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SYSTEMATIC REVIEW AND META-ANALYSIS

ADHD Diagnosis and Treatment in Children and Adolescents

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None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help healthcare decision makers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of healthcare services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of healthcare in the United States. The Patient-Centered Outcomes Research Institute (PCORI) requested this report from the EPC Program at AHRQ. AHRQ assigned this report to the Southern California Evidence-based Practice Center (Contract No. 75Q80120D00009).

AHRQ EPC reviews provide comprehensive, science-based information on common, costly medical conditions, and new healthcare technologies and strategies.

The Patient-Centered Outcomes Research Institute was established to fund research that helps patients and caregivers make better informed healthcare choices. To fulfill its authorizing mandate, PCORI partners with AHRQ to generate evidence synthesis products and make comparative effectiveness research more available to patients and providers.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, go to www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that the EPC evidence reports and technology assessments, when appropriate, will inform individual health plans, providers, and purchasers as well as the healthcare system as a whole by providing important information to help improve healthcare quality. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the website (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input.

If you have comments on this evidence report, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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Key Informants

In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

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In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

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Peer Reviewers

Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report do not necessarily represent the views of individual reviewers. AHRQ may also seek comments from other Federal agencies when appropriate.

Peer Reviewers must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential nonfinancial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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ADHD Diagnosis and Treatment in Children and Adolescents

Abstract

Objective. The systematic review assessed evidence on the diagnosis, treatment, and monitoring of attention deficit hyperactivity disorder (ADHD) in children and adolescents to inform a planned update of the American Academy of Pediatrics (AAP) guidelines.

Data sources. We searched PubMed®, Embase®, PsycINFO®, ERIC, clinicaltrials.gov, and prior reviews for primary studies published since 1980. The report includes studies published to June 15, 2023.

Review methods. The review followed a detailed protocol and was supported by a Technical Expert Panel. Citation screening was facilitated by machine learning; two independent reviewers screened full text citations for eligibility. We abstracted data using software designed for systematic reviews. Risk of bias assessments focused on key sources of bias for diagnostic and intervention studies. We conducted strength of evidence (SoE) and applicability assessments for key outcomes. The protocol for the review has been registered in PROSPERO (CRD42022312656).

Results. Searches identified 23,139 citations, and 7,534 were obtained as full text. We included 550 studies reported in 1,097 publications (231 studies addressed diagnosis, 312 studies addressed treatment, and 10 studies addressed monitoring). Diagnostic studies reported on the diagnostic performance of numerous parental ratings, teacher rating scales, teen/child self-reports, clinician tools, neuropsychological tests, EEG approaches, imaging, and biomarkers. Multiple approaches showed promising diagnostic performance (e.g., using parental rating scales), although estimates of performance varied considerably across studies and the SoE was generally low. Few studies reported estimates for children under the age of 7. Treatment studies evaluated combined pharmacological and behavior approaches, medication approved by the Food and Drug Administration, other pharmacologic treatment, psychological/behavioral approaches, cognitive training, neurofeedback, neurostimulation, physical exercise, nutrition and supplements, integrative medicine, parent support, school interventions, and provider or model-of-care interventions. Medication treatment was associated with improved broadband scale scores and ADHD symptoms (high SoE) as well as function (moderate SoE), but also appetite suppression and adverse events (high SoE). Psychosocial interventions also showed improvement in ADHD symptoms based on moderate SoE. Few studies have evaluated combinations of pharmacological and youth-directed psychosocial interventions, and we did not find combinations that were systematically superior to monotherapy (low SoE). Published monitoring approaches for ADHD were limited and the SoE is insufficient.

Conclusion. Many diagnostic tools are available to aid the diagnosis of ADHD, but few monitoring strategies have been studied. Medication therapies remain important treatment options, although with a risk of side effects, as the evidence base for psychosocial therapies strengthens and other nondrug treatment approaches emerge.

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Executive Summary

Main Points

Diagnosis:

- Multiple approaches showed promising diagnostic performance (e.g., using parental rating scales), but estimates of performance varied considerably across studies, and the strength of evidence (SoE)was generally low.
- Diagnostic test performance likely depends on whether youth with attention deficit hyperactivity disorder (ADHD) are being differentiated from typically developing children or from clinically referred children who had some kind of mental health or behavioral problem.
- Rating scales for parent, teacher, or self-assessment as a diagnostic tool for ADHD have high internal consistency but poor to moderate reliability between raters, indicating that obtaining ratings from multiple informants (the youth, both parents, and teachers) may be valuable to inform clinical judgement.
- Studies evaluating neuropsychological tests of executive functioning (e.g., Continuous Performance Test) used study-specific combinations of individual cognitive measures, making it difficult to compare performance across studies.
- Diagnostic performance of biomarkers, EEG, and MRI scans show great variability across studies and their ability to aid clinical diagnosis for ADHD remains unclear. Studies have rarely assessed test-retest reliability, no findings have been replicated prospectively using the same measure in independent samples, and real-world effectiveness studies of diagnostic performance have not been conducted.
- Very few studies have assessed performance of diagnostic tools for ADHD in children under the age of seven years and more research is needed.
- The identified diagnostic studies did not assess the adverse effects of being labeled correctly or incorrectly as having a diagnosis of ADHD.

Treatment:

- We found that several treatment modalities improve core ADHD symptoms compared to control groups (e.g., placebo). These include FDA-approved medications and psychosocial interventions with high or moderate strength of evidence.
- FDA-approved stimulant (e.g., methylphenidate, amphetamine) and non-stimulant (e.g., atomoxetine, alpha agonist) medications had the strongest evidence across interventions for significantly improving ADHD symptoms and additional outcomes, including broadband measures and functional impairment.
- Head-to-head comparisons did not detect statistically significant differences between stimulant and non-stimulant medications for most effectiveness outcomes and adverse events.
- We found little evidence that combination therapies of medication plus psychosocial therapies produce better results than medication alone, but existing research evaluated unique combinations of intervention components.
- Despite the large body of research, comparative effectiveness and safety information is limited and more research is needed to help choose between treatments.
- Data were insufficient to assess the effect of co-occurring disorders on treatment effects.

- We found too few studies reporting on diversion to quantify the risk of diversion of pharmacological treatment.

Monitoring:

- Very few monitoring studies have been reported, and more research is needed on how youth with ADHD should be monitored over time.
- Different assessment modalities may provide valid but different perspectives, and more than a single assessment modality may be required for comprehensive and effective monitoring of ADHD outcomes over time.

Background and Purpose

ADHD is the single most prevalent behavioral and mental health problem in youth. Approximately 10 percent of U.S. children have received a clinical diagnosis of ADHD, and clinical diagnoses have increased steadily over time.

Commissioned by the Patient-Centered Outcomes Research Institute (PCORI), this review assesses evidence on important gaps in knowledge related to the diagnosis of ADHD; concerns about treatment strategies, including over- and under-treatment; and how to best monitor ADHD patients over time.

This review updates prior AHRQ reviews on ADHD,[1-3] and is meant to inform a planned update of the American Academy of Pediatrics (AAP) guidelines.

Methods

The methods for this evidence review follow the Methods Guide for the Evidence-based Practice Center (EPC) Program.[4] The evidence report is based on a systematic review protocol. The evidence review team was supported by a Technical Expert Panel, a diverse panel of relevant perspectives. The Key Questions (KQs) and the protocol were posted on the AHRQ Effective Health Care website (https://effectivehealthcare.ahrq.gov/products/attention-deficit-hyperactivity-disorder/protocol) to allow additional public input. KQs addressed the diagnosis, treatment, and monitoring strategies for ADHD in children and adolescents.

We abstracted diagnostic performance measures as reported by the individual study authors. We converted to scale-independent standardized mean differences (SMD) and relative risks (RR) together with the 95 percent confidence interval (CI) for treatment studies. For monitoring studies, we reported all information on the success and impact of the monitoring strategy. We reported the range of reported diagnostic performance for diagnostic studies; treatment studies were summarized in random effects meta-analyses; monitoring studies were summarized narratively. We differentiated high, moderate, low, and insufficient strength of evidence (SoE).

Results

The searches identified 23,139 citations. Of these, we obtained 7,534 as full text. In total, 550 studies reported in 1,097 publications met the eligibility criteria. This included 231 studies addressing diagnosis (KQ1), 312 studies addressing treatment (KQ2), and 10 studies addressing monitoring (KQ3). The risk of bias in included studies varied considerably. The median minimum age in included studies was six years old and the median number of girls included in the studies was 25 percent.

We identified a large number of diagnostic approaches. Studies reported on the diagnostic performance for parental ratings, teacher ratings, teen/child self-reports, clinician tools, neuropsychological tests, EEG approaches, imaging, and biomarkers. Multiple approaches showed promising diagnostic performance (e.g., parental rating scales) but estimates of performance varied considerably across studies and the SoE was generally low. Diagnostic test performance likely depends on whether youth with ADHD are being differentiated from typically developing children (i.e., a discrimination of little clinical relevance) or from clinically referred children who have some kind of mental health or behavioral problem.

Rating scales for parent, teacher, or self-assessment as a diagnostic tool for ADHD have high internal consistency but poor to moderate reliability between raters, indicating that obtaining ratings from multiple informants (the youth, both parents, and teachers) may be valuable to inform clinical judgement. Studies evaluating neuropsychological tests of executive functioning (e.g., Continuous Performance Test) used unique and study-specific combinations of individual cognitive measures, making it difficult to compare performance across studies.

Diagnostic performance of biomarkers, EEG, and MRI scans show great variability across studies and their ability to aid clinical diagnosis for ADHD remains unclear. Studies have rarely assessed test-retest reliability, no findings have been replicated prospectively using the same measure in independent samples, and real-world effectiveness studies of diagnostic performance have not been conducted.

Very few studies have assessed performance of each of the diagnostic tools for ADHD in children under the age of seven years and more research is needed. Furthermore, the identified studies did not assess the adverse effects of being labeled correctly or incorrectly as having a diagnosis of ADHD.

Treatment studies evaluated FDA-approved pharmacologic treatment and other pharmaceutical agents, psychological or behavioral approaches, combined pharmacological and behavior, cognitive training, neurofeedback, neurostimulation, physical exercise, nutrition and supplements, integrative medicine, parent support, school interventions, and provider or model of care interventions aiming to treat or manage ADHD.

We found that several treatment modalities improve core ADHD symptoms compared to control groups (e.g., placebo). These included FDA-approved medications (SMD -0.61; CI -0.69, -0.52; 49 studies, n=7685; RR 1.71, CI 1.33, 2.19; 13 studies, n=1918; high SoE) and psychosocial interventions (SMD -0.35, CI -0.51, -0.19; 14 studies, n=1686; RR 1.75; CI 1.14, 2.71; 1 study, n=114; moderate SoE).

FDA-approved medications had the strongest evidence for significantly improving additional outcomes, including measures describing child behavior more broadly beyond ADHD symptoms (SMD 0.57; CI 0.48, 0.67; 28 studies, n=4467; RR 0.51; CI 0.43, 0.60; 25 studies, n=3959; high SoE) and functional impairment (SMD 0.50; CI 0.05, 0.96; 10 studies, n=1703; moderate SoE). Medication studies typically did not include children under six years of age. Head-to-head comparisons did not detect statistically significant differences between stimulants and non-stimulants for most effectiveness outcomes, such as ADHD symptoms (SMD 0.23; CI -0.03, 0.49; 7 studies, n=1611; low SoE) and adverse events, such as appetite suppression (RR 0.82; CI 0.53, 1.26, 8 studies, n=1463; low SoE). Identified combination therapies of medication plus youth-directed psychosocial interventions did not systematically produce better results than medication alone (e.g., ADHD symptoms SMD -0.36; CI -0.73, 0.01; 7 studies, n=841; low SoE), although existing research evaluated unique intervention bundles, and the evidence base is limited.

Despite the large body of research, comparative effectiveness and safety information is limited. Across studies, medication therapy evaluations reported more adverse events than non-medication interventions.

Data were insufficient to assess the effect of co-occurring disorders on treatment effects. We found too few studies reporting on diversion to quantify the risk of diversion of pharmacological treatment.

We identified only a very small number of evaluations of strategies monitoring ADHD over time. Studies did not provide information on key comparative effectiveness and safety outcomes, and SoE is insufficient.

Strengths and Limitations

Our comprehensive review addresses numerous important diagnostic and treatment questions relevant to clinical practice. Despite the large number of identified studies, some areas remain the subject of future research, including identifying key effect modifiers explaining variation in diagnostic performance and comparative effects of ADHD treatments. In addition, the evidence base for ADHD monitoring strategies is very limited.

Implications and Conclusions

A large number of diagnostic tools are available to inform the clinical diagnosis of ADHD, but there is great variability across studies. Medication therapy remains a central treatment modality, though with a risk of side effects, even as evidence for non-pharmacological therapies strengthen and as novel treatment approaches emerge. Few monitoring strategies have been evaluated.

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1. Introduction

1.1 Background

Attention deficit hyperactivity disorder (ADHD) is the single most prevalent behavioral and mental health problem in youth. Approximately 10 percent of U.S. children have received a clinical diagnosis of ADHD.[1] Clinical diagnoses have increased steadily over time,[2] though the higher rates may be attributable to changing clinical practices (including changes in diagnostic criteria, awareness, clinical practice guidelines, and educational policies that motivated clinical assessment and diagnosis), rather than to an increase in true population rates. The prevalence of ADHD based on rigorous diagnostic procedures is approximately 5.3 percent, a rate that is similar across geographic regions worldwide and that has remained constant over more than 20 years when diagnostic criteria have remained constant.[3] This rate, when compared with the much higher rates of clinical diagnoses, suggests that a large number of youth may be receiving a diagnosis when they should not be. Alternatively, the increasing rates of diagnosis could represent the clinical recognition of youth who have clinically significant and functionally impairing ADHD symptoms but who may not meet full, formal diagnostic criteria,[4] since increasing evidence suggests that ADHD symptoms are continuously distributed quantitative traits and therefore lie on a continuum of severity in the general population.[5-7] Some youth, however, are misdiagnosed as having ADHD when they in fact have symptoms of other disorders that are similar to, or overlap with, the symptoms of ADHD – difficulty concentrating, for example, is a symptom that occurs in many other conditions.[8] ADHD is more than twice as likely to be diagnosed in boys than in girls,[1] though this sex-specific difference in prevalence is thought to derive at least in part from diagnostic biases and cultural influences, in addition to true underlying biological determinants.[9, 10] ADHD is a more prevalent diagnosis in youth from low-income families[11] and in Caucasian compared to Black, Hispanic, and Asian youth,[12] although diagnostic bias, ethnocentrism, and cultural influences may again contribute to these socioeconomic, ethnic, and racial disparities in diagnostic rates.[13, 14]

The first question patients, parents, teachers, and clinicians ask when considering ADHD is, "Does this child truly have ADHD?" Unfortunately, *clinician judgement*, especially by non-specialist clinicians in primary care, is poor in diagnosing ADHD[15] compared with expert, research-grade diagnoses by mental health clinicians.[16] Accurately identifying youth who have ADHD has proved difficult at a population level, in part because diagnoses are often made using subjective clinical impressions and limited diagnostic tools. These tools include structured and semi-structured parent, youth, and teacher questionnaires. They represent an improvement over unsupported clinician judgement, but they are nevertheless highly subjective, prone to disagreement across eporters,[17] and likely overestimate the prevalence of ADHD.[18, 19] More objective diagnostic tools have been proposed, including activity monitors,[20] neuropsychological test measures,[21-24] biomarkers such as genotyping,[25] electrophysiological indices,[26, 27] and magnetic resonance imaging (MRI) measures,[28, 29] though they are not yet established diagnostic tools.

It is essential to know how the comparative accuracy of these diagnostic tools varies by clinical setting, including primary care or specialty clinic, and/or patient subgroup, including age, sex, socioeconomic status, racial or ethnic group, co-occurring mental, emotional, or developmental disorders, or other risk factors associated with ADHD. The accuracy of an ADHD diagnosis is thought to be especially poor in preschool-aged children, for whom hyperactivity, general rambunctiousness, and difficulties with impulse control are often relatively normative and difficult to distinguish from ADHD-related behaviors. Preschool youth also typically do not have the same classroom expectations for behavioral self-regulation that are expected of children in elementary school,[30] further obscuring the distinction between ADHD and neurotypical early childhood behaviors. Numerous population-based studies have found that the youngest children in a school year are much more likely to be diagnosed as having ADHD or to receive ADHD medication than their older classmates.[31]

ADHD diagnosis is normally based on an assessment to determine whether the patient meets the criteria described in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition, text revision (DSM-5-TR).[32] Rating scales, which can be completed by parents, teachers, and/or patients, are used to evaluate the frequency and severity of each of the 18 symptoms in DSM-5-TR[32] (9 symptoms related to inattention, and 9 symptoms related to hyperactivity/impulsivity), as well as the degree of symptom-related impairment across settings (e.g., home, school, work). Rating scale data are integrated with a clinical interview to determine the onset, course, duration, and impairment associated with symptoms. In addition, screening and clinical evaluation of potential co-occurring psychiatric conditions is a key part of the diagnostic process. Important questions remain about the accuracy of this approach in primary care settings. A particular challenge 2opular2ng ADHD from other conditions that may appear similar (e.g., anxiety, conduct disorders) and determining whether another condition may better explain ADHD symptoms or is present as a co-occurring diagnosis. Co-occurring problems are the rule, as approximately half of youth with ADHD are diagnosed with an oppositional defiant or conduct disorder diagnosis, one-third have an anxiety disorder, and 20 percent have depression.[2]

Inaccurate diagnoses of ADHD can lead either to the administration of treatments, usually stimulant medications, in children who do not need them, or to the withholding of treatment and services for those who would benefit from such treatments.[30, 33] Prescription of stimulant medications across the U.S. population has doubled in the last decade,[34] with a prevalence in 2019 of approximately six percent, and as high as 14 percent regionally.[35] These rates are higher than the 5.3 percent population prevalence of rigorously diagnosed ADHD,[36] suggesting that many youth may be receiving stimulants when they do not have ADHD.[36, 37] These trends have created alarm in the lay public, policy makers, and healthcare providers.[37, 38] Adding to their concern is that diversion and abuse of stimulants is common, particularly in college students[39] and not infrequently by parents.[40] Little is known or understood about how the risk for diversion and abuse of stimulant medications approved for ADHD varies with patient characteristics (e.g., as a function of age, race/ethnicity, or socioeconomic status). Conversely, only about half of U.S. children who receive a clinical diagnosis of ADHD are treated with stimulants,[41] suggesting a large number of children are not receiving medication when perhaps they should be.

Additional important consequences of an incorrect diagnosis can include stigmatizing youth unnecessarily with a diagnosis of ADHD[30, 42] on the one hand (i.e., “labeling harms,” which can impair self-esteem or reduce future educational attainment or career opportunities[43-45] or failing to provide a correct diagnostic framework for appropriate, timely, and evidence-based interventions on the other. Misdiagnosis of ADHD not only leads to its overdiagnosis or underdiagnosis, but it can also can lead to incorrectly diagnosing as ADHD other conditions that share symptoms with ADHD (e.g., anxiety, conduct disorders, bipolar disorder, complex trauma, difficult home environments, attachment problems, sleep disturbances, other medical disorders/diseases, speech or language delay, or developmental disorders).[46-49] Thus, treating disorders misconstrued as ADHD may withhold appropriate psychosocial and psychological therapies for those conditions and instead inappropriately treat them with stimulants and other ADHD therapies that may have little or no effectiveness in treating those conditions.

Once a diagnosis of ADHD is made, patients and their parents ask, “What treatment should be undertaken?” The answer to this question is challenging for most clinicians and requires a detailed and accurate understanding of the comparative safety and effectiveness of pharmacologic and behavioral treatments for improving not only the immediate symptoms of ADHD, but also the long-term impact that ADHD has on academic and occupational success, mental health, substance abuse, and conduct or antisocial behaviors.[50] This answer, however, is always conditioned on characteristics of the individual child or the child’s environment that are known to modify response to treatment. These “tailoring variables” can include patient age, ADHD presentation (primarily inattentive, hyperactive/impulsive, or combined), socioeconomic status, race and ethnicity, prior trauma history, co-occurring conditions (e.g., depression or anxiety), family conflict, and biomarker status (e.g., genotype, cognitive testing profile).[51, 52] Possible benefits of medication must be weighed against risks and side effects. Many parents and clinicians do not have ready access to information that can help them identify and assess these potential risks and whether their child is likely to respond better or worse to any specific possible treatment they might undertake.

Treatment strategies for ADHD are diverse and can be divided into pharmacologic and nonpharmacologic therapies. The main categories of pharmacologic therapies include stimulants (either methylphenidate or amphetamine derivatives) or non-stimulants (norepinephrine reuptake inhibitors, alpha-2 agonists, and antidepressants). The current frontline treatment for ADHD is stimulant medication, with or without combined psychological and behavioral therapies. Nonpharmacologic therapies include *psychosocial interventions* (e.g., homework, organizational, and social skills training, sleep-focused interventions, dialectical behavior therapy, cognitive behavior therapy, and mindfulness training), *school-based interventions* (e.g., psychoeducation and expert consultation for class-room based interventions by teachers), *cognitive training* (e.g., training of working memory, executive function, and motor skills using interactive games and tasks), *parent support* (e.g., behavioral training for parents, in-home nurse visits, group psychotherapy, telephone-assisted self-help, psychoeducation, and parental friendship coaching), *provider interventions* (e.g., psychoeducation and training of providers, support for monitoring therapeutic response, and expert consultation) *neurofeedback* (e.g., learning to modulate electroencephalogram [EEG] activity), *nutritional or dietary supplements* (e.g., Omega-3, vitamins, herbs), *complementary, alternative, or integrative medicine* (acupuncture, homeopathy, physical therapy, and chiropractic treatment).

1. Introduction

In children over the age of 5, the American Academy of Pediatrics (AAP) recommends stimulants as the first line of therapy.[18] Whether combining behavioral therapy with stimulant medication confers a significant benefit over stimulants alone, or whether nonpharmacologic therapy alone may be effective, is at present unclear. Adverse effects of pharmacologic treatment depend on the specific intervention and may include gastrointestinal symptoms, changes in appetite, slowed somatic growth, and sleep disturbance.[53] Treatment can also lead to personality changes or perceived loss of spontaneity. Individuals who are initially misdiagnosed or who have inadequate monitoring may be overtreated with stimulant medications. Overtreatment leads to the risk of treatment with little or no benefit or to unnecessary side effects. Long-term adherence to medication regimens is often poor in youth who have ADHD and can limit the long-term, real-world effectiveness of medication.[54]

Long-term outcomes for both medication and non-medication therapies have been less well studied,[53] and little is known about which treatment to begin first and for whom, or how best to sequence treatments for ADHD when the first intervention proves ineffective or insufficient. Recent advances in the development and testing of novel therapies for ADHD warrant a systematic review of their efficacy and effectiveness that will provide information eagerly awaited by the field. These novel therapeutics include cognitive training, game-based digital devices such as EndeavorRx, approved by the Food and Drug Administration (FDA), and neuromodulation techniques such as repetitive Transcranial Magnetic Stimulation and the FDA-approved external Trigeminal Nerve Stimulator.[55-66]

Once treatment is begun, the central question is, "Is the treatment working?" The answer to this question is not as straightforward as it may at first appear, as ADHD symptoms and the capacity to compensate for them may vary over time and with circumstance (e.g., school day or weekend, the presence of psychosocial stress), by symptom presentation (e.g., hyperactivity, inattention, impulsivity), and by functional domain (academics, risk-taking behaviors, socialization). Thus, valid and reliable methods are needed to monitor treatment response easily and accurately. If the current treatment is not producing the desired response, or if side effects are limiting the dose of medication prescribed, the final question is what to do next to improve short- and long-term outcomes. For example, is it better to optimize dosing of the current medication, switch to another first-line medication, switch to a second-line medication, add an additional medication, or add an adjunctive psychological or behavioral therapy? And how does a clinician or parent prevent the complete abandonment of treatment, which is exceedingly common, when the first line treatment is ineffective or produces troubling side effects?[67]

After a child is diagnosed with ADHD and an initial treatment strategy is determined, a monitoring strategy is applied to ensure that outcomes are evaluated over time, and modification of treatments are made when needed.[68] Ideally, repeat monitoring should provide the opportunity to intervene (e.g., modify the treatment) before the undesirable or adverse outcomes associated with ADHD occur or determine whether and which treatment for remains clinically indicated. Several instruments are available to assess treatment response and adverse effects over time, including the Vanderbilt, Conners, ADHD Rating Scale-5, and Swanson, Nolan, and Pelham Rating Scale (SNAP)-IV rating scales. Monitoring may also include assessment of any adverse treatment effects. The frequency of monitoring may depend on the age of the child, the specific treatment, duration of treatment, previous symptoms, co-occurring conditions, and family and healthcare provider preferences. For example, monitoring into adulthood is often desirable or needed, as one-third to one-half of patients with ADHD will have clinically significant symptoms that persist into adulthood. Monitoring for long-term adverse outcomes in domains distinct from ADHD symptom severity is important, since youth with ADHD are at increased risk for future problems associated with risk-taking, such as substance abuse, motor vehicle accidents, unprotected sexual intercourse, and criminal behavior. They are also at considerable risk as adults for chronic health problems, including diabetes, heart disease, and poor oral health, in part because they engage in behaviors that increase risk for these conditions, and they often fail to adhere to health-protective behaviors. They are also at risk for future depression, anxiety, suicide attempts, and problematic peer and family relationships.[2, 50] In addition, the long-term effectiveness of standard and novel interventions for ADHD, and their potential long-term adverse effects, are not well known[69-73] and are difficult to detect and document for these diverse outcomes,[74-76] even though they are critically important considerations for patients, parents, and clinicians as they make treatment decisions. Knowledge of the ways in which unique patient characteristics modify these short- and long-term treatment outcomes is essential to tailor and personalize care for individual patients.[77]

1.2 Purpose and Scope of the Systematic Review

This review updates prior AHRQ reviews on ADHD.[11, 53, 78] It builds on the previous reports and will address important gaps in knowledge related to the diagnosis of ADHD, concerns about overtreatment and undertreatment, and conflicting literature about the effectiveness of long-term treatment. The review is especially intended to be a resource for clinicians, researchers, and policymakers, although through them, we hope the review will benefit the many youth who have ADHD, as well as their families and teachers. We anticipate that the analyses and results will be difficult for most parents, educators, and lay persons to understand, although the executive summary, key points, and discussion are intentionally crafted to be accessible to a much wider audience. Finally, this systematic review aims to inform a planned update of the current American Academy of Pediatrics (AAP) clinical guidelines for the diagnosis, evaluation, and treatment of ADHD.

Since the last AHRQ report was published, further diagnostic and treatment strategies have been suggested, warranting an update of the literature. Identified references address predominantly diagnostic questions such as the diagnostic validity of specific tests and suggested diagnostic tools. Furthermore, key studies that provide important information on the diagnosis of ADHD predate the most recent ADHD report. Hence, the current systematic review will include older studies. Searches for studies of diagnostic tools will extend back to 1980, when the diagnosis of ADHD and its diagnostic criteria were first introduced in the DSM as Attention Deficit Disorder with or without hyperactivity (DSM-III).[79]

In addition, since the last AHRQ review, several studies have been published that explore novel interventions, such as game-based cognitive therapy or computer training. Furthermore, key studies that predate the most recent ADHD report provide important information on the treatment of ADHD. Hence, the current systematic review also includes older treatment studies. Searches for studies of ADHD interventions will therefore extend back to 1980, when long-acting stimulants were introduced, heralding the modern era of ADHD pharmacotherapy.

Given that the 2018 AHRQ report on ADHD identified no monitoring study, we removed limits on the search date for this question and will aim for a comprehensive review that considers older studies (the 2018 report included only studies published to 2009). Based on discussions and preliminary literature searches, we still do not expect to identify many studies for monitoring strategies and long-term outcomes, although we anticipated that some data may be available from the educational and school psychology literature, such as Response to Intervention – Behavioral (RTI-B) strategies to monitor behavioral and psychosocial interventions in the classroom that aim to improve ADHD outcomes.

To our knowledge, no prior reviews of ADHD have been as comprehensive as the current review in the range of diagnostic tools, treatments, clinical outcomes, participant ages, and year of publication for the included studies. We hope that it will be a valuable resource for patients, families, clinicians, educators, policymakers, and researchers for years to come.

2. Methods

2.1 Review Approach

The methods for this evidence review follow the Methods Guide for Evidence-based Practice Center (EPC) Program. Appendixes provide supplementary information. Appendix A contains the methods. Appendix B lists the excluded studies as well as the background studies. Appendix C contains the evidence tables for the included studies. Appendix D has the critical appraisal and applicability tables for each included study, and Appendix E lists the included studies.

The topic of this report was developed by the Patient-Centered Outcomes Research Institute (PCORI) in consultation with the Agency for Healthcare Research and Quality (AHRQ). Key Questions (KQs) were posted on AHRQ's Effective Health Care (EHC) website for public comment in August 2021 for 3 weeks. PCORI conducted an online townhall meeting to discuss the comments in November 2021 (Appendix F). The protocol was refined following this input through public posting of the KQs, the townhall meeting, input from Key Informants, and a Technical Expert Panel. The final protocol is posted on the EHC website. A panel of technical experts provided high-level content and methodological expertise throughout development of the review protocol. The protocol for the review has been registered in PROSPERO (CRD42022312656). Appendix G includes the PCORI checklist.

2.1.1 Key Questions

The KQs proposed for the systematic review, addressing diagnosis (KQ1), treatment (KQ2), and monitoring (KQ3) of ADHD, were refined following input from Key Informants, input through public posting, and a townhall organized by PCORI.

We obtained input from eight Key Informants. Key Informants included a parent of an underserved, ethnic minority (Hispanic) youth with attention deficit hyperactivity disorder (ADHD), an advocate from the national advocacy group CHADD (Children and Adults with ADHD), an expert in medical safety, an expert in testing and assessment, a representative from the Association for Child and Adolescent Counseling (ACAC), a family medicine representative, and members of the guideline group who will use the review to update the guidelines. The Key Informants showed strong support for the importance and relevance of the KQs. They suggested relevant references and provided important input on terminology relevant to the literature searches. There were discussions about developments since the last report and about where the field is now from the perspective of each participant.

Additional input on the project was received through public posting of the review questions on the AHRQ website. The posting aimed to ensure that the review is addressing the right questions, and all aspects have been considered. A submission from the American Psychological Association (APA) and a submission from a researcher at Immaculata University addressed all review questions. For KQ1, input stressed the importance of minimizing false positive diagnoses from the presence of co-occurring conditions; costs and reliability of electroencephalogram (EEG) diagnostic information; that a developmental lens should be adopted (e.g., does a child's relative age and developmental maturity in comparison to classmates influence the odds of receiving a diagnosis of ADHD?); that the role of sleep, trauma, and language development should be considered; and that annual reassessments of behaviors and impairment are important. For KQ2, input addressed the importance of reviewing the effects of medications and the risk of diversion of pharmacological treatment; of treatment fidelity; of adherence to and persistence of medication use; of behavioral treatment, including use of different modalities (in person, video, online); and of the Multimodal Treatment of ADHD study, specifically. For KQ3, the input targeted the conduct of routine assessments, including reports from parents, teachers, and the children/adolescents, that should be accessible to all parties; and that routine monitoring should be part of the child/adolescent's record.[68]

Finally, at the online townhall meeting in November 2021 hosted by PCORI, there were passionate discussions and advocacy for changes in ADHD policy and research. Some participants felt strongly that both important policies and data were lacking across the board. Specific areas identified by this group included lumping ADHD-Inattentive with the Combined presentation, the lack of empirical data on executive function training and executive function coaches, the general lack of specific and feasible non-pharmacological interventions that parents can use easily and have access to, as well as the lack of availability of parent training programs being offered before initiating stimulant medication.

Following Key Informant and public input, the KQs are as follows:

KQ1. For the diagnosis of ADHD:

a. What is the comparative diagnostic accuracy of approaches that can be used in the primary care practice setting or by specialists to diagnose ADHD among individuals younger than 7 years of age?
b. What is the comparative diagnostic accuracy of EEG, imaging, or approaches assessing executive function that can be used in the primary care practice setting or by specialists to diagnose ADHD among individuals aged 7 through 17?
c. For both populations, how does the comparative diagnostic accuracy of these approaches vary by clinical setting, including primary care or specialty clinic, or patient subgroup, including, age, sex, or other risk factors associated with ADHD?
d. What are the adverse effects associated with being labeled correctly or incorrectly as having ADHD?

KQ2. What are the comparative safety and effectiveness of pharmacologic and/or nonpharmacologic treatments of ADHD in improving outcomes associated with ADHD?

a. How do these outcomes vary by presentation (inattentive, hyperactive/impulsive, and combined) or other co-occurring conditions?
b. What is the risk of diversion of pharmacologic treatment?

KQ3. What are the comparative safety and effectiveness of different empirical monitoring strategies to evaluate the effectiveness of treatment in improving ADHD symptoms or other long-term outcomes?

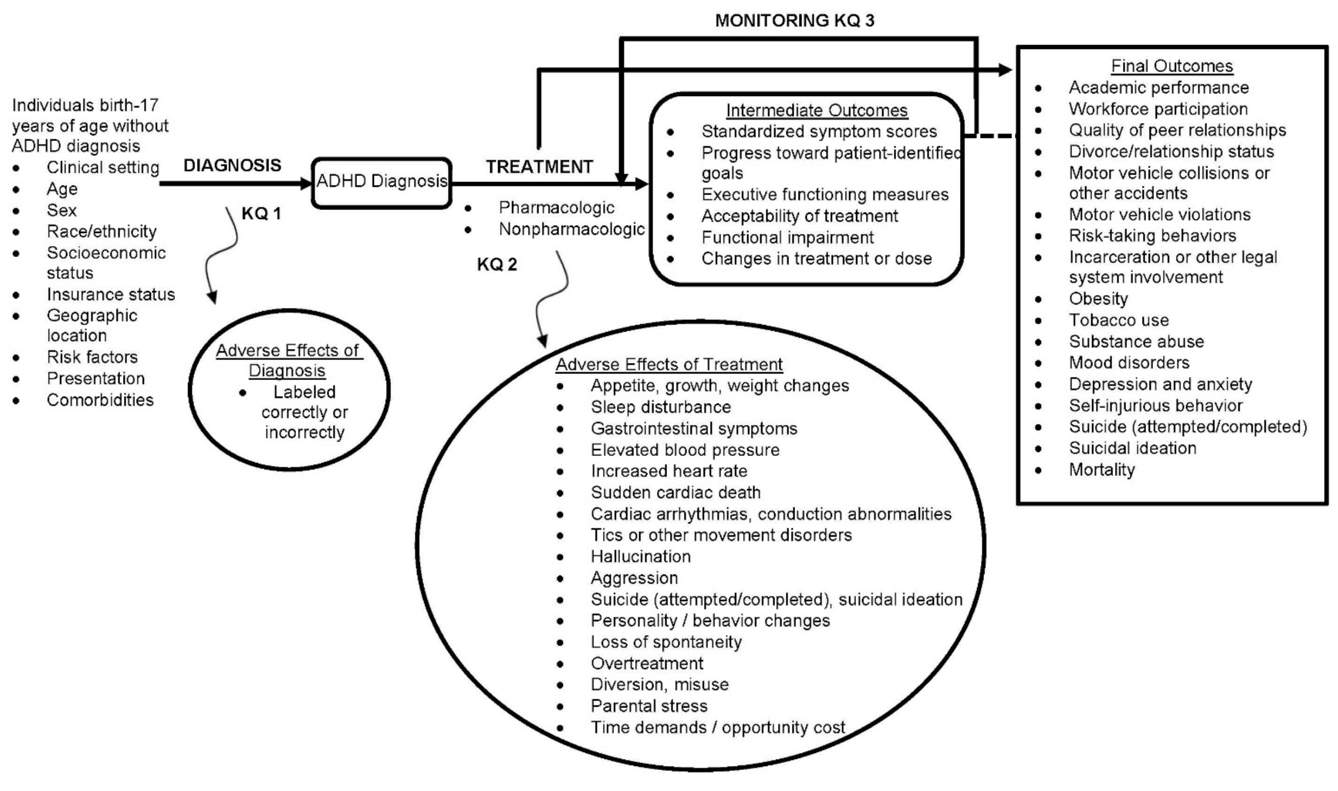
While the diagnosis and treatment KQs are unchanged from the 2018 AHRQ EPC report on the topic, the KQ regarding monitoring ADHD over time was rephrased for clarity. The restricted age range for sub-question 1b is based on recognition that most of these specialized technologies require the child to remain very still, which is difficult for children younger than seven. Neuropsychological tests as well as genetic markers are included in 1a and 1b. In question

1d, we will assess whether the literature suggests whether these adverse effects differ for those youth who are on the threshold of clinical or subclinical diagnoses. Co-morbidities may include co-occurring conditions such as conduct disorder, mood disorders, autism spectrum disorders, Williams syndrome, Down syndrome, learning and language disabilities, and developmental coordination disorder. Questions 2 and 3 address effectiveness as well as adverse outcomes.

2.1.2 Analytic Framework

The analytic framework (Figure 1) depicts the KQs and outcomes to evaluate the diagnosis, treatment, and monitoring strategies for ADHD.

Figure 1. Analytic framework



Notes: ADHD = Attention deficit hyperactivity disorder, KQ = Key Question

2.2 Study Selection

The eligibility criteria are organized in a PICOTSO (population, intervention, comparator, outcome, timing, setting, study design, and other limiters) framework. The report includes studies published from 1980 to June 2023.

2.2.1 Search Strategy

For primary research studies, we searched the database PubMed® (biomedical literature), Embase® (pharmacology emphasis), PsycINFO (psychological research), and ERIC (education research). We also searched the U.S. trial database – ClinicalTrials.gov – to capture all relevant data regardless of the publication status. Increasingly trial registries include data and a complete record of adverse events, making them an important evidence review tool to identify all relevant data and to reduce publication bias.

We used existing reviews for reference-mining; these were identified through the same databases used for primary research plus searching the Cochrane Database of Systematic Reviews, Campbell Collaboration, What Works in Education, and PROSPERO. Scoping searches identified several published reviews. These often address medication treatment with an increased focus on safety.[80-84] Given that many practice guidelines are now based on systematic reviews, we also searched the ECRI Guidelines Trust, G-I-N, and ClinicalKey. Using external systematic reviews in addition to building on prior AHRQ reports increases the certainty that all relevant studies have been captured.

The literature searches for this project were built on prior ADHD reports published by AHRQ. KQ1 searches covered 1980 to 2011, and 2016 to present. Since research published between 2011 and 2016 was thoroughly screened by the 2018 review, we used the identified studies listed in the 2018 AHRQ report to cover 2011 to 2016. KQ2 searches covered 1980 to 2011 and 2016 to date, omitting search terms covered in the 2011 AHRQ report, and adding the adolescent population, which was not previously fully covered. We used the identified studies in the AHRQ report and reference-mining of pertinent reviews to identify relevant studies. KQ3 searches were not limited by date. We simplified the search strategies and removed filters for specific interventions for key databases to ensure that no existing test or intervention evaluation would be missed. Searches were designed, executed, and documented by the evidence review center librarian. The search strategy underwent peer review to ensure high quality searches. The search strategies for the databases are shown in the methods appendix (Appendix A). Furthermore, we used information provided by content experts,[85] and the Technical Expert Panel reviewed the list of included studies to ensure that all relevant literature has been captured.

We used detailed pre-established criteria to determine eligibility for inclusion and exclusion of publications in accordance with the AHRQ Methods Guide for Effectiveness and Comparative Effectiveness Reviews. To reduce reviewer errors and bias, all citations were reviewed by a human reviewer and screened by a machine learning algorithm. Citations deemed potentially relevant were obtained as full text. Each full-text article was reviewed for eligibility by two literature reviewers, including any articles suggested by peer reviewers or that arose from the public posting process, submission through the SEADS (Supplemental Evidence And Data for Systematic reviews) portal, or response to Federal Register notice. Any disagreements were resolved by consensus. We maintain a record of studies excluded at the full-text level with reasons for exclusion (see Appendix B).

The SEADS portal was open from July 1st through August 15th 2022. We received two submissions, including one from the American Academy of Child and Adolescent Psychiatry. Submissions include comments on the need for an evidence review of ADHD research, the usefulness of the review as outlined in the posted protocol, and in total four published studies were submitted to be considered for the systematic review.

While the draft report was under peer review and open for public comment, we updated the search and included any eligible studies identified either during that search or through peer or public review suggestions in the final report.

2.2.2 Eligibility Criteria

The detailed inclusion and exclusion criteria are listed in Table 1.

2. Methods

Table 1. Eligibility criteria

PICOTSO Element	KQ1 (Diagnosis)	KQ2 (Treatments)	KQ3 (Monitoring)
Population	Individuals birth through 17 years of age without the diagnosis of ADHD **Exclusion**: Individuals 18 years of age or older unless findings are reported separately for younger participants	Individuals birth through 17 years of age with a diagnosis of ADHD **Exclusion**: Individuals 18 years of age or older unless findings are reported separately for younger participants	Individuals birth through 17 years of age who have previously begun treatment for ADHD **Exclusion**: For long-term studies, the age of the individuals were greater than 17, but these studies were only considered for inclusion if the age at enrollment in the study was 18 years or younger, and administrative claims data used for diagnosis of ADHD
Interventions	Any ADHD diagnostic strategy for the diagnosis of ADHD in children through 17 years **Exclusion**: Validation studies or not reporting on diagnostic performance; non-English language questionnaires and interview guides	Any treatment of ADHD, alone or in combination. **Exclusion**: Studies with less than 4 weeks of treatment	Follow-up visit methods and frequencies for monitoring, independent of treatment, including remote monitoring or telehealth strategies
Comparators	Confirmation of diagnosis by a specialist (gold standard), such as a psychologist, psychiatrist or other care provider using a well-validated and reliable process of confirming a clinical diagnosis of ADHD **Exclusion**: Comparison to diagnosis with a non-validated instrument	Specific treatments compared with other treatments as described above or to no treatment **Exclusion**: Comparisons to other patient groups rather than treatments	Follow-up compared with differing frequencies of follow-up or different settings of follow-up for monitoring strategies; no restrictions for long-term outcomes
Outcomes	Diagnostic accuracy (e.g., sensitivity, specificity, accuracy, area under the curve, positive predictive value, negative predictive value, likelihood ratios, false positives, false negatives, false negatives, false positives, misdiagnosis, stigma, and costs following diagnosis comparing those with and without ADHD	Patient health outcomes, global clinical impression, social and family functioning, functional impairment, executive functioning, academic performance outcomes, acceptability of treatment, adverse events of treatment, loss of spontaneity, progress toward patient-identified goals, quality of peer relationships, motor vehicle collisions or other accidents, risk-taking behaviors and interactions with the legal system	Monitoring strategy success (e.g., feasibility, uptake), changes in treatment or dose, adverse effects of treatment, changes in intermediate and final outcomes
Timing	• For assessment of diagnostic accuracy: diagnostic follow-up must be within 4 months of the initial evaluation and must be completed before treatment is initiated • For labeling: any time after the ADHD diagnosis	Any	Any
Setting	Primary or specialty care settings	Any (including remote monitoring and telehealth)	Any (including remote monitoring and telehealth)

PICOTSO Element	KQ1 (Diagnosis)	KQ2 (Treatments)	KQ3 (Monitoring)
Study Design	• RCTs • For diagnostic accuracy, observational studies, are eligible if they include patients with diagnostic uncertainty and direct comparison of diagnosis in primary care to diagnosis by a mental health specialist • Controlled clinical trials and prospective and retrospective observational studies with comparator for non-drug treatments **Exclusion**: Editorials, nonsystematic reviews, letters, case series, case reports, pre-post studies. Systematic reviews are not eligible for inclusion but will be retained.	• RCTs • Controlled clinical trials and prospective and retrospective observational studies with comparator for non-drug treatments **Exclusion**: Editorials, nonsystematic reviews, letters, case series, case reports, pre-post studies. Studies with fewer than 100 participants had to report a power calculation to determine that studies had sufficient power to detect effects. Systematic reviews are not eligible for inclusion but will be retained	• RCTs • No study size restriction **Exclusion**: Editorials, nonsystematic reviews, letters, case series, case reports, pre-post studies. Systematic reviews were not eligible for inclusion but will be retained
Other limiters	• English-language publications • Published after 1980 **Exclusion**: Non-English language and abbreviated publications (abstracts, letters)	• English-language publications • Published after 1980 **Exclusion**: Non-English language and abbreviated publications (abstracts, letters)	• English-language publications • Monitoring strategies and long-term effects have no publication year restriction • Journal manuscripts and trial record data with results **Exclusion**: Non-English language and abbreviated publications (abstracts, letters)

Notes: ADHD = Attention deficit hyperactivity disorder, KQ = Key Question, PICOTSO = Population, Intervention, Comparators, Timing, Outcomes, Setting, Other limiters, RCT = Randomized controlled trial

Compared to the prior 2018 report on ADHD, the eligibility criteria were simplified and now includes all tests used to diagnose ADHD and all treatments for ADHD treatments. In addition, randomized controlled trials (RCTs) are no longer limited by sample size given that RCTs allow strong evidence statements; however, treatment studies with fewer than 100 participants had to report a power calculation indicating sufficient power for at least one patient outcome to ensure that the studies were designed to detect a difference between the intervention and comparison group. Not all studies can be combined in meta-analyses to aggregate data, because the intervention, comparator, and reported outcome combinations are often unique to the study; hence we required individual studies to show sufficient power to detect effects. We specified that intervention studies had to have a treatment duration of four weeks; we excluded experiments of shorter duration (e.g., proof of concept studies) and focused on treatment for ADHD. Finally, no comparator is needed anymore for monitoring studies, and these are not restricted by publication date, given the small evidence base (the 2018 report found no relevant study).

Relevant systematic reviews and meta-analyses were retained as background or for reference-mining but will not be included as evidence. Publications reporting on the same participants were consolidated into one study record. Studies exclusively published in non-English language publications remain excluded given the high volume of literature, the focus on the review on populations in the U.S., the scope of the KQs, and the aim to support a U.S. clinical practice guideline.

2.3 Data Extraction

We abstracted detailed information regarding study characteristics, participants, methods, and results. The review team created data abstraction forms for the KQs in DistillerSR, an online program for systematic reviews. Forms included extensive guidance to support reviewers, both to aid reproducibility and standardization of data collection. One literature reviewer abstracted the data, and a second reviewer checked for accuracy and completeness. Further data checks were conducted while synthesizing results across studies. Disagreements were resolved by consensus.

We designed the data abstraction forms to collect the data required to evaluate the study, as well as demographic and other data needed for determining outcomes, informed by existing research.[86-89] We paid particular attention to describing the details of the treatment (e.g., pharmacotherapy dosing, methods of behavioral interventions), patient characteristics (e.g., ADHD presentation, co-occurring disorders, age), and study design (e.g., RCT versus observational), which may influence the reported outcome results. In addition, we carefully described comparators, as treatment standards may have changed during the period covered by the review. In addition, data necessary for assessing quality and applicability as described in the EPC Methods Guide were abstracted. Forms were pilot-tested with a sample of included articles to ensure that all relevant data elements are captured and that ambiguity is avoided.

The abstracted information was used for analyses as well as to populate the evidence tables in Appendix C showing characteristics for each included study. Final abstracted data will be uploaded to SRDR per EPC requirements and will be publicly available.

2.4 Risk of Bias Assessment

The critical appraisal for individual studies applied criteria consistent with QUADAS-2 for diagnostic studies and the RoB 2 guidance for common sources of bias in intervention studies adapted for the eligible study designs.[90, 91]

QUADAS-2 evaluates four domains: *patient selection*, *index test* characteristics, *reference standard* quality, as well as *flow and timing:*[91]

- **Patient selection:** The domain *patient selection* addresses whether the selection of patients could have introduced bias, taking into account whether the study enrolled a consecutive or random sample, whether the data are not based on a retrospective case-control design, and whether the study avoided inappropriate or problematic exclusions from the patient pool.
- **Index test:** The *index test* domain evaluates whether the conduct or interpretation of the test could have introduced bias, taking into account whether the results of the test were interpreted without knowledge of the results of the reference standard and whether any thresholds or cut-offs were pre-specified (e.g., instead of determined during the study to maximize diagnostic performance).
- **Reference standard:** The domain *reference standard* evaluates whether the reference standard, its conduct, or its interpretation may have introduced bias, taking into account the quality of the reference standard in correctly classifying the condition and whether the reference standard test results were interpreted without knowledge of the results of the index test.
- **Flow and timing:** The last domain, *flow and timing*, evaluates whether the conduct of the study may have introduced bias. The assessment takes into account whether the interval between the test and the reference standard was appropriate, whether all patients received

the reference standard and whether they received the same reference standard, and whether all patients were included in the analysis. For each domain, we assessed the potential risk of bias in the study in order to identify high risk of bias and low risk of bias studies. We evaluated for each study and appraisal domain whether there are concerns regarding the applicability of the study results to the review question (Appendix D). This encompassed whether the patients included in the studies match the review question; whether the test, its conduct, or interpretation differ from the review question; or whether the target condition as defined by the reference standard fully matches the review question.

For treatment and monitoring studies, we assessed the six domains selection, detection, performance, attrition, reporting, and study-specific sources of bias:

- **Selection bias:** For *selection bias*, we assessed the randomization sequence and allocation concealment in RCTs as well as baseline differences and potential confounders in all studies.
- **Performance bias:** *Performance bias* evaluated whether patient- or caregiver knowledge of the intervention allocation or circumstances such as the trial context may have affected the outcome, and whether any deviations from intended interventions were balanced between groups.
- **Attrition bias:** *Attrition bias* considered the number of dropouts, any imbalances across study arms, and whether missing values may have affected the reported outcomes.
- **Detection bias:** *Detection bias* assessed whether outcome assessors were aware of the intervention allocation, whether this knowledge could have influenced the outcome measurement, and whether the outcome ascertainment could differ between arms.
- **Reporting bias:** *Reporting bias* assessment includes an evaluation of whether a pre-specified analysis plan exists (e.g., a published protocol), whether the numerical results likely have been selected on the basis of the results, and whether key outcomes were not reported (e.g., an obvious effectiveness indicator is missing) or inadequately reported (e.g., anecdotal adverse event reporting).
- **Study-specific sources of bias:** In addition to the types of bias listed above, we assessed *other potential sources of bias* such as inadequate reporting of intervention details.

Each study was initially appraised by the data abstractor for the study. In a second step, we reviewed risk of bias results across studies to ensure consistency of ratings. Risk of bias results informed the study limitation assessment in the quality of evidence assessment across studies. Appendix D has the critical appraisal and applicability tables.

2.5 Data Synthesis and Analysis

We summarized key features of the included studies, including study design; participant characteristics; diagnostic, treatment, and monitoring strategies; and frequent outcomes in a narrative overview. We answered each KQ with the available evidence using quantitative syntheses across studies where possible to increase statistical power, to increase precision, and to objectively summarize results across all available evidence. We ordered our findings by diagnostic, treatment, and monitoring strategy, i.e., the KQs.

We broadly characterized tests (KQ1), interventions (KQ2), and monitoring strategies (KQ3). For diagnostic studies, we reported the range of reported diagnostic performance. For KQ2, we differentiated effectiveness and comparative effectiveness results (i.e., comparing to a passive comparison in the form of a control group, or an active comparator in the form of an alternative intervention). We documented results by the pre-specified key outcomes. We consistently abstracted the longest follow up for each study. We converted reported standard errors and confidence intervals to standard deviations to compute effect sizes. We reversed originally reported outcomes where necessary to facilitate comparisons across studies.

For statistical pooling, we used random-effects models corrected for small numbers of studies where necessary to synthesize the available evidence quantitatively.[92] We computed standardized mean differences (SMD) for continuous outcomes and relative risks (RR) for categorical outcomes to document results across studies. We present summary estimates and 95 percent confidence intervals for all summary estimates. Where more than one study could be combined in an analysis, we showed the results in a forest plot. The forest plots document the results for each study reporting on the outcomes, including the size of the effect, the direction of effects, the confidence interval surrounding the point estimate, the proximity to the point of no effect (RR = 1, SMD = 0), and the results in relation to other studies. Forest plots visually document the consistency of effects across studies, and they can show outliers clearly.

We determined whether the pooled effect was statistically significantly different from the comparison group and documented the identified systematic effects. We also documented results that were not statistically significant; in these cases, we stated that we did not detect a systematic effect – while we cannot rule out that the intervention may work for some children, across participants and studies the effect was indistinguishable from chance. For all interventions and outcomes that reported a continuous and a categorical effect estimate, we reviewed both estimates for each key outcome.

We assessed heterogeneity using graphical displays and the I-squared statistics. The statistic ranges from zero to 100 percent and we noted in particular results where heterogeneity exceeded 70 percent. We anticipated that intervention effects may be heterogeneous across studies. We explored potential sources of heterogeneity, while recognizing that the ability of statistical methods to detect individual sources of heterogeneity may be limited in the presence of multiple sources of heterogeneity.[93] We hypothesized that the methodological rigor of individual studies and patients' underlying clinical presentations are potentially associated with the intervention effects. We performed meta-regression analyses to examine these hypotheses and reported sensitivity analyses where necessary. We assessed the potential for publication bias for all key outcomes using the Begg and the Egger test.[94, 95] The trim and fill method provides alternative estimates where evidence of publication bias was detected.[96]

Pre-defined subgroups for KQ1 included children younger than seven years of age and children and adolescents, seven through 17. We assessed whether diagnostic performance is associated with the age of participants using reported sensitivity and specificity estimates in a regression analysis across studies. In addition, we assessed the effect of treatment and diagnosis in participants with concomitant morbidities; the racial and ethnic composition of study samples; and the potential effect of the diagnostic, treatment, and monitoring setting in meta-regressions across studies and KQs. We differentiated primary care, specialty care, school settings, and other settings (e.g., participants were part of a larger research study), mixed settings (e.g., participant recruiting through primary care and schools), and not reported.

For KQ3, we documented outcomes as reported by the original authors.

2.5.1 Applicability Assessment

Applicability was assessed in accordance with the AHRQ Methods Guide. Factors that may affect applicability, which we have identified *a priori*, include patient, intervention, comparisons, outcomes, and settings. For each study, we assessed the population included in the study to identify those with narrow eligibility criteria, that excluded participants with comorbidities, that had more complex participants than typically seen in the community, and those that had run-in periods where adherence was tested and participants were excluded for non-adherence. Regarding interventions, we assessed whether studies described tests or treatments not used as recommended or commonly used in practice, dosing of medications not reflective of current practice, the presence of co-interventions that were likely to modify the effectiveness, and the presence of highly trained tester or treatment team. Regarding the comparisons, we assessed whether diagnostic studies used tools differently than recommended, treatment studies that used inadequate intervention or substandard care as comparators, and those where the comparator was unclear. Regarding outcomes, we assessed whether studies used outcome assessors that were not qualified for the assessment, surrogate or composite outcomes with limited applicability, and follow-ups too short for effects to manifest. Regarding the setting, we assessed whether studies were conducted in a setting which has a level of care that is different from that in the community. Literature reviewers could also flag additional applicability concerns.

We used this information to assess the situations in which the evidence is most relevant and to evaluate applicability to real-world clinical practice in typical U.S. settings, summarizing applicability assessments qualitatively. The information is reflected in the discussion of the review findings.

2.6 Grading the Body of Evidence

The strength of evidence assessment documents uncertainty, outlines the reasons for insufficient evidence where appropriate, and communicates our confidence in the findings.

The strength of evidence for each body of evidence (based on the KQ, diagnostic and treatment approach, comparator, and outcome) was initially assessed by one researcher with experience in determining strength of evidence for each primary clinical outcome by following the principles for adapting GRADE (Grading of Recommendations Assessment, Development and Evaluation), outlined in the AHRQ Methods Guide.[97] The initial assessment was then discussed in the team.

2.6.1 Key Outcomes

We prioritized outcomes with the help of the Technical Expert Panel in combination with team expertise. The panelists reviewed a large number of possible outcomes. We considered outcomes most clinically relevant and important to patients and clinicians to guide clinical practice. The following outcomes were selected for the strength of evidence assessment:

- Key Question 1:
    - Sensitivity
    - Specificity
    - Costs
    - Rater agreement
    - Internal consistency
    - Test-retest reliability
    - Misdiagnosis impact
- Key Question 2:
    - Behavior changes

    - Broadband scale scores
    - Standardized symptom scores
    - Functional impairment
    - Acceptability of treatment
    - Academic rating scale scores
    - Appetite changes and growth suppression
    - Number of participants with adverse events
- Key Question 3:
    - Functional impairment
    - Broadband scale scores
    - Standardized symptom scores
    - Progress toward patient-identified goals
    - Acceptability of treatment
    - Academic rating scale scores
    - Any long-term effects
    - Growth suppression
    - Quality of peer relationships

For diagnostic studies in KQ1, we abstracted the number of true positive and true negatives in order to compute diagnostic performance measures, but we also abstracted all values as reported by the authors. We added information on the specific cut-off and model used to achieve the diagnostic performance where reported. The impact of misdiagnosis included the risk of missed conditions that can appear as ADHD as well as being incorrectly labeled as having or not having ADHD.

For treatment studies in KQ2, we abstracted numerical values for all key outcomes to facilitate meta-analysis. We also abstracted a brief narrative for the evidence table for each outcome focusing on the comparison to a control or a comparator group (rather than pre-post data). In addition, we summarized study-specific health outcomes and reported adverse events to complete the evidence table for all included studies. For the *behavior change* domain, we abstracted individual behaviors such as aggression or conduct problems, either from direct observations or behavior ratings, where studies reported these in addition to global impression or symptom scales. We used global psychological, mental health, and child development assessments, such as the CGI (Clinical Global Impression)[98] and total scores of the Conners rating scales, that go beyond assessing individual ADHD symptoms as *broadband scale scores*. For *standardized symptom scores*, we included summary measures for ADHD symptoms, such as ADHD-RS-IV (ADHD Rating Scale Version IV),[99, 100] or, when unavailable, subclasses of individual symptoms for ADHD, such as inattention. For *functional impairment*, we abstracted functional measures such as the Weiss Functional Impairment Rating Scale.[101, 102] For acceptability of treatment we abstracted child, parent, or teacher satisfaction with intervention, depending on what was reported. We abstracted *academic rating scale scores* where reported, in the absence of these, we used broad academic performance measures such as GPA (grade point average). Other, narrower performance measures, such as specific cognitive skills, were summarized in the free text field in the evidence table. For *appetite changes* and *growth suppression*, we abstracted indicators such as decreased appetite or growth during the study period. The *number of participants with adverse events* was restricted to documenting the total number of patients reporting at least one adverse event in each study arm. Other adverse event measures (such as the total number of adverse events or the number of serious adverse events) were summarized in the free adverse event text field in the evidence table.

For monitoring studies eligible for KQ 3, we abstracted all information provided by the authors on the suitability of the applied monitoring strategy in addition to all pre-specified outcomes.

The synthesis documented the presence and the absence of evidence for the key outcomes for all included diagnostic tests, treatment interventions, and monitoring strategies in the respective sections.

2.6.2 Strength of Evidence Assessments

In determining the quality of the body of evidence, the following domains were evaluated:

- **Study limitations:** The extent to which studies reporting on a particular outcome are likely to be protected from bias. The aggregate risk of bias across individual studies reporting an outcome is considered; graded as low, medium, or high level of study limitations.
- **Inconsistency:** The extent to which studies report the same direction and/or magnitude of effect or show statistical heterogeneity for a particular outcome; graded as consistent, inconsistent, or unknown (in the case of a single study or the absence of studies).
- **Indirectness:** Describes whether the intervention (test, treatment, or strategy) and the comparator were directly compared (i.e., in head-to-head trials) or indirectly (e.g., through meta-regressions across studies). In addition, indirectness can reflect whether the outcome is directly or indirectly related to health outcomes of interest. The domain is graded as direct or indirect.
- **Imprecision:** Describes the level of certainty of the estimate of effect for a particular outcome, where a precise estimate is one that allows a clinically useful conclusion. When quantitative synthesis is not possible, sample size and assessment of variance within individual studies are considered. Graded as precise or imprecise.
- **Reporting bias:** Occurs when publication or reporting of findings is based on their direction or magnitude of effect. Publication bias, selective outcome reporting, and selective analysis reporting are types of reporting bias. Reporting bias is difficult to assess as systematic identification of unpublished evidence is challenging. When possible, we reviewed Begg and Egger test results and used trim and fill methods to assess the robustness of effect estimates.

Bodies of evidence consisting of RCTs were initially considered as high strength, while bodies of comparative observational studies began as low-strength evidence. The strength of the evidence could be downgraded based on the domains described above. There are also situations where evidence may be upgraded (e.g., large magnitude of effect, presence of dose-response relationship, or plausible unmeasured confounders could potentially increase the magnitude of effect) as described in the AHRQ Methods guides.[97] A final strength of evidence grade for each evidence statement was assigned by evaluating and weighing the combined results of the above domains. We differentiated an overall grade of high, moderate, low, or insufficient according to a four-level scale outlined in Table 2.

Table 2. Definitions of the grades of overall strength of evidence[103]

Grade	Definition
High	We are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. We believe that the findings are stable (i.e., another study would not change the conclusions).
Moderate	We are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains.
Low	We have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.
Insufficient	We have no evidence, we are unable to estimate an effect, or we have no confidence in the estimate of effect for this outcome. No evidence is available, or the body of evidence has unacceptable deficiencies, precluding reaching a conclusion.

Summary tables include reasons for downgrading or upgrading the strength of evidence.

2.7 Peer Review and Public Commentary

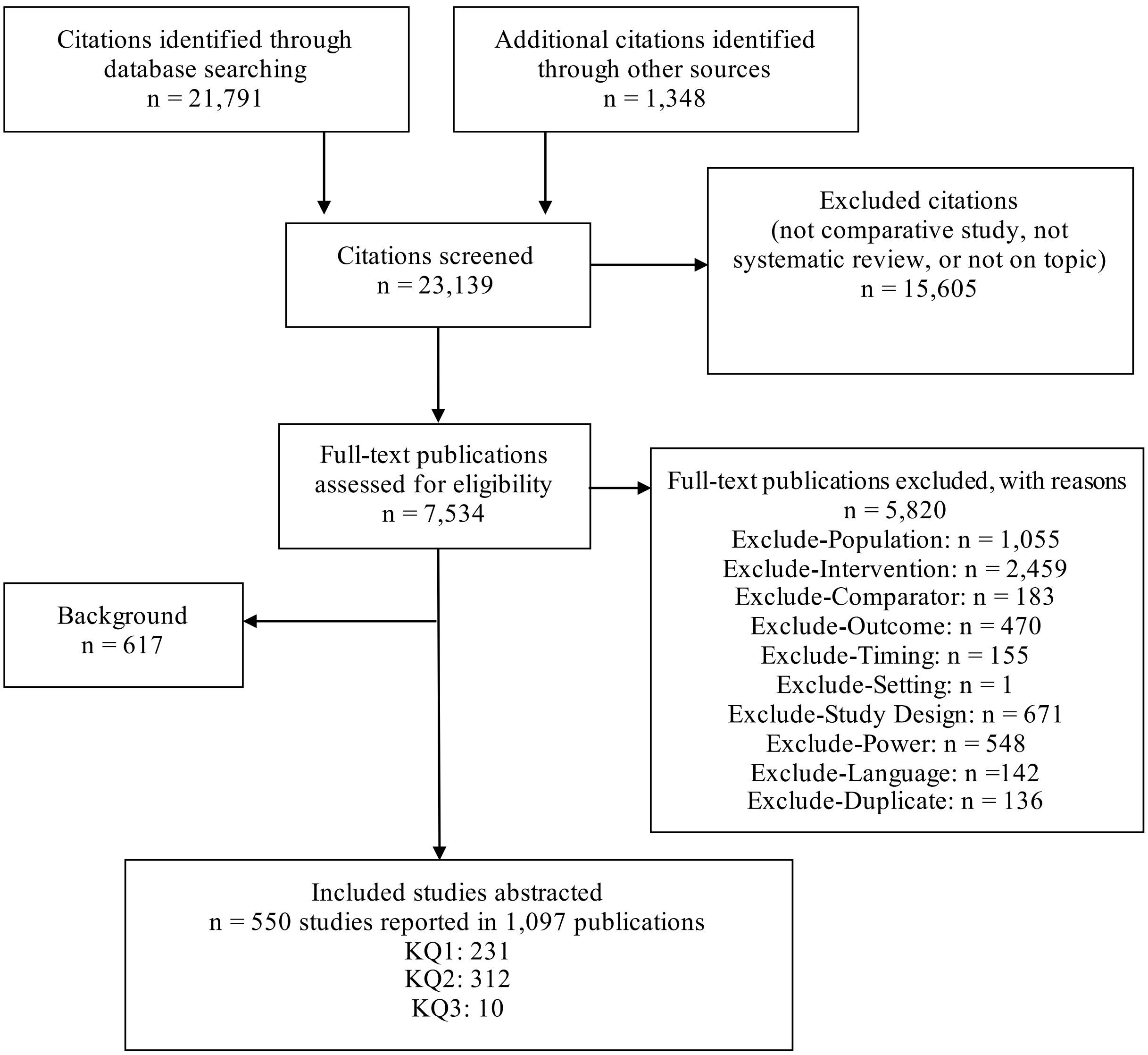
The report was updated after having undergone peer review and was posted for public commentary. The report was posted for public comment for 45 days. The disposition of comments document will be posted about three months after the final report is posted.

3. Results: Description of Included Evidence

Below we provide the report results, including the Key Points for each Key Question (KQ), and describe the included evidence, as well as the data synthesis and a summary of the strength of evidence. Details on results of literature searches, included studies, and the strength of evidence can be found in Appendixes A, C. D, and E. The list of excluded studies can be found in Appendix B.

The searches Identified 23,139 citations. Of these, we obtained 7,534 as full text. The flow diagram (Figure 2) describes the study flow through the literature review.

Figure 2. Flow diagram



Notes: KQ = Key Question

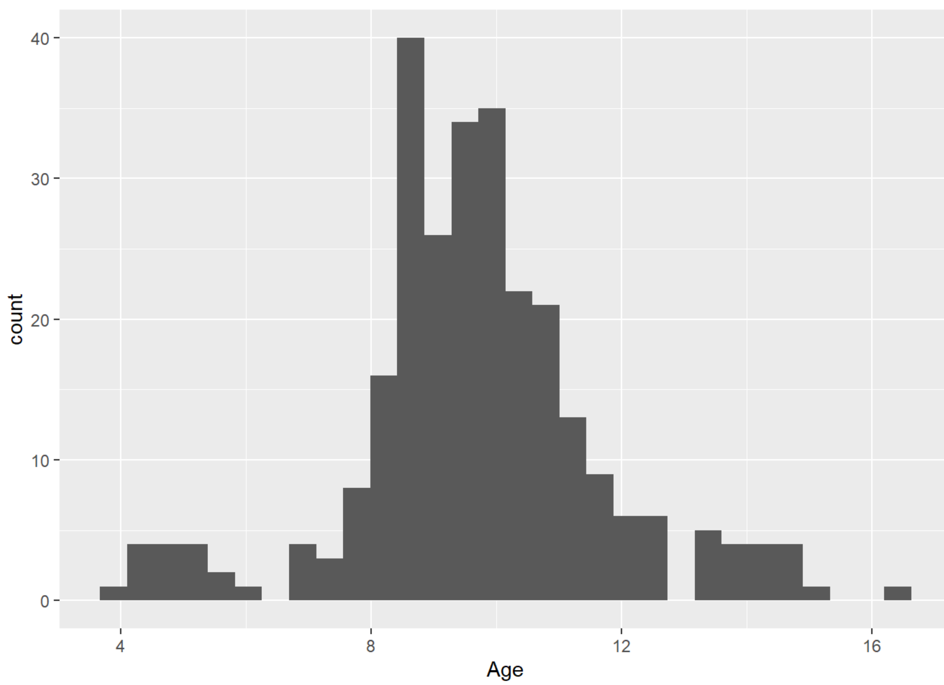
3. Results

In total, 550 studies reported in 1,097 publications met the eligibility criteria.[18, 21, 24, 27, 28, 56, 104-1194] This included 231 studies addressing KQ1, 312 studies addressing KQ2, and 10 studies addressing KQ3 (three studies contributed to more than one review question). Appendix E includes a list of included studies. Throughout the report, included studies are listed by the study ID which is composed of the first author's last name of a key publication reporting on the study and the publication year of the key publication. The evidence table in the appendix shows the study ID and cites the main publication selected for the study and all multiple publications providing additional input on the study.

The flow diagram summarizes the main reason for exclusion from the review. In addition, it shows that we retained a large number of papers as background. The list of excluded studies and background studies is listed in Appendix B. In most cases, these were existing systematic reviews addressing an individual aspect of attention deficit hyperactivity disorder (ADHD) research that were then reference-mined to ensure that all eligible studies had been included in the report.

Studies included different age ranges. Figure 3 plots the mean age for each study.

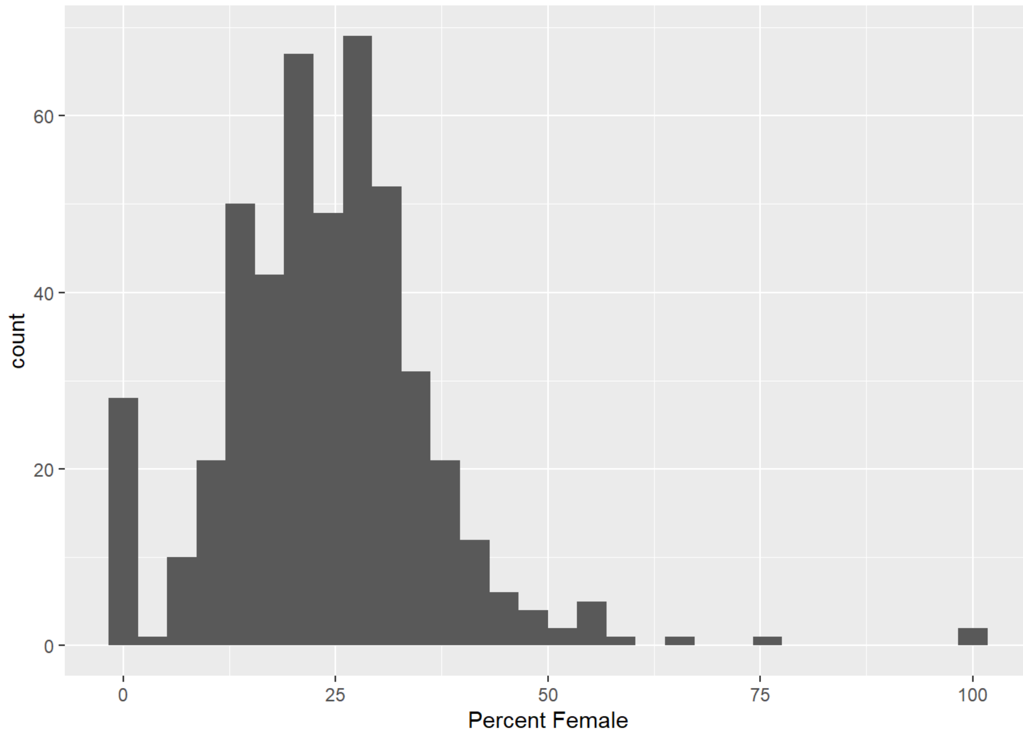
Figure 3. Mean age across studies



The median minimum age in included studies was 6 years old.

The number of included girls was low. Figure 4 plots the proportion of female participants across the research studies.

Figure 4. Proportion of female participants across studies



The median number of girls included in the studies was 25 percent.

The following subchapters address each Key Question: Chapter 4 presents the results on diagnosing ADHD, Chapter 5 presents the results on treating ADHD, and Chapter 6 presents the results of approaches to monitoring ADHD.

4. Results: Diagnosis of ADHD

The Key Question (KQ) is divided into four subquestions:

- KQ1a. What is the comparative diagnostic accuracy of approaches that can be used in the primary care practice setting or by specialists to diagnose attention deficit hyperactivity disorder (ADHD) among individuals younger than 7 years of age?
- KQ1b. What is the comparative diagnostic accuracy of electroencephalogram (EEG), imaging, or approaches assessing executive function that can be used in the primary care practice setting or by specialists to diagnose ADHD among individuals aged 7 through 17?
- KQ1c. For both populations, how does the comparative diagnostic accuracy of these approaches vary by clinical setting, including primary care or specialty clinic, or patient subgroup, including, age, sex, or other risk factors associated with ADHD?
- KQ1d. What are the adverse effects associated with being labeled correctly or incorrectly as having ADHD?

The gold standard or reference standard against which diagnostic tools were compared was diagnosis by a mental health specialist, such as a psychologist, psychiatrist or other care provider. In many cases, clinicians used published scales or semi-structured diagnostic interviews to ensure a well-validated and reliable process of confirming the diagnosis of ADHD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM), as outlined in more detail in the evidence table. Many identified studies included a broader age range rather than differentiating clearly between younger (KQ1a) or older (KQ1b) than seven years of age. Hence, we added a section describing the results for parental ratings, teacher ratings, clinician tools, and biomarkers before addressing the Key Questions. The section summarizes results by test and most studies evaluated a combined sample of children and adolescents. The KQ1a section describes all diagnostic approaches for children younger than seven years of age regardless of the applied test. The KQ1b section describes EEG, imaging, and executive function tests for children seven and up.

4.1 KQ1, ADHD Diagnosis Key Points

Key points pertaining to the diagnosis of ADHD are as follows.

- Multiple approaches showed promising diagnostic performance (e.g., using parental rating scales), but estimates of performance varied considerably across studies, and the strength of evidence (SoE) was generally low.
- Diagnostic test performance likely depends on whether youth with ADHD are being differentiated from typically developing children or from clinically referred children who had some kind of mental health or behavioral issue.
- Rating scales for parent, teacher, or self-assessment as a diagnostic tool for ADHD have high internal consistency but poor to moderate reliability between raters, indicating that obtaining ratings from multiple informants (the youth, both parents, and teachers) may be valuable to inform clinical judgement.
- Studies evaluating neuropsychological tests of executive functioning (e.g., Continuous Performance Test) used study-specific combinations of individual cognitive measures, making it difficult to compare performance across studies.

4. Results: Diagnosis of ADHD

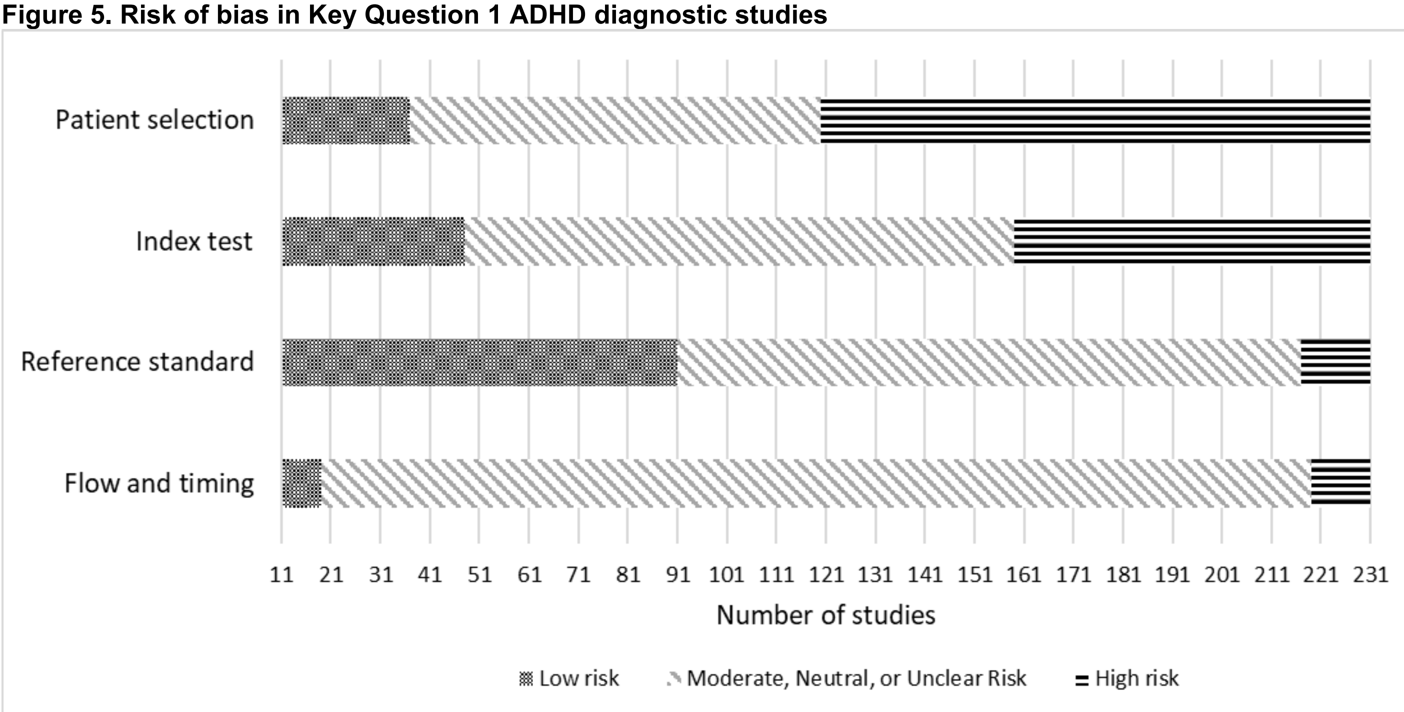
Diagnostic performance of biomarkers, EEG, and magnetic resonance imaging (MRI) scans show great variability across studies and their ability to aid clinical diagnosis for ADHD remains unclear. Studies have rarely assessed test-retest reliability, no findings have been replicated prospectively using the same measure in independent samples, and real-world effectiveness studies of diagnostic performance have not been conducted.

- Very few studies have assessed performance of diagnostic tools for ADHD in children under the age of 7 years and more research is needed.
- The identified diagnostic studies did not assess the adverse effects of being labeled correctly or incorrectly as having a diagnosis of ADHD.

4.2 KQ1, ADHD Diagnosis Summary of Findings

We identified 231 studies addressing the performance of tests aiming to diagnose ADHD.[18, 21, 24, 27, 28, 111, 112, 115, 117, 119-121, 124, 134, 135, 140-143, 152, 153, 157, 159, 162, 167-170, 172, 177, 179, 181-192, 197, 198, 210, 211, 213, 214, 218, 223, 230, 231, 233, 234, 237, 241, 242, 244-246, 251, 253, 260, 263, 267, 276, 277, 282-285, 287, 293, 297-301, 303, 307, 309, 311, 312, 314-316, 319, 322, 323, 327, 331, 336, 338-340, 342, 344, 346, 347, 351, 352, 355, 356, 359, 362, 365, 366, 369, 370, 379, 382, 385, 388-391, 393-395, 397, 400-405, 407, 408, 412, 413, 415-417, 420-424, 427, 429, 434, 436-438, 445-450, 462-465, 467-470, 473, 475, 477, 479, 482, 486, 487, 491, 493-496, 498-502, 506, 514-516, 518, 519, 524, 527, 528, 536, 537, 541-543, 546-549, 553, 558, 559, 563, 564, 566, 570, 571, 576, 580-584, 587, 591, 592, 599, 600, 603, 605, 607, 614, 615, 625, 627, 630-633, 635, 638, 639, 641, 642, 644, 647] The methodological rigor and the reporting varied substantially in the identified studies. The potential for risk of bias in the studies is documented in Figure 5. The critical appraisal for the individual studies is in Appendix D.

Figure 5. Risk of bias in Key Question 1 ADHD diagnostic studies

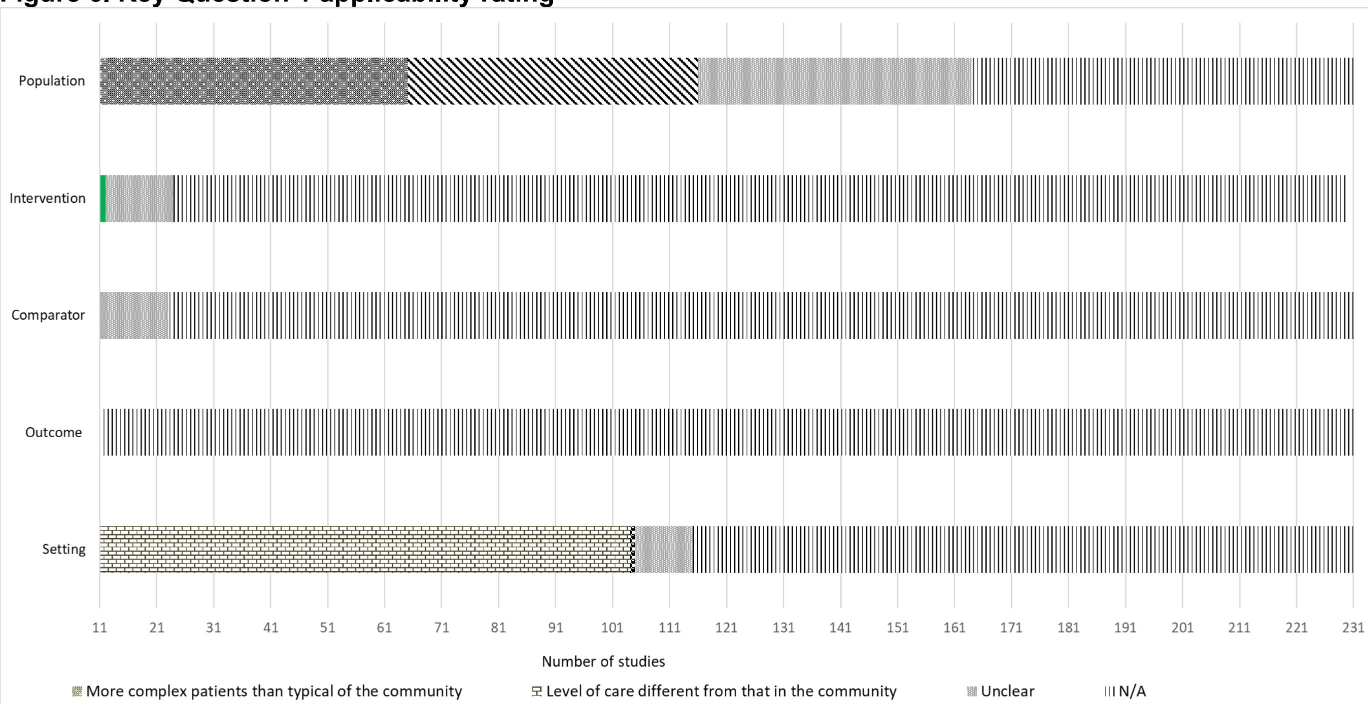


Notes: ADHD = attention deficit hyperactivity disorder

Selection bias was likely present in two thirds of studies. Often samples were restricted and did not necessarily represent the full range of children with ADHD. For example, studies explicitly reported using a convenience sampling strategy. Index test issues were present in ten percent of studies. Although the review was restricted to studies reporting a clinical diagnosis of ADHD for participants, reference standard issues were also present in a small number of studies, in particular due to lack of details on procedures and/or diagnosticians.[111, 142, 233, 342, 405, 412, 450, 516, 553, 642] Flow and timing was rated as high risk of bias in several studies.[111, 121, 143, 162, 172, 312, 319, 351, 379, 501] Typically this was due to an unclear participant flow (e.g., it was unclear whether the diagnosis was known before the results of the index test was known).

We also assessed possible applicability issues that could influence the generalizability of the reported data. Figure 6 shows the summary of rated applicability. The applicability for the individual studies is in [Appendix D](#).

Figure 6. Key Question 1 applicability rating



Notes: N/A = Not applicable

In several studies, samples were employed that do not represent the general population of children with ADHD, usually because children with co-morbidities were excluded. In addition, several papers took place in specialty care settings with diagnostic and treatment options that go beyond the standard course of action for children with ADHD.

4.3 Summary ADHD Diagnosis by Tests for All Age Groups

We broadly differentiated between parental ratings, teacher ratings, tools for clinicians, teen self-reports, neuropsychological tests, imaging, EEG, biomarker, activity markers, and other (e.g., electrocardiogram [EKG] indicators). Studies evaluated a large number of different tools within the broader categories. In addition, where studies used the same diagnostic tool (e.g., a rating scale), authors used different components of the tool (e.g., specific subscales) or combined components in a variety of ways (e.g., different neuropsychological parameter). We identified 68 studies that used machine learning algorithms to determine the best diagnostic approach.[28, 115, 120, 121, 143, 152, 157, 172, 179, 181, 182, 185-188, 191, 211, 214, 223, 233, 234, 245, 253, 282, 283, 299, 303, 322, 323, 340, 355, 356, 369, 370, [388, 394, 400, 402, 403, 407, 408, 412, 420, 429, 434, 438, 449, 450, 467, 468, 473, 494, 495, 518, 541, 543, 571, 581, 582, 591, 592, 599, 603, 630-633, 641] Studies were published since 2012[28] and came from 21 different countries, but primarily the United States[28, 152, 223, 233, 234, 282, 299, 323, 400, 403, 412, 467, 495, 518, 1188] and China.[185, 187, 188, 191, 394, 407, 408, 571, 581, 630, 632, 641] A third of identified studies used EEG markers as the data source[115, 120, 143, 157, 172, 179, 187, 188, 322, 340, 370, 394, 412, 438, 449, 468, 473, 494, 592, 883] with another third of the studies using MRI[191, 282, 495, 518, 571, 581, 630, 633, 1188] The remaining studies used neuropsychological test components, rating scale scores, activity estimates, or other sources. Some studies were able to achieve 100 percent sensitivity with the help of machine learning (corresponding specificity 100%)[143, 152] Other studies maximized specificity, and some achieved 100 percent specificity in machine learning supported diagnostic models (corresponding sensitivities 100, 97, 75, 98, and 100% respectively).[121, 143, 152, 370, 450] Across machine-learning supported studies, accuracy ranged from 61 percent[282] to 100 percent.[143, 152, 468]

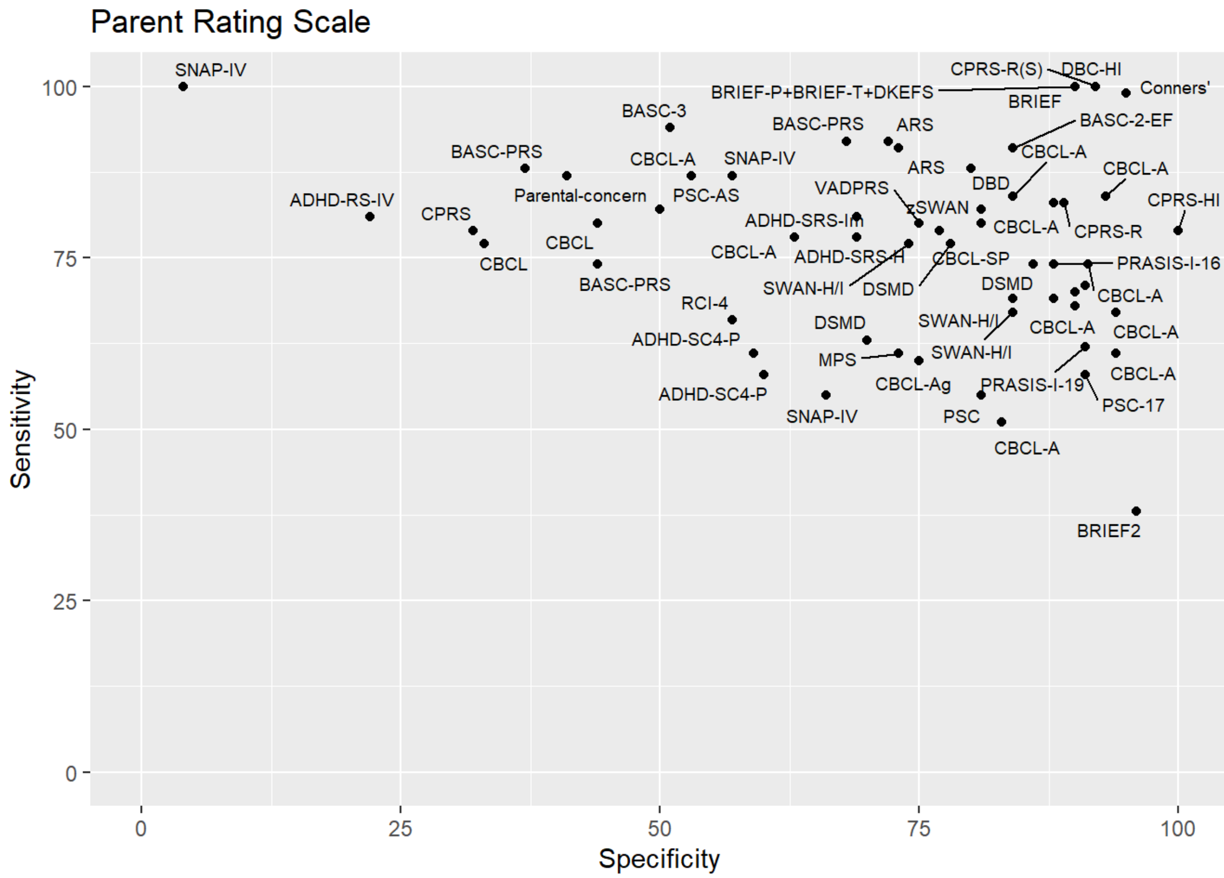
Given that most studies included younger (typically 5- and 6-year-olds) and older children, the following section describes diagnostic tools relevant to all age groups. Some studies evaluated more than one test (e.g., a parental rating and a teacher rating).

4.3.1 Parental Ratings

We identified 59 studies using Parental ratings to diagnose ADHD.[18, 117, 134, 168, 169, 190, 218, 223, 230, 233, 234, 241, 242, 244, 251, 263, 285, 287, 297, 300, 301, 311, 314, 331, 336, 339, 342, 344, 359, 362, 390, 391, 423, 424, 427, 447, 448, 463, 464, 482, 487, 491, 498, 502, 514-516, 519, 527, 528, 547, 553, 558, 559, 584, 587, 605, 638, 642] The earliest study meeting inclusion criteria was published in 1985.[514] Evaluations of parental rating tools came from five different English-language speaking countries, but most studies were from the United States.[134, 169, 190, 230, 233, 234, 241, 242, 244, 251, 263, 285, 297, 299, 311, 331, 336, 339, 342, 344, 359, 390, 391, 423, 424, 427, 448, 463, 464, 482, 487, 491, 498, 502, 514-516, 519, 527, 528, 547, 553, 558, 559, 584, 605, 638, 642]The populations studied were predominately males and included participants ranged between the ages of two and 18. Four studies exclusively included children younger than seven years old.[331, 516, 519, 559] For studies that distinguished between ADHD presentations, most of the participants were diagnosed with the combined or inattentive presentations. In one study focusing on preschool age children who presented with disruptive behavior disorders, 57 percent of participants were diagnosed with the hyperactive/impulsive presentation.[331] While ADHD participants with co-occurring disorders were not excluded from most studies, only a few purposely included children with specific co-occurring disorders such as disruptive behavior disorders[331] or autism.[234, 447] However, about half of identified studies came from clinical samples, rather than general neurotypically developing children–- i.e., they identified children undergoing a diagnostic workup for a potential diagnosis of ADHD, conduct disorders, autism, or depression.

In half of the identified studies, White participants made up more than 70 percent of the sample. One study evaluated diagnostic accuracy a sample in which over 50 percent of participants were Black/African American,[462, 536] and one study was identified in which 85 percent of participants were Hispanic or Latino.[553] Studies reported predominantly on the estimated sensitivity and specificity. Some studies also reported on the area under the curve (AUC) as a summary test performance, but other key outcomes were less frequent. Figure 7 plots the sensitivity and specificity for the parental rating scale evaluated in the study.

Figure 7. Sensitivity and specificity of parental rating scales



Notes: Evaluated tools: ADHD-RS-IV, ADHD-SC4-P, ADHD-SRS-H, ADHD-SRS-Im, ARS, BASC-2-EF, BASC-3, BASC-PRS, BRIEF, BRIEF2, BRIEF-P+BRIEF-T+DKEFS, CBCL, CBCL-A, CBCL-AD/H, CBCL-Ag, CBCL-SP, Conner'', Conners-3-P(S)+CBCL, CPRS, CPRS-HI, CPRS-R, CPRS-R(S), DBC-HI, DBD, DSMD, MPS, Parental-concern, PRASIS-I-16, PRASIS-I-19, PRASIS-I-30, PSC, PSC-17, PSC-AS, RCI-4, SNAP-IV, SWAN, SWAN-H/I, VADPRS. More information can be found in Appendix C, Table C.1.

The studies reporting sensitivity and specificity (the measures are not independent from each other, and high sensitivity can come at a cost of low specificity and vice versa) show the wide variation in diagnostic accuracy estimates. The figure also shows that studies evaluated a large range of different parental rating scales, with few studies reporting on the same tool.

The most frequently evaluated diagnostic tool was the CBCL (Child Behavior Checklist), either alone or in combination with other scales, using different cutoffs, and evaluating different subscales (the attention deficit/hyperactivity problems subscale most frequently). Reported sensitivity for the CBCL ranged from 71 percent in a study differentiating ADHD and oppositional defiance disorder[331] to 84 percent in two studies, one using an outpatient pediatric medical clinic, the other one a sample of children with traumatic brain injury.[190, 605] Reported specificity for this parental scale ranged from 33 percent[587] to 93 percent[190] in the pediatric medical clinic sample. The reported AUC ranged from 0.55[344] to 0.93[190] with three independent studies reporting estimates of 0.83 or 0.84 for this diagnostic measure for the CBCL.[251, 331, 498] The evidence table in the appendix shows the results for all diagnostic and psychometric outcomes of interest for all identified studies.

Table 3 shows the findings for the outcomes of interest together with the number of studies and study identifiers for parental rating scales. For the main results, we report findings from population samples that differentiated ADHD from neurotypical developing children separately from results obtained in clinical samples, given that the study population was identified as one of the sources of heterogeneity in reported results as documented in KQ1c. Results are shown across studies and tools for the main analyses. Where at least two different author groups reported on the same rating scale, we provide results for a specific scale.

Table 3. KQ1 summary of findings and strength of evidence for parental ratings

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 Parental Ratings	Sensitivity	36 studies[18, 134, 168, 190, 218, 223, 230, 242, 244, 251, 285, 287, 301, 314, 331, 336, 339, 359, 390, 424, 427, 448, 482, 487, 502, 514, 515, 528, 547, 553, 558, 559, 584, 587, 605, 642]	Sensitivity ranged from 61% for a Maternal Perinatal Scale (corresponding specificity 73%)[427] to 94% for the BASC-3 (corresponding specificity 51%) differentiating ADHD and neurotypical development Sensitivity showed more variation and ranged from 38% using the BRIEF (corresponding specificity 96%)[339] to 100% using the CPRS-R or the SNAP-IV (corresponding specificities 92% and 4%)[287, 314] differentiating ADHD in clinical samples	S, I	Low
KQ1 CBCL	Sensitivity	7 studies[190, 242, 251, 331, 336, 587, 605]	Sensitivity ranged from 71% (corresponding specificity 91%)[331] to 84% (corresponding specificity 93 and 84)[190, 605]	S	Moderate for moderate sensitivity
KQ1 DSMD	Sensitivity	2 studies[244, 547]	Sensitivity ranged from 63% (corresponding specificity 70%)[547] to 77% (corresponding specificity 78%)[244]	S, I	Low
KQ1 SNAP-IV	Sensitivity	2 studies[482 314]	Sensitivity ranged from 55% (corresponding specificity)[547] to 100% (corresponding specificity 4)[314]	S, I	Low
KQ1 SWAN	Sensitivity	2 studies[168, 223]	Sensitivity ranged from 67% (corresponding specificity 84%)[223] to 82% (corresponding specificity 81%)[168]	S, I	Low
KQ1 Parental Ratings	Specificity	36 studies[18, 134, 168, 190, 218, 223, 230, 242, 244, 251, 285, 287, 301, 314, 331, 336, 339, 359, 390, 424, 427, 448, 482, 487, 502, 514, 515, 528, 547, 553, 558, 559, 584, 587, 605, 642]	Specificity ranged from 37% using the BASC-PRS (corresponding sensitivity 88%)[230] to 100% using the Conners Parent Rating Scale Hyperactivity Index (corresponding sensitivity 79%)[515] differentiating ADHD and neurotypical development Specificity ranged from 4% using the SNAP-IV (corresponding sensitivity 100%)[314] to 96% (corresponding sensitivity 38%)[339] differentiating ADHD in clinical samples	S, I	Low
KQ1 CBCL	Specificity	6 studies[190, 251, 331, 336, 587, 605]	Specificity ranged from 33% (corresponding sensitivity 77%)[587] to 93% (corresponding sensitivity 84)[190]	S, I	Low
KQ1 DSMD	Specificity	2 studies[244, 547]	Specificity ranged from 70% (corresponding sensitivity 63%)[547] to 88% (corresponding sensitivity 69%) in a second sample[547]	S, I	Low
KQ1 SNAP-IV	Specificity	2 studies[314, 482]	Specificity ranged from 4% (corresponding sensitivity 100%)[72] to 66% (corresponding sensitivity 55%)[482]	S, I	Low
KQ1 SWAN	Specificity	2 studies[168, 223]	Specificity ranged from 74% (corresponding sensitivity 77%)[223] to 84% (corresponding sensitivity 69%) in a second sample[223]	S, I	Low

4. Results: Diagnosis of ADHD

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 Parental Ratings	Accuracy	11 studies[18, 169, 223, 251, 331, 339, 427, 487, 547, 587, 605]	Accuracy was 67% using the Maternal Perinatal Scale[427] differentiating ADHD and neurotypical development Accuracy ranged from 59% using the CBCL to 95% using the BRIEF[18] differentiating ADHD in clinical samples	S, I	Low
KQ1 CBCL	Accuracy	3 studies[251, 331, 605]	Accuracy ranged from 80%[331] to 84%[605]	S	Moderate for good accuracy
KQ1 Parental Ratings	AUC	23 studies[168, 190, 218, 230, 233, 234, 241, 251, 263, 285, 287, 297, 301, 311, 331, 339, 342, 344, 359, 464, 498, 502, 553]	AUC ranged from 0.73 using the PSC-AS[553] to 0.95 for a combination of BRIEF 2 and Conners 3[464] differentiating ADHD and neurotypical development AUC ranged from 0.55 using the CBC attention deficit / hyperactivity problem scale[344] to 0.97 using the SRS[234] differentiating ADHD in clinical samples	S, I	Low
KQ1 CBCL	AUC	6 studies[190, 241, 251, 331, 344, 498]	The reported AUC ranged from 0.55[344] to 0.93[190] with three independent studies reporting estimates of 0.84 or 0.83[251, 331, 498]	S	Moderate for acceptable AUC
KQ1 Parental Ratings	Rater agreement	2 studies[218, 423]	ICC 0.51 for inattention, 0.56 for hyperactivity, and 0.58 for impulsivity between mother and father subscale ratings on the *DSM-ADHD-Symptom Rating Scale*[423] in a sample of children with ADHD ICC between parent and teacher total scores using CPRS-R and CTRS-R was 0.19[218]	S, I	Low
KQ1 Parental Ratings	Internal consistency	10 studies[168, 218, 287, 339, 342, 359, 423, 424, 447, 516]	Across children with ADHD, autism, and neurotypically developing Cronbach's alpha SCQ 0.93[447] In neurotypical samples: Cronbach's alpha SWAN 0.95[168]; Cronbach's alpha BASC-2 Executive Function Screener parent rating global sum score 0.91[359]; Cronbach's alpha DBDRS Inattention 0.94, hyperactivity / impulsivity 0.91[527] In clinical samples: Cronbach's alpha BRIEF2 global executive composite summary score 0.97[339]; Cronbach's alpha CBCL Attention Problems 0.76[342] and CPRS-R 0.84[218]; Cronbach's alpha DBC-HI 0.93[287]; Cronbach's alpha DIPA 0.92[516] Cronbach's alpha DSM-ADHD-Symptom Rating Scale total 0.90 for mother's rating, 0.91 for father's rating[423]; Cronbach's alpha PSC attention subscale 0.90[424]	S, I	Low
KQ1 Parental Ratings	Test-retest reliability	2 studies[134, 391]	Test-retest correlations in a high-risk sample were .91 for inattention, .92 for hyperactive/impulsive, .95 for conduct/oppositional, .87 for anxiety/depression, .82 for performance subscales[134]	S, C	Low

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
			CHAOS test-retest reliability ranged from 0.74 to 0.87[391] over four subscales in a *clinical* sample		
KQ1 Parental Ratings	Misdiagnosis impact	0 studies	No data	C	Insufficient
KQ1 Parental Ratings	Costs	0 studies	No data	C	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, AUC = area under the curve, BASC = Behavior Assessment System for Children, BRIEF2 = Behavior Rating Inventory of Executive Function, Second Edition, C = inconsistency, CBCL = Child Behavior Checklist, CPRS-R = Revised Conners Parent Rating Scale, CHAOS = Conduct-Hyperactive-Attention Problem-Oppositional Symptom scale, DBC-HI = Developmental Behaviour Checklist Hyperactivity Index, DBDRS = Parent Disruptive Behavior Disorder Ratings Scale, DIPA-L = diagnostic infant and preschool assessment, I = imprecision, KQ = Key Question, PSC = Pediatric Symptom Checklist, S = study limitation, SCQ = Social Communication Questionnaire, SoE strength of evidence, SRS = Social Responsiveness Scale, SWAN = Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Rating Scale

Parental ratings reported mainly on the sensitivity and specificity. A few studies reported perfect diagnostic performance for parental ratings for either sensitivity or specificity, but not both together. Little information was provided in these diagnostic studies regarding the reliability of the measures given the large range of different measures evaluated by study authors. We downgraded the strength of evidence for study limitation (lack of detailed reporting), imprecision (large variation in reported diagnostic performance) and for inconsistency (when consistency could not be assessed because no study was identified, or only one study was identified reporting on the test and outcome of interest and results have not been replicated by another author group, or only limited data points were available). None of the included studies provided information on the effect of misdiagnosis. None of the identified studies reported the costs associated with obtaining parental ratings.

4.3.2 Teacher Ratings

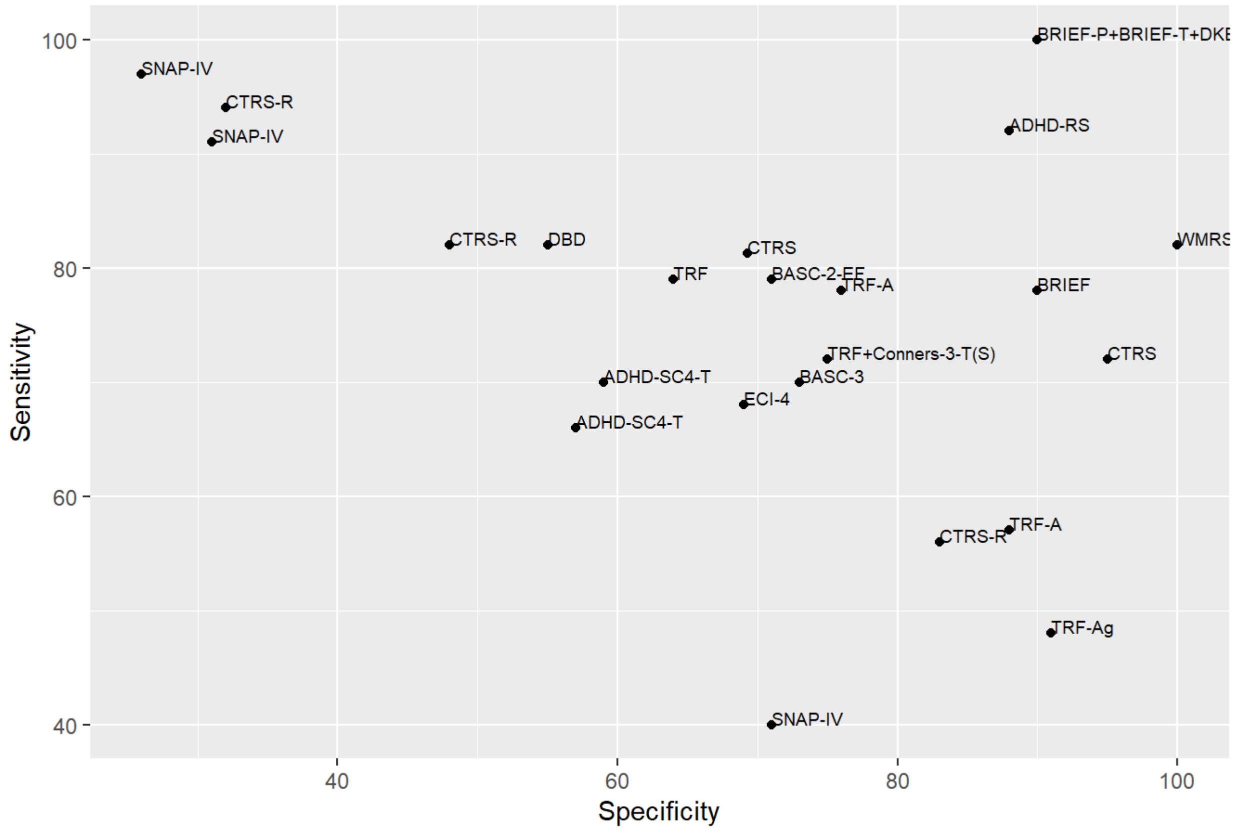
We identified 23 studies using Teacher ratings to diagnose ADHD.[18, 119, 183, 218, 242, 299, 301, 314, 342, 359, 362, 391, 463, 479, 482, 491, 519, 527, 528, 558, 559, 587, 642] The earliest study meeting eligibility criteria was published 1998[479] from four different English-speaking countries, primarily the United States.[242, 299, 342, 359, 391, 463, 479, 482, 491, 519, 527, 528, 558, 559, 642] The populations studied were predominately males between the ages of three and 18. Two studies exclusively included children younger than seven years old[519, 559] and two exclusively in children eight years or older.[119, 359] For studies that distinguished between ADHD presentations, most of the participants were diagnosed with the combined or inattentive presentations. Almost all of the studies mention race and ethnicity demographics, with 14 studies where White participants made up greater than 70 percent of the sample, and one study in which over 85 percent of the participants were Black/African American.

ADHD participants with co-occurring disorders were not excluded from most of the studies. Studies were divided into clinical samples and those recruited from a less selective population. None of the studies included children who all had a dual diagnosis, such as ADHD and conduct disorder.

4. Results: Diagnosis of ADHD

Studies reported a variety of outcomes, with sensitivity and specificity being the most frequently reported outcomes. Figure 8 plots the reported sensitivity and specificity for teacher rating scales.

Figure 8. Sensitivity and specificity of teacher rating scales



Notes: Evaluated tools: ADHD-RS, ADHD-RS-IV-I, ADHD-SC4-T, BASC-2-EF, BASC-3, BRIEF, BRIEF-P+BRIEF-T+DKEFS, CTRS, CTRS-R, DBD, ECI-4, SNAP-IV, TRF, TRF+Conners-3-T(S), TRF-A, TRF-Ag, WMRS. More information can be found in the evidence table in the appendix

The figure shows the large range in reported sensitivity and specificity. It also shows that studies have evaluated many different teacher rating tools.

The Teacher Report Form, alone or in combination with Conners teacher rating scales, and using the total or the subscale of attention problems, was evaluated in more than one study.[242, 301, 342, 587] Reported sensitivity ranged from 72 percent[301] to 79 percent.[587] Reported specificity estimates ranged from 64 percent[587] to 76 percent.[242] Two of the studies reported on AUC and found 0.65[342] for the attention problem subscale and 0.77[301] in combination with the Conners 3 teacher short form. No two studies reported on rater agreement, internal consistency, or test-retest reliability for the same teacher rating scale.

Table 4 shows the findings for the outcomes of interest together with the number of studies and study identifiers.

Table 4. KQ1 summary of findings and strength of evidence for teacher ratings

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 Teacher Ratings	Sensitivity	17 studies[18, 119, 183, 218, 242, 299, 301, 314, 359, 479, 482, 527, 528, 558, 559, 587, 642]	Sensitivity ranged from 70% using the BASC-3 (corresponding specificity 73%)[642] to 92% using the ADHD-RS (corresponding specificity 88%)[299] differentiating ADHD and neurotypical development Sensitivity ranged from 40% using the SNAP-IV (corresponding specificity 71%)[482] to 97% using the SNAP-IV (corresponding specificity 26%)[314] in clinical samples	S, I	Low
KQ1 TRF	Sensitivity	3 studies[242, 301, 587]	Reported sensitivity ranged from 72% (corresponding specificity 75%)[301] to 79% (corresponding specificity 64%)[587]	S, C	Low
KQ1 SNAP-IV	Sensitivity	2 studies[314, 482]	Reported sensitivity ranged from 40% (corresponding specificity 71%)[482] to 97% (corresponding specificity 26%)[314]	S, C	Low
KQ1 Teacher Ratings	Specificity	16 studies[18, 119, 183, 218, 242, 299, 301, 314, 359, 482, 527, 528, 558, 559, 587, 642]	Specificity ranged from 55% using the DBD (corresponding sensitivity 82%)[528] to 88% for the ADHD-RS (corresponding sensitivity 92%)[299] differentiating ADHD and neurotypical development Specificity ranged from 48% using the CTRS-R (corresponding sensitivity 82%)[183] to 91% for the TRF aggressive behavior scale (corresponding sensitivity 48%)[301] in clinical samples	S, I	Low
KQ1 TRF	Specificity	4 studies[242, 301, 342, 587]	Reported specificity ranged from 64%[587] to 76%[242]	S, C	Low
KQ1 SNAP-IV	Specificity	2 studies[314, 482]	Reported specificity ranged from 26% (corresponding sensitivity 97%)[314] to 71% (corresponding sensitivity 40%)[482]	S, C	Low
KQ1 Teacher Ratings	Accuracy	4 studies[18, 299, 559, 587]	Accuracy was 91%[299] using the ADHD-RS to differentiate ADHD and neurotypical development Accuracy ranged from 69 using the ECI-4[559] to 76% using the TRF[587] in clinical samples	C	Low
KQ1 Teacher Ratings	AUC	5 studies[218, 301, 342, 359, 479]	AUC was 0.83 using the BASC-2[359] differentiating ADHD and neurotypical development AUC ranged from 0.65 for TRF[342] to 0.84 for the ADHD RS-IV teacher rating inattention scale[479] in clinical samples	S, I	Low

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 TRF	AUC	2 studies[301, 342]	AUC ranged from 0.65%[342] to 0.77 when combined with Conners-3-T(S)[301]	S, C	Low
KQ1 Teacher Ratings	Rater agreement	4 studies[218, 362, 391, 463]	In clinical samples: Correlations between teacher and parent ratings ranged from 0.17 to 0.41 over four subscales on the CHAOS scale,[391] the reported kappa range was 0.29 between teacher and parent ratings on the ADHD RS-IV,[362] up to 0.68 for Symptom Inventories Teacher rating[463]; ICCs comparing teacher and parent scores of the Conners rating scales were 0.19[218]	S, I	Low
KQ1 Teacher Ratings	Internal consistency	6 studies[218, 342, 359, 391, 527, 528]	In neurotypical samples: Cronbach's alpha 0.94 for both teacher-rated inattention and hyperactivity symptom counts on the DBD[528] Cronbach's alpha was 0.95 for BASC-2[359] Cronbach's alpha was 0.94 for the DBD[527] In clinical samples: Cronbach's alpha was 0.95 for the TRF attention problems subscale[342]; Cronbach's alpha ranged from 0.64 to 0.91 over four subscales of the CHAOS scale[391], Cronbach's alpha was 0.80 for CTRS-R[218]	S, I	Low
KQ1 Teacher Ratings	Test-retest reliability	1 study[391]	Pearson correlations ranged from 0.74 to 0.87 over four subscales of the CHAOS scale, retest between 1 and 829 days[391] in a clinical sample	C	Low
KQ1 Teacher Ratings	Misdiagnosis impact	0 studies	No data	C	Insufficient
KQ1 Teacher Ratings	Costs	0 studies	No data	C	Insufficient

Notes: AUC = area under the curve, KQ = Key Question, Attention-Deficit/Hyperactivity Disorder Rating Scale, 4th edition, ASEBA = Achenbach System of Empirically Based Assessment, BASC = Behavior Assessment System for Children, C = inconsistency, CHAOS = Hyperactive-Attention Problem- Oppositional Symptom, CTRS-R = Connor Teacher Rating Scale Revised, DBD = Disruptive Behavior Disorder rating scale, I = imprecision, S = study limitation, SNAP-IV = Swanson, Nolan, and Pelham Questionnaire, SoE = strength of evidence, TRF = Teacher Report Form

Across all teacher rating studies, reported sensitivity in individual studies were up to 97 percent in a clinical sample, but the corresponding specificity was only 26 percent.[314] We downgraded the strength of evidence for imprecision (large variation in reported diagnostic performance) and for inconsistency (when consistency could not be assessed because only one study was identified reporting on the test and outcome of interest and results had not been replicated by another author group). Identified diagnostic accuracy studies did not report on several of the other key outcomes.

4.3.3 Teen/Child Self-Reports

We identified six studies using teen/child self-reports to diagnose ADHD.[142, 168, 231, 297, 491, 506] The earliest study was published in 2002[506] and data came from two countries, the United States[231, 297, 491] and Canada,[142, 168, 506] respectively. Self-reports were primarily completed by adolescents, however one study provided a research assistant to help read the questions for participants under 11 years old.[297] Only one study documented the ADHD presentation: 10 percent inattentive presentation, 4 percent hyperactive/impulsive presentation, and 25 percent combined presentation.[491] Two studies mentioned race and ethnicity demographics. In one study, White participants made up 61 percent of the sample[297] and one study reported 89 percent of the participants were Black/African American.[491]

Studies reported a limited number of outcomes, with sensitivity, specificity, and AUC being the most frequently reported outcomes. No two identified studies reported on the same self-report measure. Reported diagnostic success varied widely. Table 5 shows the findings for the outcomes of interest together with the number of studies and study identifiers. None of the tools was evaluated in more than one study.

Table 5. KQ1 summary of findings and strength of evidence for self reports

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 Self-reports	Sensitivity	4 studies[142, 168, 297, 506]	Sensitivity ranged from 57% (corresponding specificity 81%) using the SWAN self report[168] to 86% for the DIA-R (corresponding specificity 70%)[142] differentiating ADHD and neurotypical development Sensitivity ranged from 53% using the Brown ADD Scale for Adolescents (corresponding specificity 98%)[142] to 78% using the Brown ADD scale plus CWASR in clinical samples	C	Low
KQ1 Self-reports	Specificity	4 studies[142, 168, 297, 506]	Specificity ranged from 70% using the DIA-R (corresponding sensitivity 86%)[506] to 81% (corresponding sensitivity 57%) using the SWAN self report,[168] differentiating ADHD and neurotypical development Specificity was 98% for the Brown ADD Scale for Adolescents (corresponding sensitivity 53%)[506] in clinical samples	C	Low
KQ1 Self-reports	Accuracy	1 study[506]	Accuracy ranged between 78 and 87% using the Brown ADD scale for Adolescents in samples of children with reading disabilities[506]	C	Insufficient
KQ1 Self-reports	AUC	4 studies[142, 168, 297, 491]	AUC ranged from 0.71 for the SWAN self report,[168] and the Kiddie-Computerized adaptive test (K-CAT)[297] to 0.85 using the DIA-R[142] differentiating ADHD and neurotypical development AUC was 0.56[491] for the ASEBA in clinical samples[491]	C	Low
KQ1 Self-reports	Rater agreement	1 study[506]	Spearman correlation between child self-report and parent report ranged from .164 for subscales of the Conners and Child Behavior Checklist to .747 for the Brown ADD self-report vs the K-SADS parent report[506]	C	Low
KQ1 Self-reports	Internal consistency	1 study[168]	Cronbach's alpha was above 0.80 for the DIA-R[142] and 0.88 for the SWAN self report[168] differentiating ADHD and neurotypical development	C	Low

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 Self-reports	Test-retest reliability	1 study[142]	Test-retest ICC was between 0.82 to 0.84 across clinical and neurotypical developing subsamples using the DIA-R[142]	C	Low
KQ1 Self-reports	Misdiagnosis impact	0 studies	No data	C	Insufficient
KQ1 Self-reports	Costs	0 studies	No data	C	Insufficient

Notes: AUC = area under the curve, KQ = Key Question, ASEBA = Achenbach System of Empirically Based Assessment, C = inconsistency, DIA-R = Dominic Interactive for Adolescents-Revised, I = imprecision, K-SADS = Kiddie Schedule for Affective Disorders and Schizophrenia, S = study limitation, SoE = strength of evidence, SWAN = Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Rating Scale

The reported diagnostic performance of teen self-reports was limited. We downgraded for the domain inconsistency (inability to judge the consistency across studies because only one study was identified reporting on the test and outcome of interest). In several cases, our searches identified no studies and the strength of evidence is insufficient for the outcome.

4.3.4 Combined Ratings

We identified 13 studies that assessed the diagnostic performance of ratings combined across informants.[18, 189, 277, 297, 303, 405, 467, 479, 527, 548, 559, 570, 600] The studies compared the information from multiple raters to the reference standard. Studies combined information sources in different ways, often selecting individual variable with the help of machine learning. Only one of these studies compared the performance when combining data from multiple informants to that of single informants: it found negligible improvement when combining youth self-report to the parent report alone using an adaptive testing questionnaire (AUC youth only 0.71; parent only 0.85; combined 0.86) in a treatment-seeking population.[297]

The studies reported only on selected accuracy measures. One study combined parent and teacher ratings on the Conners scales by requiring youth to meet diagnostic cutoffs (T-score ≥65) in one setting and substantial symptoms in the other setting (T-score ≥60). It reported a diagnostic sensitivity of 84 percent and specificity of 36 percent for the combined rating when distinguishing ADHD from other clinically referred youth.[18] One study reported findings from a discriminant function analysis of mother, father, and teacher ratings on the Conners scale when distinguishing ADHD youth who were considered either intellectually gifted or not from typically developing, intellectually gifted youth. It found that the discriminant function using all three informants distinguished the typically developing youth from the two ADHD groups but did not distinguish the two ADHD groups from one another.[277] A study in four to seven year old children used machine learning to combine parent and teacher ratings on the BRIEF in distinguishing youth with ADHD from typically developing controls. It reported an average diagnostic accuracy of 0.93, with teacher ratings being the most informative in the machine learning algorithm, though it did not formally compare accuracy for combined informants with accuracy for either informant alone. The study also found that the addition of neuropsychological test measures and cortical thickness measures to the machine learning algorithm did not meaningfully improved diagnostic performance over use of the BRIEF alone.[467] The best AUC was reported by a machine learning supported study combining parent and teacher ratings (AUC 0.98).[405]

The studies did not report reliability measures for ratings combined across informants; studies reported only psychometric performance in individual informant groups. For example, one of the studies reported that individual ratings of the BRIEF using parent and teacher ratings found intraclass correlation coefficients (ICCs) from 0.31 to 0.59 across subscales.[570]Another study reported the range of Cronbach's alpha estimates across teacher and parent ratings for individual scales, all indicating substantial internal consistency (with the lowed Cronbach's also of 0.72, all other values were above 0.90).[467]

4.3.5 Clinician Tools

We identified 24 of studies evaluating additional tools that could be used by clinicians or the healthcare system (beyond neuropsychological tests; parent, teacher, or self-report ratings; biomarkers; or imaging) to aid the diagnosis of ADHD.[27, 121, 167, 181, 298, 299, 311, 338, 355, 362, 385, 388, 389, 400, 403, 407, 416, 417, 434, 437, 499, 542, 566, 627] The earliest identified study was published in 2009.[627] Evaluations were published in three different countries, including eight from the United States.[27, 299, 311, 389, 400, 403, 542, 566] The populations studied were predominately males and included youth were between the ages of three and 18. Most studies did not distinguish between ADHD presentations but three studies restricted to the combined ADHD type.[121, 416, 627] Where studies mentioned race and ethnicity demographics of the sample composition, the percentage of White children ranged from 52 to 100 percent, the number of Black or African American children ranged from two to 44 percent, Hispanic/Latino children three to 20 percent, and Asian children one to three percent.

Studies used different tools, including diagnostic interview guides and observation tools. Several studies measured child activity levels as an objective test, for example through an actometer or commercially available activity tracker[121, 181, 298, 355, 400, 403, 416, 437, 627] and two evaluated direct observation as a diagnostic tool.[167, 362] Three studies used insurance claim-based algorithms or medical health record indicators[434, 542, 566] The remaining studies addressed unique interventions and questions, for example, one study focused on the clinical utility of International Classification of Diseases [ICD]-11 diagnostic guidelines[499] and a clinician diagnosis combined with an assessment aid that involved integrating EEG and theta/beta ratio data.[27]

Studies are difficult to compare since they assess different tools and approaches. Studies reported a variety of outcomes, with sensitivity and specificity being the most frequently reported outcomes. Table 6 shows the findings for the key outcomes of interest together with the number of studies and study identifiers. Where all identified studies evaluated the same tool, the first column of the study indicates the tool, otherwise estimates are reported across all tools.

Table 6. KQ1 summary of findings and strength of evidence for clinician tools

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 Clinician tool	Sensitivity	14 studies[27, 121, 167, 181, 298, 299, 355, 388, 400, 403, 407, 416, 417, 434]	Sensitivity ranged from 25 (corresponding specificity 94%) using actigraph measures taken during CPT task[417] to 100% (corresponding specificity 99%) using extended activity measurement[355] differentiating ADHD and neurotypical development Sensitivity ranged from 63% (corresponding specificity 74%) using a combination of medical record indicators[434] to 93% using smart chair data[181] in a clinical sample	C, I	Low

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 Clinician tool	Specificity	14 studies[27, 121, 167, 181, 298, 299, 355, 388, 400, 403, 407, 416, 417, 434]	Specificity ranged from 79% using an observational assessment tool (corresponding sensitivity 87%)[167] to 100% (corresponding sensitivity 98%)[121] using activity measures differentiating ADHD and neurotypical development Specificity ranged from 36% using interview notes and family history data (corresponding sensitivity 89%)[434] to 95% (corresponding sensitivity 67%)[181] using smart chair data in a clinical sample	C, I	Low
KQ1 Clinician tool	Accuracy	12 studies[27, 121, 181, 298, 299, 355, 388, 403, 407, 416, 434, 437]	Accuracy ranged from 0.68[437] to 0.99[121] using activity measures to differentiate ADHD and neurotypical development Accuracy ranged from 0.61 for individual clinical impressions[27] to 0.92 using smart chair data[181] in a clinical sample	S, I	Low
KQ1 Clinician tool	AUC	12 studies[121, 167, 181, 311, 355, 385, 389, 400, 407, 416, 434, 627]	Activity measures ranged from AUC 0.79[627] to 0.9996[355] differentiating ADHD and neurotypical development AUC ranged from 0.66 using a combination of medical record indicators[434] to 0.98 using smart chair data in a clinical sample	S, I	Low
KQ1 Clinician tools	Rater agreement	2 studies[167, 499]	ICC was 0.92 for raters using the DB-DOS[167] differentiating ADHD and neurotypical development Kappa between a clinician interviewer and clinician observing the interview was 0.46[499] in a clinical sample	C	Low
KQ1 Clinician tools	Internal consistency	2 studies[167, 385]	Cronbach's alpha was 0.82 for the DB-DOS[167] differentiating ADHD and neurotypical development Cronbach's alpha was 0.86 for the HDS[385] in a clinical sample	C	Low
KQ1 Clinician tools	Test-retest reliability	1 study[167]	Test-retest reliability was ICC 0.64 for the DB-DOS[167] differentiating ADHD and neurotypical development	C	Insufficient
KQ1 Clinician tools	Misdiagnosis impact	0 studies	No data	C	Insufficient
KQ1 Clinician tools	Costs	0 studies	No data	C	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, AUC = area under the curve, C = inconsistency, DB-DOS = Disruptive Behavior Diagnostic Observation Schedule, HDS= InterRAI child and Youth Mental Health Hyperactive/Distraction scale, I = imprecision, KQ = Key Question, S = study limitation; SoE = strength of evidence

We downgraded the strength of evidence for imprecision (very large variation in reported diagnostic performance) and for inconsistency (when consistency could not be assessed because only one study was identified reporting on the test, and outcome of interest and results had not been replicated by another author group). The tools were difficult to compare and answered study-specific questions.

4.3.6 Biomarkers

We identified seven studies using proposed biomarkers obtained from biospecimen to diagnose ADHD.[309, 501, 563, 583, 603, 635, 644] EEG and imaging approaches are reported in section

4.3.7 and the evidence table (Appendix C, Table C.1.) shows additional, more unique approaches using other approaches such as eye movement tracking to diagnose ADHD. Five identified studies used blood measures, including membrane potential ratio[563] and erythropoietin/erythropoietin receptor,[309] and three of these studies analyzed miRNA obtained from blood samples.[603, 635, 644] The other studies evaluated urine indicators.[501, 583] The earliest identified study was published in 2007.[501] Evaluations were published in five different countries, including one from the United States.[563]

The populations studied were predominately males between the ages of six and 17. Most studies required participants to not be taking stimulant medication. For studies that distinguished between ADHD presentations, most of the participants were diagnosed with the combined presentation.[563, 635, 644] Only two studies mentioned race and ethnicity demographics, one where all of the participants were Han Chinese[603] and the other where the majority of participants were Black/African American.[563] None of the studies used a clinical sample or children with a consistent co-morbidity.

Table 7 shows the findings for the outcomes of interest together with the number of studies and study identifiers. Given the clinical diversity of the biomarkers (e.g., differences in invasiveness and technological requirements of tests), we include results across all biospecimen evaluations, blood markers, miRNA specifically, and urine indicators where more than one study was identified that reported on the outcome.

Table 7. KQ1 summary of findings and strength of evidence for biomarkers

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 Biomarkers (biospecimen)	Sensitivity	7 studies[309, 501, 563, 583, 603, 635, 644]	Sensitivity ranged from 56% (corresponding specificity 95%)[501] to100% (corresponding specificity 100%) using a serum marker[309] differentiating ADHD and neurotypical development	S, I	Low
KQ1 Blood biomarkers	Sensitivity	2 studies[309, 563]	Sensitivity ranged from 79% (corresponding specificity 25%)[563] to 100% (corresponding specificity 100%) using a serum marker[309]	S, I	Low
KQ1 miRNA biomarkers	Sensitivity	3 studies[603, 635, 644]	Sensitivity ranged from 68% (corresponding specificity 71%)[635] to 90% (corresponding specificity 80%)[603]	S, I	Low
KQ1 urine markers	Sensitivity	2 studies[501, 583]	Sensitivity ranged from 56% (corresponding specificity 95%)[501] to 94% (corresponding specificity 83%)[583]	S, I	Low
KQ1 Biomarkers (biospecimen)	Specificity	7 studies[309, 501, 563, 583, 603, 635, 644]	Specificity ranged from 25% (corresponding sensitivity 79%)[563] to 100% (corresponding sensitivity 100%) using a serum marker[309] differentiating ADHD and neurotypical development	S, I	Low
KQ1 Blood biomarkers	Specificity	2 studies[309, 563]	Specificity ranged from 25% (corresponding sensitivity 79%)[563] to 100% (corresponding sensitivity 100%)[309]	S, I	Low
KQ1 miRNA biomarkers	Specificity	3 studies[603, 635, 644]	Specificity ranged from 71% (corresponding specificity 68%)[635] to 95% (corresponding sensitivity 82%)[635]	S, I	Low
KQ1 urine markers	Specificity	2 studies[501, 583]	Specificity ranged from 80% (corresponding sensitivity 88%)[501] to 95% (corresponding sensitivity 56%)[501]	S, I	Low

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 Biomarkers (biospecimen)	Accuracy	2 studies[563, 603]	Accuracy ranged from 55% using a blood marker[563] to 85% using miRNA[603] differentiating ADHD and neurotypical development	S, C	Low
KQ1 Biomarkers (biospecimen)	AUC	4 studies[309, 583, 603, 644]	AUC ranged from 0.68[603] using mIRNA[635] to 1.00[309] using a serum marker differentiating ADHD and neurotypical development	S, C	Low
KQ1 Biomarkers (biospecimen)	Rater agreement	0 studies	No data	C	Insufficient
KQ1 Biomarkers (biospecimen)	Internal consistency	0 studies	No data	C	Insufficient
KQ1 Biomarkers (biospecimen)	Test-retest reliability	0 studies	No data	C	Insufficient
KQ1 Biomarkers (biospecimen)	Misdiagnosis impact	0 studies	No data	C	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, AUC = area under the curve, C = inconsistency, I = imprecision, Key Question = Key Question, S = study limitation, SoE = strength of evidence

Biomarker studies reported mainly on sensitivity and specificity. Selected studies achieved very high sensitivity.[309] Little information was provided in the studies regarding the reliability of the markers or combinations of markers. None of the included studies provided information on the effect of misdiagnosis. None of the identified studies reported the costs associated with analyzing biomarkers.

4.3.7 EEG

We identified 45 studies using EEG markers to diagnose ADHD.[27, 111, 115, 120, 124, 143, 157, 172, 179, 182, 186-189, 192, 197, 245, 312, 322, 340, 351, 356, 365, 366, 370, 394, 395, 397, 404, 408, 412, 413, 415, 420, 438, 449, 465, 468, 473, 487, 494, 546, 548, 592, 641] The earliest identified study was published in 2003.[546] EEG evaluations were published in 17 different countries, primarily Iran and China, with four studies published in the United States.[27, 412, 487, 548] The populations studied were predominately males between the ages of six and 17, with only three studies including children as young as four years old.[157, 340] One study included only female participants,[197] and seven studies included only males.[111, 179, 412, 413, 449, 468, 473] In several studies, participants were required to demonstrate an IQ of 80 or higher and almost half of the studies required that participants not take stimulant medication or stop medication several days before testing. For studies that distinguished between ADHD presentations, most focused on the combined and inattentive presentations. Race and ethnicity demographics were not mentioned in most studies.

While ADHD participants with co-occurring disorders were not excluded from most studies, only a few studies purposely included specific co-occurring disorders to evaluate the diagnostic test performance in children with co-occurring conduct disorder or other behavioral disorders.[143] The large majority of studies had unselected samples, i.e., comparing children with ADHD to neurotypical developing children.

Studies used EEG signals obtained during a resting state with eyes closed, eyes open, while performing neuropsychological tests, and/or recording event-related potentials. Studies varied in the reported detail (e.g., number of electrodes, channels, frequency and duration of the recording); the documented information is shown in the evidence table in the appendix. Two thirds of studies used machine learning algorithms to select parameter for classification. Several studies explicitly reported combining EEG data with specific demographic variables or rating scale results.[27, 124, 143, 189, 192, 312, 351]

Table 8 shows findings for the outcomes of interest together with the number of studies and study identifiers.

Table 8. KQ1 summary of findings and strength of evidence for EEG

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 EEG	Sensitivity	27 studies[27, 111, 115, 120, 124, 143, 157, 172, 179, 182, 186, 189, 197, 245, 340, 351, 356, 370, 395, 397, 408, 413, 473, 487, 546, 548, 592]	Sensitivity ranged from 46% (corresponding specificity 74%)[197] to 100% (corresponding specificities 71% to 100%)[143, 245, 413] differentiating ADHD and neurotypical development Sensitivity ranged from 82% (corresponding specificity 94%)[27] to 97% (corresponding specificity 100%)[487] in clinical samples	S, I	Low
KQ1 EEG combined with ratings or demographics	Sensitivity	6 studies[27, 124, 143, 157, 189, 197]	Sensitivity ranged from 76% (corresponding specificity 74%)[124] to 100% (corresponding specificity[157] 100%)[143]	S, I	Low
KQ1 EEG	Specificity	27 studies[27, 111, 115, 120, 124, 143, 157, 172, 179, 182, 186, 189, 197, 245, 340, 351, 356, 370, 395, 397, 408, 413, 473, 487, 546, 548, 592]	Specificity ranged from 38% (corresponding sensitivity 95%)[197] to 100% (corresponding specificities 71% or 100%)[143, 413] differentiating ADHD and neurotypical development Sensitivity ranged from 83% (corresponding specificity 84%)[395] to 100% (corresponding specificity 94%)[487] in clinical samples	S, I	Low
KQ1 EEG combined with ratings or demographics	Specificity	6 studies[27, 124, 143, 157, 189, 351]	Specificity ranged from 74% (corresponding sensitivity 76%)[124] to 100% (corresponding sensitivity[27] 100%)[143]	S, I	Low
KQ1 EEG	Accuracy	35 studies[27, 111, 115, 120, 143, 157, 172, 182, 186-189, 197, 245, 312, 322, 340, 351, 356, 366, 370, 394, 397, 408, 420, 438, 449, 468, 473, 487, 494, 546, 548, 592, 641]	Accuracy ranged from 58%[197] to 100%[143, 245, 340, 468, 494] differentiating ADHD and neurotypical development Accuracy ranged from 88%[27] to 98%[370] in clinical samples	S, I	Low
KQ1 EEG combined with ratings or demographics	Accuracy	5 studies[27, 143, 189, 312, 322, 351]	Accuracy ranged from 86%[189] to 98%[312]	S, I	Low
KQ1 EEG	AUC	13 studies[120, 179, 186, 187, 189, 197, 245, 340, 404, 412, 413, 415, 438]	AUC ranged from 0.63[197] to 1.00[245] differentiating ADHD from neurotypical development	S, I	Low
KQ1 EEG	Rater agreement	1 study[120]	Kappa for classifiers ranged from 0.73 to 0.78[120] across different models differentiating ADHD and neurotypical development	C	Insufficient
KQ1 EEG	Internal consistency	0 studies	No data	C	Insufficient

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 EEG	Test-retest reliability	1 study[27]	ICC was 0.83 for Theta/Beta ratio; repeated measures collected on two different visits in a clinical sample[27]	C	Low
KQ1 EEG	Misdiagnosis impact	0 studies	No data	C	Insufficient
KQ1 EEG	Costs	0 studies	No data	C	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, AUC = area under the curve, C = inconsistency, EEG = electroencephalogram; I = imprecision, KQ = Key Question, S = study limitation, SoE strength of evidence

EEG studies predominantly reported accuracy estimates. Sensitivity in individual studies ranged widely from 46 percent[197] to perfect sensitivity (corresponding specificities 71%);[143, 413] the range was reduced in studies restricting to older children. Studies in clinical samples reported a reduced range of sensitivity and specificity compared to studies differentiating children with ADHD from neurotypically developing children, but the identified samples were either small or they augmented EEG predictions with demographic variables. Some studies combined EEG data with demographics; the achieved sensitivity was reported as 100 percent (corresponding specificity 100%) in one study.[143] We downgraded the strength of evidence for imprecision (large variation in performance across studies). In addition, we downgraded for study limitations as diagnostic approaches were often not well described. For some outcome measures, no study was identified that assessed it and determining the effects associated with the test was not possible.

4.3.8 Imaging

We identified 19 studies using neuroimaging.[28, 191, 282, 319, 400, 464, 467, 495, 518, 524, 549, 571, 580, 581, 591, 630, 631, 633] Studies were predominantly published in the U.S. and China. A publicly available dataset (ADHD-200) produced numerous analyses.[191, 282, 495, 581] The populations studied were predominately males between the ages of six and 17, with one study including only male participants.[630] In several studies, participants were required to demonstrate an IQ of 80 or higher to be included in the sample.[495, 549, 571, 630, 631] A quarter of the studies required participants not be taking stimulant medication or to stop medication several days before testing.[571, 630, 633] A third of the studies included only right-handed participants[400, 495, 571, 630] In studies that distinguished between ADHD presentations, most focused on the combined and inattentive presentations. A minority specified including individuals with the hyperactive/impulsive presentation.[191, 282, 549, 633] Nearly all studies did not include race and ethnicity demographics.

While ADHD participants with co-occurring disorders were not excluded from most of the studies, no studies specifically assessed test performance in children with specific co-occurring disorders. One study differentiated children with ADHD from those with dyslexia.[524] One evaluated the diagnostic performance of an algorithm differentiating ADHD from autism.[282] All studies used unselected, general samples, rather than clinical samples referred for further diagnostic workup (where a large proportion of children will either be diagnosed with ADHD, conduct disorders, autism, or depression).

All but two imaging studies used MRI to diagnose ADHD. However, studies utilized MRI in different ways. Some studies used functional MRI, some structural MRI, some used combinations of structural and functional MRI, with or without magnetic resonance spectroscopy. Two studies used near-infrared spectroscopy but the applications and diagnostic models differed.[211, 631] Most of the imaging studies used a large number of indicators and utilized machine learning algorithms to detect markers to optimize the classifications. The reporting of the variable selection process varied, and it was often not clearly reported which exact indicators were included in the model used to determine diagnostic accuracy. Sone of the identified studies combined imaging parameter with demographic or other clinical data for the prediction model.[191, 211, 282, 400, 467, 495, 631, 633]

Reported diagnostic accuracy estimates varied widely. Table 9 shows the findings for the outcomes of interest, together with the number of studies and study identifiers. The table summarizing findings across all imaging studies, findings for MRI studies specifically, and imaging studies that combine imaging parameters with other variables (e.g., demographics) for predictions.

Table 9. KQ1 summary of findings and strength of evidence for neuroimaging

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 Imaging (MRI, NIRS) to diagnose ADHD	Sensitivity	15 studies[28, 191, 211, 282, 319, 400, 467, 495, 518, 549, 571, 581, 591, 630, 631]	Sensitivity ranged from 42% (corresponding specificity 95%) using morphometric MRI[549] to 99% (corresponding specificity 100%) utilizing fMRI in a complex machine learning approach[581] differentiating ADHD and neurotypical development	S, I	Low
KQ1 MRI to diagnose ADHD	Sensitivity	13 studies[28, 191, 282, 319, 400, 467, 495, 518, 549, 571, 581, 591, 630]	Sensitivity ranged from 42% (corresponding specificity 95%) using morphometric MRI[549] to 99% (corresponding specificity 100%) utilizing fMRI in a complex machine learning approach[581] differentiating ADHD and neurotypical development	S, I	Low
KQ1 NIRS to diagnose ADHD	Sensitivity	2 studies[211, 631]	Sensitivity ranged from 73% (corresponding specificity 87%)[211] to 89% (corresponding specificity 84%)[631]	S, I	Low
KQ1 Imaging combining data with non-imaging variables	Sensitivity	3 studies[211, 282, 631]	Sensitivity ranged from 73% (corresponding specificity 65%) using near-infrared spectroscopy for functional measures in a multi-domain profile of measures to 93% (corresponding specificity 95%) in a complex machine learning model based on fMRI[282]	S, I	Low
KQ1 Imaging (MRI, NIRS) to diagnose ADHD	Specificity	14 studies[28, 191, 211, 282, 319, 400, 495, 518, 549, 571, 581, 591, 630, 631]	Specificity ranged from 55% (corresponding sensitivity 95%) in a model using resting state fMRI[518] to 100% (corresponding sensitivity99%) utilizing fMRI in complex machine learning approaches[581] differentiating ADHD and neurotypical development	S, I	Low
KQ1 MRI to diagnose ADHD	Specificity	12 studies[28, 191, 282, 319, 400, 495, 518, 549, 571, 581, 591, 630]	Specificity ranged from 55% (corresponding sensitivity 95%) in a model using resting state fMRI[518] to 100% (corresponding sensitivity 100%) utilizing fMRI in a complex machine learning approach[581]	S, I	Low
KQ1 Imaging combining data with non-imaging variables	Specificity	3 studies[211, 282, 631]	Specificity ranged from 84% (corresponding sensitivity 89%) using a combination of NIRS and other data[631] to 95% (corresponding sensitivity 93%) utilizing fMRI and non-imaging data[282]	S, I	Low
KQ1 NIRS to diagnose ADHD	Specificity	2 studies[211, 631]	Specificity ranged from 84% (corresponding specificity 89%)[631] to 87% (corresponding specificity 73%)[211]	S, I	Low

4. Results: Diagnosis of ADHD

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 Imaging (MRI, NIRS) to diagnose ADHD	Accuracy	14 studies[191, 211, 282, 319, 400, 467, 495, 518, 571, 581, 591, 630, 631, 633]	Accuracy ranged from 61% using sMRI[467] to 99.6% utilizing resting state fMRI in complex machine learning approaches[191, 581] differentiating ADHD and neurotypical development	S, I	Low
KQ1 MRI to diagnose ADHD	Accuracy	12 studies[191, 282, 319, 400, 467, 495, 518, 571, 581, 591, 630, 633]	Accuracy ranged from 61% using sMRI[467] to 99.6% utilizing resting state fMRI in complex machine learning approaches[191, 581] differentiating ADHD and neurotypical development	S, I	Low
KQ1 NIRS to diagnose ADHD	Accuracy	2 studies[211, 631]	Accuracy ranged from 81%[211] to 86%[631]	S, I	Low
KQ1 Imaging combining data with non-imaging variables	Accuracy	6 studies[211, 282, 495, 518, 631]	Accuracy ranged from 68% in a model using resting state fMRI[518] to 95% utilizing fMRI in combination with phenotypic data in a complex machine learning procedure[631]	S, I	Low
KQ1 Imaging (MRI, NIRS) to diagnose ADHD	AUC	13 studies[191, 211, 319, 400, 464, 467, 518, 549, 580, 581, 591, 631, 633]	AUC ranged from 0.58 in a multimodal imaging model[400] to 0.997 in a model based on fMRI[581] differentiating ADHD and neurotypical development	S, I	Low
KQ1 MRI to diagnose ADHD	AUC	10 studies[191, 319, 400, 467, 518, 549, 580, 581, 591, 633]	AUC ranged from 0.58[400] in a multimodeal imaging model to 0.997 in a model based on fMRI[581]	S, I	Low
KQ1 Imaging combining data with non-imaging variables	AUC	3 studies[211, 631, 633]	AUC ranged from 0.70 using sMRI, fMRI, and diffusion-tensor MRI plus age, sex, and IQ[633] to 0.898 in a model based on resting state fMRI[631]	S, I	Low
KQ1 NIRS to diagnose ADHD	AUC	2 studies[211, 631]	AUC ranged from 0.80[211]to 0.90[631]	S, I	Low
KQ1 Imaging to diagnose ADHD	Rater agreement	0 studies	No data	C	Insufficient
KQ1 Imaging to diagnose ADHD	Internal consistency	0 studies	No data	C	Insufficient
KQ1 Imaging to diagnose ADHD	Test-retest reliability	0 studies	No data	C	Insufficient
KQ1 Imaging to diagnose ADHD	Misdiagnosis impact	0 studies	No data	C	Insufficient
KQ1 Imaging to diagnose ADHD	Costs	0 studies	No data	C	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, AUC = area under the curve, C = inconsistency, fMRI = functional magnetic resonance imaging, I = imprecision, KQ = Key Question, MRI = magnetic resonance imaging, sMRI = structural MRI, NIRS = near-infrared spectroscopy, S = study limitation, SoE strength of evidence

Studies reported primarily on sensitivity, specificity, and accuracy. Across all neuroimaging studies, reported sensitivity varied widely. We downgraded the strength of evidence for imprecision (large variation in performance reported across studies). In addition, we downgraded for study limitations as the individual diagnostic models were often not well described and the number and type of predictor variables feeding into the model was unclear. For some outcomes, no study was identified, and it was not possible to determine the effects associated with the diagnostic modality. Some studies combined neuroimaging data and demographics, though the relevance is unclear, since the only demographic characteristic that is likely associated with a diagnosis of ADHD is sex, with a higher prevalence in males.

4.3.9 Neuropsychological Tests

We identified 74 studies using neuropsychological tests, assessing executive function and/or encompassing a variety of cognitive assessments, including continuous performance tests, to diagnose ADHD.[18, 21, 24, 112, 119, 135, 140, 141, 152, 153, 159, 162, 170, 177, 184, 185, 190, 198, 213, 237, 246, 253, 263, 267, 276, 284, 293, 298, 307, 315, 316, 323, 327, 346, 347, 351, 352, 379, 382, 393, 401, 402, 417, 421, 422, 436, 445, 446, 450, 462, 467, 469, 470, 475, 477, 482, 486, 493, 496, 500, 515, 537, 541, 543, 564, 576, 607, 614, 615, 625, 627, 632, 639, 647] Rating scales of executive function are described in the parent and teacher rating section in the beginning of the chapter.

The earliest study evaluating a neuropsychological tests as diagnostic tools was published in 1999[496] and evaluations came from 18 different countries, primarily the United States. The populations studied were predominately males between the ages of six and 18. Three studies included three and four year old children.[162, 315, 467] In several studies, participants were required to demonstrate an IQ of 70 or higher[24, 346, 352, 365, 467, 469, 500] with some studies requiring IQ to be at least 80[21, 152, 253, 647] or 85.[379, 446, 486] Two thirds of the studies required participants not take stimulant medication or stop medication several days before testing. For studies that distinguished between ADHD presentations, most of the participants were diagnosed with the combined or inattentive presentations. About a third of the studies mentioned race and ethnicity demographics, with seven studies where White participants made up half or more of the sample,[21, 162, 170, 263, 462, 607] one study where all of the participants were Asian,[393] one study where over 50 percent were Black/African American,[462] and one study where 83 percent of the participants were Hispanic or Latino.[467]

ADHD participants with co-occurring disorders were not excluded from most of the studies. Some studies used clinical samples with participants who were referred for diagnostic work-up where all children presented with attention issues or other symptoms indicative of ADHD or a different clinical diagnosis.[24, 153, 162, 263, 315] One study specifically looked at distinguishing between children with ADHD, developmental dyslexia, and those who had both disorders.[446] The remaining studies used samples of neurotypically developing children as controls rather than clinical samples.

ADHD participants with co-occurring disorders were not excluded from most of the studies. Some studies used clinical samples with participants who were referred for diagnostic work-up where all children presented with attention issues or other symptoms indicative of ADHD or a different clinical diagnosis[24, 153, 162, 263, 315] One study specifically looked at distinguishing between children with ADHD, developmental dyslexia, and those who had both disorders.[446] The remaining studies used samples of neurotypically developing children as controls rather than clinical samples.

Studies described a wide range of test batteries, but over 50 studies used continuous performance testing (CPT) to diagnose children and adolescents. CPTs provide multiple behavioral outputs relevant to ADHD, including omission errors (reflecting inattention), commission errors (reflecting impulsivity), and reaction time standard deviation (or reflecting moment-to-moment response variability). Studies varied in their use of traditional visual CPTs, such as the TOVA (Test of Variables of Attention), or more novel, multifaceted CPT approaches. These latter “hybrid” CPT paradigms included CPTs that combined auditory and visual attentional processing demands together in the same task, those that monitored physical movements during task administration, and virtual reality CPTs built upon environments designed to emulate real-world distractibility in a classroom setting. The included studies used idiosyncratic combinations of individual cognitive measures to achieve the best performance. However, multiple studies reported on attention and impulsivity measures included in the continuous performance tests.

Studies reported a variety of statistical parameters to determine the accuracy of the diagnostic approach. Sensitivity, specificity, and accuracy were the most frequently reported diagnostic measures. Table 10 shows the findings for the outcomes of interest together with the number of studies and study identifiers for all key outcomes. Where we found more than one study reporting on the same test or test component, the table also summarizes the performance for those, specifically.

Table 10. KQ1 summary of findings and strength of evidence for neuropsychological tests

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 Neuropsychological tests	Sensitivity	52 studies[18, 21, 112, 119, 141, 152, 153, 162, 170, 177, 190, 198, 213, 246, 253, 267, 276, 293, 298, 307, 323, 327, 346, 347, 351, 352, 379, 393, 417, 421, 422, 436, 445, 446, 450, 462, 467, 470, 475, 477, 482, 486, 493, 496, 515, 537, 543, 564, 614, 615, 639, 647]	Sensitivity ranged from 28% (corresponding specificity 95%)[445] to 100% (corresponding specificity up to 100%)[141, 152] differentiating ADHD and neurotypical development Sensitivity ranged from 22% (corresponding specificity 96%)[564] to 91% (corresponding specificity 22%)[639] in clinical samples	S, I	Low
KQ1 CPT	Sensitivity	35 studies[21, 112, 119, 141, 152, 153, 162, 189, 190, 198, 246, 253, 276, 298, 307, 323, 346, 347, 407, 417, 421, 436, 450, 462, 469, 470, 475, 482, 496, 515, 537, 543, 564, 639, 647]	Sensitivity ranged from 22% (corresponding specificity 96%)[564] to 100% (corresponding specificity 100%) for a brief neuropsychological measure supported by machine learning	S, I	Low
KQ1 CPT Attention	Sensitivity	3 studies[21, 24, 162]	Sensitivity ranged from 48% (corresponding specificity 83%)[24] to 68% (corresponding specificity 76%,)[21]	S, I	Low
KQ1 CPT Impulsivity	Sensitivity	2 studies[24, 162]	Sensitivity ranged from 48% (corresponding specificity 83%)[24] to 55% (corresponding specificity 64%)[162]	S, I	Low
KQ1 Neuropsychological tests	Specificity	54 studies[18, 21, 112, 119, 124, 152, 153, 162, 170, 177, 190, 198, 213, 246, 253, 267, 276, 284, 298, 307, 323, 327, 346, 351, 352, 379, 388, 393, 402, 407, 417, 421, 422, 436, 445, 446, 450, 462, 469, 470, 475, 477, 482, 486, 493, 496, 515, 537, 543, 564, 614, 615, 639, 647]	Specificity ranged from 46% (corresponding sensitivity 85%)[469] to 100% (corresponding sensitivity 100% and 75% respectively)[152, 450] differentiating ADHD and neurotypical development Specificity ranged from 22% (corresponding sensitivity 91%)[639] to 85% (corresponding sensitivity 63%)[153] in clinical samples	S, I	Low

4. Results: Diagnosis of ADHD

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
KQ1 CPT	Specificity	33 studies[21, 112, 119, 152, 153, 162, 189, 190, 198, 246, 253, 276, 298, 323, 346, 347, 407, 417, 421, 436, 450, 462, 469, 470, 475, 482, 496, 515, 537, 543, 564, 639, 647]	Specificity ranged from 22% (corresponding sensitivity 91%) using TOVA[639] to 100% (corresponding sensitivity 89%) using the PANDAS[450]	S, I	Low
KQ1 CPT Attention	Specificity	3 studies[21, 24, 162]	Specificity ranged from 64% (corresponding sensitivity 55%)[162] to 83% (corresponding sensitivity 48%)[24]	S, I	Low
KQ1 CPT Impulsivity	Specificity	2 studies[24, 162]	Specificity ranged from 64% (corresponding sensitivity 55%)[162] to 83% (corresponding sensitivity 48%)[24]	S, I	Low
KQ1 Neuropsychological tests	Accuracy	40 studies[18, 112, 141, 152, 159, 162, 170, 184, 185, 198, 213, 253, 284, 293, 298, 307, 316, 323, 327, 346, 351, 388, 402, 407, 417, 421, 422, 450, 462, 467, 469, 470, 475, 493, 500, 537, 541, 543, 607, 632]	Accuracy ranged from 34% using the TOVA[500] to 100%[152] for a brief neuropsychological measure supported by machine learning differentiating ADHD and neurotypical development Accuracy ranged from 67%[162] in children with co-occurring oppositional defiance disorder to 95% for a combination measure[18]	S, I	Low
KQ1 CPT	Accuracy	26 studies[112, 141, 152, 162, 185, 189, 198, 253, 298, 307, 316, 323, 346, 407, 417, 421, 450, 462, 465, 469, 470, 475, 500, 537, 543, 632]	Accuracy ranged from 57% using a virtual reality CPT[500] to 95% using TOVA[141]	S, I	Low
KQ1 Neuropsychological tests	AUC	26 studies[140, 170, 177, 190, 198, 246, 263, 267, 316, 346, 347, 352, 382, 393, 401, 407, 445, 446, 467, 469, 477, 486, 493, 564, 576, 627]	AUC ranged from 0.65[469] to 0.93 for individual Go/No-Go task measures[393] differentiating ADHD and neurotypical development AUC ranged from 0.59[564] to 0.87[263] in clinical samples	S, I	Low
KQ1 CPT	AUC	15 studies[140, 189, 190, 198, 246, 263, 316, 346, 347, 382, 401, 407, 469, 564, 576]	AUC ranged from 0.65 using the Advanced Test of Attention[469] to 0.92 using the MOXO CPT[140]	S, I	Low
KQ1 Neuropsychological tests	Rater agreement	3 studies[170, 263, 639]	Neurotypical samples: Kappa was 0.55 between *Cognitive Assessment System* discriminant function analysis classifications and a priori diagnosis[170] Clinical samples: Kappa 0.15 between *Groundskeeper* game and *Conners* subscales, 0.18 between *Groundskeeper* game and CPT, and 0.3 between *Conners* subscales and Conners CPT[263] Kappa 0.15 between *Test of Variables of Attention* and diagnosis by clinical assessment[639]	S, I	Low
KQ1 Neuropsychological tests	Internal consistency	2 studies[198, 500]	Cronbach's alpha ranged from 0.906 to 0.987 across 15 variables in the diagnosis-supported decision support	C	Low

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	Reasons for Downgrading	SoE
			system (DS-ADHD) across all children[198] Cronbach's alpha for a virtual reality instrument was 0.72[500]		
KQ1 Neuropsychological tests	Test-retest reliability	1 study[213]	ICC less than 0.5 for the ADHD group on all visual and auditory test variables on The *Advanced Test of Attention* repeated after 2 weeks[469]	C	Insufficient
KQ1 Neuropsychological tests	Misdiagnosis impact	0 studies	No data	C	Insufficient
KQ1 Neuropsychological tests	Costs	1 study[315]	£31 [~$42] for QbTest including 30-minute appointment, £108 a consultation within the UK Medway NHS Trust at the time of audit[315] in a clinical sample	C	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, AUC = area under the curve, C = inconsistency, CPT = continuous performance test, I = imprecision, KQ = Key Question, QB test = Quantified Behavioral Test, S = study limitation, TOVA = Test of Variables of Attention, SoE = strength of evidence

Studies evaluating neuropsychological tests reported predominantly on sensitivity and specificity. Although selected studies reported perfect diagnostic performance for neuropsychological tests,[152] those studies reported the diagnostic performance for composite measures (unique and study-specific combinations of individual cognitive measures), making it difficult to compare test performance across studies. The wide range in performance was narrower in studies restricting to children seven and above. Reliability measures were rarely reported in the identified studies. No study addressed the effects of misdiagnosis. Costs were reported in only one study. We downgraded the strength of evidence for imprecision (large variation in performance reported across studies). For some outcome measures, no study was identified, and it was not possible to determine the effects associated with the test.

4.4 KQ1a. What is the comparative diagnostic accuracy of approaches that can be used in the primary care practice setting or by specialists to diagnose ADHD among individuals younger than 7 years of age?

We identified only 12 studies that reported exclusively on children younger than seven years of age.[162, 167, 189, 316, 331, 412, 416, 437, 467, 516, 519, 559] The earliest identified study was published in 2002[559] and data came from the United States, Portugal, Spain, The Netherlands, Germany, Taiwan, and New Zealand. The percent female ranged from none to 41 percent, where reported, and the proportion of Caucasian children ranged from 54 to 90 percent. We identified three studies that explicitly reported on diagnostic performance data collected in primary care.[162, 445, 605] Several studies used clinic populations of children referred for diagnostic purposes and children often presented with multiple co-occurring disorders.

Studies evaluated parent ratings, teacher ratings, combined ratings, activity, EEG, imaging, and neuropsychological tests. Studies reported a variety of outcomes, with sensitivity and specificity being the most frequently reported outcomes. Sensitivity achieved in this age group reached up to 97 percent in a study evaluating the use of activity ratings,[416] while a study evaluated a continuous performance tests showed the lowest sensitivity (42%).[189] Reported specificity was 91 percent in a study using parental ratings to diagnose ADHD[331], but EEG data achieved only a specificity of 38 percent.[189] Few of these diagnostic studies reported reliability measures. The results across studies for the key outcomes are shown in the summary of findings table at the end of the chapter, all other measures (where reported) are shown in the evidence table in the appendix. We did not identify any study reporting on the adverse effect following a misdiagnosis (not being diagnosed or being incorrectly diagnosed) in this age group. In addition, none of the diagnostic studies mentioned costs of tests in this subsample.

The summary of findings table at the end of this chapter shows the diagnostic performance in this young age group in more detail. The table summarizes the limited available evidence across identified studies, together with the strength of evidence. Strength of evidence was either low due to the limited evidence, or insufficient due to the lack of studies in this age group reporting on the outcomes of interest.

4.5 KQ1b. What is the comparative diagnostic accuracy of EEG, imaging, or approaches assessing executive function that can be used in the primary care practice setting or by specialists to diagnose ADHD among individuals aged 7 through 17?

We identified 61 studies that reported exclusively on children aged seven and older. The earliest identified study was published in 1989. Data came from 23 different countries, most frequently U.S. and Chinese studies. Six studies restricted to boys, but one study included 75 percent girls.[446] The proportion of White children ranged from 44[464] to 100[112] percent. The proportion of Hispanic or Latino children ranged from one[607] to 20[400] percent. The proportion of Black or African American children ranged from five[359] to 34[607] percent. The proportion of Asian children ranged from one[570] to 100[641] percent. The proportion of multiracial youth (where reported) ranged from eight[400] to 20[464] percent.

Studies evaluated parent ratings, teacher ratings, combined ratings, teen/child self-report, continuous performance, executive functioning, activity, EEG, MRI imaging, and neuropsychological tests. Studies reported a variety of outcomes, with sensitivity and specificity being the most frequently reported outcomes. Few of these diagnostic studies reported reliability measures. We did not identify any study reporting on the adverse effect following a misdiagnosis (not being diagnosed or incorrectly diagnosed) in this age group. In addition, none of the diagnostic studies mentioned costs of tests in this subsample. The results across studies for the key outcomes and interventions are shown in the summary of findings table at the end of the chapter, all other measures (where reported) and results for other interventions evaluated in this age group are shown in the Appendix C, Table C.1.

4.5.1 Diagnostic Accuracy of EEG in Youth Aged 7 Through 17

We identified 16 studies that used EEG to diagnose youth.[111, 120, 172, 245, 312, 351, 370, 394, 397, 408, 438, 449, 465, 494, 546, 641] The first study meeting eligibility criteria was published in 2003.[111, 120, 172, 245, 312, 351, 370, 394, 397, 408, 438, 449, 465, 494, 546, 641] Study locations included 11 different countries, with several studies being conducted in China[351, 394, 408, 641] and Iran[245, 438, 494] The proportion of included girls ranged from none[111, 449] to 56 percent[394] Race and ethnicity was rarely reported, one study included 100% Asian youth.[351] The ADHD presentation was often not reported but where reported, but two studies reported two thirds of children with combined presentation[312, 465] and one study restricted to inattentive ADHD[351] Studies did usually not exclude children with comorbidities but only one study specifically assessed the effect of ODD (oppositional defiant disorder) co-morbidity on diagnostic accuracy.[370]

Reported sensitivity, specificity, accuracy and AUC values ranged widely across studies as documented in the summary of findings table. Studies varied in how much detail they provided on the parameters that contributed to the diagnostic performance, which in combination with the wide range of reported diagnostic performance resulted in low strength of evidence statement for these outcomes of interest.

Studies did not report on rater agreement between EEG readers, internal consistency of measurements, or test-retest reliability. Identified studies also did not describe the impact of misdiagnosis and they did not mention costs. Hence, the evidence was determined to be insufficient for these outcomes of interest.

4.5.2 Diagnostic Accuracy of Imaging in Youth Aged 7 Through 17

We identified eight studies that used imagining for diagnosing in this age group, all evaluated the use of MRI.[191, 282, 400, 464, 495, 518, 571, 581] The first studies meeting eligibility criteria published data in 2018[191, 571] Study locations were the United States and China. The proportion of included girls ranged from 14[571] to 45[282] percent. Race and ethnicity was rarely reported, but in studies that provided a participant breakdown, the proportion of White children was 44 and 55 percent, Hispanic 19 and 20 percent, Black six and 14 percent, and Asian two and six percent in two U.S. studies.[400, 464] Several studies stated that youth with all ADHD presentations were included. Studies typically did not exclude youth with other comorbidities, but only one study assessed the effect of autism on the diagnostic accuracy.[518]

The reported sensitivity, specificity, accuracy, and AUC values varied widely across studies. Given the wide range of reported diagnostic accuracy measures in this age group, strength of evidence was judged to be low regarding successfully diagnosing ADHD with imaging data. Rater agreement for human imaging readers, internal consistency, test-retest reliability, impact of misdiagnosis, and costs were not described. The strength of evidence was insufficient for evidence statements for these outcomes of interest.

4.5.3 Diagnostic Accuracy of Executive Function in Youth Aged 7 Through 17

While a number of studies evaluated neuropsychological tests in this age group, not all emphasized utilizing executive function characteristics for the diagnosis of ADHD. We identified 14 studies with an emphasis on executive function assessment.[119, 153, 159, 213, 284, 351, 352, 379, 446, 465, 541, 607, 614, 625] The earliest study was published in 1989.[159] Evaluations were conducted in six countries, with the United States being the most frequent country.[159, 213, 607, 625] The reported proportion of girls ranged from none[352, 614] to 74 percent[446] across studies. Race and ethnicity was rarely reported, but several identified studies included only or predominantly White youth.[112, 213, 607, 625] Several studies restricted to or predominantly included youth with combined ADHD presentation,[119, 253, 352, 625] Studies typically did not exclude youth with comorbidities but none of the samples assessed the effect of a specific comorbidity on the diagnostic performance of the executive function test.

Sensitivity, specificity, accuracy, and AUC values ranged widely within and across the identified studies as documented in the summary of findings table. None of the identified studies assessed the performance of the same diagnostic test, and most of the studies described unique combinations of test components that were used to diagnose ADHD. All identified studies are documented in detail in the appendix. We determined the strength of evidence to be low for diagnostic outcomes of interest.

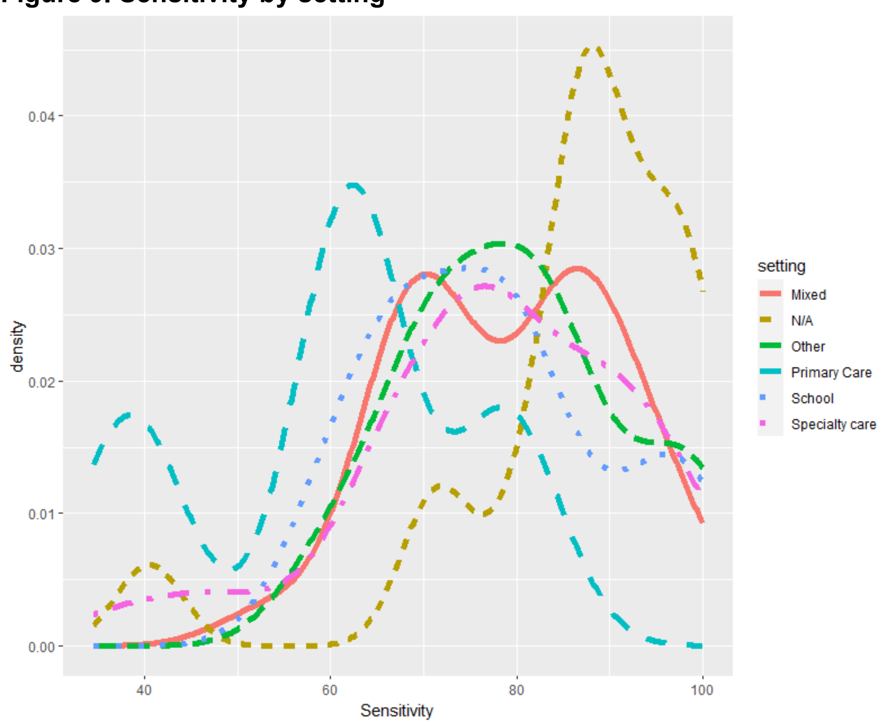
Studies did not report on rater agreement or internal consistency of the test components, but one study reported on temporal stability. The study reported correlations between tests on two occasions of 0.81 ($p<0.05$) for the total test score in a Tower of London–- Drexel task (assessing total move and rule violation scores), 0.79 ($p<0.05$) for total time violations, and 0.42 ($p<0.005$) for total rule violations.[213] Studies did not report on the impact associated with a misdiagnosis or costs of the tests. Given the lack of studies or our inability to judge consistency reported in results across studies, we determined the strength of evidence to be insufficient.

4.6 KQ1c. For both populations, how does the comparative diagnostic accuracy of these approaches vary by clinical setting, including primary care or specialty clinic, or patient subgroup, including age, sex, or other risk factors associated with ADHD?

We did not identify studies comparing the accuracy in different settings in direct, head-to-head comparisons. Hence, we had to address this KQ in indirect analyses across studies. Our analyses were further limited by studies providing insufficient details on the accuracy of performance (e.g., reporting clearly on the false positives and false negatives) and could not be based on a meta-analytic model. Instead, we used the reported summary performance measures as reported by the study authors to explore potential effect modifiers. The most common reported diagnostic performance measures were sensitivity and specificity and most analyses were only possible for these outcomes.

Figure 9 plots reported sensitivity by setting.

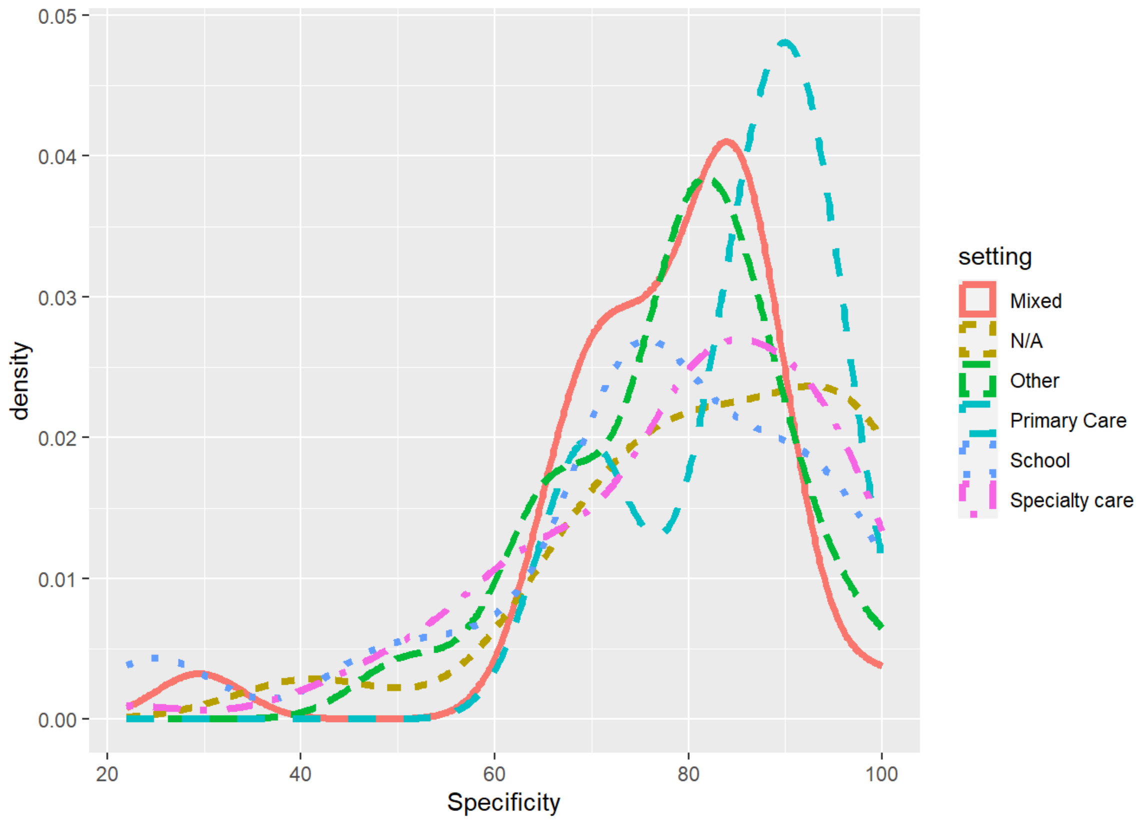
Figure 9. Sensitivity by setting



Notes: N/A = not available

The figure plots the sensitivity in different settings that are included in the dataset. It also shows the range within and across settings. Comparing the reported sensitivities, a simple regression analysis indicated that setting is associated with reported sensitivity (p 0.03). However, the result should be interpreted with caution, as it does not take study size or quality into account, and it was not established within a meta-analytic model. The corresponding reported specificities are shown in Figure 10.

Figure 10. Specificity by setting



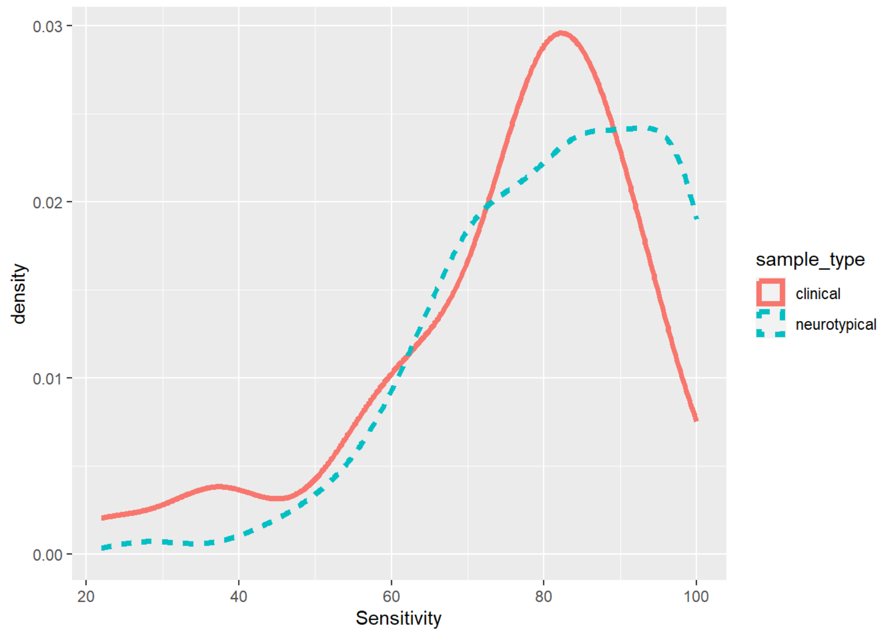
Notes: N/A = not available

Reported specificity values ranged considerably, within as well as across settings. Comparing the reported specificities, a simple regression analysis did not indicate that setting is systematically associated with reported specificity (p 0.70). However, the result should be interpreted with caution, as it does not take study size or quality into account, and it was not established within a meta-analytic model. The equivalent analyses for reported accuracy (p 0.006) indicated that the reported estimate is statistically significantly associated with setting. The analysis for AUC was not significant (p 0.28).

We also evaluated whether the studies in clinical samples (i.e., referred for a clinical diagnosis, oppositional defiance disorder, or autism) and those with primarily neurotypical developing children reported different diagnostic performance values. The figure plots the sensitivity results for the two participant populations (Figure 11).

4. Results: Diagnosis of ADHD

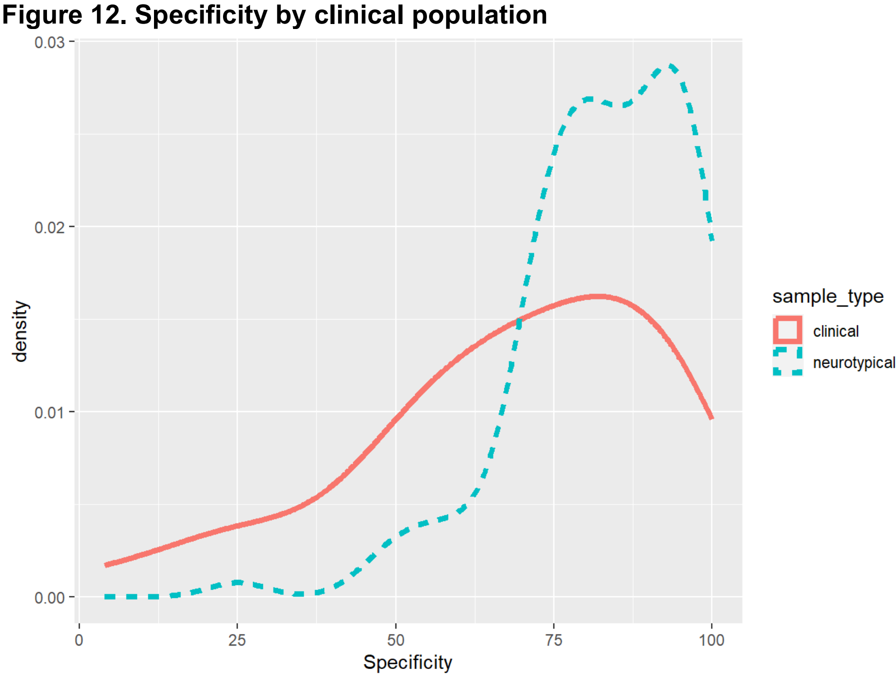
Figure 11. Sensitivity by clinical population



Across studies, analyses detected a statistically significant difference in reported sensitivity results depending on whether a study reported on a clinical sample or children were compared to neurotypically developing children (p 0.04). On average, the sensitivity was lower in clinical samples compared to studies differentiating youth with ADHD from neurotypically developing youth (mean 75, SD 18 vs mean 81, SD 15). However, the analysis should be interpreted with caution, as it does not use a meta-analytic model for the analysis and uses reported sensitivity values as reported by the original authors.

Figure 12 plots the specificity stratified by population.

Figure 12. Specificity by clinical population

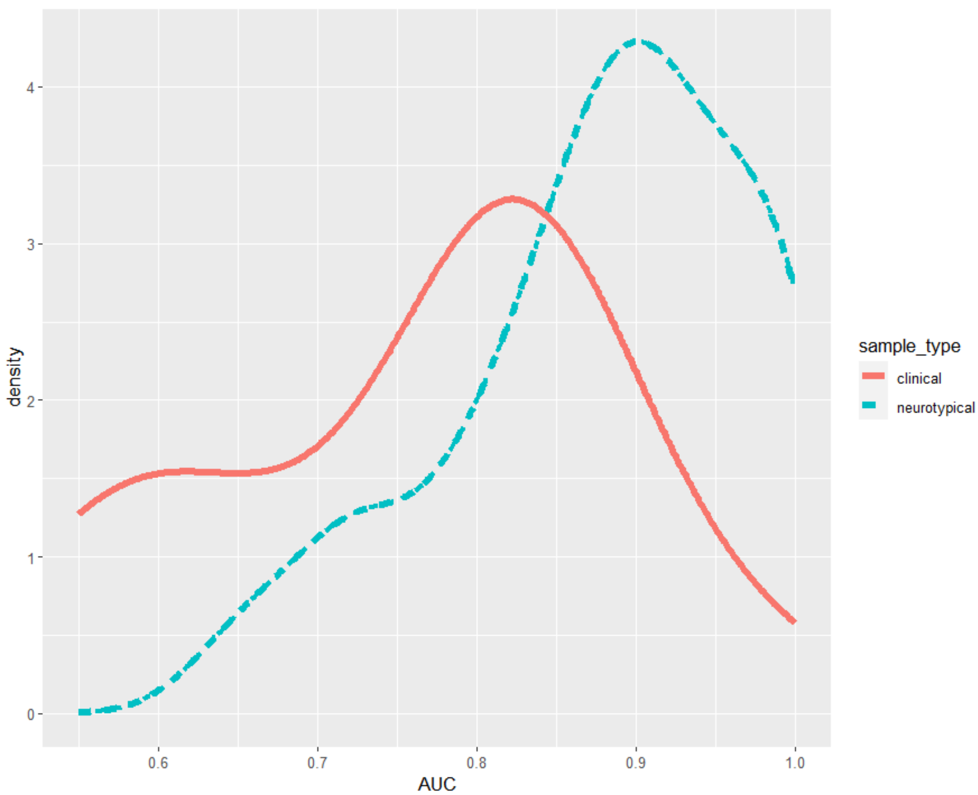


4. Results: Diagnosis of ADHD

The analysis indicated that the reported specificity was associated with the population that was used to establish diagnostic accuracy (p<0.001). On average, clinical samples reported lower specificities than studies in neurotypical samples (mean 68, SD 24 vs mean 83, SD 14). The result suggests that the clinical population appears to be a source of heterogeneity seen in the studies. However, the result should be interpreted with caution as the data were not analyzed in a meta-analytical model and used the diagnostic performance data as reported by the original authors.

Figure 13 plots the AUC values reported in included studies stratified by clinical versus neurotypical samples.

Figure 13. Specificity by clinical versus neurotypical samples

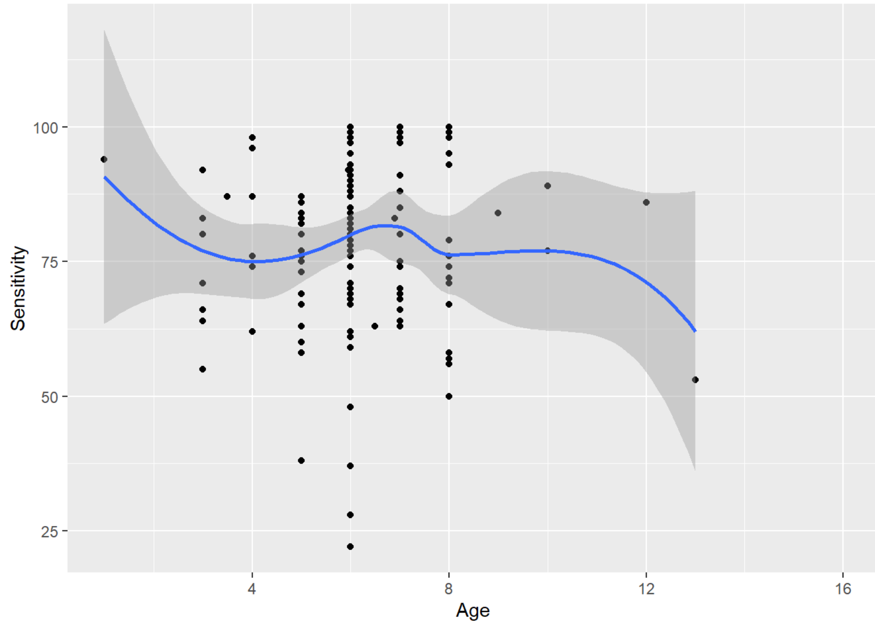


The analyses also detected a statistically significant difference in the reported accuracy based on the population included in the evaluation sample (p<0.001). On average, the reported accuracy was lower in clinical samples than in studies that differentiated youth with ADHD from neurotypically development youth (mean 0.76, SD 0.13 versus mean 0.88, SD 0.09). However, the analysis should be interpreted with caution as it is not based on a meta-analytic model, and the number of included datapoints is smaller than for sensitivity and specificity. There were insufficient data available for analyses of other outcomes.

We further aimed to investigate whether the age of the participants is associated with the achieved diagnostic performance. Most studies included a range of ages, but studies differed in whether they included young children. Figure 14 plots sensitivity by minimum age in the sample.

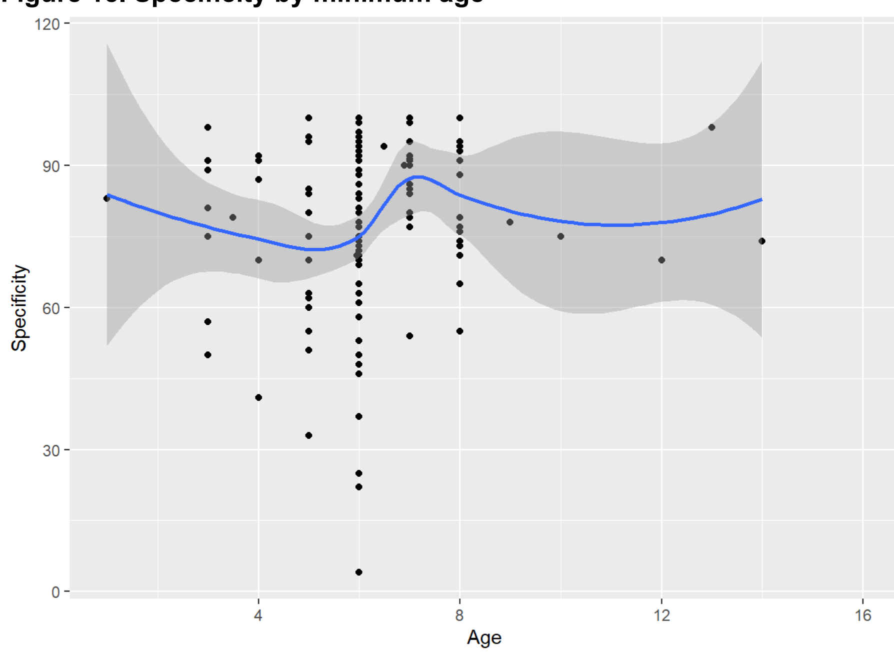
4. Results: Diagnosis of ADHD

Figure 14. Sensitivity by minimum age



Across studies, we did not detect a statistically significant linear association between samples including younger children versus not on reported sensitivity (p 0.54). However, it should be noted that the number of studies that included smaller children was low and thus hindered statistical power to detect differences and this is an indirect comparison across studies that also does not take study size into account and hence should be interpreted with caution. The equivalent figure for the specificity is shown in Figure 15.

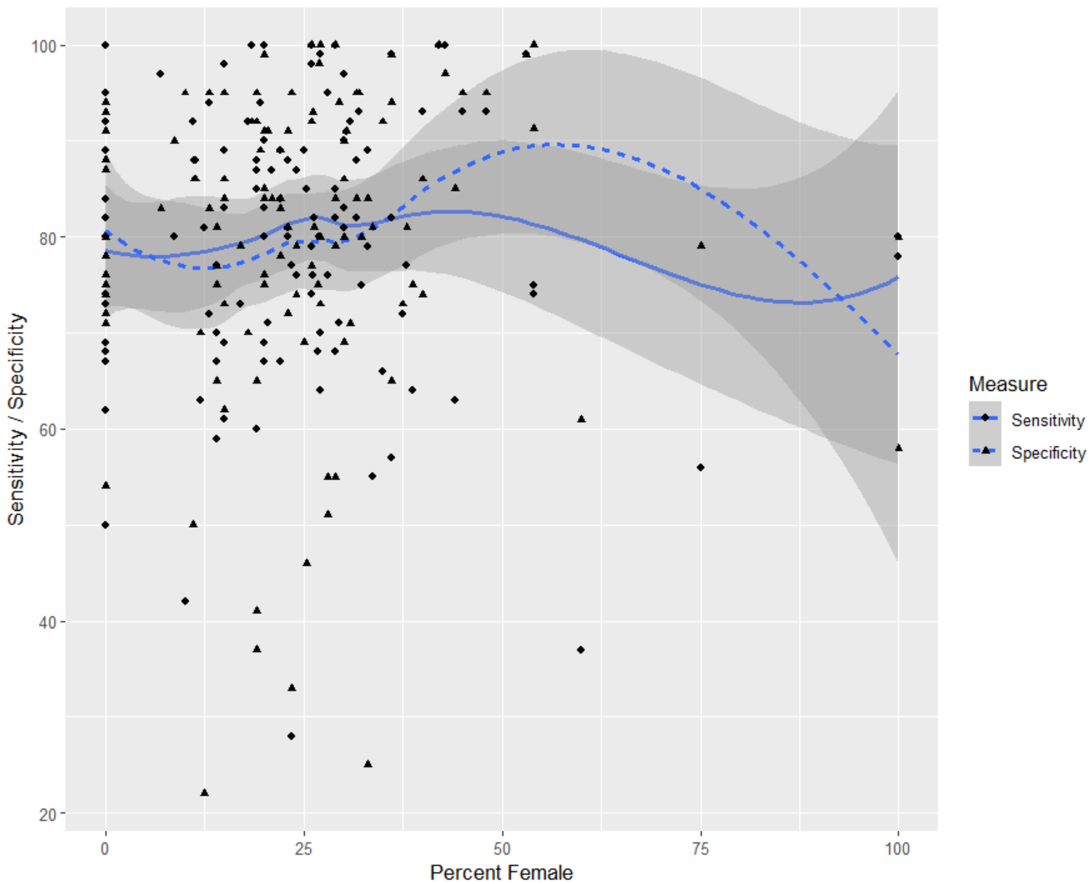
Figure 15. Specificity by minimum age



Across studies, we did not detect a statistically significant linear association between samples including younger children or not on reported specificity (p 0.37). However, this analysis is an indirect analysis across studies which is also not based on the meta-analytic model and should therefore be interpreted with caution. We also categorized studies as younger versus older children. Using a dichotomous indicator differentiating between young (under 7) and older children (7 and over) also did not indicate a systematic effect for sensitivity (p 0.98), specificity (p 0.35), accuracy (p 0.09), or AUC (p 0.28).

We also analyzed the gender distribution in the identified studies, as the reported accuracy of a diagnosis may be associated with the gender of the participants. Figure 16 plots the percent female participants, the sensitivity, and specificity.

Figure 16. Sensitivity and specificity by proportion of female participants



Across samples, the proportion of girls was not associated with reported sensitivity (p 0.63) or specificity (p 0.80). Analysis for reported accuracy also did not detect an effect (p 0.34) nor did an analysis of the reported AUCs (p 0.90) and there were insufficient data for further analyses. However, the number of female participants was small across studies, which lowers the statistical power to detect an effect.

There were insufficient numbers of studies to evaluate any other risk factors or participant variables on the diagnostic outcomes of interest.

4.7 KQ1d. What are the adverse effects associated with being labeled correctly or incorrectly as having ADHD?

Identified studies did not address consequence for patients correctly or not correctly receiving a diagnosis of ADHD or adverse effects associated with being labeled correctly or incorrectly as having ADHD. One study highlighted that a missed diagnosis has implications for accessing funding in the Australian healthcare system (e.g., national Disability Insurance Scheme) but provided no further empirical data.[447] None of the included studies reported on stigma associated with being diagnosed or labeled with ADHD.

4.8 Summary of Findings. KQ1a-d

Table 11 provides a very broad overview of the identified research. Results of the individual studies are shown in the evidence table in Appendix C, Table C.1.

Table 11. KQ1 summary of findings and strength of evidence for the diagnosis of ADHD

Tests To Diagnose ADHD	Outcome	Number of Studies; Study Design; IDs	Findings	Reasons for Downgrading	SoE
KQ1a Diagnostic tests for under 7 year olds	Sensitivity	7 studies[162, 167, 189, 416, 467, 559]	Sensitivity ranged from 64% (corresponding specificity 75%) for a neuropsychological test[162] to 97% (corresponding specificity 84%) for an activity measure[416]	S, I	Low
KQ1a Diagnostic tests for under 7 year olds	Specificity	6 studies[162, 167, 189, 331, 416, 559]	Specificity ranged from 38% (corresponding sensitivity 95) using EEG data[189] to 91% (corresponding sensitivity 71%) for the *Child Behavior Checklist* for ages 1.5 to 5 Attention-Deficit/Hyperactivity Problems scale[331]	S, I	Low
KQ1a Diagnostic tests for under 7 year olds	Accuracy	6 studies[162, 189, 331, 416, 467, 559]	Accuracy ranged from 64%[467] combining different executive function tasks to 93%[467] combining teacher and parent ratings, both in a model supported by machine learning	S, I	Low
KQ1a Diagnostic tests for under 7 year olds	AUC	7 studies[167, 189, 316, 331, 412, 416, 467]	AUC ranged from 0.68[189] using EEG data to 0.98[467] for combined teacher and parent ratings	S, I	Low
KQ1a Diagnostic tests for under 7 year olds	Rater agreement	1 study[167]	ICC was 0.92 between researchers administering the *Disruptive Behavior Diagnostic Observation Schedule*[167]	C	Insufficient
KQ1a Diagnostic tests for under 7 year olds	Internal consistency	3 studies[167, 467, 516]	Cronbach's alpha 0.92 for parent ratings on the DIPA-L[516] Cronbach's alpha *Behavior Rating Inventory of Executive Function* preschool version 0.976 for teacher ratings and 0.970 for parent ratings; child version 0.724 for teacher ratings and 0.978 for parent ratings[467] Cronbach's alpha was 0.83 for the K-BDS in the sample of ADHD children[167]	S, I	Low
KQ1a Diagnostic tests for under 7 year olds	Test-retest reliability	1 study[516]	ICC 0.91 and Kappa 0.84 for parent ratings on the *Diagnostic Infant and Preschool Assessment Likert version* (DIPA-L), 30 days or less between interviews[516]	C	Insufficient
KQ1a Diagnostic tests for under 7 year olds	Misdiagnosis consequences	0 studies	No data	C	Insufficient
KQ1a Diagnostic	Costs	0 studies	No data	C	Insufficient

4. Results: Diagnosis of ADHD

Tests To Diagnose ADHD	Outcome	Number of Studies; Study Design; IDs	Findings	Reasons for Downgrading	SoE
tests for under 7 year olds					
KQ1b Diagnostic tests for 7-18 year olds	Sensitivity	EEG: 9 studies[111, 120, 172, 245, 351, 370, 397, 408, 546] Imaging: 8 studies[191, 282, 400, 495, 518, 571, 581] Executive function tests:7 studies[119, 213, 351, 352, 379, 446, 614]	EEG: Sensitivity ranged from 57% (corresponding specificity 63%)[546] to 100% (corresponding specificity 100%)[245] MRI imaging: Sensitivity ranged from 57% (corresponding specificity 65%)[400] to 99% (corresponding specificity 100%)[581] Neuropsychological test with executive function component: Sensitivity ranged from 41% (corresponding specificity 65%) using Conners K test[119] to 84% (corresponding specificity 72%) using the CCTT[352]	S, I	Low
KQ1b Diagnostic tests for 7-18 year olds	Specificity	EEG: 9 studies[111, 120, 172, 245, 351, 370, 397, 408, 546] Imaging: 7 studies[191, 282, 400, 495, 518, 571, 581] Executive function tests: 8 studies[119, 213, 284, 351, 352, 379, 446, 614]	EEG Specificity ranged from 63% (corresponding sensitivity 57%)[546] to 100% (corresponding sensitivity 94-100%)[245, 370] MRI imaging: Specificity ranged from 55% (corresponding sensitivity 95%)[518] to 100% (corresponding sensitivity 100%)[191] Neuropsychological test with executive function component: Specificity ranged from 62% (corresponding sensitivity 63%) using the BANC[446] to 94% (corresponding sensitivity 74%) using a combination of reaction time and visuo-spatial working memory tests[614]	S, I	Low
KQ1b Diagnostic tests for 7-18 year olds	Accuracy	EEG: 15 studies[111, 120, 172, 245, 312, 351, 370, 394, 397, 408, 438, 449, 494, 546, 641] Imaging: 7 studies[191, 282, 400, 495, 518, 571, 581] Executive function tests: 7 studies[159, 213, 284, 351, 465, 541, 607]	EEG: Accuracy ranged from 59%[546] to 100%[245, 494] MRI imaging: Accuracy ranged from 64[400] to 99.6[191] Neuropsychological test with executive function component: Accuracy ranged from 65% using components of a test battery developed to assess right hemisphere function[284] to 88 using NCAT[351]	S, I	Low
KQ1b Diagnostic tests for 7-18 year olds	AUC	EEG: 3 studies[120, 245, 312] Imaging: 5 studies[191, 400, 464, 518, 581] Executive function tests: 2 studies[352, 446]	EEG: AUC values ranged from 0.89[120] to 1.0[245] MRI imaging: AUC ranged from 0.58[400] to 0.997[581] Neuropsychological test with executive function component: AUC values ranged from 0.73 for the Coimbra Neuropsychological Assessment Battery[446] to 0.80 for part 2 of the Children's Color Trail Test[352]	S, I	Low

4. Results: Diagnosis of ADHD

Tests To Diagnose ADHD	Outcome	Number of Studies; Study Design; IDs	Findings	Reasons for Downgrading	SoE
KQ1b Diagnostic tests for 7-18 year olds	Rater agreement	0 studies	No data	C	Insufficient
KQ1b Diagnostic tests for 7-18 year olds	Internal consistency	0 studies	No data	C	Insufficient
KQ1b Diagnostic tests for 7-18 year olds	Test-retest reliability	1 study[213]	EEG: No data MRI imaging: No data Neuropsychological test with executive function component: test-retest correlation of 0.81 ($p<0.05$) for the total test score in a Tower of London–- Drexel	C	Insufficient
KQ1b Diagnostic tests for 7-18 year olds	Misdiagnosis consequences	0 studies	No data	C	Insufficient
KQ1b Diagnostic tests for 7-18 year olds	Costs	0 studies	No data	C	Insufficient
KQ1c (effect modifier) setting	Sensitivity	N/A	Indirect analyses (regression) indicated that the setting may be associated with reported results (p 0.03)	D	Low
KQ1c (effect modifier) setting	Specificity	N/A	Indirect analyses (regression) did not indicate that the setting is associated with reported results (p 0.70)	D	Low
KQ1c (effect modifier) setting	Accuracy	N/A	Indirect analyses (regression) indicated that the setting may be associated with reported results ($p<0.01$)	D	Low
KQ1c (effect modifier) setting	AUC	N/A	Indirect analyses (regression) did not indicate that the setting is associated with reported results (p 0.22)	D	Low
KQ1c (effect modifier) population	Sensitivity	N/A	Indirect analyses (regression) indicated that the population may be associated with reported results (p 0.04)	D	Low
KQ1c (effect modifier) population	Specificity	N/A	Indirect analyses (regression) indicated that the population may be associated with reported results ($p<0.001$)	D	Low
KQ1c (effect modifier) population	Accuracy	N/A	Indirect analyses (regression) indicated that the population may be associated with reported results ($p<0.001$)	D	Low
KQ1c (effect modifier) age	Sensitivity	N/A	Indirect analyses (regression) did not detect an association (p 0.90, p 0.58)	D	Low
KQ1c (effect modifier) age	Specificity	N/A	Indirect analyses (regression) did not detect an association (p 0.35, 0.45)	D	Low
KQ1c (effect modifier) gender	Sensitivity and specificity	N/A	Indirect analyses (regression) did not detect an association (p 0.80) but the number of female participants was small	D	Insufficient
KQ1d (labeling)	Any outcome	0 studies	No data	C	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, AUC = area under the curve, BANC = Coimbra Neuropsychological Assessment Battery, C = inconsistency, CCTT = children's color trails test; D = indirectness, DIPA-L = Diagnostic Infant and Preschool Assessment Likert version, EEG = Electroencephalogram, I = imprecision, KQ = Key Question, ICC = intraclass correlation coefficient, K-DBDS = Kiddie-Disruptive Behavior Disorder Schedule, MRI = magnetic resonance imaging, N/A = not applicable, NCAT = neurocognitive assessment tool, S = study limitation, SoE = strength of evidence

As documented in the summary of findings table, tests to diagnose ADHD were very diverse, and studies reported a large range of diagnostic and psychometric performance. Strength of evidence assessments for this group were low or insufficient for all outcomes. We downgraded results for study limitation (lack of details on the selected tests, employed machine learning algorithm used to select variables, and lack of details on the exact variables included in the final model contributing to the effect estimate), imprecision (large variation in reported diagnostic performance across studies), and/or lack of replication in more than one study assessing the same test (i.e., consistency could not be assessed). Few studies were available to diagnose ADHD in young children. More studies were available for the older children; however, studies did not report on all outcomes of interest. We downgraded the strength of evidence for study limitations where the evidence base consisted primarily of studies that provided insufficient detail on the diagnostic strategy (e.g., which cut offs, which variables exactly entered models). We downgraded for imprecision where studies reported a large range of possible diagnostic performance. The strength of evidence for other outcomes was downgraded for the domain inconsistency because consistency could not be assessed as no replication of the document effect has been identified.

Effect modifier analyses were hindered by the lack of reported detail needed to assess effects in meta-regressions. Indirect analyses using simple regression indicated that the diagnostic setting may influence diagnostic accuracy estimates. Further analyses assessing study population characteristics (e.g., whether the comparison is to neurotypical developing or was made in clinical samples) may affect estimates. Given that both aspects (e.g., clinical samples are seen in specialty care) may be associated with key outcomes for this review, we stratified the test-specific result presentation by neurotypical or clinical sample.

We did not identify studies reporting on the impact of correctly or incorrectly labeling youth as having ADHD or the impact of an incorrect diagnosis, and the strength of evidence is insufficient to make any evidence statements.

5. Results: Treatment of ADHD

This section describes studies reporting on a treatment of attention deficit hyperactivity disorder (ADHD). Key points are listed first, followed by a summary of findings section before going into the effects and comparative effects of specific interventions.

5.1 KQ2, ADHD Treatment Key Points

- We found that several treatment modalities improve core ADHD symptoms compared to control groups (e.g., placebo). These include medications approved by the Food and Drug Administration (FDA) and psychosocial interventions with high or moderate strength of evidence.
- FDA-approved stimulant (e.g., methylphenidate, amphetamine) and non-stimulant (e.g., atomoxetine, alpha agonist) medications had the strongest evidence for significantly improving ADHD symptoms and additional outcomes, including broadband measures and functional impairment.
- Head-to-head comparisons between stimulants and non-stimulants did not detect statistically significant differences for most effectiveness outcomes and adverse events.
- We found little evidence that combination therapies of medication plus psychosocial therapies produce better results than medication alone, but existing research evaluated unique combinations of intervention components.
- Despite the large body of research, comparative effectiveness and safety information is limited, and more research is needed to help choose between treatments.
- We did not detect differential treatment effects associated with ADHD presentation, but analyses were based on indirect comparisons and should be interpreted with caution.
- Data were insufficient to assess the effect of co-occurring disorders on treatment effects.
- We found too few studies reporting on diversion to quantify the risk of diversion of pharmacological treatment.

5.2 KQ2, ADHD Treatment Results

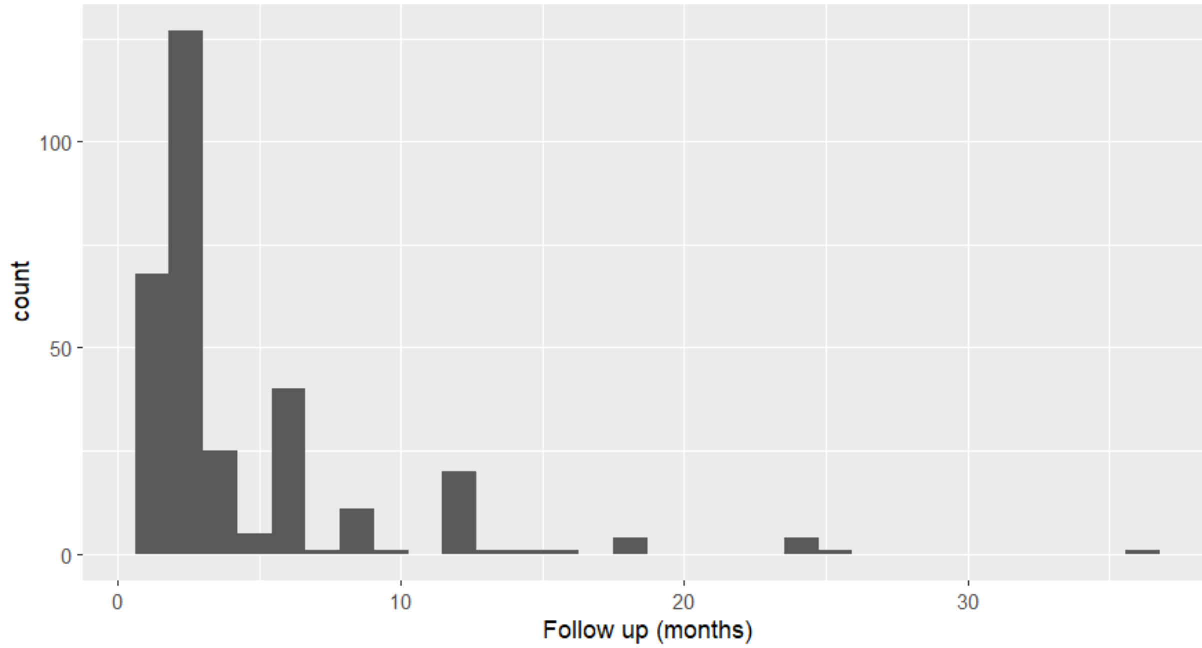
We identified 312 studies evaluating a treatment for ADHD.[56, 104-110, 113, 114, 116, 118, 122, 123, 125-133, 136-139, 144-151, 154-156, 158, 160, 161, 163-166, 171, 174-176, 178, 180, 193-196, 199-202, 204-209, 212, 215-217, 219-222, 224-229, 232, 235, 236, 238-240, 243, 247-250, 252, 254-259, 261, 262, 264-266, 269-273, 275, 278-281, 286, 288-292, 294-296, 302, 304-306, 308, 310, 313, 317, 318, 320, 321, 324-326, 328-330, 332-335, 337, 341, 343, 345, 348-350, 353, 354, 357, 358, 360, 361, 363, 364, 367, 368, 371-378, 380, 381, 383, 384, 386, 387, 392, 396, 398, 399, 406, 409-411, 414, 418, 419, 425, 426, 428, 430-433, 435, 439-444, 451-461, 466, 471, 472, 474, 476, 478, 480, 481, 483-485, 488-490, 492, 497, 503-505, 507-513, 517, 520-523, 525, 526, 529-535, 538-540, 544, 550-552, 554-557, 560-562, 565, 567-569, 572-575, 577-579, 585, 586, 588-590, 593-598, 601, 602, 604, 606, 608, 610-613, 616-624, 626, 628, 634, 636, 637, 640, 643, 645, 646] Although studies from 1980 were eligible, the earliest treatment studies meeting inclusion criteria were published in 1995. Studies were published in 30 different countries, although about 40 percent were U.S. studies (contributing 127 included studies).

The summary of findings table broadly summarizes the available evidence for the key outcomes across identified treatment studies.

5. Results: Treatment of ADHD

Figure 17 plots the followup periods across treatment studies.

Figure 17. Followup in KQ2 ADHD treatment studies

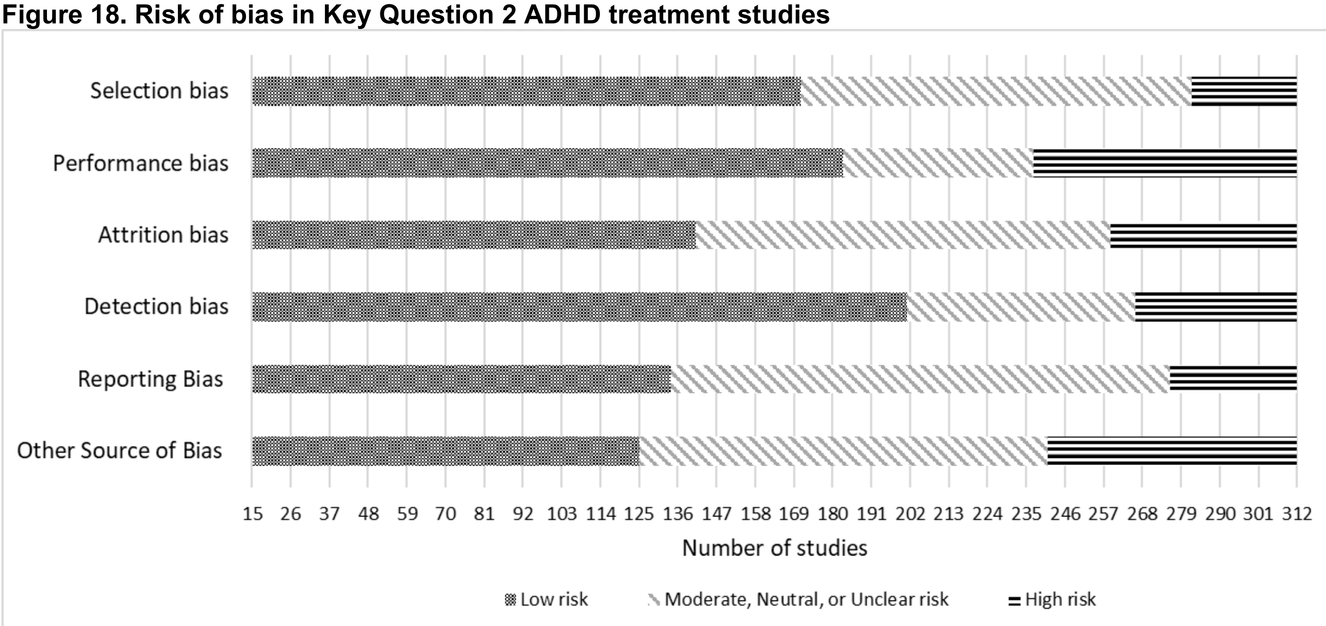


Notes: ADHD = attention deficit hyperactivity disorder

With few exceptions, studies reported short-term effects.

The potential for risk of bias in Key Question (KQ) 2 studies is documented in Figure 18. The critical appraisal for the individual studies is in Appendix D.

Figure 18. Risk of bias in Key Question 2 ADHD treatment studies

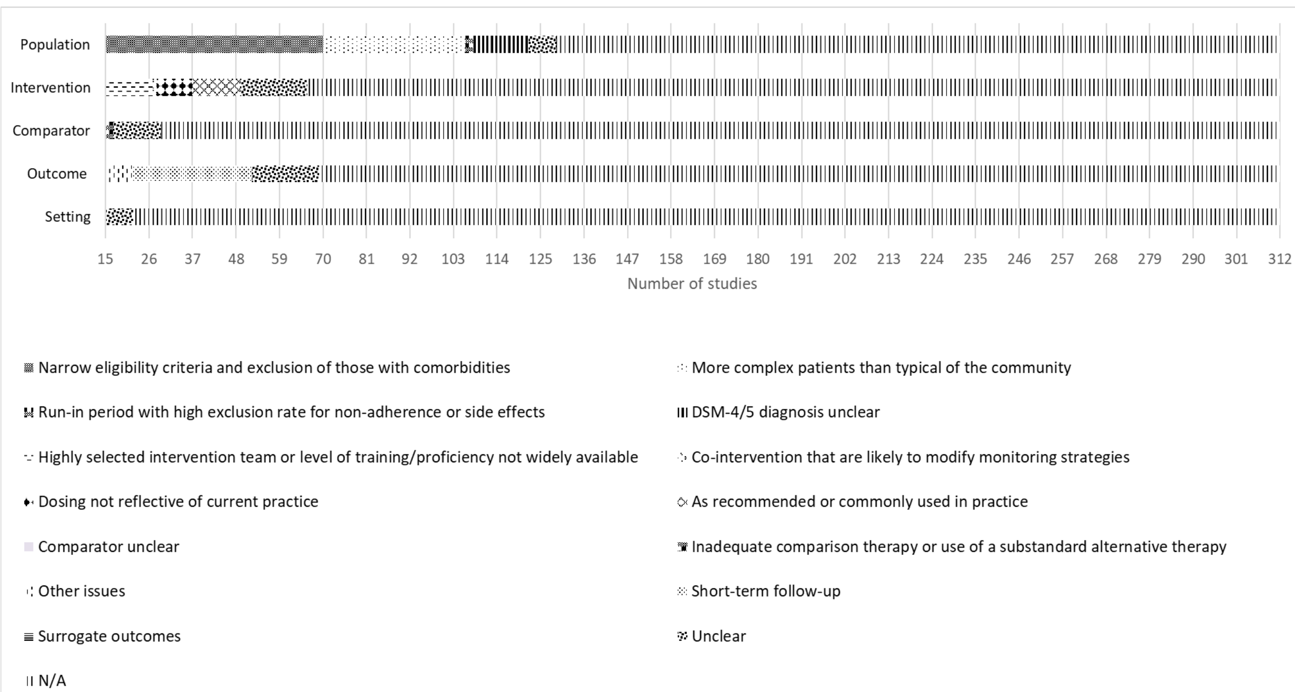


Notes: ADHD = attention deficit hyperactivity disorder

Across studies, *selection bias* was likely present in multiple identified studies. This was predominantly attributable to highly selected samples and exclusions, or a biased allocation into groups because of study logistics. The review was open to all studies evaluating intervention in youth with a ADHD without further limitations, but some included studies reported a number of additional inclusion and exclusion criteria. *Performance bias* was noted in half of the included studies. An example of this kind of bias is that participants deviated from protocol medication administration (e.g., parents frequently reduced weekend medication use on their own). *Attrition bias* was also often noted, with large numbers of participants being unavailable for follow-up assessments. *Detection bias* was detected in many studies where blinding was not possible or would be very difficult and the outcome assessors (often the parents of the participants) were aware of the participants' intervention assignment. *Reporting bias* was also suspected in some of the studies, usually indicating that the study did not report on key ADHD outcomes, and no study protocol was published specifying that prospectively. Other sources of bias were identified in a third of studies, concerning small samples or inadequate descriptions of either the interventions or study flow.

Figure 19 shows the distribution of KQ2 studies with applicability issues. The applicability for the individual studies is documented in Appendix D.

Figure 19. KQ2 ADHD treatment applicability rating



Notes: ADHD = attention deficit hyperactivity disorder, DSM = Diagnostic and Statistical Manual of Mental Disorders, N/A = Not applicable

Applicability issues primarily concerned the participant samples in the identified studies. Some of the samples were less diverse than the typical population seen in clinical practice, often because of very strict inclusion criteria for the study (e.g., excluding children with co-occurring disorders). A large number of studies did not report any characteristics that flagged the comparator or the setting as different from the level of care in the community (listed as not applicable in the figure).

The 78 populations studied were predominately males, and some studies (2%) were restricted to boys; samples included on average a quarter of female participants. The youngest children in individual studies were three years old. Race and ethnicity demographics were not mentioned in over half of the studies. For studies that distinguished between ADHD presentations, the most prevalent type was the combined type.

The following sections summarize the effects of interventions on the key outcomes. This is a very broad analysis; however, it is an important question whether ADHD characteristics can be changed at all with interventions. For each section, a narrative summary is followed by a summary of findings table. Summary tables report on each of the key outcomes. Subgroup results are only added to the summary tables when a direct or indirect analysis suggested empirically different results and more than one study contributed to the effect estimate. Additional information on study-specific primary outcomes are documented in the evidence table in the appendix.

5.2.1 Effects of ADHD Treatment on Behavior

The results for any achieved changes in problem behavior (e.g., conduct problems) across the diverse ADHD interventions evaluating a continuous outcome (and reporting sufficient information to allow effect size calculations) showed a positive effect compared to passive control groups (standardized mean difference [SMD] -0.34; confidence interval [CI] -0.49, -18; 34 studies, n=3507). There was evidence of heterogeneity (I-squared 66%). We tested whether the intervention type was a key source of heterogeneity to explain differences in effects; results indicated that effect estimates for behavior depend on the type of intervention (p 0.04). Analyses suggested publication bias (Begg p 0.01, Egger p<0.0001), indicating that publication bias should be considered for individual analyses. We also estimate in a sensitivity analysis whether the result was mainly driven by high risk-of-bias studies; after removing 13 high risk-of-bias studies, the estimate was similar (SMD -0.32; CI -0.48, -0.17). Across studies, only three studies were identified reporting on categorical outcomes (e.g., assessing whether or not behavior had improved). Results indicated reductions in problematic behavior associated with ADHD treatment (RR [relative risk] 0.46; CI 0.24, 0.87; 3 studies, n=154). In this small set of studies, there was no evidence of heterogeneity or publication bias. None of the studies was classified as high risk.

5.2.2 Effects of ADHD Treatment on Broadband Measures

The results for broadband scales describing a child's behavior more generally showed positive effects of ADHD interventions (SMD 0.39, CI 0.31, 0.47; 72 studies, n=9027). There was evidence of heterogeneity (I-squared 68%). We tested whether the intervention was the key source of heterogeneity to explain differences in effects, but we did not detect an effect (p 0.29). There was no evidence of publication bias. We removed 25 high risk-of-bias studies in a sensitivity analysis, but the effect estimate remained similar (SMD 0.42, CI 0.33, 0.52). Multiple studies also reported on these global impressions as categorical variables and the effect was similar for the categorical broadband measures, indicating improvement associated with ADHD treatment (RR 0.57; CI 0.48, 0.66; 40 studies, n=6033). There was evidence of heterogeneity (I-squared 81%). We tested whether the intervention was the key source of heterogeneity to explain differences in effects, but we did not detect a systematic effect (p 0.34). There was evidence of publication bias (Begg p 0.01, Egger p<0.001) and an alternative estimate using the trim and fill method showed a somewhat smaller effect (RR 0.64; CI 0.55, 0.75). We also conducted a sensitivity analysis to determine whether results are robust when removing six high risk-of-bias studies; the estimate was very similar to the original results (RR 0.57; CI 0.48, 0.68).

5.2.3 Effects of ADHD Treatment on ADHD Symptoms

A large number of studies reported on standardized symptom assessment tools. Standardized mean difference results across studies using continuous data found a positive effect of interventions successfully reducing ADHD symptom severity (SMD -0.47, CI -0.54, -0.40; 150 studies, n=18746). There was evidence of heterogeneity (I-squared 80%). We tested whether the intervention was the key source of heterogeneity to explain differences in effects and found that the reported effect size was not systematically associated with the type of intervention evaluated (p 0.13). There was some indication of publication bias (Begg p 0.09, Egger, p 0.02), but an alternative effect estimate using the trim and fill method found a very similar estimate SMD -0.47; CI -0.55, -0.40). Excluding 49 high-risk-of-bias studies in a sensitivity analysis resulted in a similar estimate (SMD -0.47, CI -0.55, -0.38) and heterogeneity was not reduced. A smaller number of studies reported on a dichotomous outcome for ADHD symptoms (e.g., meeting or not meeting an improvement target). Across studies, we found a positive effect of ADHD interventions (RR 1.51, CI 1.23, 1.84; 26 studies, n=3289). We detected heterogeneity (I-squared 67%), but a moderator analysis did not detect the intervention as a source of heterogeneity (p 0.18). There was evidence of publication bias (Begg p<0.004, Egger p<0.001). A more appropriate estimate of the true effect on symptom reduction may be somewhat smaller (RR 1.31, CI 1.06, 1.60). We also removed four high-risk of bias studies in a sensitivity analysis which showed the treatment effect to be robust (RR 1.58, CI 1.24, 2.00) but heterogeneity was not reduced.

5.2.4 Effects of ADHD Treatment on Functional Impairment

The results for functional impairment measures across the diverse interventions in studies reporting on a continuous outcome found a positive effect of ADHD interventions on functional impairment (SMD 0.37; CI 0.20, 0.54; 31 studies, n=3890). There was evidence of heterogeneity (I-squared 82%). We tested whether the intervention was the key source of heterogeneity to explain differences in effects, but we did not detect a systematic effect (p 0.88). There was no significant publication bias. When removing 11 high-risk of bias studies in a sensitivity analysis, the estimate remained similar (SMD 0.40; CI 0.17, 0.62) and heterogeneity was not reduced. Very few studies reported on functional impairment as a categorical variable, and only one study reported sufficient information to compute effect sizes. The study indicated improvement, but the confidence interval was wide (RR 1.29; CI 1.00, 1.66; 1 study, n=332).

5.2.5 Effects of ADHD Treatment on Acceptability of Treatment

Only one study assessed treatment acceptability formally in a rating scale for all groups and reported sufficient detail to compute effect sizes; the study did not find a statistically significant difference between groups (SMD 0.19; CI -0.12, 0.49; 1 study, n=164). One study reported categorical data to express satisfaction with the treatment; the study favored the intervention (RR 0.47; CI 0.32, 0.68; 1 study, n=198). There were insufficient data for further analyses.

5.2.6 Effects of ADHD Treatment on Academic Performance

The results for academic performance changes reported in sufficient detail across the diverse interventions favored ADHD treatment arms, but we did not detect a statistically significant difference between ADHD treatment and passive control groups on academic performance (SMD -0.29; CI -0.62, 0.03; 12 studies, n=1780). There was evidence of heterogeneity (I-squared 88%). We tested whether the intervention was the key source of heterogeneity to explain differences in effects, but the intervention type did not systematically contribute to the heterogeneity of effects (p 0.10). Publication bias tests did not indicate potential bias. Removing two high risk-of-bias studies in a sensitivity analysis showed a smaller effect, and the difference between groups remained not statistically significant (SMD -0.29; CI -0.69, 0.10). None of the studies comparing to a control group reported on a categorical outcome in sufficient detail to allow effect size calculation.

5.2.7 Effects of ADHD Treatment on Appetite Changes

We identified several studies that reported on a continuous measure to capture appetite changes or growth suppression. Across ADHD interventions, analyses indicated an effect on appetite suppression in studies reporting continuous outcomes (SMD 0.41; CI 0.01, 0.82; 11 studies, n=1321). Heterogeneity was high (I-squared 90%). The type of intervention was one source of heterogeneity, as indicated in a meta-regression (p 0.02). There was no evidence of publication bias. Removing two high-risk-of-bias studies in a sensitivity analysis found a similar point estimate (SMD 0.46; CI -0.05, 0.97) and heterogeneity was not reduced. Across all ADHD interventions, ADHD treatment was associated with decreased appetite compared to control group participants (RR 2.77; CI 2.21, 3.46; 66 studies, n=9508). A large number of studies and participants contributed to the results, and while many individual interventions did not detect statistically significant effects for this rare event, the data aggregation across studies shows a statistically significant effect. Heterogeneity was not remarkable (I-squared 53%). We tested whether the intervention type explained some of the heterogeneity and found evidence that this was the case (p 0.002). It should be noted that adverse events generally were more systematically reported in drug studies, and this outcome in particular was usually only reported in studies evaluating a pharmacological component; hence the analysis of the source of heterogeneity should be interpreted with caution. There was some evidence of publication bias (Egger p 0.01, Begg $p<0.001$). The alternative estimate of the effect using the trim and fill method to account for unpublished studies was somewhat smaller (RR 2.21; CI 1.74, 2.80). We also conducted a sensitivity analysis removing nine high risk-of-bias studies; the resulting estimate suggested an even stronger effect (RR 3.01; CI 2.38, 3.80) and heterogeneity was reduced further.

5.2.8 Effects of ADHD Treatment on Number of Participants With Adverse Events

Several identified studies reported on the number of participants experiencing at least one adverse event. Across ADHD interventions, participants undergoing active ADHD treatment were more likely to report adverse events than control group participants (RR 1.26; CI 1.19, 1.33; 64 studies, n=9632). We did not detect notable heterogeneity in this analysis (I-squared 59%). An analysis of the intervention as a potential source of heterogeneity indicated that the type of intervention was associated with the reported effect estimate ($p<0.0001$). There was no evidence of publication bias. Removing 11 high risk-of-bias studies in a sensitivity analysis did result in a similar point estimate (RR 1.25; CI 1.18, 1.33) and heterogeneity estimates were unchanged.

5.3 Effects by Intervention

The identified interventions were very diverse and addressed ADHD treatment in very different ways. In addition, exploring heterogeneity across studies indicated that for several key outcomes the type of intervention that was evaluated is a key source explaining variation in effect estimates. Hence, we broadly differentiated different types of interventions:

- Combined pharmacological and youth-directed psychosocial treatment
- FDA-approved pharmacologic treatment
- Other pharmaceutical agents
- Youth-directed psychosocial treatment
- Cognitive training
- Neurofeedback
- Neurostimulation
- Physical exercise
- Nutrition and supplements
- Complementary, alternative, and integrative medicine
- Parent support
- School interventions
- Provider intervention

These intervention categories provide broad clusters for analyses. The scope of each intervention category is described in detail in each intervention section. In addition to categorizing the type of intervention, we noted whether the intervention was tested as an 'add-on,' i.e., it was given in addition to and concurrently with stimulant medication. In these studies, the intervention as well as the control group received stimulants while the intervention group was given an additional intervention component.

The following provides an overview of the available studies for each intervention category, together with a summary of the effects of the interventions on outcomes. Each section starts broad, addressing a broad question associated with the intervention class, such as whether medication can improve outcomes at all compared to a concurrent control group or an active comparator. Each section then explores empirically whether subgroups of interventions were associated with different treatment effects. Finally, each study addresses a unique research question with a relatively unique intervention. Throughout the report, forest plots show not only the results across studies, but document also the results of each individual study. The study ID (author, publication year, unique identifier) is shown in the list of included studies in the appendix together with the full citation for the main publication of the study. In addition, intervention characteristics for particularly successful interventions are described in more detail in the text. We also refer the reader to the appendix, where for each included study a narrative summary of the results for all key outcomes are documented in a comprehensive evidence table.

5.3.1 Combined Pharmacological and Youth-Directed Psychosocial Treatment

We identified 11 eligible treatment studies that evaluated a combination of pharmacological intervention and youth-facing nonpharmacological psychosocial therapy.[107, 201, 216, 275, 343, 357, 474, 497, 560, 589, 597] The behavioral or psychological treatment had to be directed at the participating children and adolescents in order to be included in this treatment category. Studies assessing the effect of parental training in combination with medication are reported in the parent intervention section. The earliest identified set of studies were those published from the National Institute of Mental Health Multimodal Treatment Study of Children with ADHD (MTA), which dates to 1999[343] that has been reported thus far in 73 articles, as shown in the evidence table. Studies were published in six countries but half of the identified combined pharmacological and behavioral studies were conducted in the United States.[151, 275, 343, 497, 1163]

The populations studied were predominately males and the proportion of girls ranged from seven to 26. Studies included children and adolescents between the ages of five and 18. Evidence of intellectual disability (i.e., full-scale IQ < 70) was exclusionary in all studies, and most studies required full-scale IQ scores of 80 or higher. Half of the studies allowed participants to be included if they had prior exposure to stimulant treatment for ADHD, whereas the remaining studies required participants to be stimulant naïve, or else it was unclear what their inclusion criteria were regarding prior treatment with stimulant medication. For studies that distinguished between ADHD presentations (i.e., ADHD-combined type, ADHD-inattentive type, and ADHD-hyperactive/impulsive type), the most prevalent type (ranging from 54%[201] to 88%[343] of the ADHD participants) was the ADHD-combined presentation. In most studies, children were allowed to have common co-occurring conditions such as oppositional defiant disorder, conduct disorder, or dyslexia/learning disorder, but more severe neurodevelopmental conditions such as autism were exclusionary in this subarea of studies. Most studies reported at least some general information regarding the racial/ethnic makeup of their sample; on average, children of Caucasian/European ancestry comprised two thirds of sample makeup, a third were Hispanic or Latino, and a smaller percentage were African American.

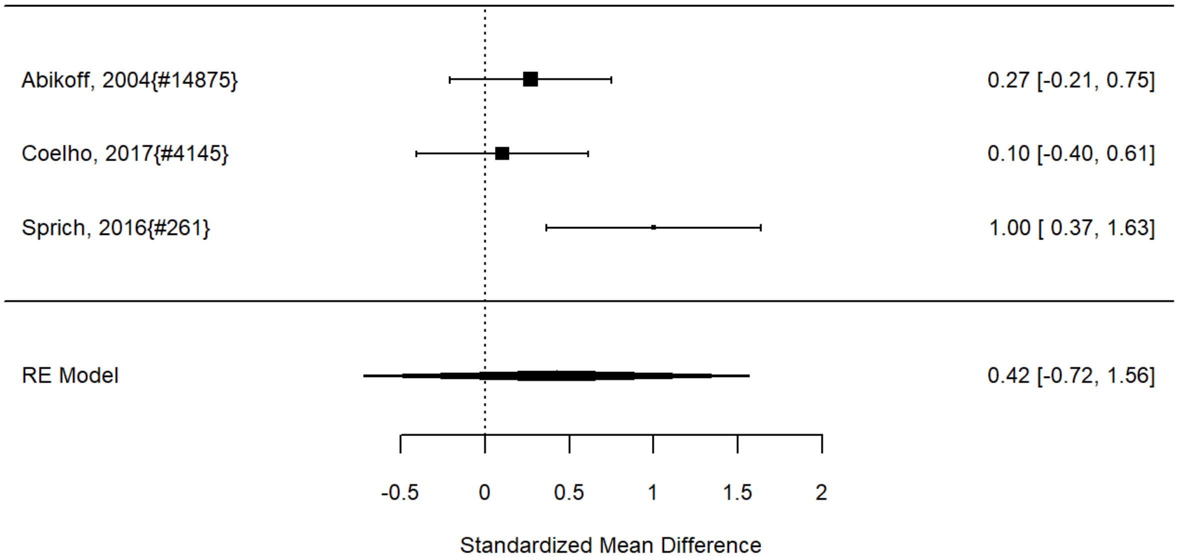
The pharmacological treatment components employed in the studies were predominantly short- or long-acting stimulants (such as methylphenidate and amphetamine)[201, 257, 343, 497] or else the non-stimulant medication atomoxetine.[216] Behavioral treatment components varied in approach and complexity. Four studies evaluated cognitive behavioral therapy[201, 216, 497, 560] and three described multi-modal psychosocial treatments.[107, 333, 343] One study each evaluated a behavioral and social skills class;[589] one a complex intervention with brief early intervention, parent component, and cognitive behavioral therapy for adolescents,[275] one a humanistic intervention,[474] and one a solution-focused approach.[357] Studies compared most frequently to pharmacology treatment alone, rather than no treatment or placebo. These "add-on" trials, where one group receives an additional intervention, predominantly evaluated whether the combination treatment was superior to the medication intervention that all participants received.

Studies reported a variety of often study-specific outcomes. In terms of pre-specified key outcomes, symptom scores were most frequently reported.

Three studies reported on changes in a specific problem behavior, but they reported different effect estimates and could not be combined into a meaningful summary estimate shown by the large confidence interval; none detected statistically significant difference between the intervention and a control group (SMD -1.28; CI -7.56, 5.00; 3 studies, n=329).[107, 275, 343] Two of the identified studies reported long-term effects, but they reported very small effects with conflicting direction of effects (SMD 0.04; CI -2.15, 2.20).[107, 343]

Studies reporting on broadband measures are shown in Figure 20.

Figure 20. Effects of combined pharmacological and youth-directed psychosocial treatment on broadband measures (SMD)

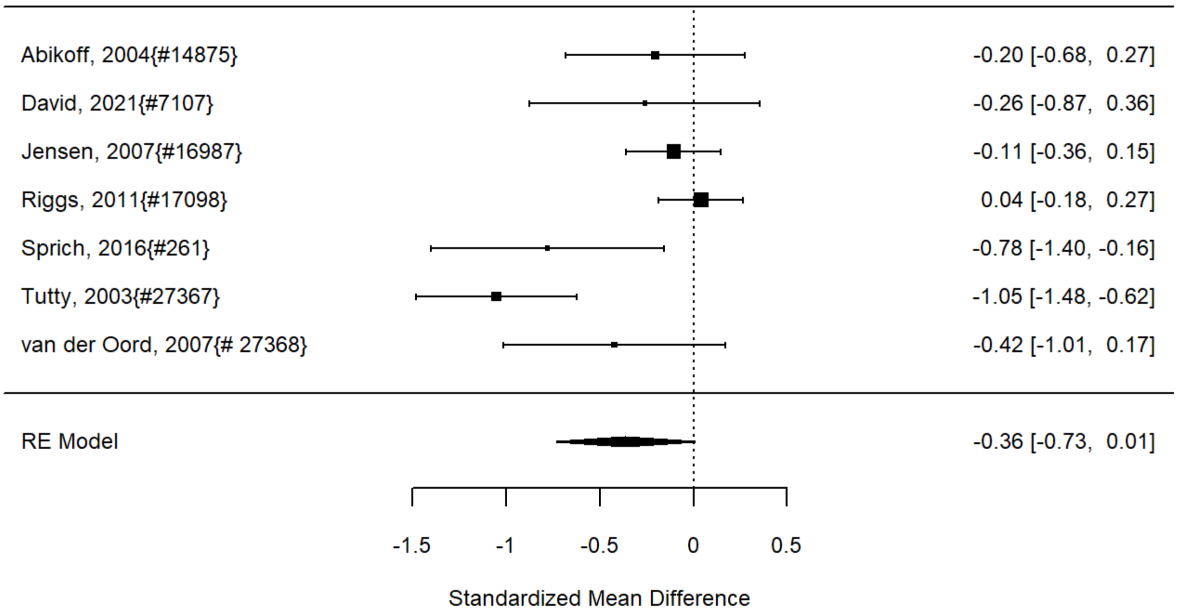


Notes: ADHD = attention deficit hyperactivity disorder, RE = random effects, SMD = Standardized Mean Difference

Across studies, we found no systematic difference between intervention and control groups (SMD 0.42; CI -0.72, 1.56; 3 studies, n=171), but it should be noted that all studies included in this analysis compared to the medication component of the combined intervention (i.e., control participants received one of the two intervention components). The included studies evaluated different interventions (multimodal psychosocial treatment plus methylphenidate;[107] group cognitive behavioral therapy (CBT) plus methylphenidate;[201] and individual CBT plus FDA-approved medication[560]) and compared to medication alone. The analysis detected some heterogeneity (I-squared 62%). There was no indication of publication bias. All three studies were judged to be high risk of bias. A study reporting on a categorical outcome also found no difference between studies (RR 0.85; CI 0.54, 1.36; 1 study, n=227).[497] Only one of the studies reported a long-term outcome; the effect of the intervention was not statistically significant (SMD 0.27; CI -0.21, 0.75).[107]

Studies reporting on ADHD symptom scales are shown in the next forest plot (Figure 21).

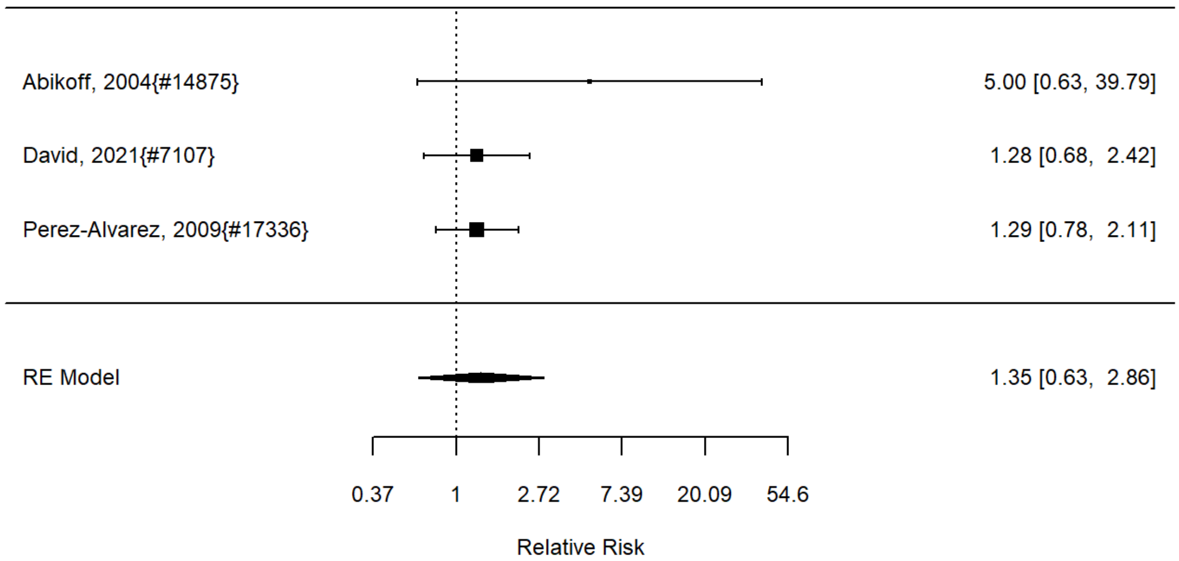
Figure 21. Effects of combined pharmacological and youth-directed psychosocial treatment on ADHD symptoms (SMD)



Notes: ADHD = attention deficit hyperactivity disorder, RE = random effects, SMD = Standardized Mean Difference

Studies did not identify a statistically significant effect of superiority of the combined pharmacological and psychological treatment versus control (SMD -0.36; CI -0.73, 0.01; 7 studies, n=841). However, the pooled effect was very close to being statistically significant and several of the individual studies reported positive (although not necessarily statistically significant) effects. The strongest effects were reported for a behavioral and social skills functioning class for children and their parents,[589] and for cognitive behavioral therapy with adolescents[560] in another study. Additionally, when interpreting the results of combined pharmacological and behavioral interventions, it should be noted that the control groups against which the intervention is compared consisted of groups that received the pharmacological intervention component alone rather than no intervention. Hence, the analysis was typically a type of comparative effectiveness analysis rather than a pure effectiveness analysis against a passive comparator. There was some indication of statistical heterogeneity (I-squared 76%). The analysis did not detect publication bias. Removing four high-risk of bias studies in a sensitivity analysis did not result in a different effect estimate, and the effect was also not statistically significant (SMD -0.35; CI -1.80, 1.10). Only the MTA study reported on a long-term outcome (36 months, SMD -0.11; CI -0.36, 0.15).[343] The study did also not detect a difference between the combined and medication alone group at post-intervention for ADHD symptoms (inattention teacher ratings at 14 months, SMD 0.01; CI -0.23, 0.26) and using this alternative estimate for the MTA study did also not detect a statistically significant effect of the combined treatment across all studies (SMD -0.34; CI -0.73, 0.04). The next forest plot (Figure 22) shows studies reporting on a categorical symptom assessment.

Figure 22. Effects of combined pharmacological and youth-directed psychosocial treatment on ADHD symptoms (RR)



Notes: RE = random effects, RR = Relative Risk

Studies did not identify a statistically significant treatment effect in the categorical outcome either (RR 1.35; CI 0.63, 2.86; 3 studies, n=155) that would suggest superiority of the combined treatment compared to medication alone. There was no indication of heterogeneity in this small set of studies and further analyses were not possible due to the small number of studies. Of these, two studies reported on outcomes of 12 months or more; because effect estimates differed widely, no meaningful summary estimate could be derived (RR 1.72; CI 0.00, 2038).[107, 474]

Studies reporting on functional impairment reported conflicting results and no meaningful summary estimate could be derived due to wide confidence intervals (SMD 0.02; CI -2.54, 2.56; 2 studies, n=261). Heterogeneity was negligible, but the number of studies was small and no further analyses could be conducted. The estimate included the MTA study that reported a long-term effect of the intervention (36 months, SMD 0.11; CI -0.14, 0.36, 14 months SMD -0.05; CI -0.38, 0.27).

The MTA study also reported on an academic performance measure and did not detect a statistically significant effect (36-months SMD -0.12; CI -0.37, 0.13; 1 study, n=243; 14 months SMD -0.10; CI -0.34, 0.14).[343] No other study reported on academic performance. We did not identify studies reporting on treatment satisfaction.

One study reporting on appetite suppression that reported sufficient data for effect size calculation found no difference between groups, where both received atomoxetine (RR 0.93; CI 0.29, 3.03; 1 study, n=29).[216] The MTA reported that after 14 months, children treated with methylphenidate had gained less height and less weight (-1.23 cm per year and -2.48 kg per year) than untreated children[669] and follow up into young adulthood within naturalistic subgroups of ADHD cases showed that extended use of medication was associated with suppression of adult height.[343]

One identified study reported on the number of participants experiencing adverse events and documented one hospitalization, but the outcome was considered unrelated to the study and there was no systematic difference between groups (RR 3.00; CI 0.13, 68.57; 1 study, n=32).[275]

5.3.1.1 Combined Pharmacological and Youth-Directed Psychosocial Treatment Summary of Findings

Table 12 shows the findings for all key outcomes of interest, together with the number of studies reporting on the outcome and study identifiers. The findings column shows the pooled estimate across studies. Not all studies reporting on the outcomes of interest contributed to each pooled estimate (e.g., because they did not report sufficient detail to allow effect size calculations). Results of individual studies are documented in the evidence table in the appendix and, for each study and outcome, results are summarized in a narrative summary (including results for the key outcomes that provided insufficient detail for effect size calculations).

Table 12. KQ2 summary of findings and strength of combined pharmacological and youth-directed psychosocial treatment

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 combined treatment vs control (individual component or usual care)	Behavior	3 RCTs[107, 275, 343]	No systematic difference but no meaningful summary estimate could be derived (SMD 1.28; CI -7.56, 5.00; 3 studies, n=329)	I	Insufficient
KQ2 combined treatment vs control (individual component or wait list)	Broadband measures	4 RCTs[107, 201, 497, 560]	No systematic difference (SMD 0.42; CI -0.72, 1.56; 3 studies, n=171; RR 0.85; CI 0.54, 1.36; 1 study, n=227)	I	Low for no difference
KQ2 combined treatment vs control (individual component, usual care, or wait list)	ADHD symptoms	8 RCTs[107, 216, 343, 474, 497, 560, 589, 597]	No systematic difference (SMD -0.36; CI -0.73, 0.01; 7 studies, n=841; RR 1.35; CI 0.63, 2.86; 3 studies, n=155)	S, I	Low for no difference
KQ2 combined treatment vs control (individual component or usual care)	Functional impairment	2 RCTs[275, 343]	No systematic difference (SMD 0.02; CI -2.51, 2.56; 2 studies, n=261)	S, I	Insufficient
KQ2 combined treatment vs control	Acceptability of treatment	0 studies	No data	C	Insufficient
KQ2 combined treatment vs usual care	Academic performance	1 RCT[343]	No systematic difference (SMD -0.12; CI -0.37, 0.14; 1 study, n=243)	S, C	Insufficient
KQ2 combined treatment vs control (individual component or usual care)	Appetite suppression	2 RCTs[216, 343]	No systematic difference (RR 0.93; CI 0.29, 3.03; 1 study, n=29)	I	Insufficient
KQ2 combined treatment vs no intervention	Participants with adverse events	1 RCT[275]	No systematic difference (RR 3.00; CI 0.13, 68.57; 1 study, n=32)	C	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, C = inconsistency, CI 95% = confidence interval, I = imprecision, KQ = Key Question; RCT = randomized controlled trial, RR = relative risk, S = study limitation, SMD = standardized mean differences, SoE = strength of evidence

The summary of findings table above generally shows little support that a treatment modality comprising combined medication and youth-directed psychosocial treatment as superior to control groups receiving mono-therapy (typically medication alone). For multiple outcomes we found very few or no studies to determine intervention effects. We downgraded the strength of evidence for functional impairment, academic performance, and adverse events to insufficient due to study limitation and inconsistency (downgraded by 2 given that consistency could not be determined as only one study has reported on the outcome to date). The strength of evidence for symptom improvement was downgraded for imprecision (the result was not statistically significant but the confidence interval was very close to including a positive effect for the combined intervention).

5.3.2 FDA-Approved Pharmacologic Treatment

We identified 106 studies evaluating a pharmacological intervention approved by the FDA for the treatment of ADHD.[108, 109, 118, 127, 131-133, 137, 144, 145, 154, 161, 164, 175, 193-196, 202, 205, 207, 217, 220, 224-226, 235, 247-250, 270-273, 281, 286, 288, 289, 292, 305, 306, 317, 321, 326, 337, 341, 348, 361, 373, 374, 376, 378, 380, 381, 383, 387, 414, 418, 419, 425, 431, 432, 442, 452-455, 459-461, 481, 504, 511, 512, 525, 526, 538-540, 554-557, 561, 568, 573, 575, 588, 598, 604, 608, 610-612, 616-619, 621-623, 626, 634, 645] Although studies from 1980 were eligible, the earliest studies meeting inclusion criteria were published in 1995.[540] Evaluations were published in 16 different countries (and some were conducted in multiple countries) but 60 percent of the research was U.S.-based. Although the reported percent of female participants ranged from under one percent to 56 percent, samples were predominantly male. The age minimum varied, but across all identified studies, only four studies included young children three to five years old.[109, 194, 271, 378] Studies varied in whether they required participants to be drug naïve at study beginning, while others allowed concomitant medication even during the study. The identified studies included some that explicitly tested adjunctive medication to augment stimulant treatment.[104, 107, 257, 373, 474, 488, 598, 622] Studies included different presentations of ADHD. Where reported, the combined presentation was most common in studies, on average representing two thirds of the sample. While ADHD participants with co-occurring disorders were not excluded from most of the studies, only a few studies purposely included specific co-occurring disorders, including oppositional defiant disorder or conduct disorder,[207, 220, 226, 432, 623] Tourette syndrome or tic disorder,[118, 380, 540, 556] or learning disabilities.[526, 538] Demographics were often not reported, but where studies described a breakdown by race or ethnicity, on average about 75 percent of children were White, about 15 percent Black, less than ten percent Hispanic, and about one percent were described as Asian.

Studies evaluated stimulants and non-stimulants, either alone or in combination. Interventions included the stimulant classes methylphenidate and amphetamine, and the non-stimulant classes norepinephrine reuptake inhibitor (NRI) and alpha agonists. Studies evaluated different methylphenidate hydrochloride formulations, including immediate, extended, and multilayer release formulations, methylphenidate osmotic-release oral system, and methylphenidate transdermal patch. Studies evaluated different amphetamine formulations, including amphetamine and dextroamphetamine mixed salts and lisdexamfetamine dimesylate. The NRI studies evaluated atomoxetine or extended-release viloxazine. The alpha agonist studies evaluated extended-release clonidine or extended-release guanfacine. The most commonly evaluated single medication was atomoxetine in the identified studies.

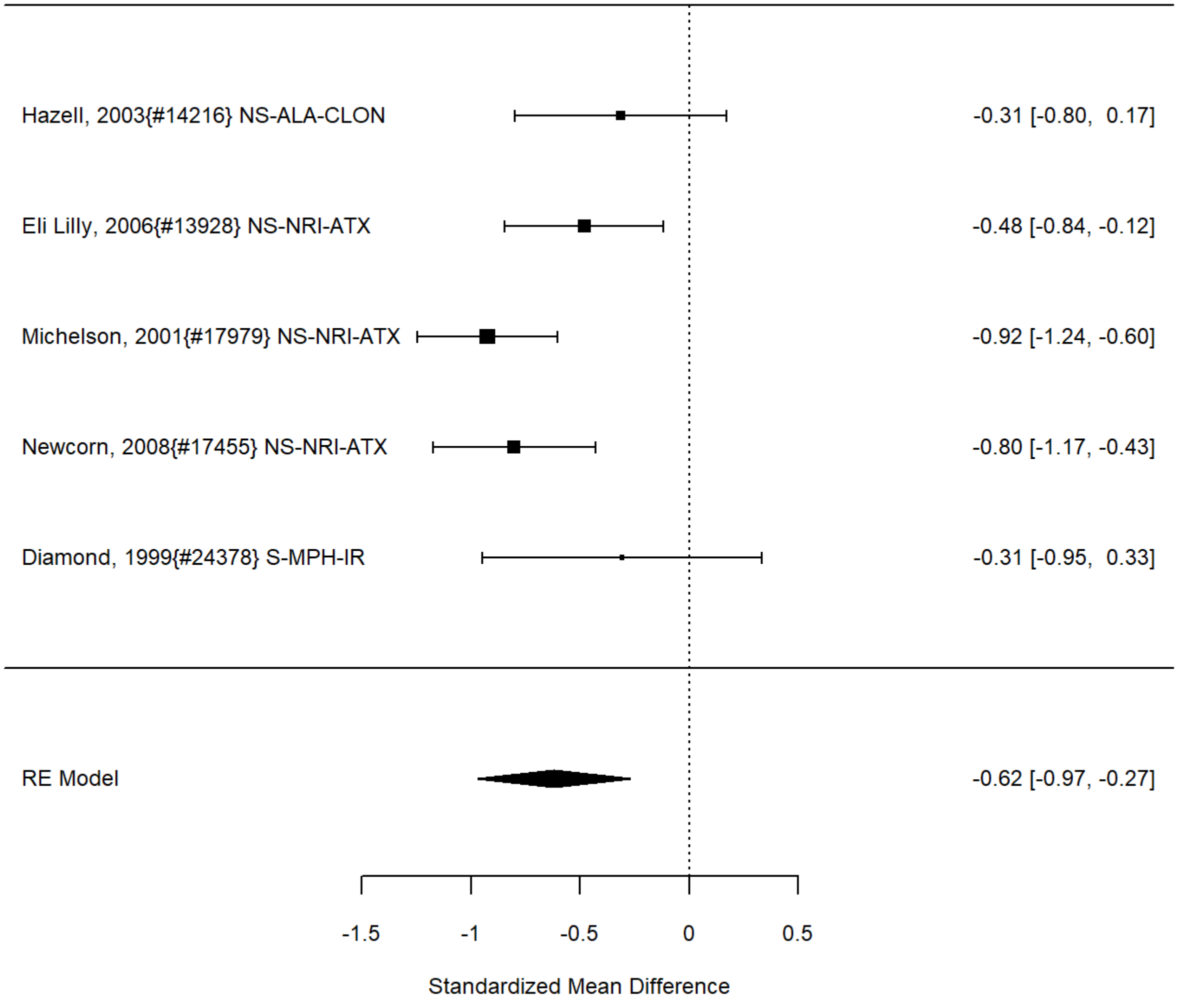
5. Results: Treatment of ADHD

Of the identified studies, the majority reported on the comparison to a control group not receiving the evaluated pharmacological treatment, and the large majority used a placebo to blind participants to the intervention allocation. Several studies provided methylphenidate as base treatment for the intervention and control group. Half of the identified studies reported on the effects of an alternative intervention, for example a different dose of the same medication or a different medication.

The following shows the effects of FDA-approved medication as a group of interventions given that whether or not subjecting children to regular medication use is a key question for parents, regardless of the pharmacological composition of the specific medication. The section is followed by a comparative effectiveness section to determine whether there are systematic differences between medication combinations (stimulants plus non-stimulants), the medications categories (stimulant or non-stimulant), drug classes (methylphenidate, amphetamine, NRIs, and alpha agonists), or individual medications (e.g., methylphenidate hydrochloride extended release, amphetamine and dextroamphetamine mixed salts, atomoxetine, or clonidine etc.).

Studies most frequently reported on ADHD symptom scale scores. Studies that reported on a control group with sufficient detail to allow effect size calculations for individual behavior changes (not already captured in broadband or symptom score measures) are shown in Figure 23. The forest plot is ordered by broad category (non-stimulant or stimulant), drug class (methylphenidate, amphetamine, NRIs, and alpha agonists, followed by the specific drug evaluated in the study (e.g., guanfacine).

Figure 23. Effects of FDA-approved pharmacologic ADHD treatment on behavior (SMD)

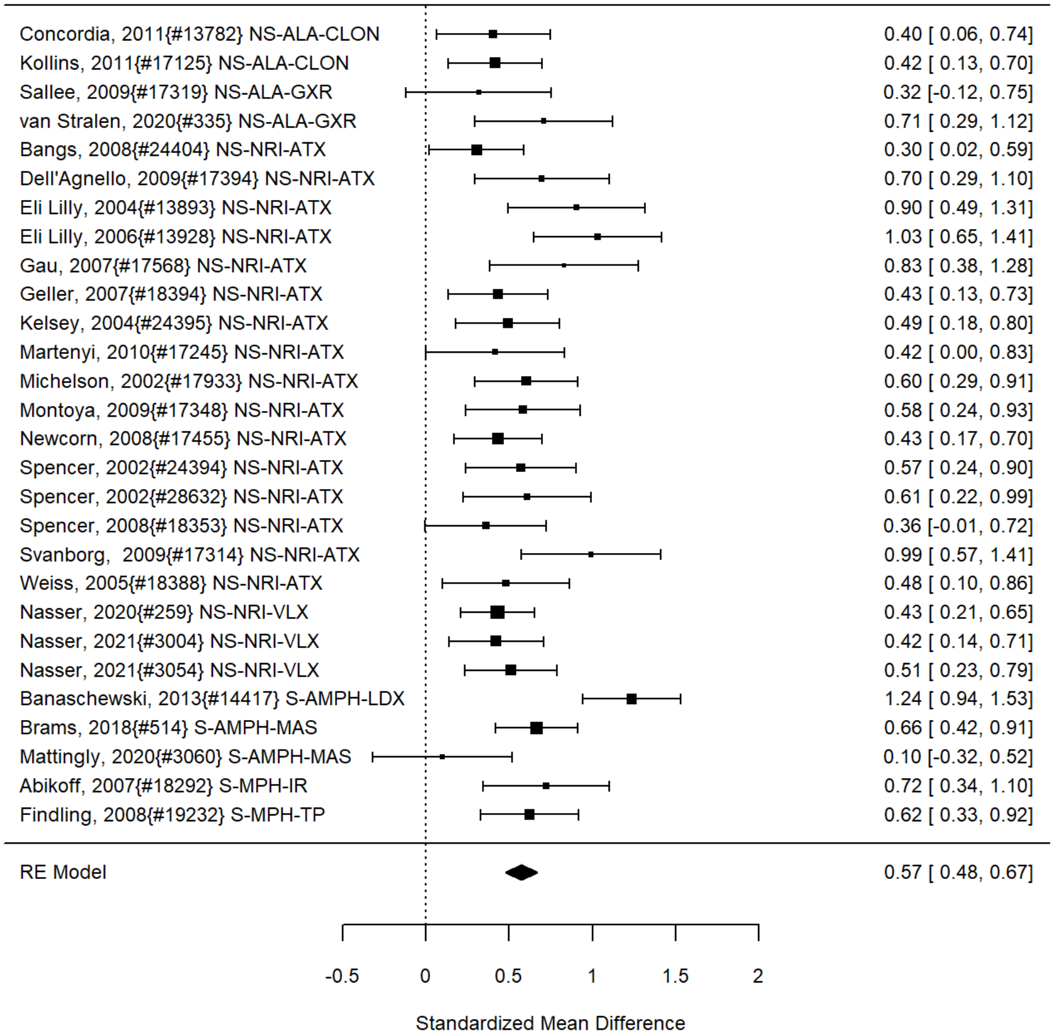


Notes: ADHD = attention deficit hyperactivity disorder, FDA = Food and Drug Administration, NS-NRI-ATX atomoxetine, NS-ALA-CLON clonidine, RE = random effects, S-MPH-IR immediate release methylphenidate, SMD = Standardized Mean Difference

Across studies, pharmacological interventions were associated with significant improvements in individual problem behaviors (SMD -0.62; CI -0.97, -0.27; 5 studies, n=561). The minimum age in the included studies was six years old. There was little evidence of heterogeneity (I-squared 45%). There was no indication of publication bias and none of the RCTs were judged to be high risk of bias. We identified one study reporting on a categorical variable based on a behavior measure and providing sufficient detail to allow effect size computation. The identified study evaluated the alpha-agonist clonidine adjunctive to psychostimulant medication[321]); the study reported positive results (RR 0.36; CI 0.17, 0.78; 1 study, n=66).

Multiple studies reported on a broadband measure (see key outcome section) describing the children's potential improvement on broader dimensions than specific ADHD symptoms, as shown in Figure 24.

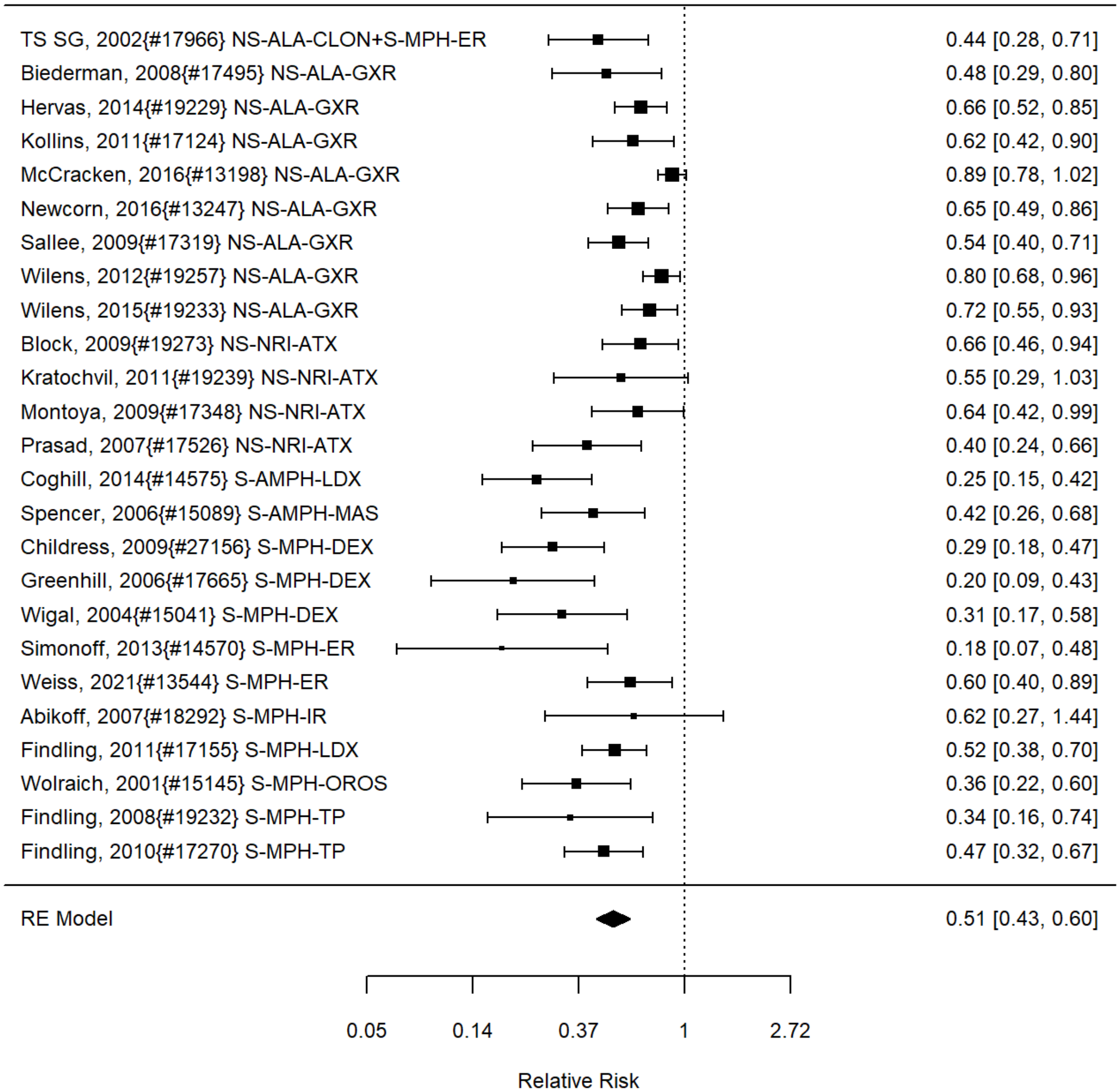
Figure 24. Effects of FDA-approved pharmacologic ADHD treatment on broadband measures (SMD)



Notes: ADHD = attention deficit hyperactivity disorder, FDA = Food and Drug Administration, NS-ALA-CLON = clonidine, NS-ALA-GXR = guanfacine, NS-NRI-ATX = atomoxetine, NS-NRI-VLX = viloxazine, S-AMPH-LDX = lisdexamfetamine dimesylate, S-AMPH-MAS = mixed amphetamine salts, S-MPH-IR = immediate release methylphenidate, S-MPH-TP = methylphenidate transdermal patch, RE = random effects, SMD = Standardized Mean Difference

Across studies, pharmacological treatment was associated with a systematic benefit on broadband scale assessments compared to control (SMD 0.57; CI 0.48, 0.67; 28 studies, n=4467). Only one study included children younger than six years old.[109] Studies assessed different medication regimes but analyses detected little heterogeneity (I-squared 50%). Large effects were reported in studies evaluating lisdexamfetamine dimesylate,[131] atomoxetine,[248] methylphenidate,[109] and extended-release guanfacine added to usual care stimulant therapy,[598] respectively. There was no evidence of publication bias. Removing six high-risk-of-bias RCTs in a sensitivity analysis found a smaller but also significant effect estimate (SMD 0.53; CI 0.38, 0.69), indicating that the documented treatment effect is not mainly based on biased studies. Multiple studies reported on broadband scale as a categorial outcome (e.g., criteria for improvement met or not) as shown in Figure 25.

Figure 25. Effects of FDA-approved pharmacologic ADHD treatment on broadband measures (RR)

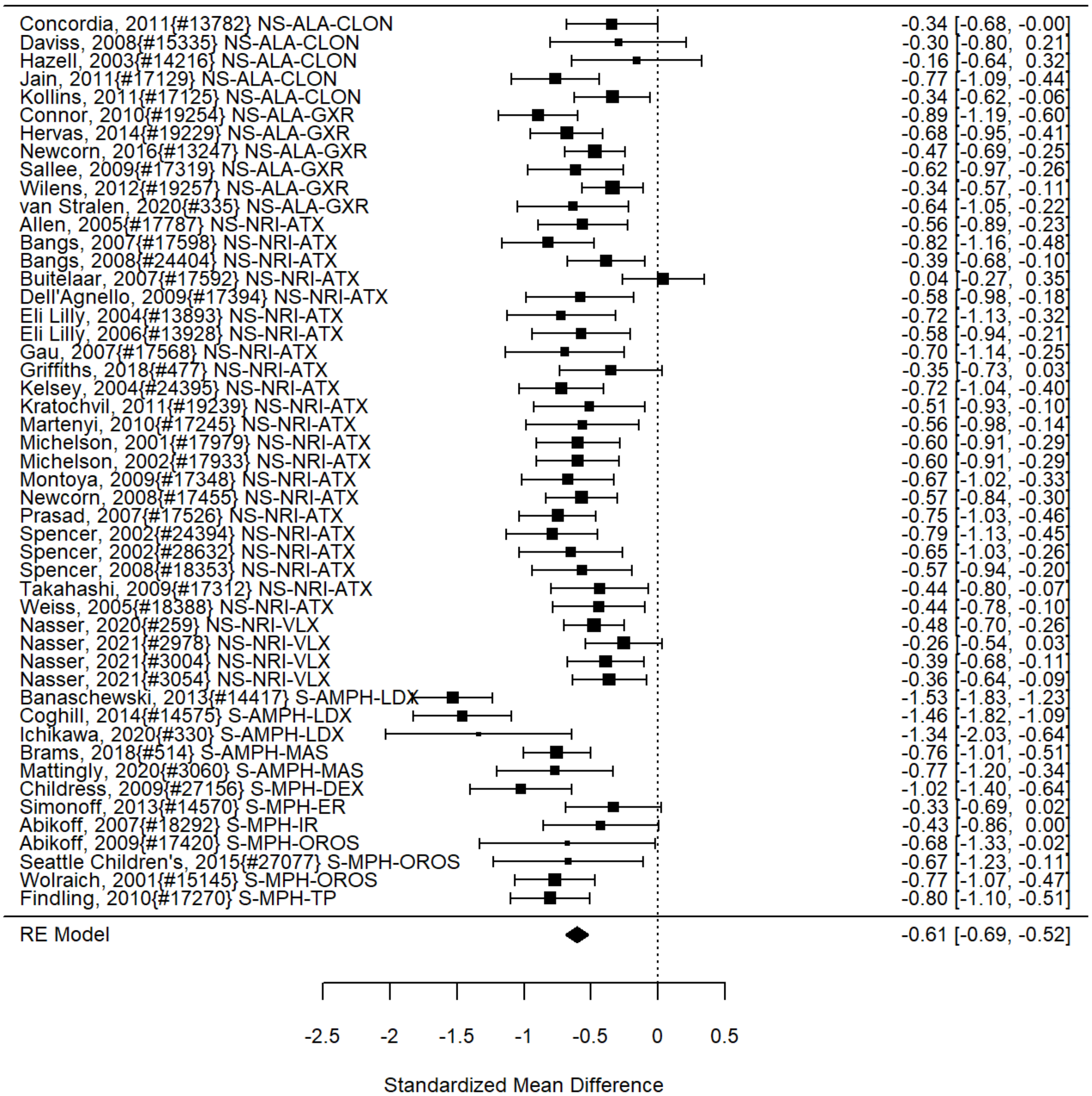


Notes: ADHD = attention deficit hyperactivity disorder, FDA = Food and Drug Administration, NS-ALA-CLON = clonidine, NS-ALA-GXR = guanfacine, NS-NRI-ATX = atomoxetine, RR = relative risk, S-AMPH-LDX = lisdexamfetamine dimesylate, S-AMPH-MAS = mixed amphetamine salts, S-AMPH-DEX = dexmethylphenidate, S-MPH-LDX = lisdexamfetamine, S-MPH-OROS = osmotic-release oral system methylphenidate, S-MPH-TP = methylphenidate transdermal patch, RE = random effects,

Across studies, results also indicated that pharmacological ADHD treatment was associated with a benefit in outcomes compared to control (RR 0.51; CI 0.43, 0.60; 25 studies, n=3959). Only two studies included children younger than 6 years old.[109, 378] Analyses detected some heterogeneity (I-squared 75%). There was evidence of publication bias (Begg p<0.001, Egger p<0.001) and an alternative estimate using the trim and fill method suggested a somewhat smaller effect (RR 0.62; CI 0.52, 0.74). When excluding six high-risk-of-bias RCTs in a sensitivity analysis, effect estimates were similar to the original effect (RR 0.49; CI 0.40, 0.59) and heterogeneity was not reduced (I-squared 80%). All studies reported on less than 12 months follow up with the exception of one study; the study found a significant improvement (SMD 4.74; CI 4.36, 5.13).[164]

A large number of studies reported on symptom improvements. Standardized mean differences are shown in Figure 26.

Figure 26. Effects of FDA-approved pharmacologic ADHD treatment on ADHD symptoms (SMD)

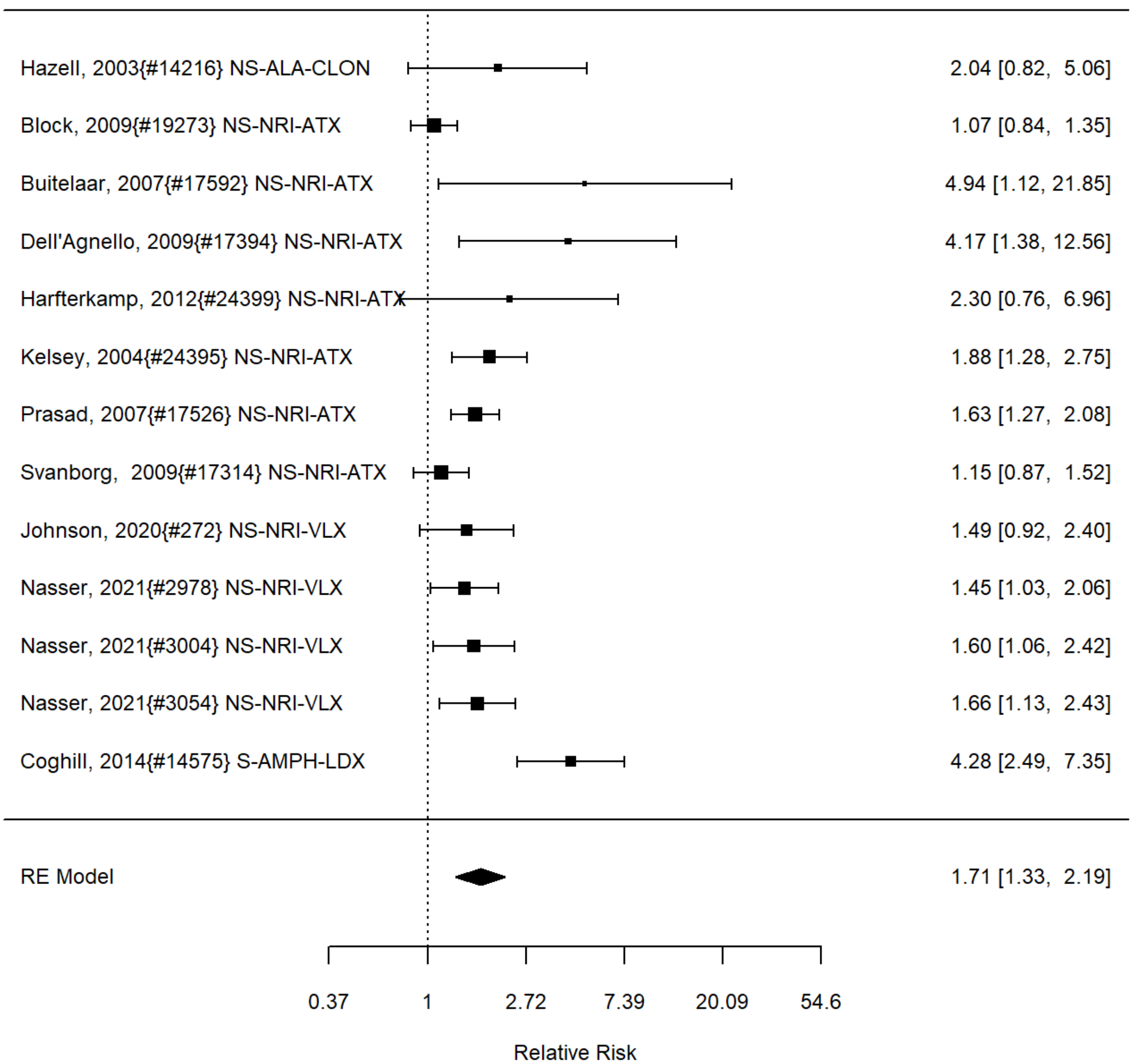


Notes: ADHD = attention deficit hyperactivity disorder, FDA = Food and Drug Administration, NS-ALA-CLON = clonidine, NS-ALA-GXR = guanfacine, NS-NRI-ATX = atomoxetine, NS-NRI-VLX = viloxazine, S-AMPH-LDX = lisdexamfetamine dimesylate, S-AMPH-MAS = mixed amphetamine salts, S-MPH-IR = immediate release methylphenidate, S-MPH-OROS = osmotic-release oral system methylphenidate, S-MPH-TP = methylphenidate transdermal patch, RE = random effects, SMD = Standardized Mean Difference

Across studies, pharmacological interventions for ADHD were associated with a systematic reduction in ADHD symptom scale scores compared to control (SMD -0.61; CI -0.69, -0.52; 49

studies, n=7685). Only two studies included children younger than six years old.[109, 378] There was some heterogeneity (I-squared 64%). Tests for publication bias were not statistically significant. Excluding nine high-risk-of-bias RCTs in a sensitivity analysis estimated similar symptom reductions, indicating that the result is not primarily driven by high-risk studies (SMD -0.60; CI -0.71, -0.49). Results for symptom measures used as categorical variables (e.g., number of improved children meeting a scale threshold) are shown in Figure 27.

Figure 27. Effects of FDA-approved pharmacologic ADHD treatment on ADHD symptoms (RR)



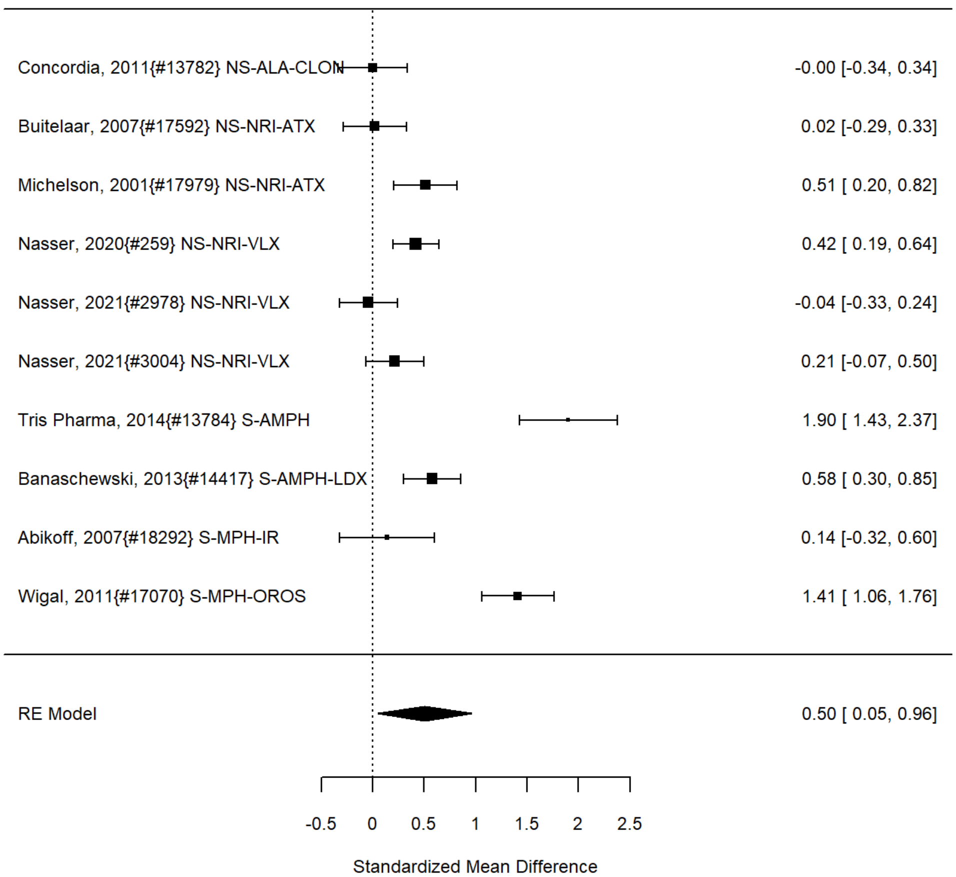
Notes: ADHD = attention deficit hyperactivity disorder, FDA = Food and Drug Administration, NS-ALA-CLON = clonidine, NS-NRI-ATX = atomoxetine, NS-NRI-VLX = viloxazine, RE = random effects, RR = relative risk, S-AMPH-LDX = lisdexamfetamine dimesylate

Results across studies also indicated a significant benefit (RR 1.71, CI 1.33, 2.19; 13 studies, n=1918). None of the studies included children under six years of age. There was some evidence of heterogeneity (I-squared 69%). There was also some evidence of publication bias (Begg p

0.02, Egger p 0.01). Applying the trim and fill method for an alternative estimate, effects were smaller (RR 1.45; CI 1.11, 1.88). When removing high-risk of bias RCTs in a sensitivity analysis, the treatment effect was similar to the main analysis (RR 1.79, CI 1.40, 2.30) and heterogeneity was further reduced, indicating that methodological rigor of the studies was one source of heterogeneity. Only one of the studies reported on a long-term outcome; the effect was not statistically significant (SMD 0.04; CI -0.27, 0.35).[164]

Some of the identified studies reported on functional outcomes as shown in Figure 28.

Figure 28. Effects of FDA-approved pharmacologic ADHD treatment on functional impairment (SMD)



Notes: ADHD = attention deficit hyperactivity disorder, FDA = Food and Drug Administration, NS-ALA-CLON = clonidine, NS-NRI-ATX = atomoxetine, NS-NRI-VLX = viloxazine, S-AMPH = amphetamine, S-AMPH-LDX = lisdexamfetamine dimesylate, S-MPH-IR = immediate release methylphenidate, S-MPH-OROS = osmotic-release oral system methylphenidate, RE = random effects, SMD = standardized mean difference

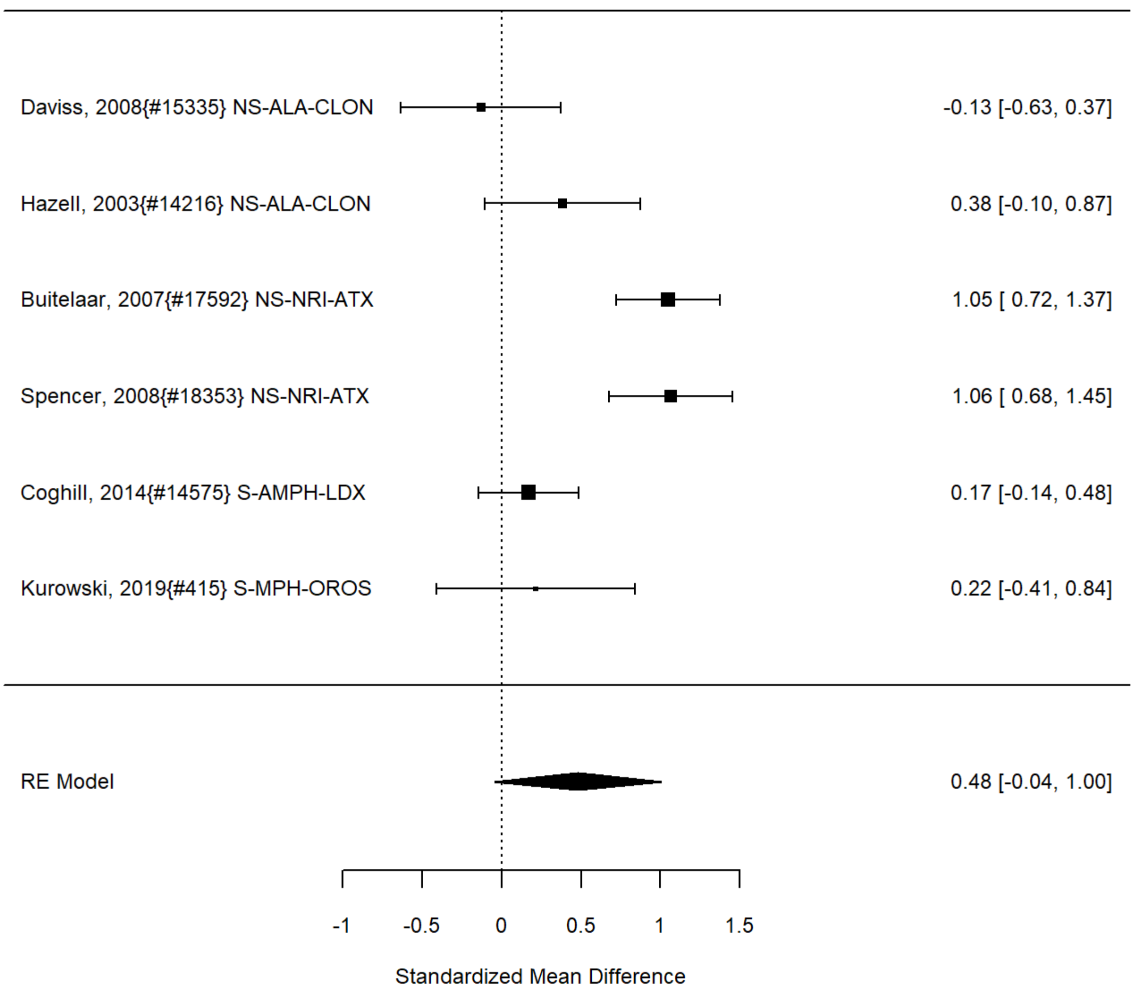
Across studies, treatment was associated with a decrease in functional impairment (SMD 0.50; CI 0.05, 0.96; 10 studies, n=1703). Only one study included children younger than six years old.[109] There was evidence of substantial heterogeneity (I-squared 93%). There was no evidence of publication bias. Excluding two high risk of bias RCTs in a sensitivity analysis did not change the effect (SMD 0.61; CI 0.05, 1.17) and heterogeneity was not reduced. We stratified studies by medication to determine whether the type of medication is a source of heterogeneity. There was some indication that heterogeneity was reduced in selected subgroups (amphetamines), but heterogeneity remained high in multiple subgroups and we did not identify broad treatment categories (stimulants, non-stimulants, the stimulant subtype amphetamines, NRIs, the NRI subtype atomoxetine) as a clear source of heterogeneity. The only study reporting a long-term effect was not statistically significant (SMD 0.02; CI -0.29, 0.33).[164]

We identified only one study that formally assessed treatment satisfaction for all study arms; it reported significant satisfaction with the alpha agonist treatment compared to placebo treatment (RR 0.47; CI 0.32, 0.68; 1 study, n=198).[207]

Only one study reported on academic performance; the study reported improvements in the methylphenidate compared to control group (SMD -1.37; CI -1.72, -1.03; 1 study, n=156) in the correct answers on the Permanent Product Measure of Performance.[618]

All studies reporting in sufficient detail on a continuous measure for appetite, weight or growth suppression that allowed us to compute measure-independent standardized mean differences are shown in Figure 29.

Figure 29. Effects of FDA-approved pharmacologic ADHD treatment on appetite suppression (SMD)

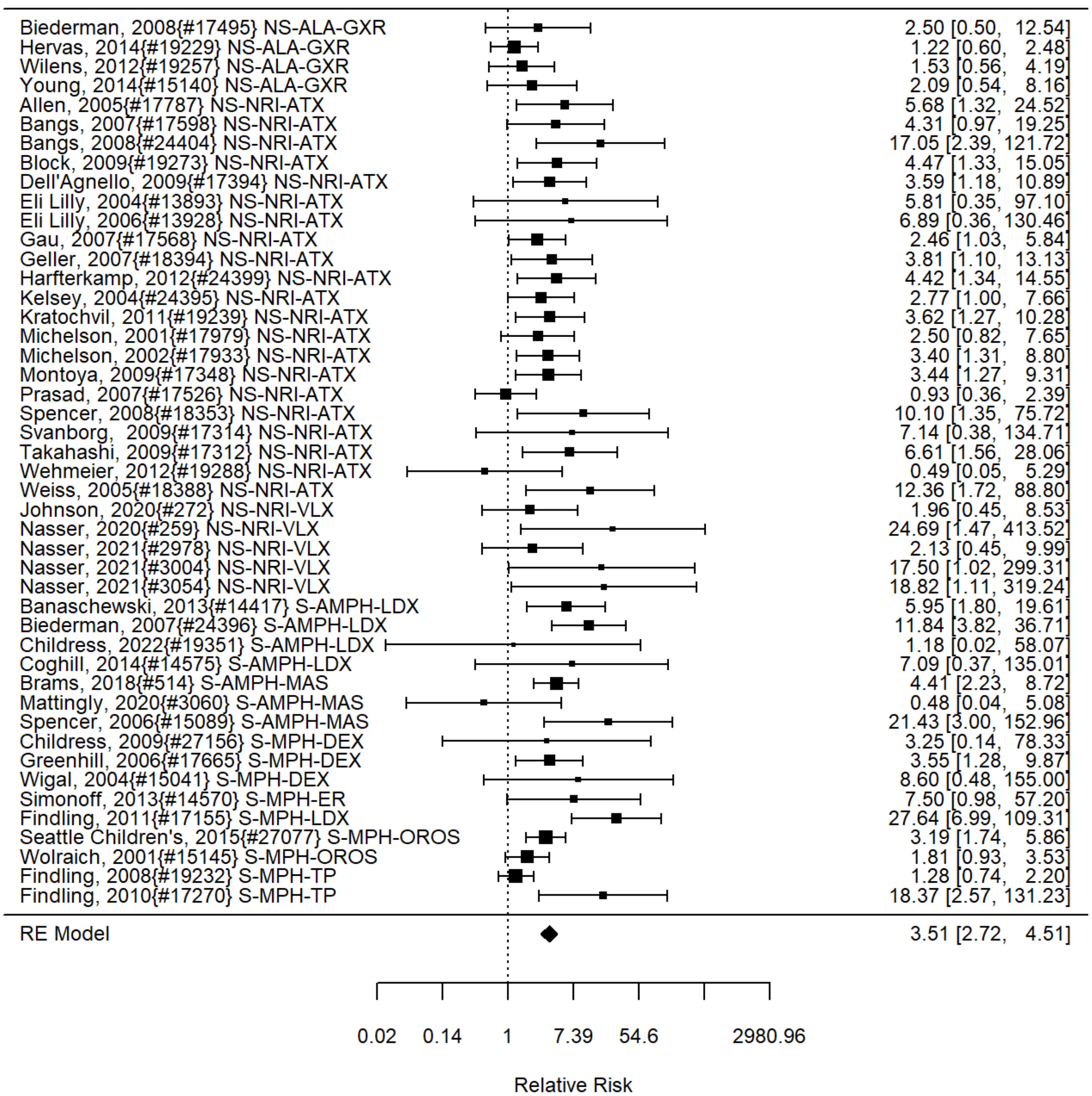


Notes: ADHD = attention deficit hyperactivity disorder, FDA = Food and Drug Administration, NS-ALA-CLON = clonidine, NS-NRI-ATX = atomoxetine, S-AMPH-LDX = lisdexamfetamine dimesylate, S-MPH-OROS = osmotic-release oral system methylphenidate, RE = random effects, SMD = standardized mean difference

5. Results: Treatment of ADHD

Across studies, pharmacological treatment indicated reduced appetite, but the effect was not statistically significant (SMD 0.48; CI -0.04, 1.00; 6 studies, n=605). There was evidence of heterogeneity (I-squared 82%). The analysis included stimulants and non-stimulants, but NRIs were only represented by atomoxetine and alpha agonists only by clonidine. Two atomoxetine studies reported a smaller increase in weight than children in the placebo group. Removing one high-risk-of-bias RCT in a sensitivity analysis did not change the finding (SMD 0.52; CI -0.13, 1.18) and heterogeneity was not reduced. We did not detect publication bias. A much larger number of studies reported on appetite suppression as a categorical measure (e.g., reported incidences per sample) indicating the number of patients reporting this adverse event as shown in Figure 30.

Figure 30. Effects of FDA-approved pharmacologic ADHD treatment on appetite suppression (RR)

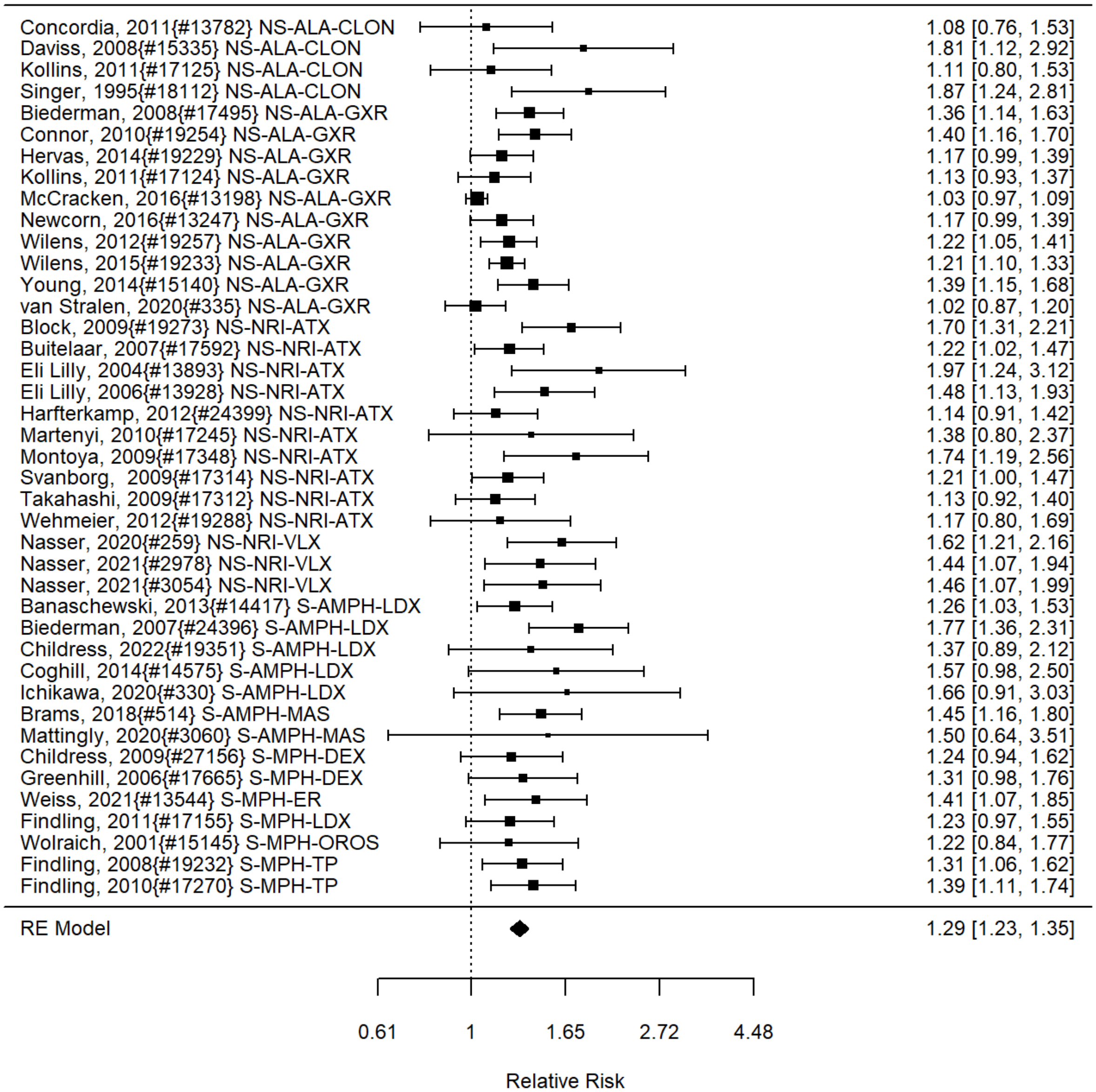


Notes: ADHD = attention deficit hyperactivity disorder, FDA = Food and Drug Administration, NS-ALA-GXR = guanfacine, NS-NRI-ATX = atomoxetine, NS-NRI-VLX = viloxazine, RE = random effects, RR = relative risk, S-AMPH-LDX = lisdexamfetamine dimesylate, S-AMPH-MAS = mixed amphetamine salts, S-MPH-DEX = dexmethylphenidate, S-MPH-OROS = osmotic-release oral system methylphenidate, S-MPH-TP = methylphenidate transdermal patch

Across studies, pharmacological treatment was associated with a suppression in appetite compared to control groups (RR 3.51; CI 2.72, 4.51; 46 studies, n=7209). Only two studies included children under the age of six.[194, 378] Heterogeneity was negligible (I-squared 41%). There was evidence of publication bias (Begg p 0.02, Egger p<0.002). An alternative treatment estimate using the trim and fill method suggested a somewhat smaller effect on appetite suppression (RR 2.66; CI 2.02; 3.50). When removing four high-risk-of-bias RCTs in a sensitivity analysis, effect estimates were similar to the main effect (RR 3.62; CI 2.77, 4.74). Only one of the studies evaluating appetite suppression reported on a long-term outcome, it indicated less weight increase compared to placebo (SMD 1.05; CI 0.72, 1.37).[164]

The number of participants experiencing any adverse event is documented in Figure 31.

Figure 31. Effects of FDA-approved pharmacologic ADHD treatment on number of participants with adverse events (RR)



Notes: ADHD = attention deficit hyperactivity disorder, FDA = Food and Drug Administration, NS-ALA-CLON = clonidine, NS-ALA-GXR guanfacine, NS-NRI-ATX = atomoxetine, NS-NRI-VLX = viloxazine, RE = random effects, RR = relative risk, S-AMPH-LDX = lisdexamfetamine dimesylate, S-AMPH-MAS = mixed amphetamine salts, S-MPH-DEX = dexmethylphenidate, S-MPH-IR = extended release methylphenidate, S-MPH-OROS = osmotic-release oral system methylphenidate, SMPH-TP = methylphenidate transdermal patch

Pharmacological interventions were associated with a higher risk of experiencing adverse events compared to control groups (RR 1.29; CI 1.23, 1.35; 41 studies, n=6926). None of the studies included children under the age of six. We detected only negligible heterogeneity (I-squared 47%). There was evidence of publication bias (Begg p 0.03, Egger p<0.001) and an alternative effect estimate using the trim and fill method suggested a smaller effect (RR 1.21; CI 1.15, 1.28). We also assessed in a sensitivity analysis whether results were mainly driven by high-risk-of-bias studies; estimates remained stable (RR 1.30; CI 1.23, 1.36) after excluding eight high-risk of bias RCTs and heterogeneity was reduced further. Only one of the identified studies reported a long-term effect; which showed more participants reporting adverse events in the intervention group compared to placebo (RR 1.22; CI 1.02, 1.47).[164]

5.3.2.1 FDA-Approved Pharmacologic ADHD Treatment Comparative Effects

We identified over 60 studies comparing pharmacological agents to an alternative treatment; however, comparators varied. Comparators were often different doses of the same medication, and some found a dose-response effect. For example, one study compared 200mg with 100mg of extended release viloxazine (an NRI) and reported improvement in both symptoms and functional impairment in both dosage groups, while the rate of children reporting decreased appetite was 7.5 percent in the 200mg group compared to 4.5 percent in the 100mg group.[453] The evidence table in the appendix shows results for dose comparisons in detail.

The following documents results of direct comparisons within head-to-head trials, followed by indirect comparisons across studies where possible.

5.3.2.1.1 Combined Effects: Non-Stimulants Plus Stimulants Versus Stimulants Alone

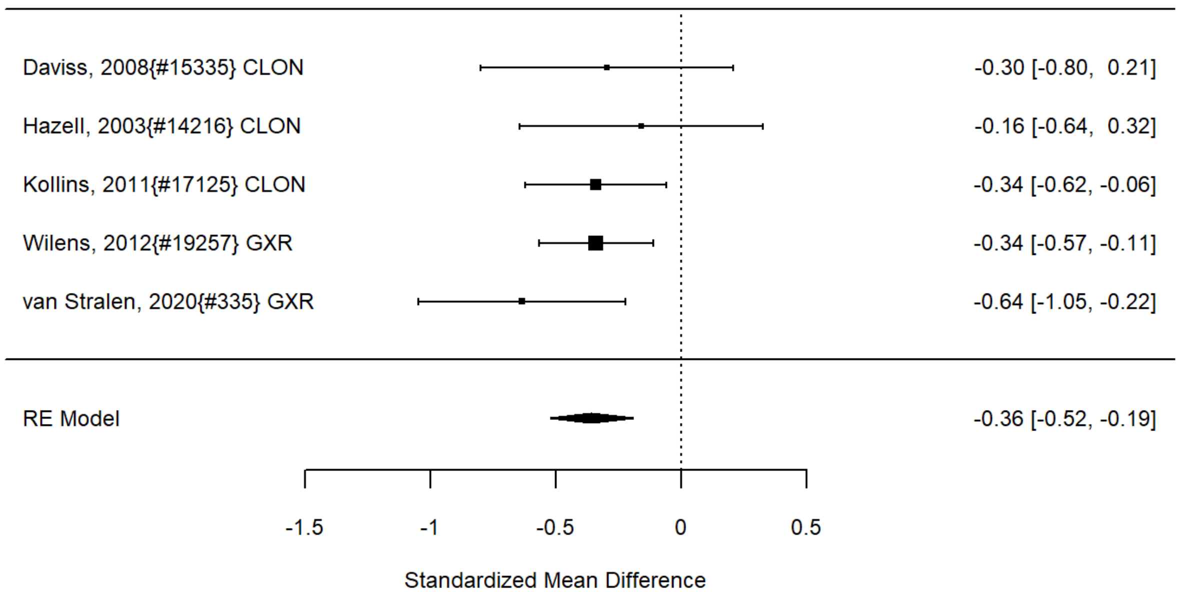
Several studies evaluated the effect of an intervention in samples already receiving treatment for ADHD. Most often the ongoing intervention was described as stimulant treatment. Hence, the group of tested non-stimulant evaluation studies included studies where participants were already receiving stimulants and the new therapy was assessed as an adjunctive treatment. The stimulant medication would be taken by both the intervention and control group participants. We systematically identified studies that augmented usual care with an additional treatment, and we determined in a meta-regression whether this intervention-comparator combination affects the treatment effects. We were particularly interested in whether medication *add-on* trials reported systematically different results from other studies. This could be either a specific stimulant, such as methylphenidate, or stimulants not further described. Often the stimulant dose was either not known, or it varied by participant based on the usual care arrangement. Most analyses for the outcomes of interest were not statistically significant: behavior (p 0.33), broadband measures (continuous p 0.81 categorical p 0.14), appetite suppression (continuous p 0.28, categorical p 0.24), participants reporting adverse events (p 0.14). For other outcomes, there were insufficient studies for the comparison (functional impairment, treatment satisfaction, academic performance). However, for ADHD symptoms using continuous outcome variables, there was indication that the effect estimate depended to some extent on whether participants were already receiving stimulants (p 0.048). The effect was not found for categorical outcome measures (p 0.77). The following analyses report on the subgroup of studies that augmented stimulant medication with a non-stimulant.

We identified one study that compared clonidine plus stimulants versus stimulants alone and that reported on a problem behavior; the study favored the combination (RR 0.36; CI 0.17, 0.78; 1 study, n=66).[321]

Two studies reported on a continuous broadband measure, but since the reported effects varied, no meaningful summary for the augmentation could be determined (SMD 0.52; CI -1.26, 2.30; 2 studies, n=292).[373, 598] However, a single study found that adjuvant treatment with guanfacine was associated with a statistically significantly greater number of improved participants (RR 0.80; CI 0.68, 0.95; 1 study, n=303).[622]

Results for ADHD symptoms for the subgroup of non-stimulants are shown in Figure 32.

Figure 32. Subgroup analysis: Non-stimulants (all alpha agonist) plus stimulants versus stimulants alone on ADHD symptoms (SMD)



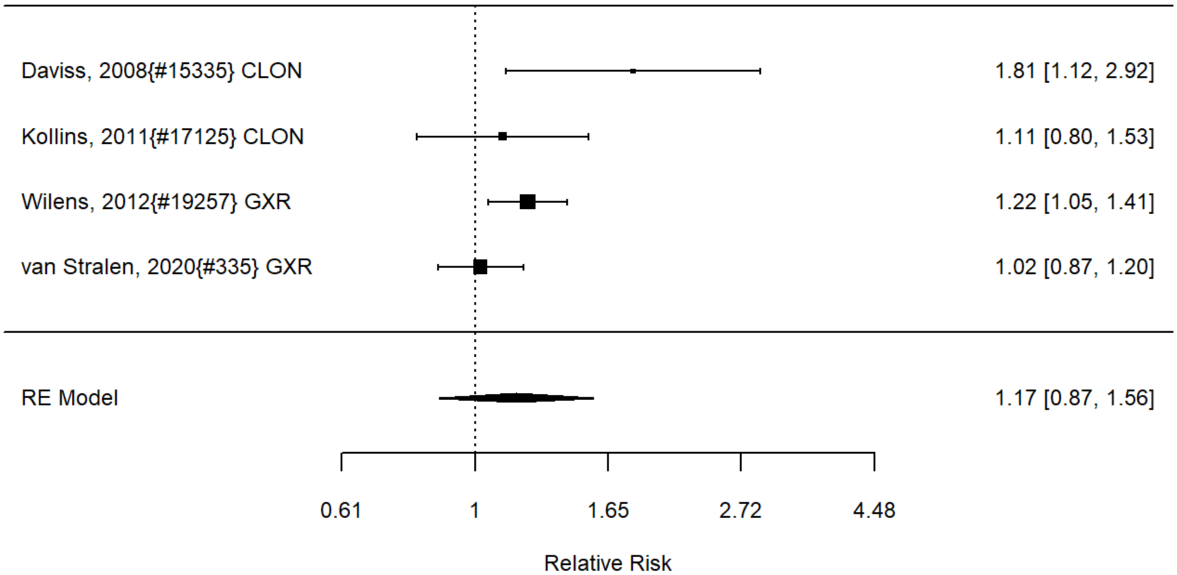
Notes: ADHD = attention deficit hyperactivity disorder, CLON = clonidine, GXR = guanfacine, RE = random effects, SMD = standardized mean difference

Across studies, non-stimulant augmentation (all studies used alpha agonists) of stimulants found a statistically significant effect for ADHD symptoms across studies (SMD -0.36; CI -0,52, -0.19; 5 studies, n=724). Only one study evaluated an add-on trial reporting on a categorical symptom outcome; the study did not detect a systematic difference (RR 2.04; CI 0.82, 5.06; 1 study, n=66).[321]

This subgroup of studies did not assess functional outcomes, treatment satisfaction, or academic performance. And although some of the studies reported on appetite suppression, the two studies that reported on a continuous outcome reported conflicting results and no meaningful summary estimate could be derived (SMD 0.13; CI -03.12, 3.39; 2 studies, n=128).[217, 321] The single study reporting a categorical outcome did not detect a statistically significant difference between treatment arms (RR 1.52; CI 0.56, 4.19; 1 study, n=303).[622]

Figure 33 shows the effects of non-stimulants plus stimulants versus stimulants alone on the number of participants with adverse events.

Figure 33. Subgroup analysis: Non-stimulants (all alpha agonist) plus stimulants versus stimulants alone on participants with adverse events (RR)



Notes: ADHD = attention deficit hyperactivity disorder, CLON = clonidine, GXR = guanfacine, RE = random effects, RR = relative risk

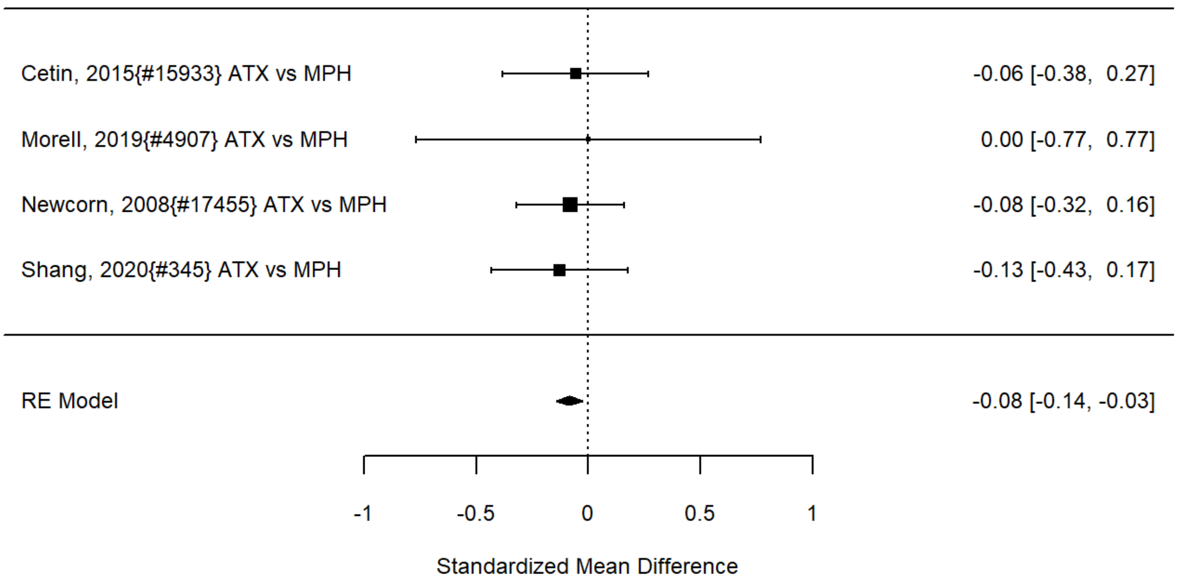
Across studies, we detected no systematically different effect of the combination treatment on appetite suppression compared to stimulant alone (RR 1.17; CI 0.87, 1.56; 4 studies, n=657).

5.3.2.1.2 Medication Category Comparison: Non-Stimulants Versus Stimulants

We also differentiated the included studies into those assessing the effects of non-stimulants and stimulant medications. We reviewed direct comparisons of a non-stimulant with a stimulant as well as meta-regressions using indirect comparisons. The indirect comparisons aimed to detect whether studies comparing non-stimulants versus control reported statistically significantly different results from stimulants versus control.

Non-stimulants versus stimulants in direct, head-to-head comparisons within identified studies for individual problem behaviors are shown in Figure 34.

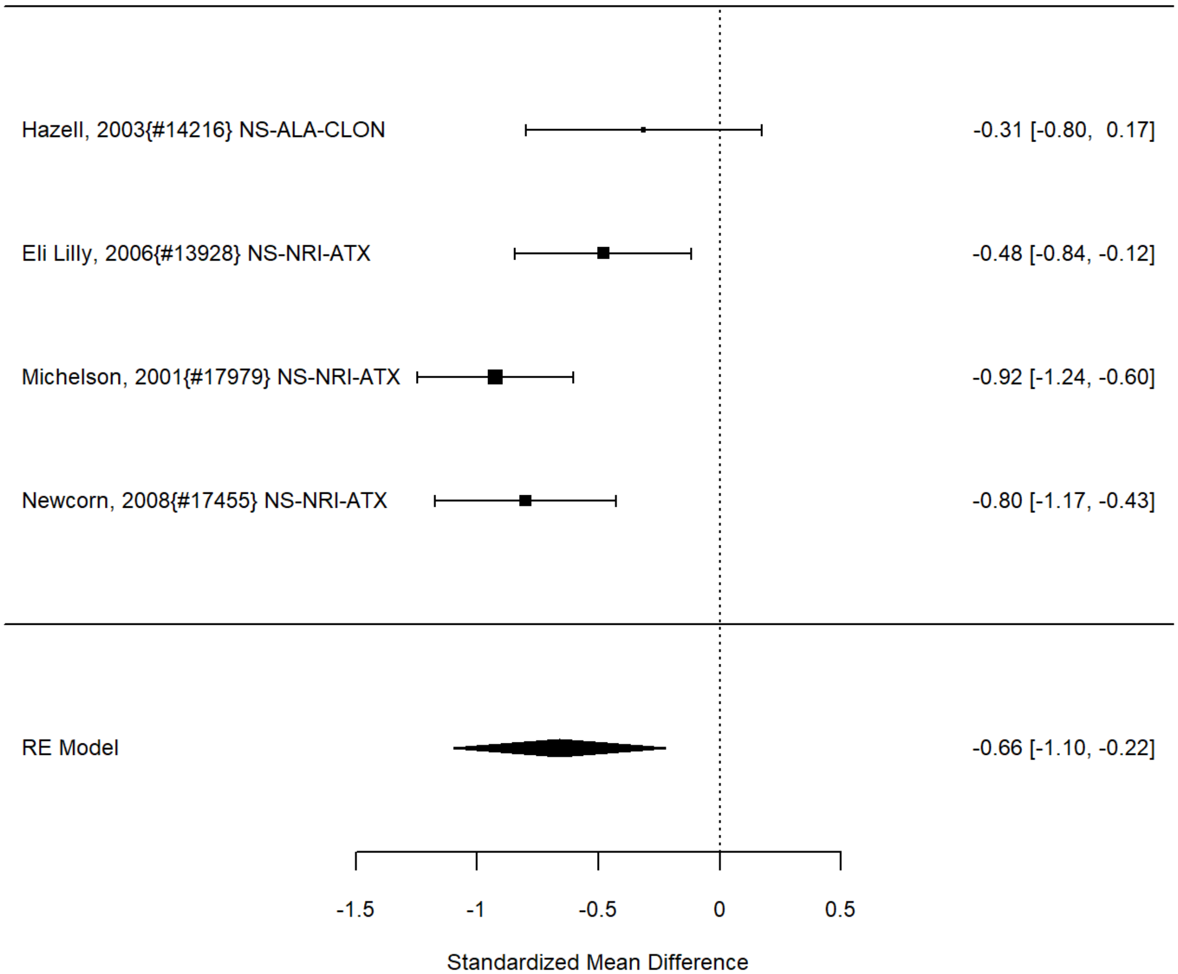
Figure 34. Comparison: Non-stimulants (all SNR, all atomoxetine) versus stimulants (all methylphenidate) on problem behaviors (SMD)



Notes: ATX = atomoxetine, MPH = methylphenidate, RE = random effects, SMD = standardized mean difference, SNR = serotonin and norepinephrine reuptake inhibitors

Across comparative effectiveness studies, non-stimulants (all NRIs) were slightly but statistically significantly associated with more reductions in individual problem behavior compared to stimulants (SMD -0.08; CI -0.14, -0.03; 4 studies, n=608); all studies compared atomoxetine versus methylphenidate specifically rather than the full range of non-stimulant or stimulant medications. None of the studies included children under the age of six. The analysis did not detect heterogeneity or evidence of publication bias. However, removing all high-risk of bias studies left only two studies, which individually did not detect a systematic difference between atomoxetine versus methylphenidate (SMD -0.10; CI -0.40, 0.20). There were insufficient studies reporting on the outcome for indirect comparisons between non-stimulant and stimulant studies. Given the difference between medications shown in the head-to-head trials, Figure 35 reports a subgroup analysis for non-stimulants on problem behavior.

Figure 35. Subgroup analysis: Non-stimulants versus control on problem behavior (SMD)

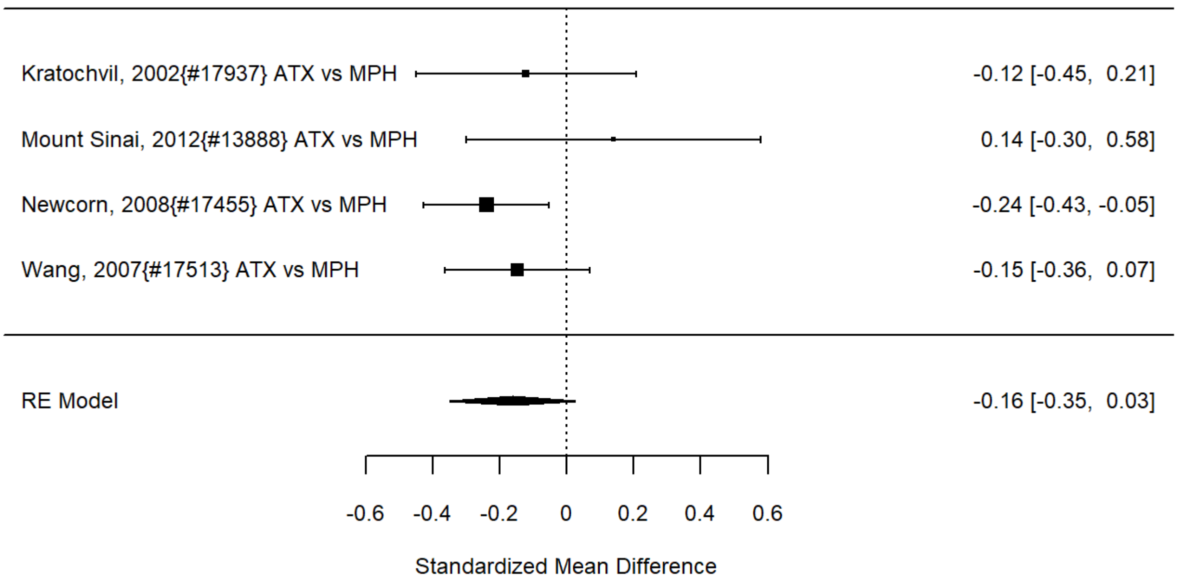


Notes: NRI = norepinephrine reuptake inhibitors, NS-NRI-ATX = atomoxetine, NS-ALA-CLON = clonidine, RE = random effects, SMD = standardized mean difference

In the subgroup of non-stimulant studies, treatment was associated with a reduction in problem behavior compared to placebo (SMD -0.66; CI -1.10, -0.22; 4 studies, n=523). However, only atomoxetine, one of the two approved NRIs for the treatment of ADHD, and clonidine, one of two approved alpha agonists, contributed to the analysis. We identified only one study that compared stimulants alone to a control group; the study did not detect a systematic difference between immediate release methylphenidate and placebo (SMD 0.31; CI -0.33, 0.95; n=91).[224]

Results for broadband measures in the comparison of non-stimulants versus stimulants are shown in Figure 36; all studies compared atomoxetine with methylphenidate medications.

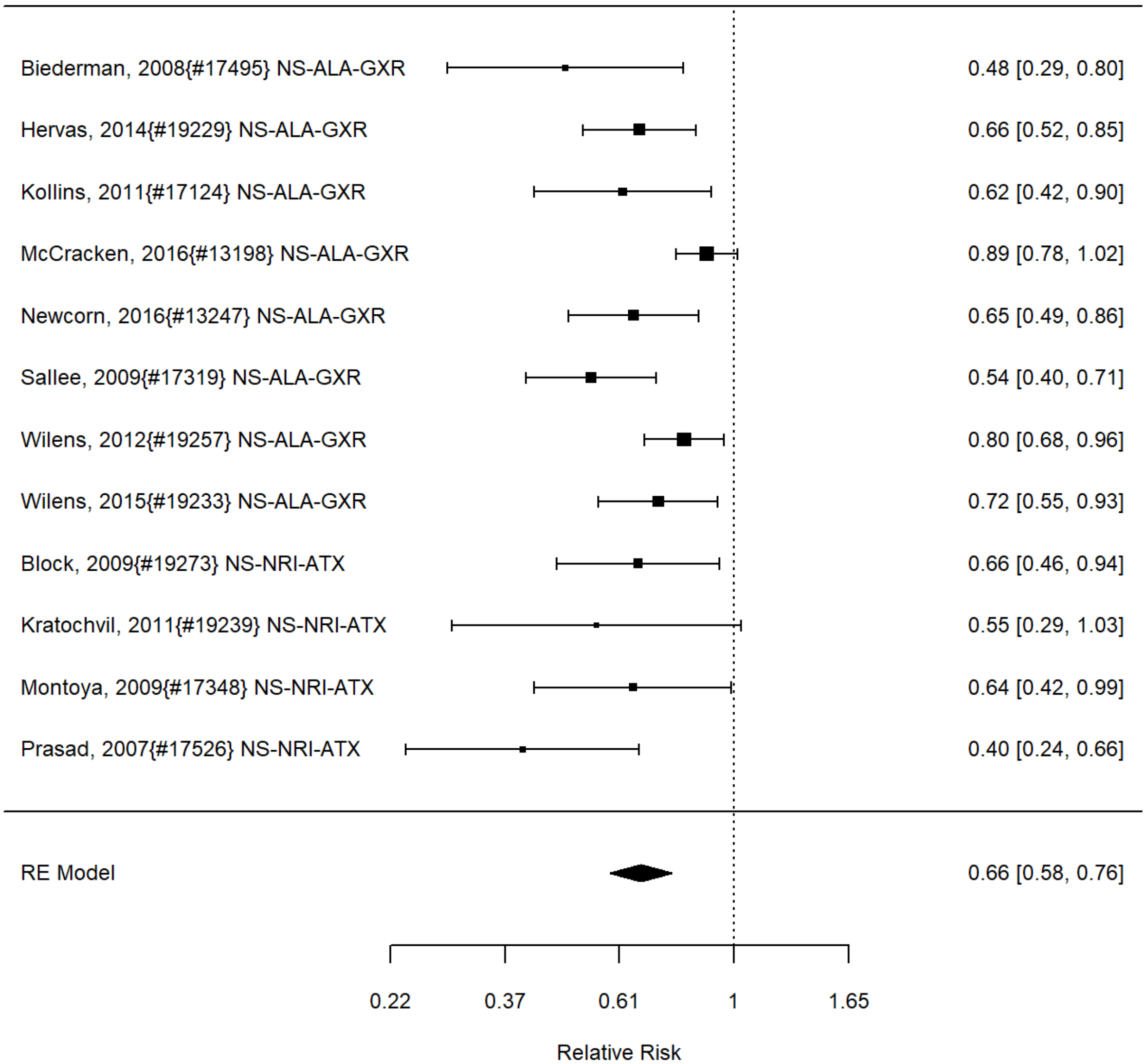
Figure 36. Comparison: Non-stimulants (all NRIs, all atomoxetine) versus stimulants (all methylphenidate) on broadband measures (SMD)



Notes: NRI = norepinephrine reuptake inhibitors, NS-NRI-ATX atomoxetine, MPH methylphenidate, RE = random effects, SMD = standardized mean difference

Across studies, we did not detect a systematic difference between stimulants and non-stimulants for continuous broadband measure outcomes (SMD -0.16; CI -0.35, 0.03; 4 studies, n=1080); all studies compared the NRI atomoxetine versus methylphenidate medications.[376, 460, 539, 604] Other stimulants (amphetamine) and non-stimulants (alpha agonists) could not be added to the analysis, due to lack of studies. We did not detect heterogeneity or evidence of publication bias in this analysis. Removing all high-risk of bias studies left only one study that reported a similar effect estimate (SMD -0.15; CI -0.37, 0.06).[604] We also assessed in indirect comparisons whether the subgroup of studies evaluating non-stimulants versus studies evaluating stimulants reported different effect sizes (both compare the intervention against a control group, rather than comparing the two drug classes directly). We did not detect differences for continuous outcomes in this analysis (p 0.88). We identified only one study that reported on a categorical assessment of a broadband impression; the study found no difference between non-stimulants and stimulants (RR 1.01; CI 0.75, 1.37; 1 study, n=237); the study compared the NRI atomoxetine versus methylphenidate medication specifically.[568] However, a meta-regression for categorical broadband measures indicated a statistically significant difference between results reported in non-stimulant versus stimulant studies (p 0.0002). Figure 37 shows the subgroup analysis results for non-stimulants.

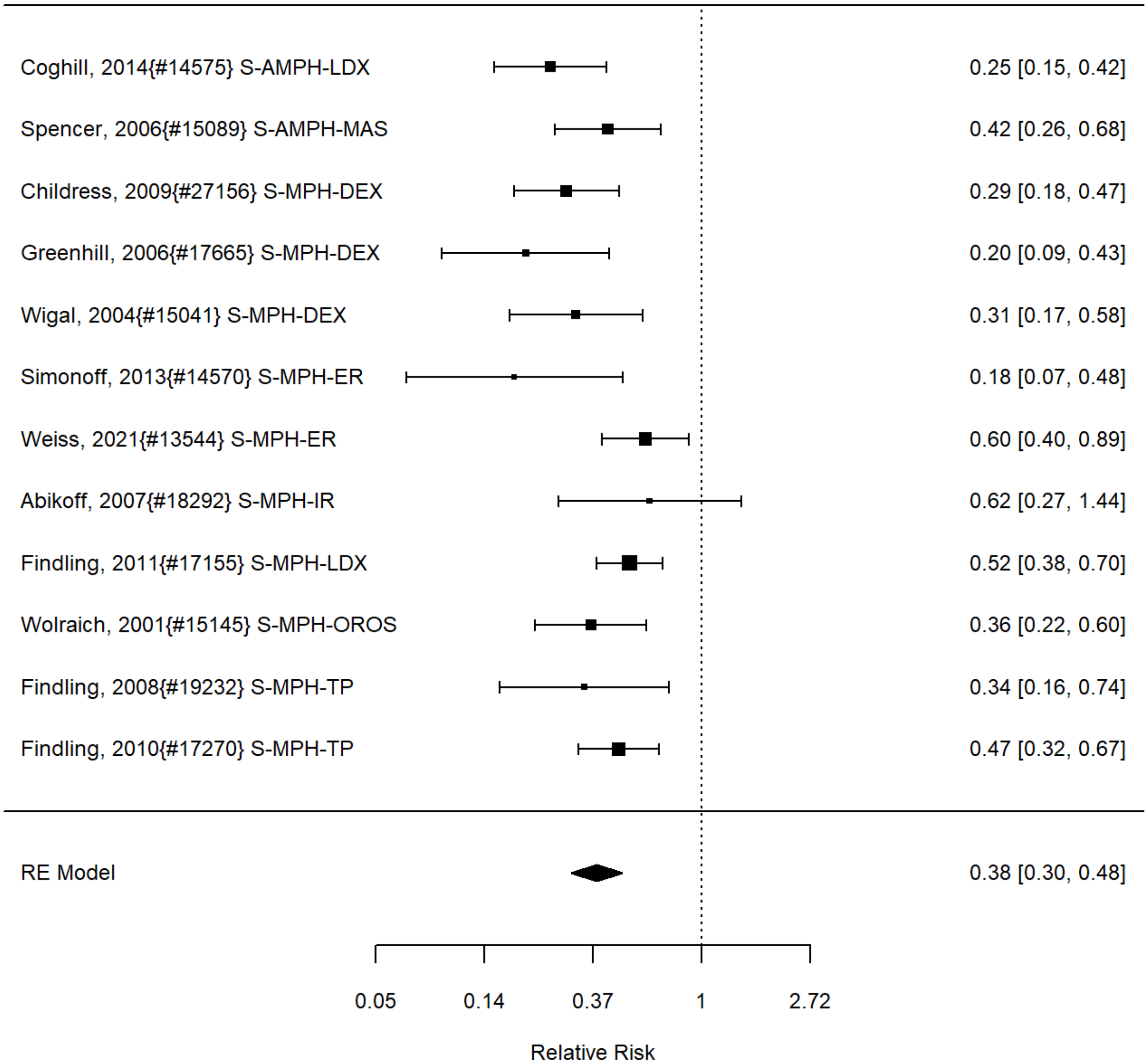
Figure 37. Subgroup analysis: Non-stimulants versus control on broadband measures (RR)



Notes: NS-NRI-ATX = atomoxetine, NS-ALA-GXR = guanfacine, RE = random effects, RR = risk ratio

In the subgroup of non-stimulant studies, treatment was associated with a reduction in broadband measures, but the effect was smaller than for stimulants (RR 0.66; CI 0.58, 0.76; 12 studies, n=2312). Only two out of four FDA-approved non-stimulant medications (atomoxetine, guanfacine) contributed to the analysis. Only one of the studies in this subgroup included children under the age of 6.[378] The subgroup analysis of stimulant studies is shown in Figure 38.

Figure 38. Subgroup analysis: Stimulants versus control on broadband measures (RR)

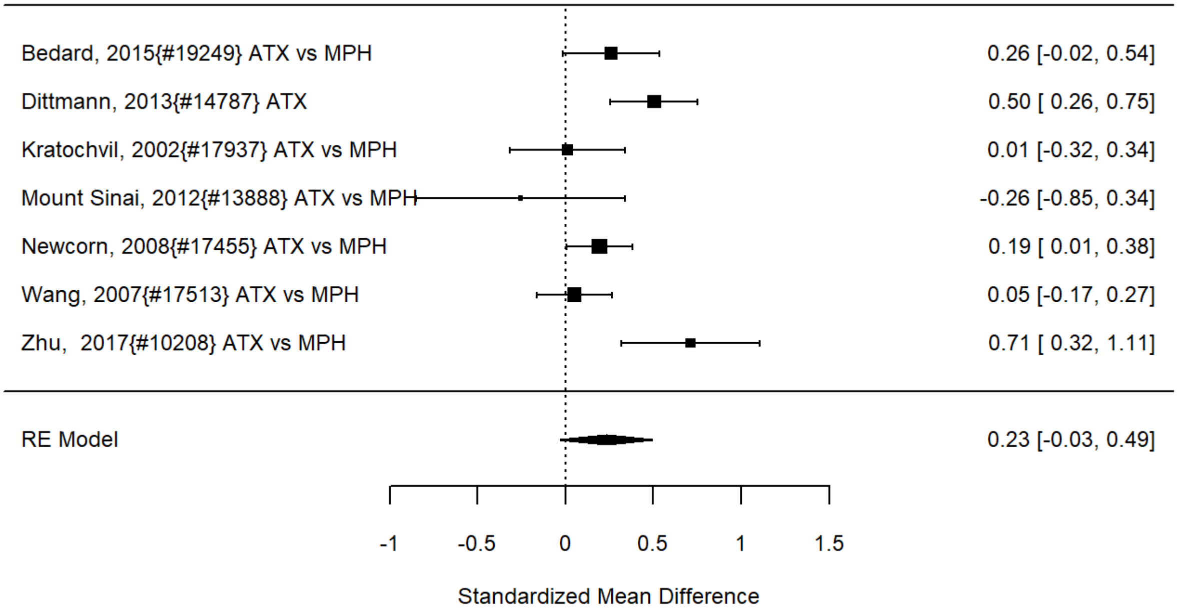


Notes: RE = random effects, RR = relative risk, S-AMPH-DEX = dexmethylphenidate, S-AMPH-LDX = lisdexamfetamine dimesylate, S-AMPH-MAS = mixed amphetamine salts, S-MPH-ER = extended-release methylphenidate, S-MRH-IR = immediate release methylphenidate, S-MPH-OROS = osmotic-release oral system methylphenidate, S-MPH-TP = transdermal patch methylphenidate

The effect estimate for stimulant studies showed a clear effect for individual studies and across studies in this medication subgroup (RR 0.38; CI 0.30, 0.48; 12 studies, n=1582). Only one study included children younger than six years old.[109]

A large number of studies reported on ADHD symptoms, and we identified a number of head-to-head comparisons. The analysis comparing non-stimulants versus stimulants for ADHD symptoms is shown in Figure 39.

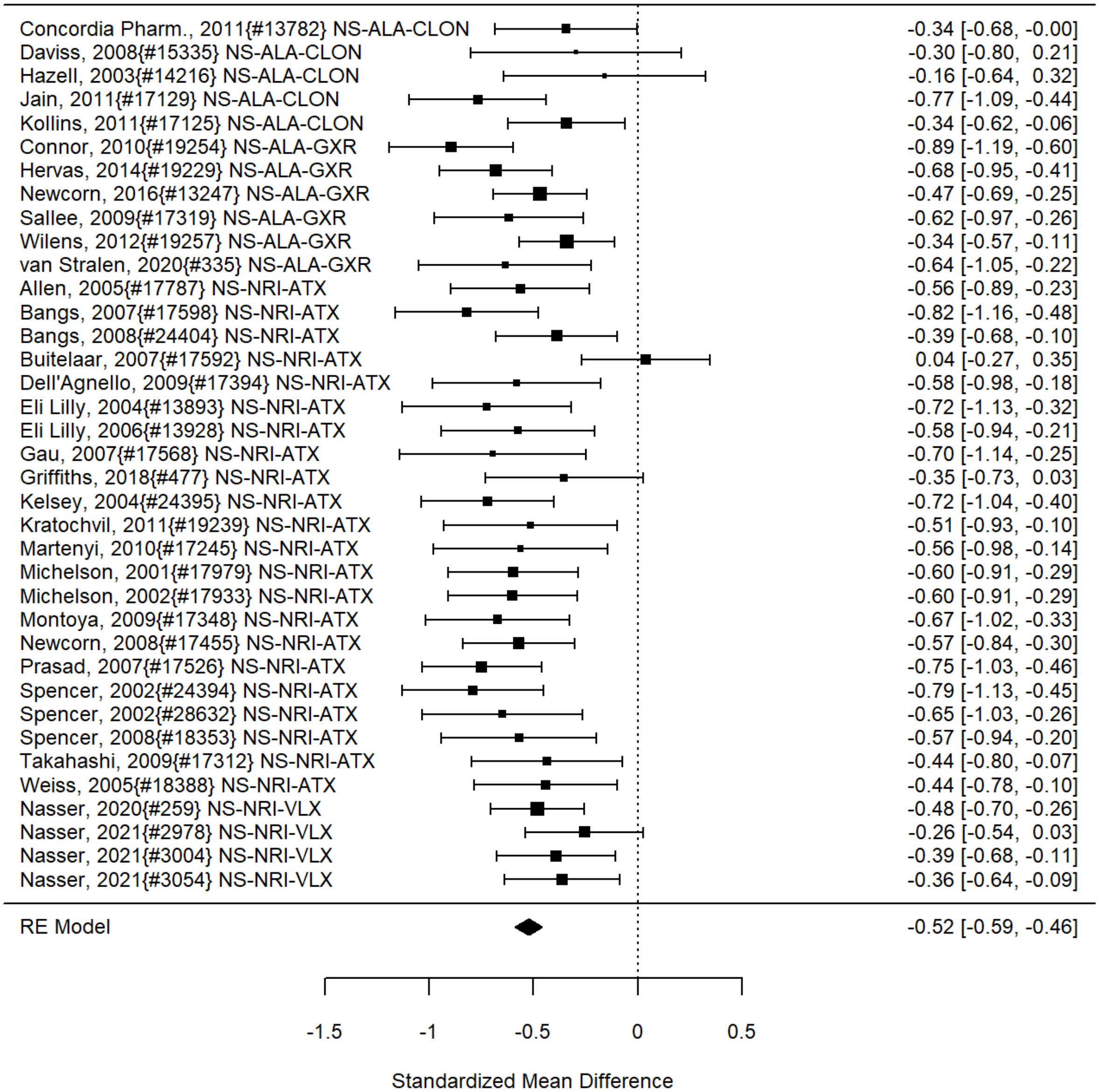
Figure 39. Comparison: Non-stimulants (all NRI) versus stimulants on ADHD symptoms (SMD)



Notes: ATX = atomoxetine, MPH = methylphenidate, one study not comparing against MPH compared to lisdexamfetamine dimesylate, NRI = norepinephrine reuptake inhibitors, RE = random effects, SMD = standardized mean difference

Although more studies favored stimulants, across studies, we did not detect a systematic difference between non-stimulants (all NRI) versus stimulants (different methylphenidate medications in all but one case) in direct comparisons for ADHD symptoms (SMD 0.23; CI -0.03, 0.49; 7 studies, n=1611). We detected some heterogeneity (I-squared 69%) in this analysis. There was no evidence of publication bias. Removing all high-risk of bias studies left three studies that also found no systematic difference between interventions (SMD 0.28; CI -0.54, 1.10). However, we also analyzed whether indirect comparisons between non-stimulant versus stimulant studies indicate systematic differences, and we found a statistically significant difference (p 0.0002). The effect estimates for the subgroups are documented in the following section. Figure 40 shows the subgroup analysis for non-stimulants reporting on ADHD symptoms.

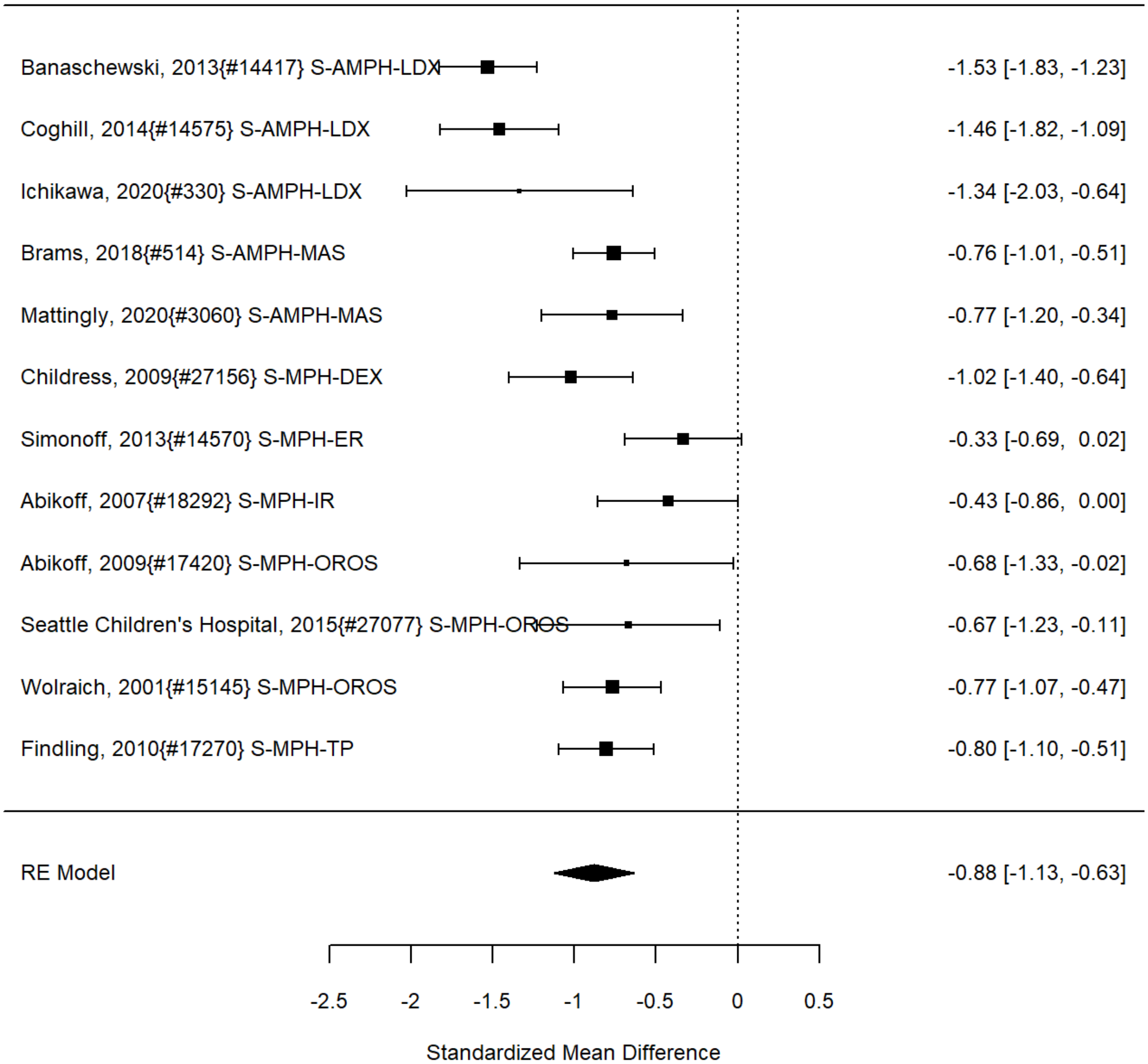
Figure 40. Subgroup analysis: Non-stimulants versus control on ADHD symptoms (SMD)



Notes: ADHD = attention deficit hyperactivity disorder, NS-NRI-ATX = atomoxetine, NS-ALA-CLON = clonidine, NS-ALA-GXR = guanfacine, NS-NRI-VLX = viloxazine, RE = random effects, SMD = standardized mean difference

In the subgroup of non-stimulant studies, results were associated with a reduction in ADHD symptoms measured as a continuous variable (SMD -0.52; CI -0.59, -0.46; 37 studies, n=6065). Only one study included children younger than six years old.[378] Results for the subgroup of stimulant studies on ADHD symptoms are shown in Figure 41.

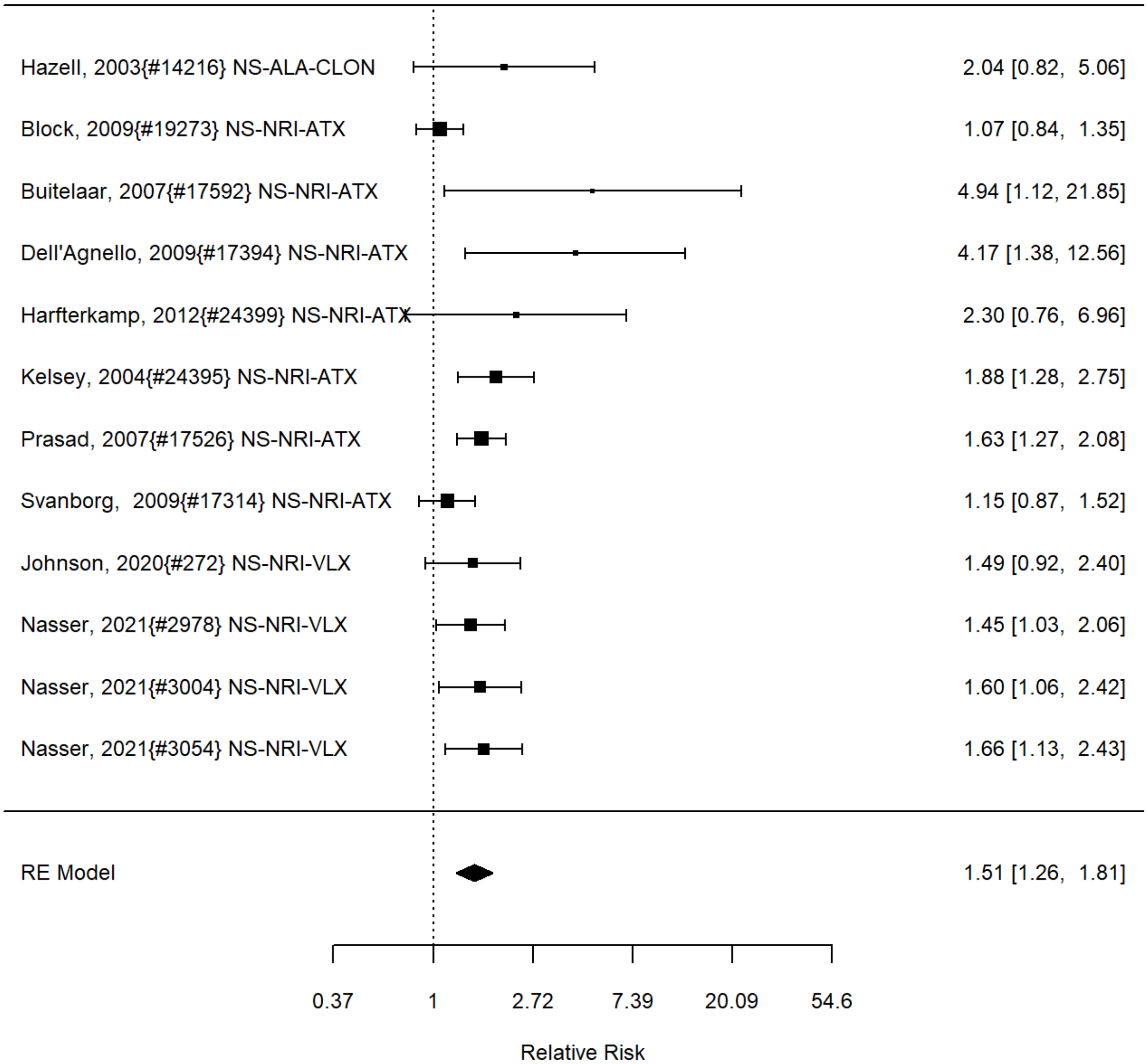
Figure 41. Subgroup analysis: Stimulants versus control on ADHD symptoms (SMD)



Notes: ADHD = attention deficit hyperactivity disorder, S-AMPH-LDX = lisdexamfetamine, S-AMPH-MAS = mixed amphetamines salts, S-MPH-DEX = dexmethylphenidate, S-MPH-ER = extended release methylphenidate, S-MPH-IR = immediate release methylphenidate, S-MPH-OROS = osmotic-release oral system methylphenidate, S-MPH-TP = dermal patch methylphenidate, RE = random effects, SMD = standardized mean difference

In the subgroup of stimulant studies, treatment was associated with a substantial reduction in ADHD symptoms (SMD -0.88; CI -1.13, -0.63; 12 studies, n=1620). Only one study included children younger than six years old.[109] None of the direct, head-to-head trials reported on symptom improvement as a categorical measure (e.g., treatment response vs not). An indirect comparison suggested that non-stimulant versus stimulant studies report statistically significantly different results for categorical ADHD symptom measures (p 0.02). The subgroups are shown separately in Figure 42 and Figure 43.

Figure 42. Subgroup analysis: Non-stimulants versus control on ADHD symptoms (RR)

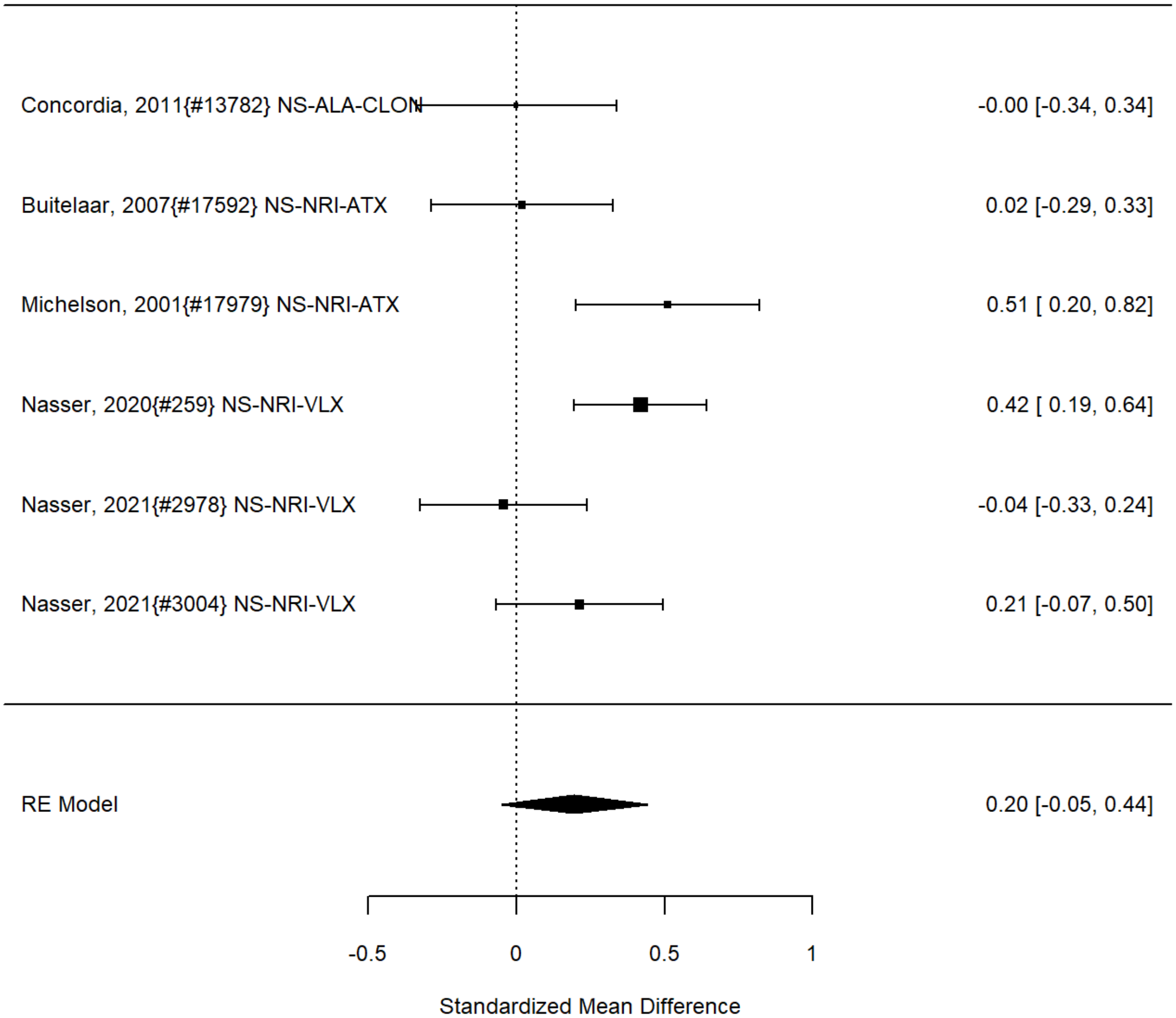


Notes: ADHD = attention deficit hyperactivity disorder, NS-NS-NRI-ATX atomoxetine, NS-ALA-CLON clonidine, NS-NRI-VLX viloxazine, RE = random effects, RR = relative risk

In the subgroup of non-stimulant studies, we found a clear treatment effect on ADHD symptoms (RR 1.51; CI 1.26, 1.81; 12 studies, n=1765). However, only three non-stimulant studies contributed to the analysis (atomoxetine, viloxazine, and clonidine). None of the studies included children under the age of six. However, the effect was not as pronounced as in the single stimulant study that was identified (evaluating lisdexamfetamine dimesylate), which reported a very large treatment effect versus control (RR 4.28; CI 2.49, 7.35; 1 study, n=153).[202]

We did not identify studies reporting on functional impairment in a head-to-head comparison. Indirect analyses comparing non-stimulant versus stimulant studies showed a statistically significant result (p 0.04). Subgroup analyses are shown in Figure 43.

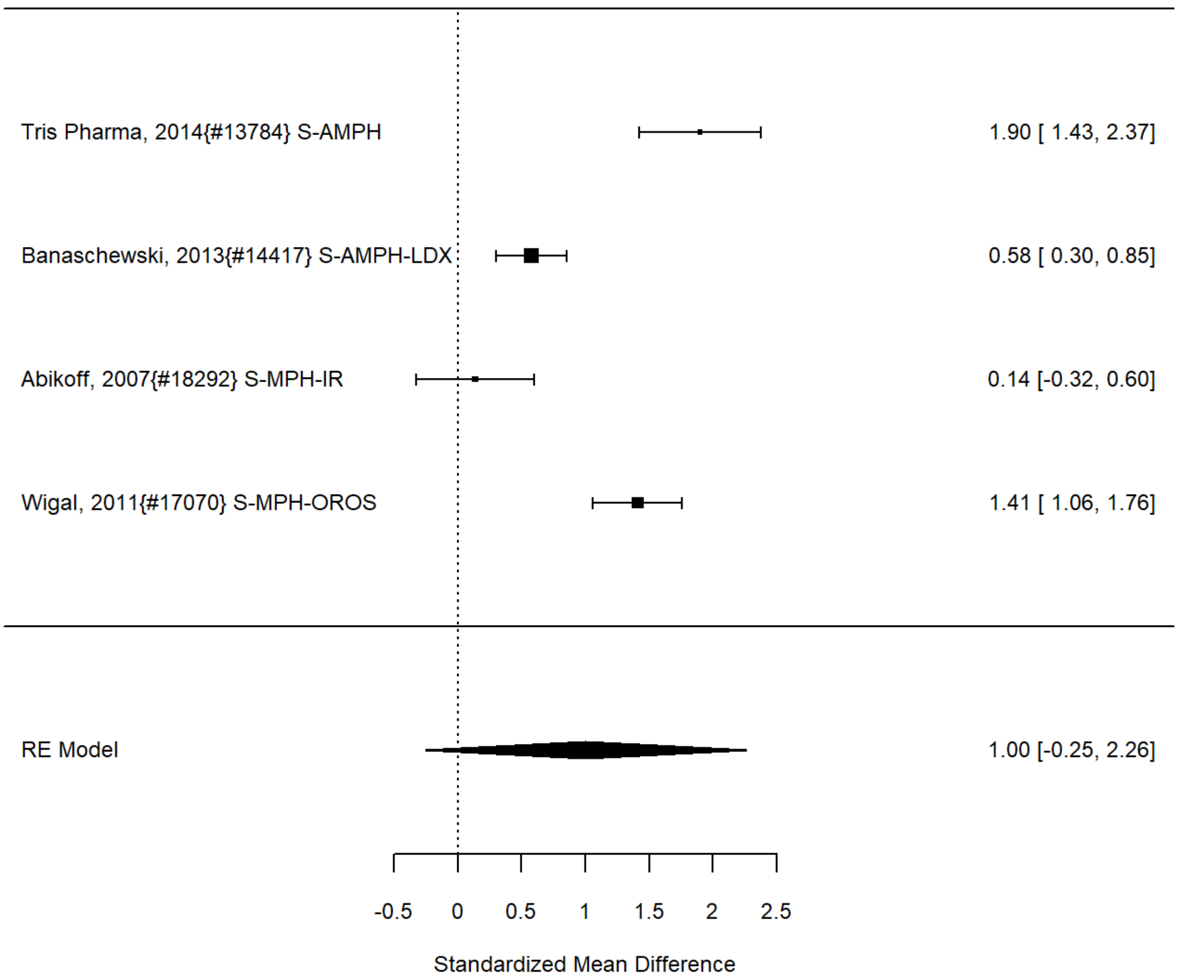
Figure 43. Subgroup analysis: Non-stimulants versus control on functional impairment (SMD)



Notes: NS-NS-NRI-ATX = atomoxetine, NS-ALA-CLON = clonidine, NS-NRI-VLX = viloxazine, RE = random effects, SMD = Standardized Mean Difference

In the subgroup of non-stimulant studies, treatment was associated with a small but not statistically significant improvement in functional impairment (SMD 0.20; CI -0.05, 0.44; 6 studies, n=1163). However, only atomoxetine, viloxazine, and clonidine studies contributed to the analysis. None of the studies included children under the age of six. The equivalent analysis for stimulant studies is shown in Figure 44.

Figure 44. Subgroup analysis: Stimulants versus control on functional impairment (SMD)



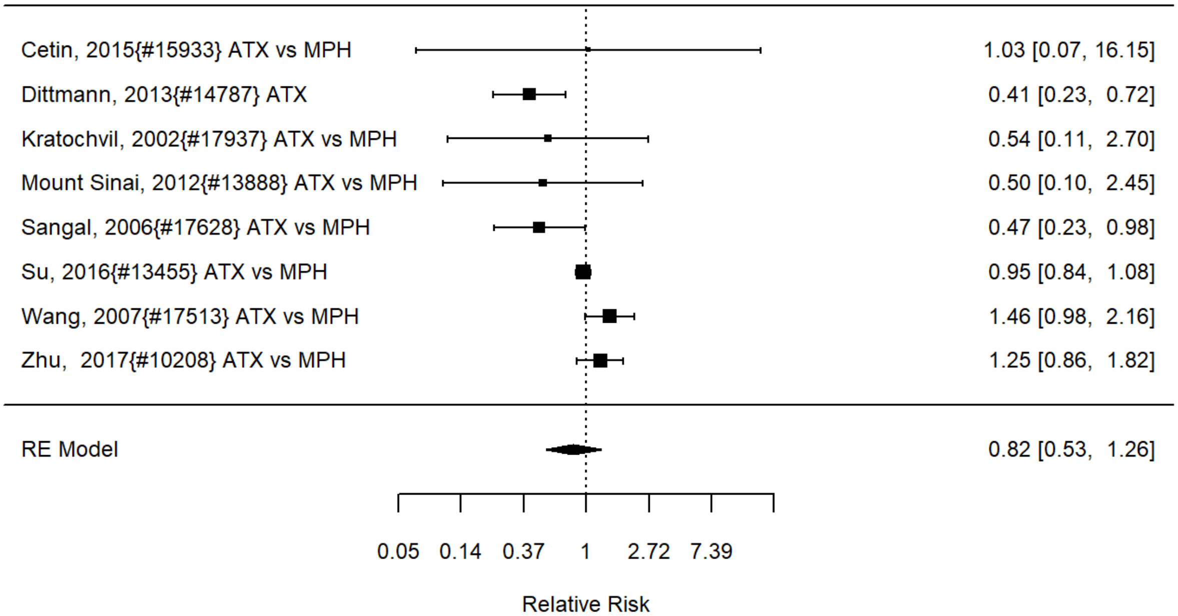
Notes: S-AMPH = amphetamine not further specified, S-AMPH-LDX = lisdexamfetamine dimesylate, S-MPH-IR = immediate release methylphenidate, RE = random effects, S-MPH-OROS = osmotic-release oral system methylphenidate, SMD = Standardized Mean Difference

In the subgroup of stimulant studies, treatment was not associated with statistically significant improvement in functional impairment across studies (SMD 1.00; CI -0.25, 2.26; 4 studies, n=540). Only one study included children younger than 6 years old.[109]

There were insufficient studies for analyses regarding treatment satisfaction as well as academic performance. Both direct and indirect comparisons could not be analyzed due to the small number of identified studies.

Results for direct comparisons between non-stimulants and stimulants for appetite suppression are shown in Figure 45.

Figure 45. Comparison: Non-stimulants (all NRI atomoxetine) versus stimulants on appetite suppression (RR)

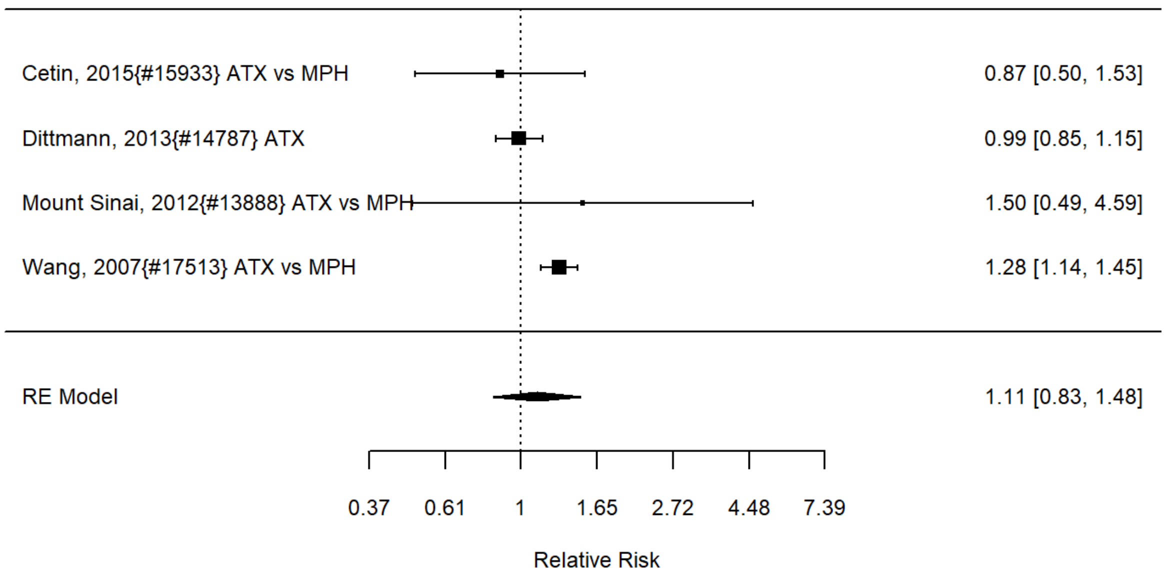


Notes: ATX = atomoxetine, MPH = methylphenidate; all comparison to MPH except one to lisdexamfetamine dimesylate, NRI = norepinephrine reuptake inhibitors, RE = random effects, RR = relative risk

Across studies, we found no systematic difference between non-stimulant (all identified studies evaluated the NRI atomoxetine) versus stimulants (RR 0.82; CI 0.53, 1.26; 8 studies, n=1463). No alpha agonists or NRIs other than atomoxetine contributed to this analysis. There continued to be heterogeneity (I-squared 78%). There was no evidence of publication bias. Removing high-risk of bias studies in a sensitivity analysis left only two studies; results remained not statistically significantly different between interventions (RR 1.34: CI 0.51, 3.52). When restricting the comparator to methylphenidate to determine whether the comparator is a source of heterogeneity, we found no systematic difference between NRI and methylphenidate medication interventions either and heterogeneity was reduced, but in this subset, all seven studies compared atomoxetine versus methylphenidate medications (RR 0.98; CI 0.67, 1.44; I-squared 58%). Results varied, sometimes favoring the NRI atomoxetine, sometimes the methylphenidate medications and across studies, no systematic difference was detected. Publication bias was not detected. An indirect comparison did not detect systematic differences between non-stimulant and stimulant studies for appetite suppression (p 0.31).

The comparative studies reporting sufficient detail to compute effect sizes for the number of participants with adverse events is shown in Figure 46.

Figure 46. Comparison: Non-stimulants (all NRI atomoxetine) versus stimulants on participants with adverse events (RR)



Notes: ATX atomoxetine, MPH methylphenidate; all studies compared to MPH except one to lisdexamfetamine dimesylate, RI = norepinephrine reuptake inhibitors, RE = random effects, RR = relative risk

Across studies, we found no systematic difference between non-stimulant (all identified studies were the NRI atomoxetine) versus stimulant interventions for the number of participants reporting adverse events (RR 1.11; CI 0.90, 1.37; 4 studies, n=756). There was some indication of heterogeneity (I-squared 63%). There was no evidence of publication bias. Removing high-risk of bias studies left one study comparing the NRI atomoxetine with methylphenidate (not further specified); the study favored stimulants (RR 1.28; CI 1.14, 1.45).[604] We also evaluated in indirect comparisons across studies whether non-stimulant and stimulant studies vary systematically in effect size reporting. However, we did not detect an effect (p 0.12).

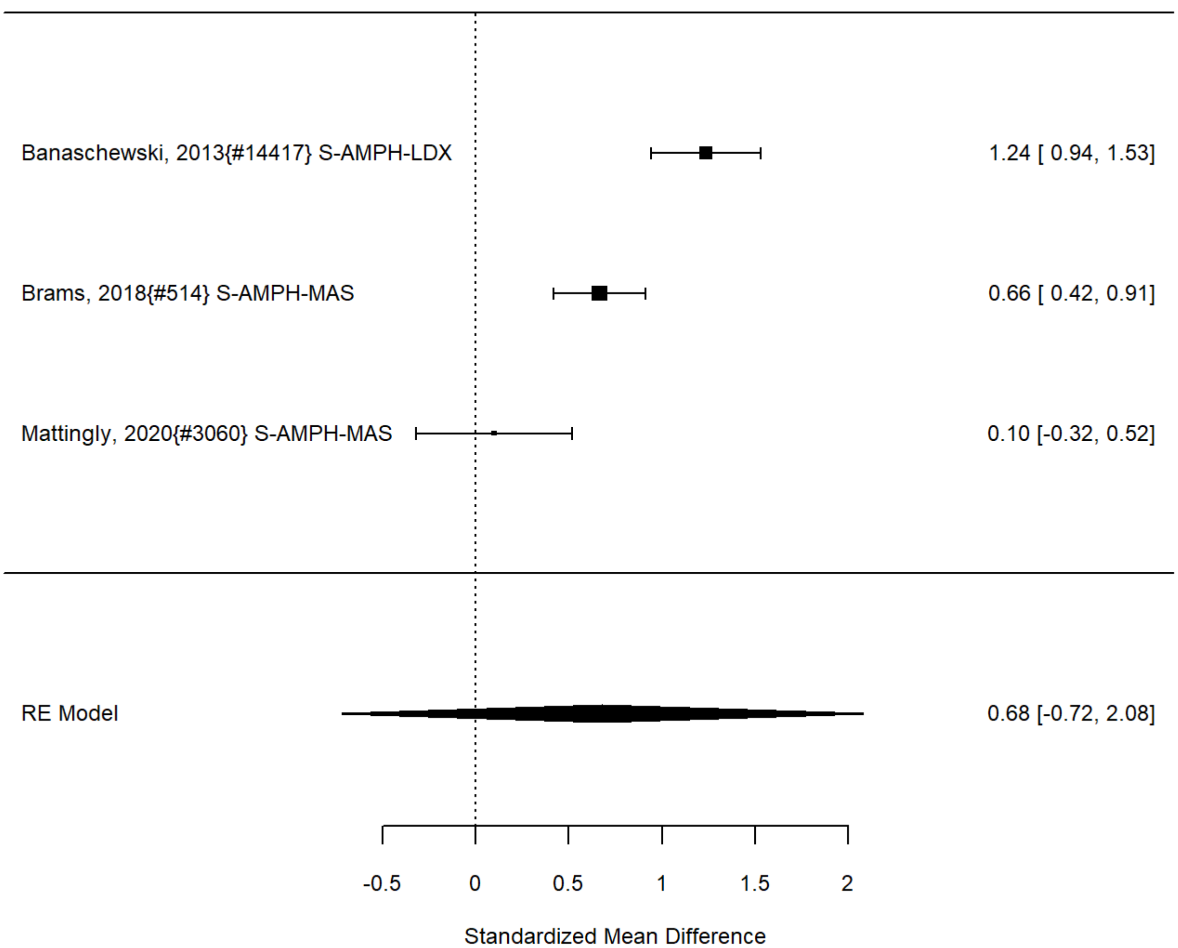
5.3.2.1.3 Stimulant Comparisons: Amphetamine Versus Methylphenidate

A small number of included studies compared amphetamine and methylphenidate in direct, head-to-head comparisons.

We did not identify any studies reporting on individual behaviors for a direct comparison of amphetamine and methylphenidate and indirect comparisons across studies also had insufficient number of studies for analyses for continuous as well as categorical outcomes.

A single study reported on a broadband measure and found more positive change in lisdexamfetamine dimesylate (an amphetamine) versus osmotic-release oral system methylphenidate (SMD 0.29; CI 0.02, 0.56; 1 study, n=211).[131] Indirect comparisons across studies did not detect a systematic difference between amphetamine and methylphenidate studies (continuous outcomes p 0.97, categorical outcomes p 0.80). Figure 47 shows the results for the subgroup of amphetamine stimulants separately from those of methylphenidate.

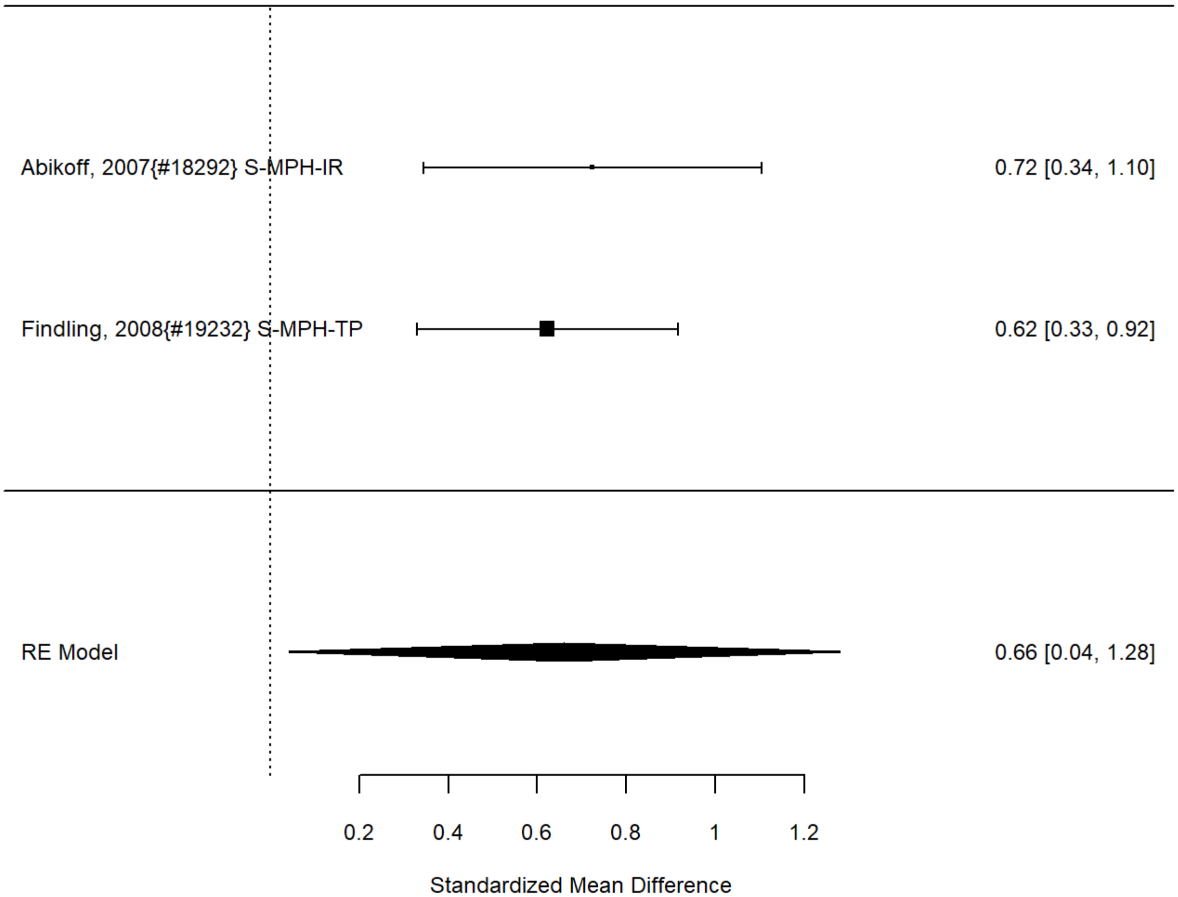
Figure 47. Subgroup analysis: Amphetamine versus control on broadband measures (SMD)



Notes: S-AMPH-LDX = lisdexamfetamine dimesylate, S-AMPH-MAS = mixed amphetamines salts, RE = random effects, SMD = standardized mean difference

Although all identified amphetamine studies in this subgroup reported positive effects, estimates varied and the pooled effect was not statistically significant (SMD 0.68; CI -0.72, 2.08; 3 studies, n=561). The analysis suggested substantial heterogeneity despite the small number of studies (I-squared 92%). There was no evidence of publication bias. None of the studies was determined to be high-risk of bias. The equivalent subgroup analysis for the stimulant methylphenidate is shown in Figure 48.

Figure 48. Subgroup analysis: Methylphenidate versus control on broadband measures (SMD)

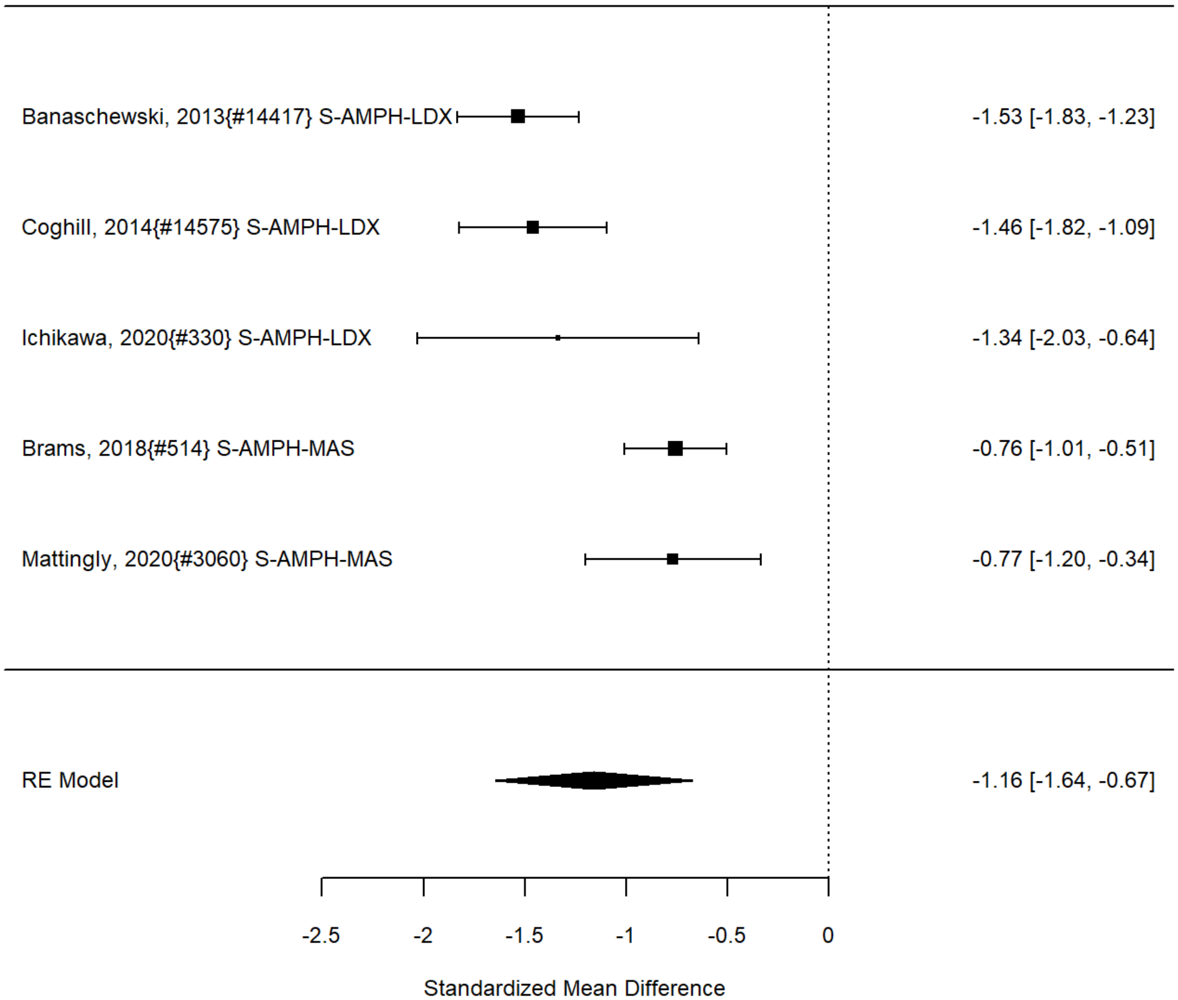


Notes: S-MPH-IR = immediate release methylphenidate, S-MPH-TP = transdermal patch methylphenidate, RE = random effects, SMD = standardized mean difference

The methylphenidate studies that compared to a passive control showed positive effects on broadband measures (SMD 0.66; 0.04, 1.28; 2 studies, n=302).

The single direct comparison study also reported better ADHD symptom control with the amphetamine lisdexamfetamine dimesylate versus osmotic-release oral system methylphenidate (SMD -0.46; CI -0.73, -0.19; 1 study, n=222).[131] Indirect comparisons detected a statistically significant difference across studies for the continuous outcome analysis (p 0.02). Figure 49 shows the results separately for the two stimulant subgroups given that one study found a difference in reported effects in a head-to-head comparison of the two types of stimulants.

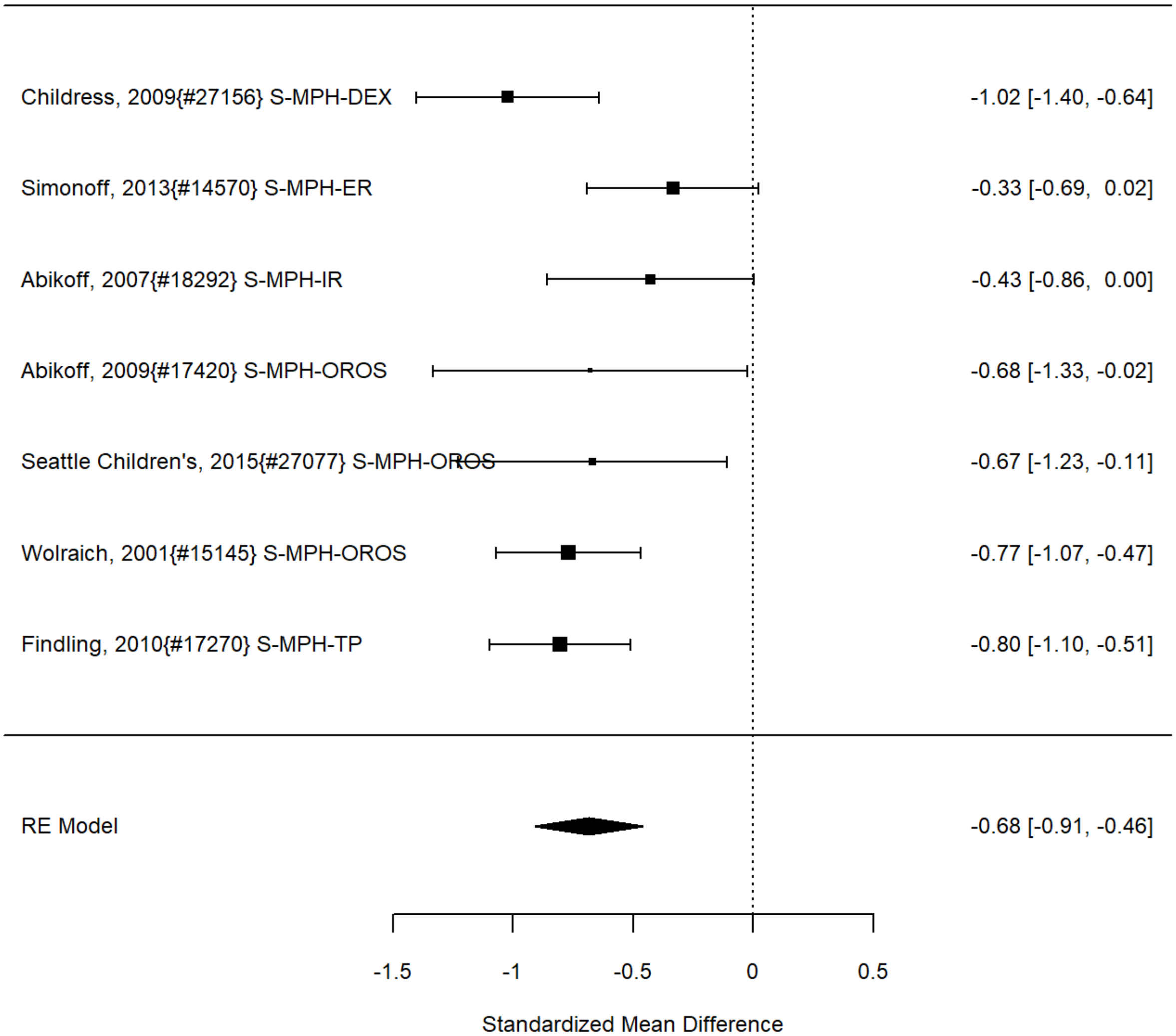
Figure 49. Subgroup analysis: Amphetamine versus control on ADHD symptoms (SMD)



Notes: ADHD = attention deficit hyperactivity disorder, S-AMPH-LDX = lisdexamfetamine dimesylate, S-AMPH-MAS = mixed amphetamines salts, RE = random effects, SMD = Standardized Mean Difference

In the subgroup of amphetamine studies, we found a significant effect of treatment (SMD -1.16; CI -1.64, -0.67; 5 studies, n=757). None of the studies included children under the age of 6. The subgroup analysis results for methylphenidate studies are shown in Figure 50.

Figure 50. Subgroup analysis: Methylphenidate versus control on ADHD symptoms (SMD)



Notes: ADHD = attention deficit hyperactivity disorder, S-MPH-DEX = dexmethylphenidate, S-MPH-ER = extended release methylphenidate, S-MPH-IR = immediate release methylphenidate, S-MPH-OROS = osmotic-release methylphenidate, S-MPH-TP = transdermal patch methylphenidate, RE = random effects, SMD = Standardized Mean Difference

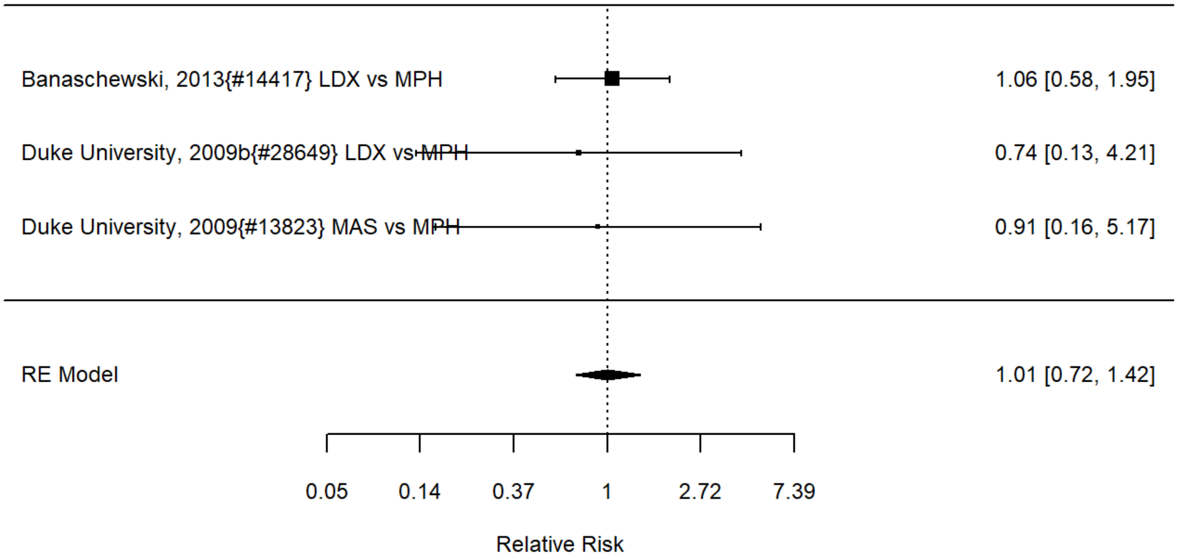
In the subgroup of methylphenidate studies, we found a significant treatment effect, but effect estimates were smaller (SMD -0.68; CI -0.91, -0.46; 7 studies, n=863). Only one study included children younger than 6 years old.[109] Indirect comparisons between amphetamine and methylphenidate using categorical data were not statistically significant (p 0.57).

There was no statistically significant difference in functional impairment in a head-to-head comparison of the two stimulants (SMD 0.16; CI -0.11, 0.43; 1 study, n=211).[131] The indirect comparison across studies did also not detect a systematic difference (p 0.68).

We identified no studies that reported on treatment satisfaction or academic performance in direct head-to-head comparisons and there were insufficient data for indirect analyses.

Results for direct comparisons between amphetamine and methylphenidate on the outcome appetite suppression are shown in Figure 51.

Figure 51. Comparison: Amphetamine versus methylphenidate on appetite suppression (RR)



Notes: LDX = lisdexamfetamine dimesylate, MPH = methylphenidate, RE = random effects, RR = relative risk

The two studies reporting on appetite suppression did not find a difference between the amphetamine lisdexamfetamine dimesylate versus osmotic-release oral system methylphenidate, lisdexamfetamine dimesylate versus methylphenidate transdermal system, or mixed amphetamines salts versus osmotic-release oral system methylphenidate (RR 1.01; CI 0.72, 1.42; 3 comparisons, n=414). Similarly, indirect comparisons across studies did also not detect a statistically significant difference between the two stimulant classes for the categorical outcome analysis (p 0.08). Although the continuous outcome analysis was borderline statistically significant (p 0.05), only one study each contributed to the analysis. Both studies compared to placebo and none found a statistically significant difference between study arms (amphetamine SMD 0.17; CI -0.14, 0.48; 1 study, n=157; methylphenidate SMD 0.22; CI -0.41, 0.84; 1 study, n=40).[202, 383]

One study documenting the number of participants reporting adverse event found no statistically significant difference between stimulant classes (RR 1.11; CI 0.93, 1.33; 1 study, n=222); the study compared lisdexamfetamine dimesylate and osmotic-release oral system methylphenidate.[131] Similarly, indirect comparisons did also not detect a difference between amphetamines and methylphenidate regarding the number of participants reporting adverse events (p 0.35).

5.3.2.1.4 Non-Stimulant Comparisons: NRIs Versus Alpha Agonists

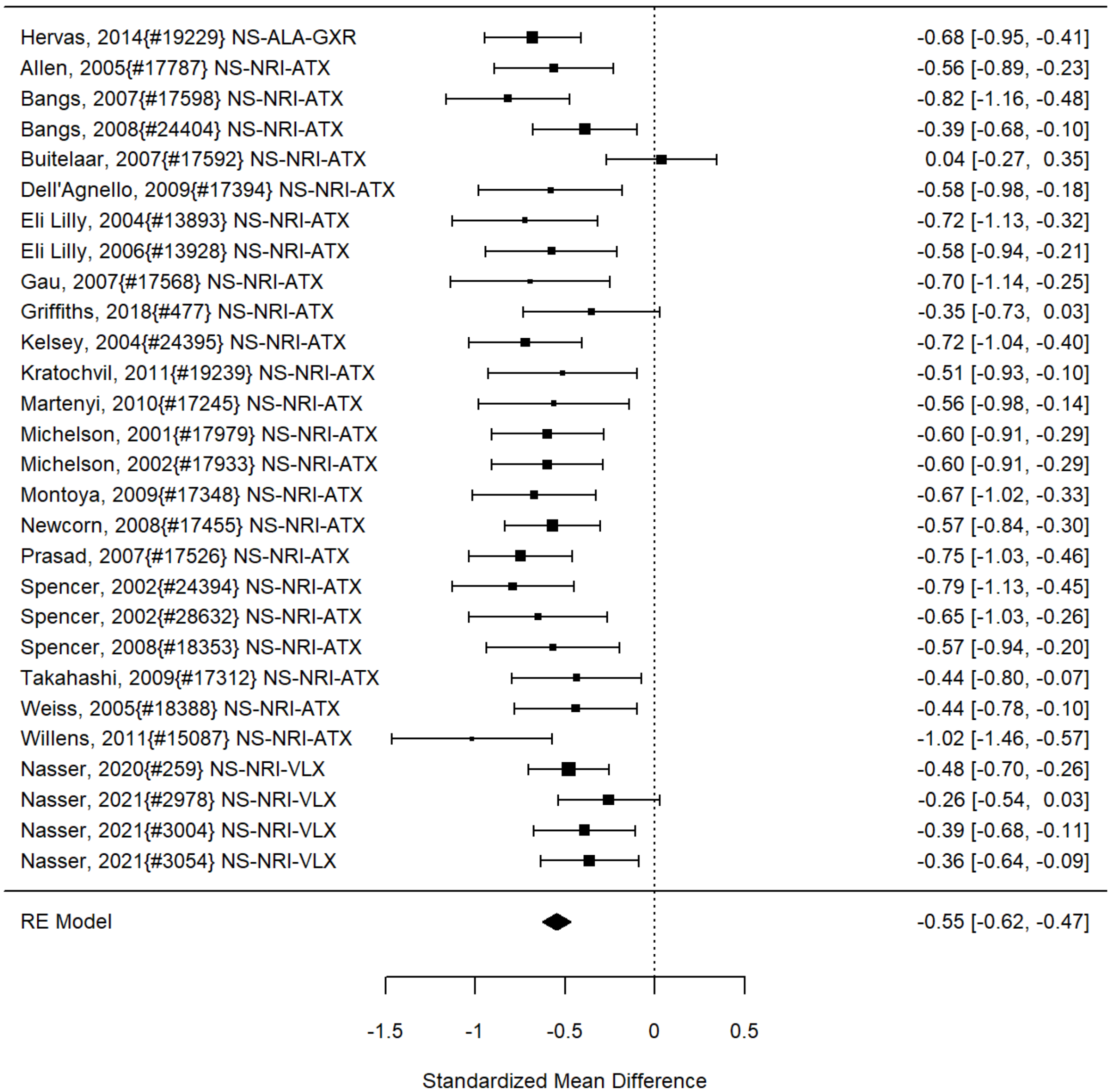
We identified a study directly comparing an alpha agonist (guanfacine) with an NRI (atomoxetine) in a head-to-head trial, but the study did not report on problem behaviors.[326] In indirect comparisons, there were no differences for problem behaviors (p 0.31).

The guanfacine versus atomoxetine study detected no difference (RR 0.84; CI 0.68, 1.04; 1 study, n=226) for a categorical broadband measure (number of improved patients per Clinical Global Impression [CGI]).[326] Indirect comparisons across studies also did not identify a systematic difference between NRIs and alpha agonists for broadband measures (continuous p 0.41, categorical p 0.19).

The same identified study comparing guanfacine with atomoxetine[326] found that ADHD symptom improvement favored guanfacine over atomoxetine (SMD -0.47; CI -0.73, -0.2; 1 study, n=226). Indirect comparisons, however, did not suggest that alpha agonists systematically report different estimates for ADHD symptoms (continuous p 0.90, categorical p 0.57).

The following shows the subgroup results for NRI studies versus control separately for ADHD symptoms, given that a direct comparison of guanfacine versus atomoxetine study found a difference in effects (Figure 52).

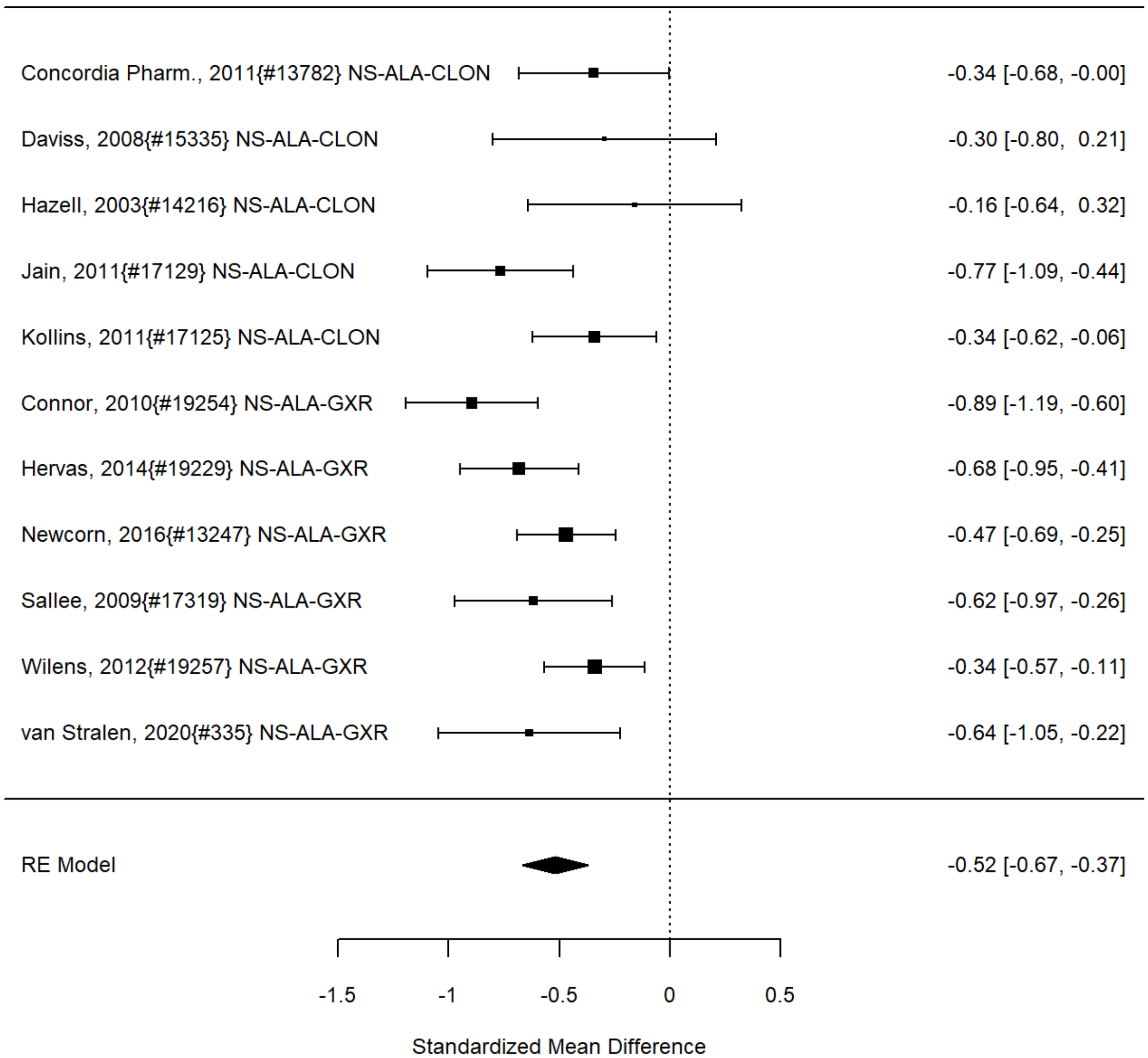
Figure 52. Subgroup analysis: NRIs versus control on ADHD symptoms (SMD)



Notes: ADHD = attention deficit hyperactivity disorder, NS-NRI-GXR/NS-NRI-ATX = atomoxetine, NS-NRI-VLX = viloxazine, RE = random effects, SMD = standardized mean difference

In the subgroup of NRI studies, we found a clear effect on ADHD symptoms (SMD -0.55; CI -0.62, -0.47; 28 studies, n=4493). Only one study included children younger than 6 years old.[378] The equivalent analysis for the subgroup of alpha agonist studies is shown in Figure 53.

Figure 53. Subgroup analysis: Alpha agonists versus control on ADHD symptoms (SMD)



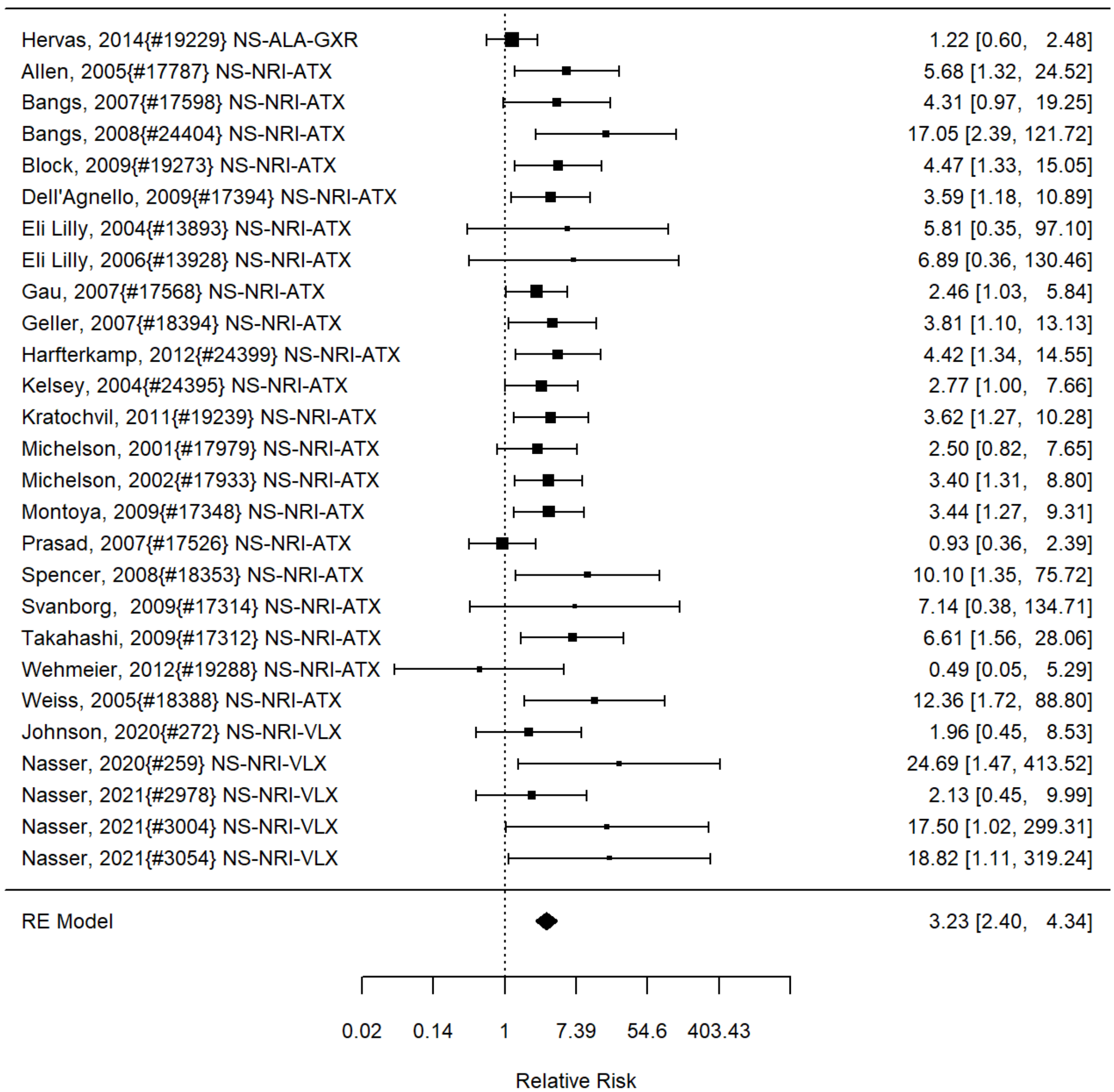
Notes: ADHD = attention deficit hyperactivity disorder, NS-ALA-CLON = clonidine, NS-ALA-GXR = guanfacine extended-release, RE = random effects, SMD = standardized mean difference

In the smaller subgroup of alpha agonist studies, we also found a clear effect on ADHD symptoms (SMD -0.52; CI -0.67, -0.37; 11 studies, n=1885). It should be noted that the small difference between NRI versus control and alpha agonists versus control effect estimates was not statistically significant and is therefore indistinguishable from chance. None of the studies in this subgroup reported on children younger than 6 years of age.

Indirect comparisons across studies did not suggest a systematic difference in effects reported by NRI versus alpha agonist studies on functional impairment (p 0.46) and we found no head-to-head comparison between NRI and alpha agonist studies. Effects for treatment satisfaction and academic performance could not be evaluated in direct or indirect analyses due to lack of data.

The only identified study that reported a direct comparison between alpha agonists and NRIs found statistically significantly fewer instances of decreased appetite for guanfacine versus atomoxetine (RR 0.48; CI 0.27, 0.83; 1 study, n=226).[326] Similarly, indirect comparisons indicated a significant difference between NRIs and alpha agonists for the outcome appetite suppression (categorical p 0.01). Subgroup results for appetite suppression are shown in Figure 54.

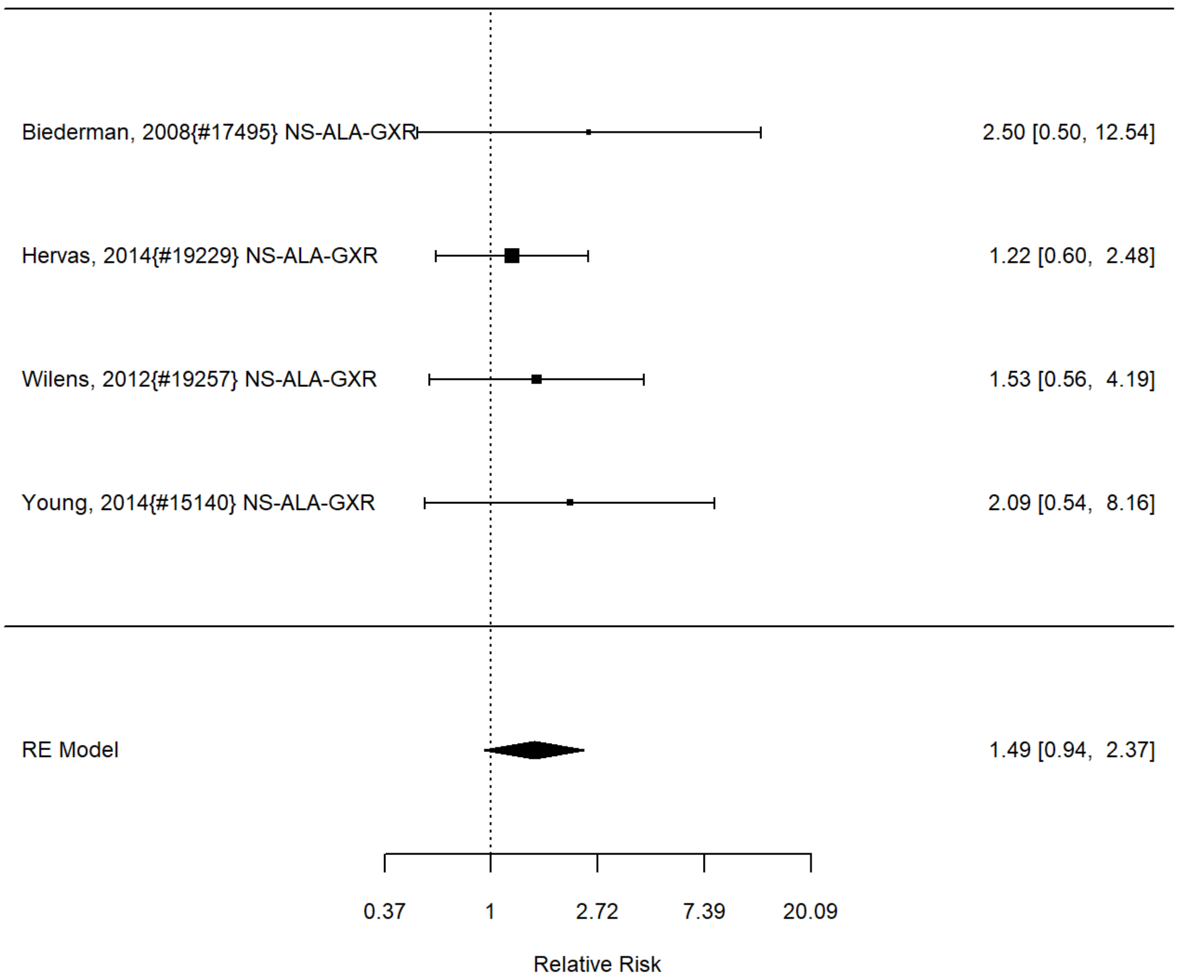
Figure 54. Subgroup analysis: NRIs versus control on appetite suppression (RR)



Notes: NRI = norepinephrine reuptake inhibitors, NS-NRI-GXR/NS-NRI-ATX = atomoxetine, NS-NRI-VLX = viloxazine, RE = random effects, RR = relative risk

In the subgroup of NRI studies, we found a substantially increased risk of appetite suppression (RR 3.23; CI 2.40, 4.34; 27 studies, n=4176). Only one study included children younger than six years old.[378] The equivalent analysis for the subgroup of alpha agonist studies is shown in Figure 55 .

Figure 55. Subgroup analysis: Alpha agonists (all guanfacine) versus control on appetite suppression (RR)



Notes: NS-ALA-GXR = guanfacine, RE = random effects, RR = relative risk

Unlike in the NRI studies, in the subgroup of alpha agonist (all guanfacine) studies, no statistically significant effect of appetite suppression was detected because confidence intervals were wider in this small subgroup (RR 1.49; CI 0.94, 2.37; 4 studies; n=919). Only guanfacine evaluations contributed to this result as no clonidine study reported on the outcome.

The one identified study that reported a direct comparison between NRIs and alpha agonists found no differences in the number of patients experiencing adverse events (RR 1.14; CI 0.97, 1.34; 1 study, n=226) between the interventions; the study compared guanfacine to atomoxetine, specifically.[326] Potential differential effects for the number of participants reporting adverse events were not statistically significant in indirect comparisons across non-stimulants (p 0.06).

5.3.2.1.5 Drug Class Comparison: Methylphenidate Versus Amphetamine Versus NRIs Versus Alpha Agonists

The review identified over 100 studies evaluating dozens of FDA-approved medication treatments for ADHD. In addition to differentiating between stimulants and non-stimulants, we also tried to determine whether there are systematic differences between the four drug classes methylphenidate (stimulant), amphetamine (stimulant), NRI (non-stimulant), and alpha agonist (non-stimulant). A meta-regression across studies evaluated whether the drug class is associated with effect sizes.

For behavior outcomes, indirect comparisons did not detect a statistically significant difference in effect sizes (p 0.42).

Indirect analyses for the outcome broadband measures, however, indicated differences between intervention class across studies (p 0.002). Specifically, the analysis suggested that amphetamine studies (p<0.001) and methylphenidate studies (p<0.001) reported larger effects than alpha agonist studies. The subgroup of amphetamine studies reported the largest effect, but estimates varied across studies, and the pooled effect was not statistically significant in this small subgroup (SMD 0.68; CI -0.72, 2.08; 3 studies, n=561). The subgroup of methylphenidate studies that compared to a passive control showed statistically significant positive effects on broadband measures (SMD 0.66; 0.04, 1.28; 2 studies, n=302). The subgroup of alpha agonist studies reported a smaller effect, but the estimate was also statistically significant (SMD 0.45; CI 0.22, 0.68; 4 studies, n=509). The subgroup of NRI studies reported statistically significant effects and the effect size was between those of the stimulant and alpha agonist studies (SMD 0.53; CI 0.44, 0.63; 20 studies, n=3183).

For ADHD symptoms, the meta-regression suggested conflicting results with a statistically significant result for the overall test (omnibus test p 0.04) but not any of the individual parameters. The subgroup of amphetamine studies reported the largest and statistically significant effect (SMD -1.16; CI -1.64, -0.67; 5 studies, n=757). The subgroup of alpha agonist studies reported smaller but statistically significant effects (SMD 0.52; CI -0.67, -0.37; 11 studies, n=1885). The subgroup of NRI studies also reported statistically significant effects with the size of effect similar to alpha agonist studies (SMD 0.55; CI -0.62, -0.47; 28 studies, n=1925). The subgroup of methylphenidate studies reported slightly larger effects than the non-stimulant studies and the effect of the intervention was also statistically significant versus control (SMD -0.68; CI -0.91, -0.46; 7 studies, n=863).

Analyses for functional impairment did not detect a statistically significant difference in effect sizes (p 0.23). Insufficient studies were available for treatment satisfaction and academic performance.

For appetite suppression, the continuous outcome analysis did not detect a statistically significant effect (p 0.10), but the categorical outcomes indicated differences between intervention classes across studies (p 0.005). Specifically, the analysis suggested that amphetamine studies (p<0.001) and NRIs studies (p 0.02) report systematically different effect estimates from alpha agonist studies. The subgroup of amphetamine studies reported the largest and statistically significant effect (RR 7.08; CI 2.72, 18.42; 8 studies, n=1229). The subgroup of NRI studies reported smaller but also statistically significant effects (RR 3.23; CI 2.40, 4.24, 27 studies, n=4176). The subgroup of alpha agonist studies reported an even smaller effect (RR 1.49; CI 0.94, 2.37; 4 studies, n=919) and the difference to the control group was not statistically significant because the confidence interval just crossed the point of no effect. However, only guanfacine studies contributed to this finding and results for the drug class of alpha agonists are not known. The subgroup of methylphenidate studies reported statistically significant effects and effect sizes were between those of NRI studies and alpha agonist studies (RR 2.80; CI 1.47, 5.32; 8 studies, n=1110).

Analysis for the total number of participants reporting adverse events showed a borderline statistically significant effect (p 0.05), suggesting potentially differential effects for amphetamine studies (p 0.02) and NRI studies (p 0.03). The subgroup of amphetamine studies reported statistically significant effects (RR 1.41; CI 1.25, 1.58; 8 studies, n=1151). The subgroup of NRI studies reported a slightly smaller but statistically significant effect (RR 1.31; CI 1.18, 1.46; 15 studies, n=2600). The subgroup of alpha agonist studies reported a slightly smaller but also statistically significant effect (RR 1.21; CI 1.11, 1.31; 14 studies, n=2544). The subgroup of methylphenidate studies reported an effect most similar to NRI studies, and the estimate was also statistically significant (RR 1.32; CI 1.25, 1.40; 6 studies, n=945).

All analyses should be interpreted with caution as they are based on an indirect analysis across studies rather than on direct, head-to-head comparisons between medications.

5.3.2.3 FDA-Approved Pharmacologic ADHD Treatment Summary of Findings

Table 13 shows the findings for the outcomes of interest, together with the number of studies and study identifiers. We report the presence and absence of evidence for outcomes of interest, regardless of the number of identified studies. Effectiveness and adverse events analysis compared to control are shown first, followed by comparative effectiveness and safety analyses relative to an active comparator. For each outcome, results across all passive control groups are shown first, followed by specific comparisons (e.g., combinations vs individual components). In the comparative effectiveness section, we report first on the comparison between medication categories (stimulant vs non-stimulant), followed by the comparison between medication classes (amphetamines, methylphenidate, NRIs, alpha agonists). All other subgroup results for individual medications or medication classes are shown in this table only when we found empirical evidence of differences in effect sizes in direct or indirect comparisons. For any additional comparative effect analyses, such as comparisons between two medications (e.g., clonidine vs guanfacine), results are shown only when more than one study reported on the comparison (given that no studies or single studies would only add a row of insufficient evidence to the table).

The table states the comparison for which evidence is available, for example, we may have tried to determine the comparative effect of stimulants versus non-stimulants, but when all identified studies happened to test atomoxetine versus lisdexamfetamine (rather than the full range of non-stimulants and stimulants), we changed the comparison description to atomoxetine versus lisdexamfetamine.

Table 13. KQ2 summary of findings and strength of evidence for FDA-approved pharmacological interventions

Intervention and Comparison	Outcome	Number of Studies and Study Design	Findings	Reasons for Downgrading	SoE
KQ2 pharmacological vs control	Behavior	11 RCTs[154, 224, 226, 248, 321, 380, 432, 460, 608, 610, 622]	Results favor intervention (SMD -0.62; CI -0.97, -0.27; 5 studies, n=523); RR 0.36; CI 0.17, 0.78; 1 study, n=66)	I	Low for benefit

5. Results: Treatment of ADHD

Intervention and Comparison	Outcome	Number of Studies and Study Design	Findings	Reasons for Downgrading	SoE
KQ2 pharmacological vs control	Broadband measures	64 RCTs[109, 131, 133, 144, 145, 161, 164, 194, 195, 202, 205, 207, 217, 220, 247, 270, 272, 273, 288, 292, 305, 326, 341, 348, 361, 373, 374, 378, 414, 419, 425, 431, 442, 452-455, 459, 461, 481, 511, 538, 554, 555, 557, 573, 598, 611, 612, 617, 619, 623, 626, 634]	Results favor intervention (SMD 0.57; CI 0.48, 0.67; 28 studies, n=4467; RR 0.51; CI 0.43, 0.60; 25 studies, n=3959)	-	High for benefit
KQ2 pharmacological vs control	ADHD symptoms	76 RCTs[108, 109, 118, 131-133, 144, 145, 154, 161, 164, 193-195, 202, 205, 207, 217, 220, 226, 247, 248, 270-273, 288, 292, 305, 306, 317, 321, 326, 337, 341, 348, 361, 373, 374, 378, 383, 414, 419, 425, 431, 432, 442, 452-455, 459-461, 481, 511, 526, 538, 540, 554-557, 573, 575, 598, 608, 610-612, 617, 619, 622, 623, 626, 634]	Results favor intervention (SMD -0.61; CI -0.69, -0.52; 49 studies, n=7685; RR 1.71, CI 1.33, 2.19; 13 studies, n=1918)	-	High for benefit
KQ2 stimulant augmentation vs stimulant alone	ADHD symptoms	5 RCTs[217, 321, 373 598, 622]	Results favor augmentation (SMD -0.36; CI -0,52, -0.19; 5 studies, n=724)	C	Low for larger effects with augmentation
KQ2 pharmacological vs control	Functional impairment	18 RCTs[109, 131, 164, 202, 205, 380, 432, 452-455, 459, 461, 588, 618, 622, 623, 634]	Results favor intervention (SMD 0.50; CI 0.05, 0.96; 10 studies, n=1703)	C	Moderate for benefit
KQ2 pharmacological vs control	Acceptability of treatment	3 RCTs[207, 573, 610]	Results favor alpha agonist intervention (RR 0.47; CI 0.32, 0.68; 1 study, n=198)	I	Insufficient
KQ2 pharmacological vs control	Academic performances	4 RCTs[526, 588, 618, 619]	Results favor intervention (SMD -1.37; CI -1.72, -1.03; 1 study, n=156)	I	Low for benefit

5. Results: Treatment of ADHD

Intervention and Comparison	Outcome	Number of Studies and Study Design	Findings	Reasons for Downgrading	SoE
KQ2 pharmacological vs control	Appetite suppression	57 RCTs[109, 118, 131-133, 144, 145, 154, 161, 164, 193-195, 202, 217, 220, 247, 248, 270, 272, 273, 288, 292, 305, 317, 321, 326, 348, 361, 378, 383, 414, 419, 431, 432, 442, 452-455, 460, 481, 511, 538, 556, 557, 573, 575, 608, 610-612, 617, 618, 622, 626, 634]	Intervention is associated with appetite suppression (SMD 0.48; CI -0.04, 1.00; 6 studies, n=605; RR 3.51; CI 2.72, 4.51; 46 studies, n=7209)	-	High for increased risk
KQ2 pharmacological vs control	Participants with adverse events	42 RCTs[131, 144, 145, 154, 161, 164, 194, 195, 202, 205, 207, 217, 247, 248, 270, 272, 273, 305, 317, 326, 337, 341, 373, 374, 414, 419, 425, 442, 452-454, 459, 540, 573, 575, 598, 608, 612, 622, 623, 626, 634]	Pharmacological treatment is associated with a higher risk of reported adverse events (RR 1.29; CI 1.23, 1.35; 41 studies, n=6926)	-	High for increased risk
KQ2 CER non-stimulants vs stimulants	Behavior	N/A (indirect comparison)	Insufficient data	D, C	Insufficient
KQ2 CER amphetamine vs methylphenidate vs NRI vs alpha agonist	Behavior	NA (indirect comparison)	No difference detected (p 0.42)	D	Low for no difference
KQ2 CER atomoxetine vs methylphenidate	Behavior	5 RCTs[175, 460, 504, 512, 525]	NRIs showed more improvement than stimulants (SMD -0.08; CI -0.14, -0.03; 4 studies, n=608)	S	Low for larger effects in NRI atomoxetine
KQ2 CER non-stimulants vs stimulants	Broadband measures	N/A (indirect comparison)	Non-stimulant studies reported smaller effects than stimulant studies (non-stimulants RR 0.66; CI 0.58, 0.76; 12 studies, n=2312 vs stimulants RR 0.38; CI 0.30, 0.48; 12 studies, n=1582; p 0.0002)	D	Low for larger effects in stimulants

Intervention and Comparison	Outcome	Number of Studies and Study Design	Findings	Reasons for Downgrading	SoE
KQ2 CER amphetamine vs methylphenidate vs NRI vs alpha agonist	Broadband measures	N/A (indirect comparison)	Amphetamine studies found no statistically effect but reported the largest effects (SMD 0.68; CI -0.72, 2.08; 3 studies, n=561); methylphenidate studies favored intervention (SMD 0.66; 0.04, 1.28; 2 studies, n=302); NRI studies favored intervention (SMD 0.53; CI 0.44, 0.63; 20 studies, n=3183); alpha agonist studies favored intervention (SMD 0.45; CI 0.22, 0.68; 4 studies, n=509); p 0.002		Insufficient
KQ2 CER atomoxetine vs methylphenidate	Broadband measures	4 RCTs[175, 460, 504, 525]	No systematic difference (SMD -0.16; CI -0.35, 0.03; 4 studies, n=1080)	S, C	Low for no difference
KQ2 CER non-stimulants vs stimulants	ADHD symptoms	N/A (indirect comparison)	Non-stimulant studies reported smaller effects than stimulant studies (SMD -0.52; CI -0.59, -0.46; 37 studies, n=6065 vs SMD -0.88; CI -1.13, -0.63; 12 studies, n=1620; p 0.0002)	D	Low for larger effects in stimulants
KQ2 CER amphetamine vs methylphenidate vs NRI vs alpha agonist	ADHD symptoms	N/A (indirect comparison)	Amphetamine studies favored intervention (SMD -1.16; CI -1.64, -0.67; 5 studies, n=757); methylphenidate studies favored intervention (SMD -0.68; CI -0.91, -0.46; 7 studies, n=863); NRI studies favored intervention (SMD 0.55; CI -0.62, -0.47; 28 studies, n=1925); alpha agonist studies favored intervention (SMD 0.52; CI -0.67, -0.37; 11 studies, n=1885); p 0.04	D	Insufficient
KQ2 CER NRIs vs stimulants	ADHD symptoms	7 RCTs[137, 225, 376, 460, 539, 604, 645]	No systematic difference (SMD 0.23; CI -0.03, 0.49; 7 studies, n=1611)	S, C	Low for no difference
KQ2 CER amphetamine vs methylphenidate	ADHD symptoms	1 RCT[131] (direct comparison), and N/A (indirect comparison)	A direct comparison shows more improvement with amphetamine vs methylphenidate (SMD -0.46; CI -0.73, -0.19; 1 study, n=222) and indirect comparisons show amphetamine studies reported more improvements than methylphenidate studies for continuous outcomes (SMD -1.16; CI -1.64, -0.67; 5 studies, n=757; SMD -0.68; CI -0.91, -0.46; 7 studies, n=863; p 0.02) but there was no systematic difference for categorical outcomes (p 0.57)	D, C	Low for larger effects of amphetamines

Intervention and Comparison	Outcome	Number of Studies and Study Design	Findings	Reasons for Downgrading	SoE
KQ2 CER NRI vs alpha agonists	ADHD symptoms	1 RCT[326] (direct comparison) and N/A (indirect comparison)	A direct comparison shows more improvement with atomoxetine (SMD -0.47; CI -0.73, -0.2; 1 study, n=226, indirect comparisons show no systematic difference (continuous p 0.90, categorical p 0.57)	C	Insufficient
KQ2 CER non-stimulants vs stimulants	Functional impairment	N/A (indirect comparison)	Non-stimulant studies reported smaller effects than stimulant studies (SMD 0.20; CI -0.05, 0.44; 6 studies, n=1163 vs SMD 1.00; CI -0.25, 2.26; 4 studies, n=540; p 0.04)	D	Low for larger effects in stimulants
KQ2 CER amphetamine vs methylphenidate vs NRI vs alpha agonist	Functional impairment	N/A (indirect comparison)	No difference detected (p 0.23)	D	Low for no difference
KQ2 CER non-stimulants vs stimulants	Acceptability of treatment	N/A (indirect comparison)	Insufficient data	D, C	Insufficient
KQ2 CER amphetamine vs methylphenidate vs NRI vs alpha agonist	Acceptability of treatment	N/A (indirect comparison)	Insufficient data	D, C	Insufficient
KQ2 CER non-stimulants vs stimulants	Academic performance	N/A (indirect comparison)	Insufficient data	D, C	Insufficient
KQ2 CER amphetamine vs methylphenidate vs NRI vs alpha agonist	Academic performance	N/A (indirect comparison)	Insufficient data	D, C	Insufficient
KQ2 CER non-stimulants vs stimulants	Appetite suppression	8 RCTs[175, 225, 376, 512, 539, 568, 645]	No systematic difference (RR 0.82; CI 0.53, 1.26; 8 studies, n=1463)	S	Low for no difference
KQ2 CER amphetamine vs methylphenidate vs NRI vs alpha agonist	Appetite suppression	N/A (indirect comparison)	Amphetamine studies reported an increased risk (RR 7.08; CI 2.72, 18.42; 8 studies, n=1229); methylphenidate studies reported an increased risk (RR 2.80; CI 1.47, 5.32; 8 studies, n=1110); NIR studies reported an increased risk (RR 3.23; CI 2.40, 4.24, 27 studies, n=4176); alpha agonist studies reported an increased but not statistically significant risk and only guanfacine was included (RR 1.49; CI 0.94, 2.37; 4 studies, n=919); p 0.005	D	Insufficient
KQ2 CER amphetamine vs methylphenidate	Appetite suppression	2 RCTs[131, 235]	No systematic difference (RR 1.01; CI 0.72, 1.42; 3 comparisons, n=414)	I	Low for no difference

Intervention and Comparison	Outcome	Number of Studies and Study Design	Findings	Reasons for Downgrading	SoE
KQ2 CER NRI vs alpha agonists	Appetite suppression	1 RCT[326] (direct comparison), and N/A (indirect comparison)	A direct comparison showed more instances of appetite suppression with NRIs (RR 0.48; CI 0.27, 0.83; 1 study, n=226); in indirect comparisons NRI studies reported more instances of appetite suppression than alpha agonist studies (NRI RR 3.23; CI 2.40, 4.34; 27 studies, n=4176 vs alpha agonist RR 1.49; CI 0.94, 2.37; 4 studies; n=919; p 0.01)	D	Low for favorin g alpha agonist studies
KQ2 CER non-stimulants vs stimulants	Participants with adverse events	N/A (indirect comparison)	No difference detected (p 0.12)	D	Low for no differe nce
KQ2 CER amphetamine vs methylphenidate vs NRI vs alpha agonist	Participants with adverse events	N/A (indirect comparison)	Amphetamine reported an increased risk (RR 1.41; CI 1.25, 1.58; 8 studies, n=1151); methylphenidate studies reported an increased risk (RR 1.32; CI 1.25, 1.40; 6 studies, n=945); NRI studies reported an increased risk (RR 1.31; CI 1.18, 1.46; 15 studies, n=2600); alpha agonist studies reported an increased risk (RR 1.21; CI 1.11, 1.31; 14 studies, n=2544); p 0.05	D	Insuffic ient
KQ2 CER NRIs vs stimulants	Participants with adverse events	4 RCTs[175, 225, 539, 604]	No difference detected (RR 1.11; CI 0.90, 1.37; 4 studies, n=756)	S	Low for no differe nce
KQ2 CER NRIs vs alpha agonists	Participants with adverse events	1 RCT[326] (direct comparison), N/A (indirect comparison)	No systematic difference (RR 1.14; CI 0.97, 1.34; 1 study, n=226) in a study comparing guanfacine and atomoxetine; indirect comparisons did also not detect an effect (p 0.06)	C	Low for no differe nce

Notes: ADHD = attention deficit hyperactivity disorder, C = inconsistency, CER = Comparative Effectiveness Review, CI = 95% confidence interval, D indirectness, I imprecision, KQ = Key Question, N/A = not applicable, NRI = norepinephrine reuptake inhibitors, RCT = randomized controlled trial, RR = relative risk, S = study limitation, SMD = standardized mean differences, SoE = strength of evidence

Across studies, we found high strength of evidence that ADHD medication had beneficial effects on broadband measures and ADHD symptom scores when comparing to passive control groups. We concluded high strength of evidence for broadband measure effects due to the consistency in direction of effects across studies, the large number of replications across independent author groups, the small amount of heterogeneity, the robustness of the finding when excluding high-risk of bias studies, and the absence of publication bias. Similarly, we concluded high strength of evidence for ADHD symptom measures due to the consistency in effects across studies, the large number of replications across independent author groups, the lack of substantial heterogeneity, the robustness of effects when excluding high-risk of bias studies, and the absence of publication bias. However, it should be noted that only few studies included children under six years of age in the evaluated interventions.

We downgraded the results for the subgroup of studies explicitly comparing the effect of non-stimulants plus stimulants to stimulants alone for inconsistency. We were unable to determine the effects across all studies as a study-level variable because identified studies varied in how rigorously they avoided co-interventions such as stimulant treatment; hence, it is unclear whether the documented subgroup is a good representation of all medication studies.

We also found moderate strength of evidence that pharmacological treatment reduces functional impairment, but we downgraded the strength of evidence due to observed heterogeneity.

Across studies, there was high strength of evidence that ADHD medication is associated with appetite suppression and that ADHD medication increases the risk of experiencing an adverse event compared to passive control groups. We concluded high strength of evidence for an increased risk due to the consistency of effects across studies, the large number of replications across independent author groups, the small amount of heterogeneity, the robustness of the finding when excluding high-risk of bias studies, and the robustness of the effect when using an alternative effect estimate that takes publication bias into account. We concluded high strength of evidence for an increased risk due to the consistency of effects across studies, the large number of replications by independent author groups, the small amount of heterogeneity, the robustness of the finding when excluding high-risk of bias studies, and the robustness of the effect when using an alternative effect estimate that takes publication bias into account.

The analyses comparing two alternative interventions and the corresponding strength of evidence were more limited. While NRIs had more favorable results than stimulants on problem behaviors, the number of studies and the effect was small, and the strength was downgraded due to study limitations. For the direct comparisons, we downgraded the strength of evidence for broadband measures and ADHD symptoms due to differences in direction of effects and study limitation. We downgraded the strength of evidence for appetite suppression for all comparisons due to differences in direction of effects, and some were further downgraded due to the small number of studies leading to imprecision All indirect comparisons were downgraded to low due to indirectness and imprecision where there were conflicting results between continuous and categorical variables.

5.3.3 Other Pharmaceutical Agents

We also identified studies evaluating a pharmaceutical agent not FDA-approved for ADHD.[105, 113, 114, 122, 146, 147, 151, 155, 158, 165, 174, 206, 219, 232, 264, 269, 304, 354, 377, 399, 439, 507, 508, 513, 572, 574, 620, 636, 637] This included new formulations, off-label use of existing medication approved for other conditions such as modafinil, amantadine, or venlafaxine, and agents no longer available in the Unites States such as agomelatine. Identified studies were published between 1996 and 2022, with some only available as a trial record. Agents were evaluated in five different countries; with the majority of studies originating in the Unites States[269, 377] and Iran.[122, 219, 232, 354, 439, 508, 636] All studies used a randomized control trial design. Nearly all children within the studies received a confirmatory diagnosis by a specialist and/or clinician; exceptions[507, 637] required only a preliminary clinical diagnosis. The populations were predominantly males between the ages of 6 and 18. Female population proportions ranged from 15 percent[507] to 29 percent[399] where reported. In nearly all studies, participants were required to demonstrate an IQ of 70 or higher. For studies that distinguished between ADHD presentations, the most prevalent (ranging from 58%[507] to 100%[354]) was the combined presentation. Approximately half of studies did not report data regarding ADHD presentation type.[113, 264, 269] The only study that addressed co-occurring disorders in the form of a dual diagnosis evaluated children with ADHD and mood disorders.[377] Race and ethnicity demographics were described only in a portion of studies.[113, 269, 377, 399]

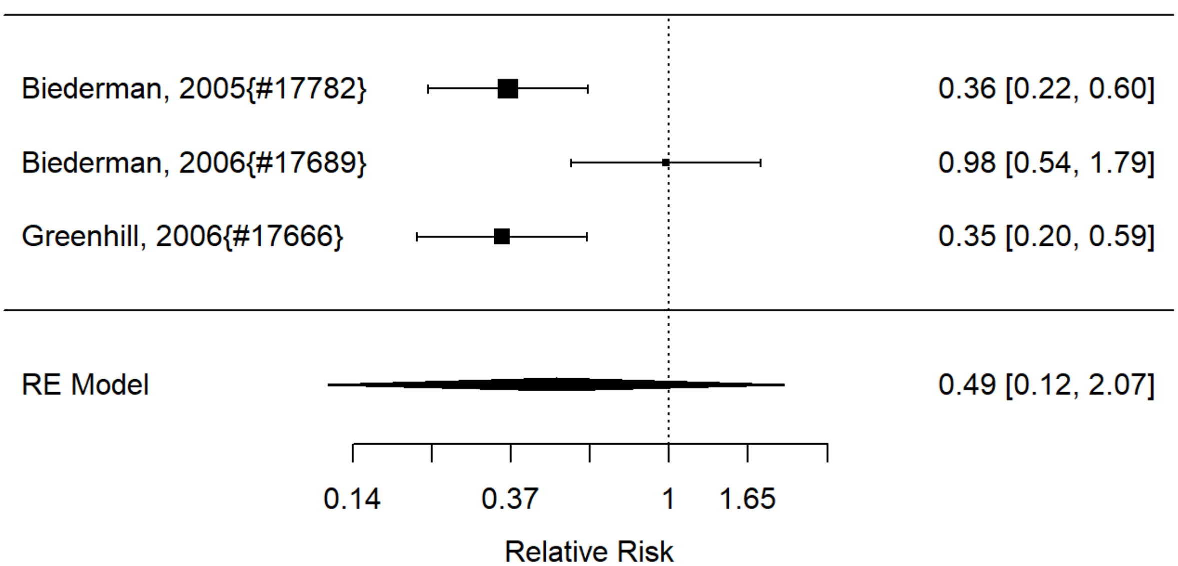
A variety of new pharmaceutical agents were tested for their efficacy in treating ADHD symptoms. Several studies evaluated the use of modafinil for youth with ADHD.[122, 146, 147, 304, 354, 574] Modafinil is a stimulant medication that has been FDA-approved for the treatment of narcolepsy and sleep apnea. Two studies evaluated ABT-089, a neuronal nicotinic receptor partial agonist.[105, 114] Two studies tested an inhibitor of G protein-coupled inward-rectifying potassium channels (GIRKs, tipepidine).[219, 507] All of the studies evaluating pharmaceutical agents reported on a control group for some of the outcomes, which was typically placebo. The most common adjunctive treatment was methylphenidate. In addition to controls, several studies reported efficacy results for comparator groups, usually composed of participants who received a reduced dose of the pharmaceutical agent being tested. Studies reported a variety of study-specific outcomes, such as treatment-related adverse effects. In terms of pre-specified outcomes, broadband scale scores, standardized symptom scores, and appetite changes were the most frequently reported outcomes.

Only some of the identified studies reported sufficient detail to compute effect sizes for our key outcomes. The identified new agents are difficult to compare, particularly as they are chemically very diverse, and it is unclear whether any represent promising approaches for ADHD treatment. However, three agents were assessed in multiple studies.

5.3.3.1 Modafinil

The identified modafinil evaluation studies that reported on a broadband measure are shown in Figure 56.

Figure 56. Effects of modafinil on broadband measures (RR)

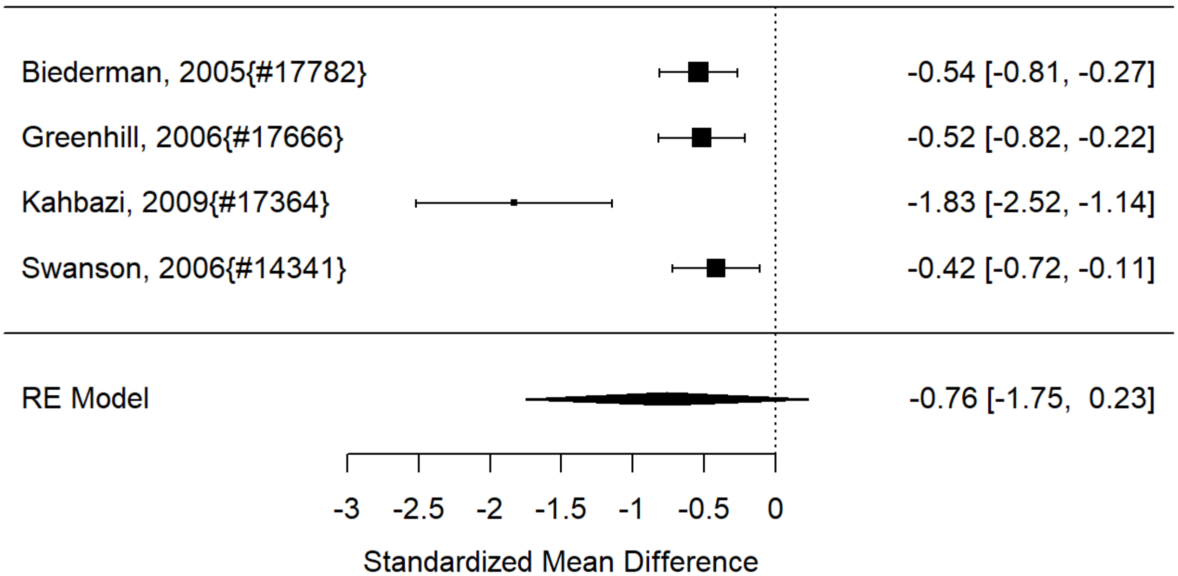


Notes: RE = random effects, RR = relative risk

Across studies, we did not detect a systematic effect of modafinil on broadband scores (RR 0.49; CI 0.12, 2.07; 3 studies, n=539). Two out of three studies were positive and there was heterogeneity (I-squared 76%). There was no indication of publication bias. None of the studies were considered high risk of bias, hence methodological rigor was not a likely source of heterogeneity.

Studies reporting on ADHD symptoms are shown in Figure 57.

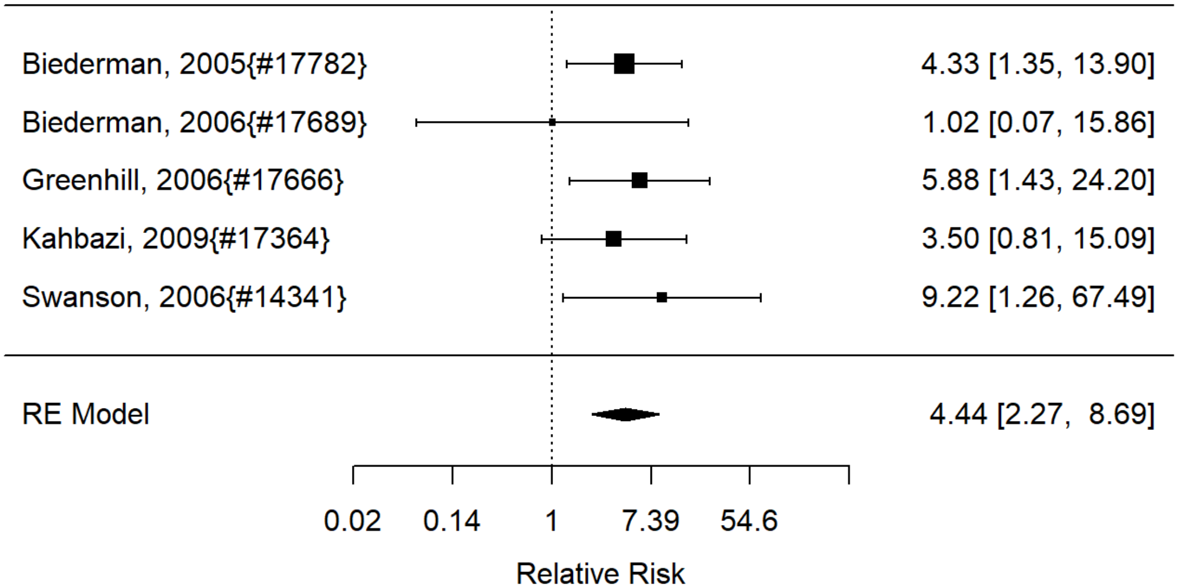
Figure 57. Effects of modafinil on ADHD symptoms (SMD)



Notes: ADHD = attention deficit hyperactivity disorder, RE = random effects, SMD = standardized mean difference

Although all studies reported a positive effect, estimates varied and we did not find a statistically significant effect on ADHD symptoms due to wide confidence intervals (SMD -0.76; CI -1.75, 0.23; 4 studies, n=667). Heterogeneity was high (I-squared 91%). Results for publication bias were borderline (Begg p 1.00, Egger p 0.05) but the alternative estimate using the trim and fill method showed the same effect estimate. One study reported on the number of responders and found a large effect size given that most of the intervention participants showed at least a 40 percent decrease in the ADHD rating scores but none of the placebo participants did (RR 37.00; CI 2.36, 578.24; 1 study, n=46).[354] Studies did not report on other outcomes other than appetite suppression (see Figure 58).

Figure 58. Effects of modafinil on appetite suppression (RR)



Notes: ADHD = attention deficit hyperactivity disorder, RE = random effects, RR = relative risk

Modafinil significantly increased the risk of appetite suppression (RR 4.44; CI 2.27, 8.69; 5 studies; n=780). We detected no heterogeneity. We also found no indication of publication bias. None of the studies were categorized as high risk, hence it is unlikely that the result is purely based on methodological flaws of the studies.

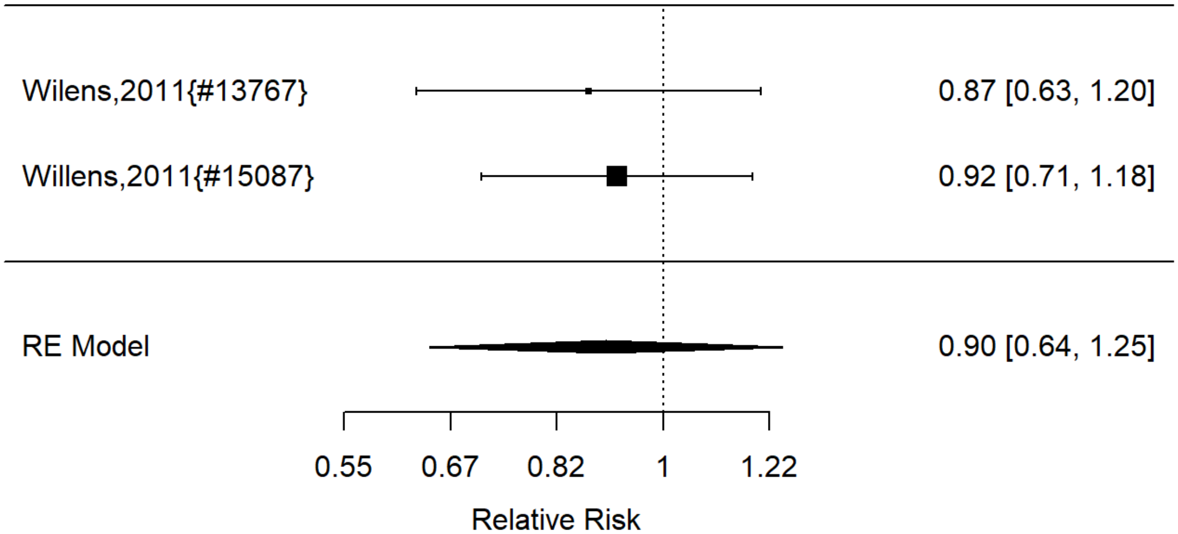
5.3.3.2 Tipepidine

One study found no difference in a broadband measure (SMD 0.38; CI -0.17, 0.93; 1 study, n=51) or appetite suppression (RR 0.30; CI 0.01, 6.98; 1 study, n=51).[219] Two studies reported on ADHD symptoms but estimates varied and no meaningful summary estimate could be derived (SMD -0.28, CI -3.59, 3.04; 2 studies, n=156).[219, 507]

5.3.3.3 ABT-089

Two studies by the same author group reported on α4β2 neuronal nicotinic receptor partial agonist for use in ADHD.[105, 620] Both studies reported on a broadband measure but reported conflicting results and no meaningful summary measure could be derived (SMD -0.02, CI -2.58, 2.53; 2 studies, n=168). One of the studies reported on ADHD symptoms and found improvement (SMD -1.02; CI -1.46, -0.57; 1 study, n=88).[624] Results for the number of participants reporting an adverse event are documented in Figure 59.

Figure 59. Effects of ABT-089 on participants reporting adverse events (RR)



Notes: ABT-089 = a neuronal nicotinic receptor partial agonist, RE = random effects, RR = relative risk

Across studies, we found no statistically significant effect for an increased risk of adverse events (RR 0.90; CI 0.64, 1.25; 2 studies, n=171). We detected no heterogeneity, there was no effect of publication bias, and none of the studies were considered high risk.

5.3.3.4 Comparative Effects of Other Pharmacological Agents

We did not identify two studies comparing the same intervention and comparator. Some studies compared two different doses of the same agent.[105, 146, 174, 269, 507, 513, 572] Multiple studies compared the evaluated intervention to methylphenidate,[122, 165, 399, 439, 508, 636] and one study compared to atomoxetine.[620] The others compared two different adjunctive treatments (risperidone vs divalproex)[151] or different medication (risperidone vs aripiprazole).[232] All individual studies are documented in detail in the evidence table in the appendix.

5.3.3.5 Summary of Findings, Other Pharmacological Agents

Given the diversity of agents that cannot be combined easily, no summary of findings across all studies could be established. Results of the individual studies are shown in Appendix C, Table C.2. The summary of findings table (Table 14) is limited to the agents assessed in multiple studies and Table 14 only shows results where effect size calculation was possible.

Table 14. KQ2 summary of findings and strength of evidence for other pharmacological agents

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 modafinil vs control	Broadband measures	3 RCTs[146, 147, 304]	No systematic effect detected (RR 0.49; CI 0.12, 2.07; 3 studies, n=539).	S	Low for no effect
KQ2 modafinil vs control	ADHD symptoms	4 RCTs RCTs[147, 304, 354, 574]	All individual studies were positive, but the pooled effect was not statistically significant due to the wide variation in effects (SMD -0.76; CI -1.75, 0.23; 4 studies, n=667; RR 37.00; CI 2.36, 578.24; 1 study, n=46)	I	Insufficient
KQ2 modafinil vs control	Appetite suppression	5 RCTs[146, 147, 304, 354, 574]	Intervention was associated with an effect (RR 4.44; CI 2.27, 8.69; 5 studies; n=780)	I	Moderate for effect
KQ2 ABT-089 vs control	Broadband measures	2 RCTs[105, 620]	No meaningful summary estimate could be derived (SMD 0.02, CI -2.58, 2.53; 2 studies, n=168)	S, I	Insufficiefi ne ent
KQ2 ABT-089 vs control	Number of participants reporting on the event	2 RCTs[105, 620]	No systematic effect (RR 0.90; CI 0.64, 1.25; 2 studies, n=171)	S, I	Low for no effect

Notes: CI = 95% confidence interval, I = imprecision, KQ = Key Question, RCT = randomized controlled trial, RR = relative risk, S = study limitation, SMD = standardized mean differences, SoE = strength of evidence

Modafinil was associated with positive effects on ADHD symptoms (low strength of evidence, downgraded due to imprecision by 2). Modafinil was also associated with appetite suppression (moderate for effect). We did not find a positive effect on broadband measure scores, but the strength of evidence was limited (downgraded for study limitations).

The research benefit of ABT-089 is limited. We could not establish a meaningful effect estimate on broadband measures (downgraded to insufficient due to heterogeneity and imprecision). There was low strength of evidence (study limitation, imprecision) indicating that the intervention is associated with adverse events.

5.3.4 Youth-Directed Psychosocial Treatment

We identified 32 studies evaluating psychological, psychosocial, or behavioral interventions for children and adolescents with ADHD.[106, 123, 160, 199, 204, 261, 290, 329, 330, 334, 335, 358, 392, 410, 426, 430, 471, 476, 480, 485, 521-523, 530, 532-535, 565, 594, 624, 643] We included studies in this section that evaluated psychosocial interventions targeting children or adolescents with ADHD, either alone or combined with components for the children's parents or their teachers. The intervention category did not include combinations of psychosocial treatments plus medication; those were described in an earlier section. In addition, all interventions conducted in a school setting are documented in the school intervention section.

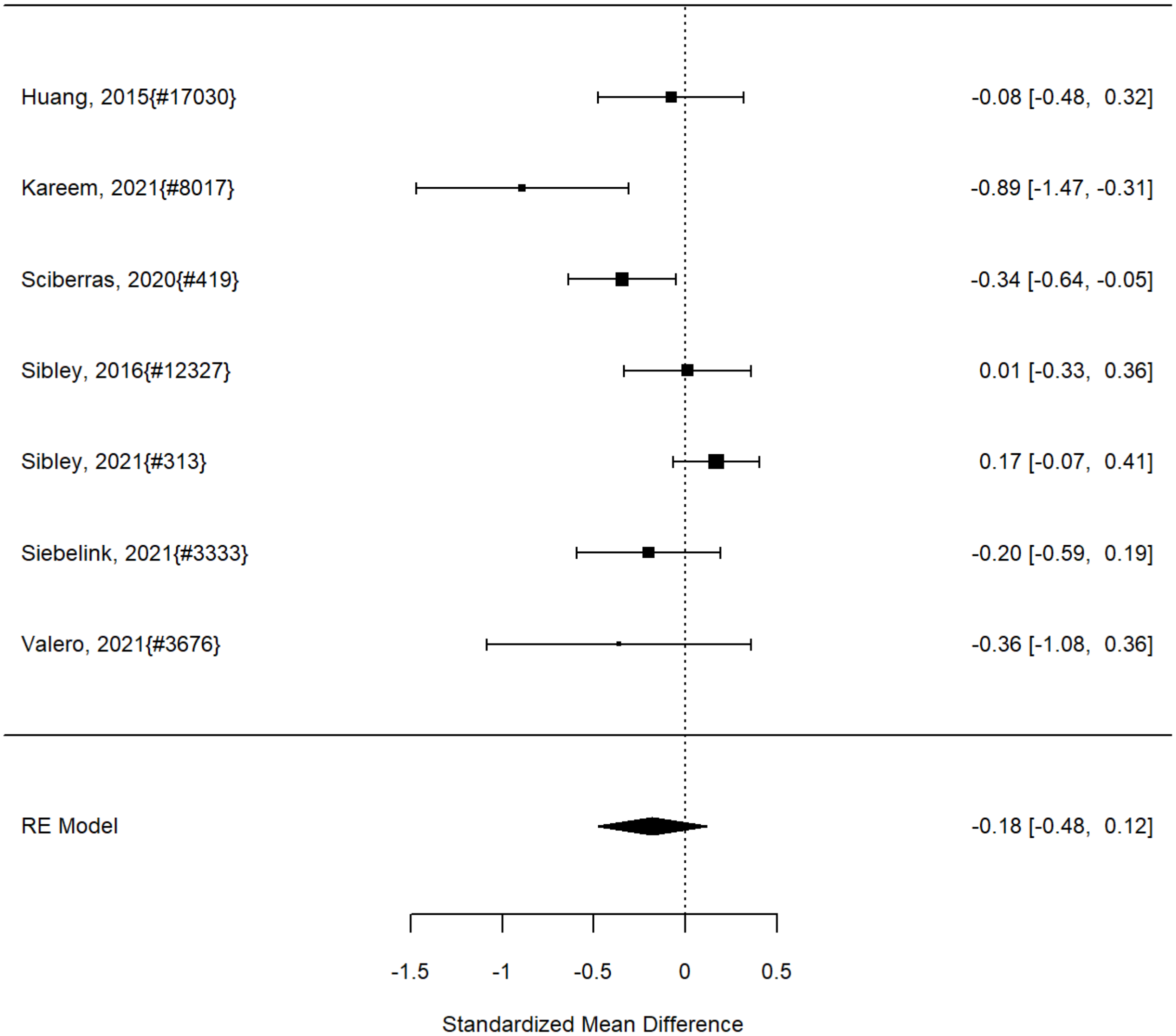
The earliest identified eligible study was published in 2003.[123] Evaluations were conducted in 11 different countries, primarily the United States.[106, 123, 204, 238, 261, 329, 476, 480, 522] The populations studied were children and adolescents with ADHD between the ages of "preschool" and 18, with half of the studies including teenagers. In studies that distinguished between ADHD presentations, the most prevalent type (ranging from 23.4%[334] to 100%[522] of the ADHD participants) was the combined presentation. While ADHD participants with co-occurring disorders were not excluded from most of the studies, three studies purposely included youth with language difficulties,[624] homework problems,[480] and organizational deficits.[106] Race and ethnicity demographics were not mentioned in most studies.

Interventions studied were diverse and they differed in complexity and intensity. Intervention approaches included skills training (e.g., executive function training, homework, or organizational skills),[106, 199, 204, 330, 426, 476, 480, 485, 521, 532-534] social skills training,[123, 335, 392, 522, 565] executive function therapy for preschoolers,[530] driving program for young drivers,[261] sleep-focused intervention,[329, 523] dialectical behavior therapy,[430] cognitive behavior therapy,[160] attention training,[358] a complex behavior modification intervention,[410] behavioral consultations with school and home components,[204] parent-child training psychotherapy for mothers and their children who had ADHD,[290] mindfulness training,[535, 594] musicotherapy,[643] play-based intervention,[624] canine-assisted therapy,[522] and one study compared a behavioral first strategy[471] (providing a behavioral intervention before using medication). Many interventions had multiple components that involved patients, parents, teachers, therapists, and counselors in addition to direct interventions for the participating children. Interventions addressing parents exclusively are documented in the parent support section. Only half of the studies reported on a control group, including attention-matched groups or no intervention (i.e., wait list); the others compared to an alternative psychosocial treatment. Several compared against treatment as usual where it varied what treatment individual children received.

The most frequently reported outcomes in the included studies were the Conners Parent Rating Scales (CPRS), CGI scores, and the ADHD Rating Scale, Version IV.

Figure 60 shows the effect of the intervention on individual problem behaviors such as tardiness, delinquency, and conduct problems, assessed in the individual studies.

Figure 60. Effects of youth-directed psychosocial interventions on behavior (SMD)



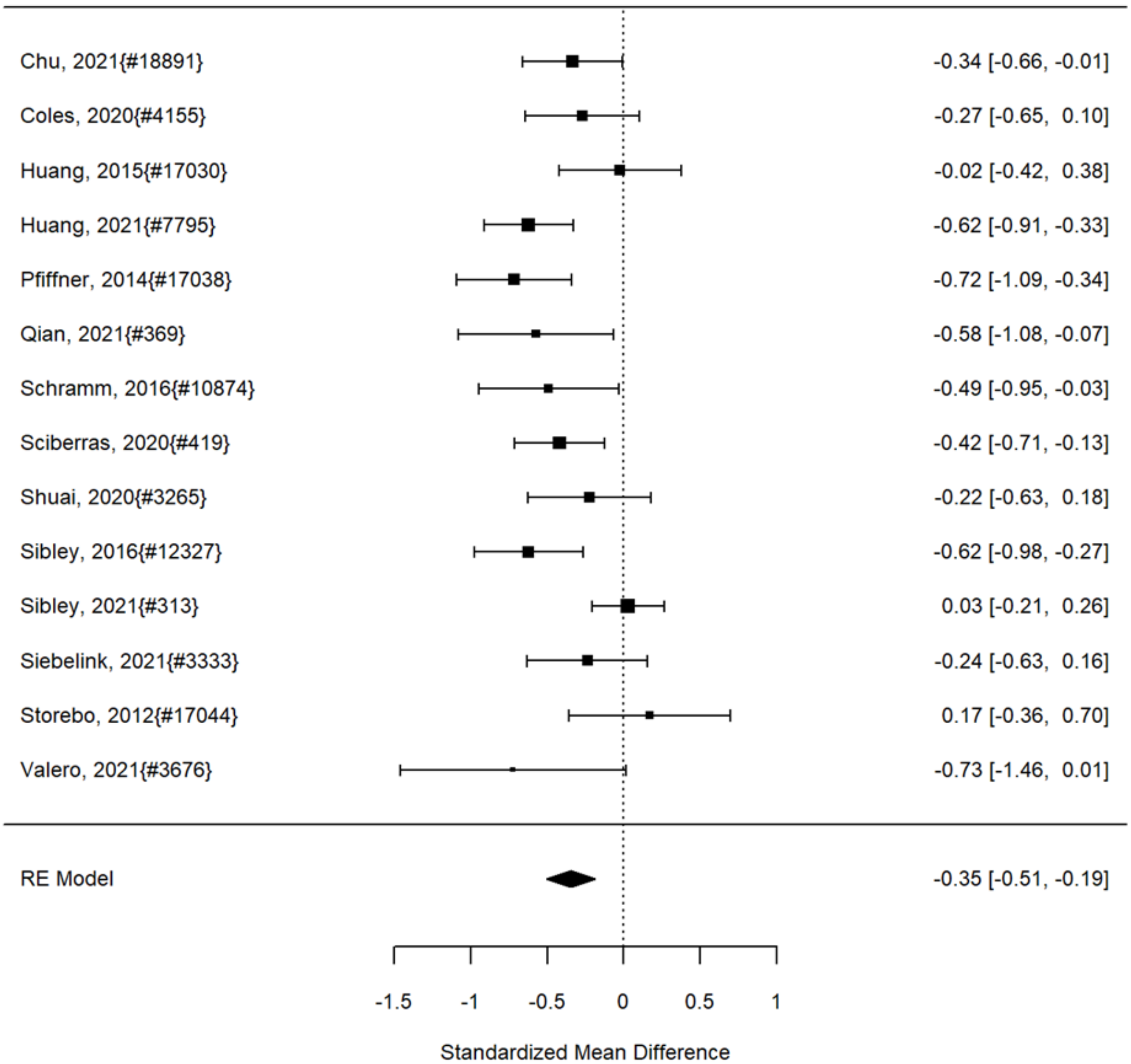
Notes: RE = random effects, SMD = standardized mean difference

Across studies, we did not detect a systematic effect of psychosocial interventions on problematic behaviors compared to control groups (SMD -0.18; CI -0.48, 0.12; 8 studies, n=947). The analysis did not detect substantial heterogeneity (I-squared 55%), but we note that one individual study unlike the other included studies reported a statistically significant effect. The training evaluated in the study focused on attention span, timetable activities, and homework compared to no intervention.[358] We did not detect publication bias. Removing high-risk of bias studies in a sensitivity analysis left only two studies and showed a different estimate with wide confidence intervals, but the effect was still not statistically significant (SMD -0.12; CI -1.04, 0.80). One of the studies (evaluating a sleep-focused intervention) reported improvements in conduct problems after one year (SMD -0.34; CI -0.64, -0.05).[523]

One study reported on a broadband measure; the RCT found a statistically significantly positive effect (SMD 0.62; 0.24, 0.99; 1 study, n=120) for a multi-component, behavioral psychosocial treatment integrated across home and school (Child Life and Attention Skills) for youth with ADHD compared to families receiving a diagnostic report and a resource list.[476]

All studies reporting sufficient detail for changes on a continuous symptom scale are shown in Figure 61.

Figure 61. Effects of youth-directed psychosocial interventions on ADHD symptoms (SMD)



Notes: ADHD = attention deficit hyperactivity disorder, RE = random effects, SMD = standardized mean difference

Analyses indicated a reduction in symptoms associated with a psychological or behavioral intervention (SMD -0.35; CI -0.51, -0.19; 14 studies, n=1686). Interventions were diverse and often included multiple components. Studies contributing to the results included a psychosocial intervention component directed at the children with ADHD; in some cases, however, an additional component addressed the parents or family specifically,[204, 334, 335, 476, 485, 523, 532, 533, 535, 594] and some interventions involved the children's teachers[204, 476] in addition to the children and parents. Two studies evaluated STAND (Supporting Teens' Academic Needs Daily), a parent-teen skills-based therapy blended with motivational interviewing that targets adolescents' organization, time management, and planning occupational training skills, as well as parental monitoring and contingency management.[532, 533] Particularly successful interventions included social skills plus parent skills training (compared to no intervention),[335] a multi-component child life and attention skills program (compared to treatment as usual and a diagnostic report),[476] ecological executive skills training with parent components (compared to waitlist),[485] a family intervention focused on sleep (compared to usual care without focus on sleep management),[523] family therapy STAND intervention (compared to usual care without family therapy),[533] and a mindfulness training for children and parents (compared to waitlist).[594] The youngest children included in the studies were 5 years old but several studies targeted pre-teens and teenagers. Statistical heterogeneity was not remarkable (I-squared 57%). There was no indication of publication bias. Most studies included in this analysis were RCTs; restricting to RCTs showed a similar effect estimate (SMD -0.36; CI -0.53, -0.19). Removing high-risk of bias studies in a sensitivity analysis left only seven studies but the effect estimate was similar (SMD -0.38; CI -0.69, -0.07).

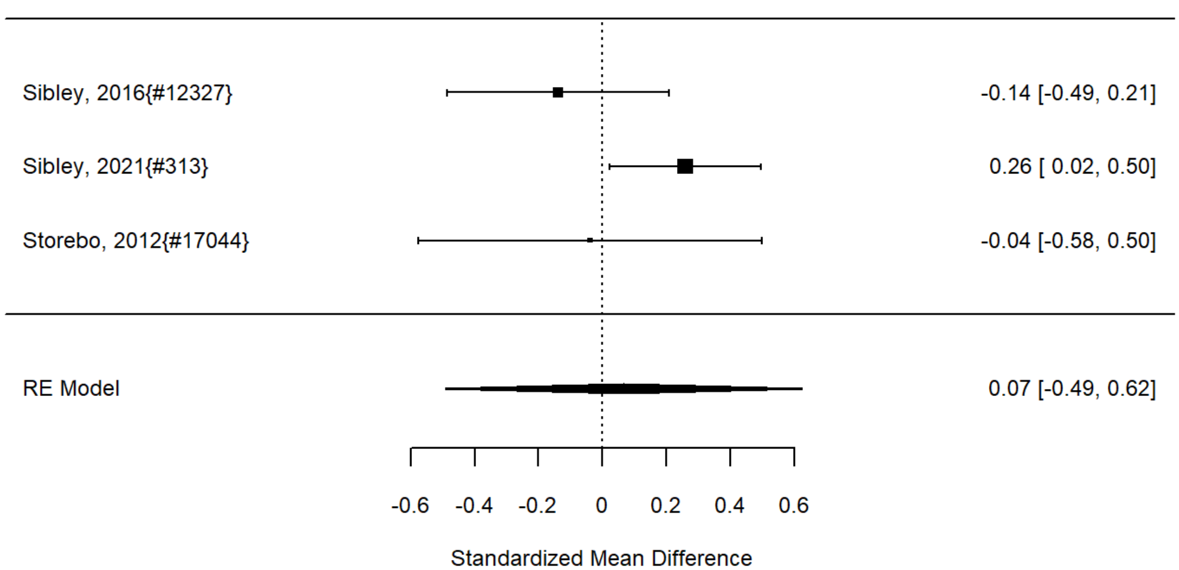
One study reported on symptom improvement as a categorical variable; the study favored a multi-component, behavioral psychosocial treatment integrated across home and school (Child Life and Attention Skills) for youth with ADHD (RR 1.75; CI 1.14, 2.71; 1 study, n=114).[476] Of all the psychosocial intervention studies, three reported long-term outcomes, which were statistically significant (SMD 0.52; CI 0.80, 0.23).[334, 521, 523]

Very few studies reported on functional outcomes. Two studies reporting on functional impairment as a categorical outcome could not be combined to a meaningful summary estimate (SMD 0.42; CI -1.13, 1.97; 2 studies, n=245).[485, 523]

Only one study reported sufficient detail to compute an effect size for treatment satisfaction, indicating no statistically significant difference between a parent-teen intervention focusing on safe driving and an attention-matched control group at the 12 month follow-up (SMD 0.19; CI -0.12, 0.49; 1 study; n=164).[261]

Studies reporting on academic outcomes and reporting sufficient detail to compute effect sizes are shown in Figure 62.

Figure 62. Effects of youth-directed psychosocial interventions on academic performance (SMD)



Notes: RE = random effects, SMD = standardized mean difference

Across studies, we did not detect a systematic effect of the intervention on academic performance compared to control groups (SMD 0.07; CI -0.49, 0.62; 3 studies, n=459). The analysis detected little heterogeneity (I-squared 49%). There was no indication of publication bias. None of the studies included in this analysis was judged to be high risk of bias, suggesting that the lack of effect is not primarily driven by high-risk of bias studies.

Only one study formally reported on the number of participants with adverse events; the study found no increased risk associated with the social skills training intervention compared to treatment as usual as none of the groups reported any adverse events (RR 0.97; CI 0.02, 47.1; 1 study, n=55).[565]

5.3.4.1 Youth-Directed Psychosocial Treatment Comparative Effects

We identified a number of studies that compared diverse psychological and behavioral interventions to an alternative therapeutic approach.[106, 160, 290, 330, 410, 430, 471, 476, 480, 521, 522, 534] None evaluated the same intervention, and comparators were also unique.

One study compared a group parent and adolescent skills training versus a dyadic skills training blended with motivational interviewing and reported similar results across assessed outcomes, including ADHD symptoms (SMD -0.23; CI -0.61, 0.16; 1 study, n=123).[534] A study comparing two cognitive behavioral therapy programs (planning skills CBT versus solution-focused therapy CBT) reported initially more favorable results for the planning skills program, but the effect was not maintained, including for ADHD symptoms (SMD -0.14; CI -0.45, 0.17; 1 study, n=159).[160] An evaluation of a problem-solving and organizational skills training for adolescents found no statistically significant difference in ADHD symptoms compared to progressive relaxation training (SMD -0.29; CI -0.74, 0.16; 1 study, n=77).[521] Another study that focused on organizational functioning, time management, and planning in elementary school children found no statistically significant difference in a functional outcome (SMD 0.24; CI -0.11, 0.60; 1 study, n=125) or academic performance (SMD 0.13; -0.22, 0.48; 1 study, n=125) compared to a performance-based intervention that precluded skills training.[106]

One study in adolescents compared dialectical behavioral therapy compared to a psychoeducational group program about ADHD. It found lower self-reported ADHD ratings (SMD -0.39; CI -0.7, -0.08; 1 study, n=164) but no statistically significant difference for functional impairment (SMD 0.23; CI -0.08, 0.53; 1 study, n=164)[430] Another of the identified studies evaluated a canine-assisted psychosocial intervention compared to behavioral parent training and social skills training.[522] The study did not report sufficient detail to allow effect size calculations for the outcomes of interest but concluded that the canine-assisted group showed better results for ADHD symptoms.

A study comparing a multi-component program (Child Life and Attention Skills, CLAS) versus a parent-focused treatment with fewer school interactions, found the intensive program to have more positive effects, but there was no statistically significant difference in broadband measures (SMD 0.20; CI -0.13, 0.52 and RR 1.23; CI 0.89, 1.71; 1 study, n=199) or ADHD symptoms (SMD -0.27; CI -0.60, 0.05 and RR 1.23; CI 0.89, 1.71; 1 study, n=199).[476] A family-school intervention versus an intervention about coping with ADHD through relationships and education (CARE) favored the family-school interventions for ADHD symptoms (SMD -0.34; CI -.061, -0.06; 1 study, n=199) but other outcomes assessed in the study did not show differences between interventions, including academic performance (SMD -0.21; -0.49, 0.07; 1

study, n=199).[480] One study (n=145) compared a multi-component intervention of motivational components, homework management and schoolwork organization training, as well as family-school partnership building versus a complex medication integration protocol that included psychoeducation, medication decision-making, and integrated medication management. There were insufficient details reported to allow effect size calculations, but the authors concluded that both interventions showed positive effects.[330] One study evaluating a complex intervention program consisting of parental training, behavior modification, sensory integration therapy, and sand tray therapy found no statistically significant difference compared to methylphenidate plus atomoxetine plus a homeopathic intervention for ADHD symptoms (SMD -0.35; CI -0.77, 0.07; 1 study, n=90).[410]

A study that included mothers with ADHD who had a child also diagnosed with ADHD evaluated parent-child training psychotherapy for mothers and children.[290] The study found no statistically significant differences compared to individual non-specific counseling for the mothers for problem behaviors (SMD -0.10; CI -0.49, 0.30; 1 study, n=101), ADHD symptoms (SMD 0.19; CI -0.20, 0.59; 1 study, n=101), or functional impairment (SMD 0.11; CI -0.31, 0.52; 1 study, n=92) in the children with ADHD.

One study addressed sequencing of interventions.[471] Children assigned to a multi-component behavioral intervention consisting of social skills training for children, parent training to establish a daily reward system, teacher consultations, and a case manager versus medication first reported significantly fewer classroom rule violations per hour than the medication first intervention (incidence rate ratio 0.66, p<0.01; 1 study, n=152). The study found no difference in the disruptive behavior disorder rating scales across groups (SMD -0.02; CI -0.34, 0.31; 1 study, n=152) or functional impairment (SMD -0.01; CI -0.33, 0.31; 1 study, n=152).

5.3.4.2 Youth-Directed Psychosocial Treatment Summary of Findings

Table 15 shows the findings for the outcomes of interest together with the number of studies and study identifiers. Findings are shown only when effect sizes could be computed.

Table 15. KQ2 summary of findings and strength of evidence for youth-directed psychosocial treatment

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 psychosocial treatment vs control	Behavior	9 RCTs and CTs[335, 358, 392, 522, 523, 532, 533, 535, 594]	No systematic effect (SMD -0.18, CI -0.48, 0.12; 8 studies, n=947)	S, I	Low for no effect
KQ2 psychosocial treatment vs control	Broadband measures	2 RCTs[106, 476]	Results favor intervention (SMD 0.62, CI -0.24, 0.99; 1 study, n=120)	S	Insufficient
KQ2 psychosocial treatment vs control	ADHD symptoms	18 RCTs and CTs[199, 204, 334, 335, 392, 426, 476, 485, 521-523, 530, 532, 533, 535, 565, 594, 643]	Results favor intervention (SMD -0.35, CI -0.51, -0.19; 14 studies, n=1686; RR 1.75; CI 1.14, 2.71; 1 study, n=114)	S	Moderate for benefit
KQ2 psychosocial treatment vs control	Functional impairment	4 RCTs[106, 476, 485, 523]	No systematic effect and no meaningful summary effect could be derived (SMD 0.42, CI -1.13, 1.97; 2 studies, n=245)	C, I	Insufficient

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 psychosocial treatment vs control	Acceptability of treatment	1 RCT[261]	No systematic effect (SMD 0.19, CI -0.12, 0.49; 1 study, n=164)	S, C, I	Insufficient
KQ2 psychosocial treatment vs control	Academic performance	4 RCTs[532, 533, 565]	No systematic effect (SMD 0.07, CI -0.52, 0.66; 3 studies, n=459)	S	Low for no effect
KQ2 psychosocial treatment vs control	Appetite suppression	0 studies	No data	C	Insufficient
KQ2 psychosocial treatment vs control	Participants with adverse events	1 RCT[565]	No systematic effect and no meaningful summary effect could be derived (RR 0.97; CI 0.02, 47.01; 1 study, n=55)	C	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, CI = 95% confidence interval, C = inconsistency, CT = controlled trial without random assignment, I = imprecision, KQ = Key Question, RCT = randomized controlled trial, RR = relative risk, S = study limitation, SMD = standardized mean differences, SoE = strength of evidence

The majority of psychological and behavioral interventions were multicomponent interventions and we found favorable effects of these on ADHD symptoms with a moderate strength of evidence. We downgraded all outcomes for study limitation as studies were at high or moderate risk of bias, often because studies of behavioral interventions versus no intervention cannot be blinded, and unblinded parents provided the outcome data. We found low strength of evidence that psychological interventions do not improve problem behaviors across studies and the evidence was insufficient for broadband measure scores. These findings were also downgraded for the domain inconsistency (direction of effects varied). There was insufficient evidence for functional outcomes due to additional imprecision as it was not clear whether or not psychological interventions influence functional impairment. Meta-analysis across studies found no difference in academic outcomes; strength of evidence is low due to inconsistency of direction and risk of bias. Only one study reported sufficient detail to compute effect sizes for treatment acceptability; the strength of evidence was rated insufficient. No studies reported on appetite changes or growth suppression, and only one study reported on the number of participants with adverse events; strength of evidence was determined to be insufficient, given the lack of data or inability to determine the consistency of effects where only one study reported on the outcome of interest.

The comparative effectiveness strength of evidence was determined to be insufficient due to the lack of studies reporting on similar interventions and comparators.

5.3.5 Cognitive Training

We identified 22 studies evaluating cognitive training to treat ADHD.[56, 129, 139, 148, 166, 221, 222, 227, 229, 243, 258, 313, 367, 368, 372, 456, 457, 489, 578, 595, 613, 628] The earliest identified studies were from 2013.[243, 578] Evaluations were published in 14 different countries, including the United States[368, 372] and Iran.[129, 456, 457]

The populations studied were predominately males aged six to 17 years, with only one study including children as young as three years old.[489] Evidence of intellectual disability (i.e., full-scale IQ < 70) was exclusionary in all studies, and eight studies required full-scale IQ scores of

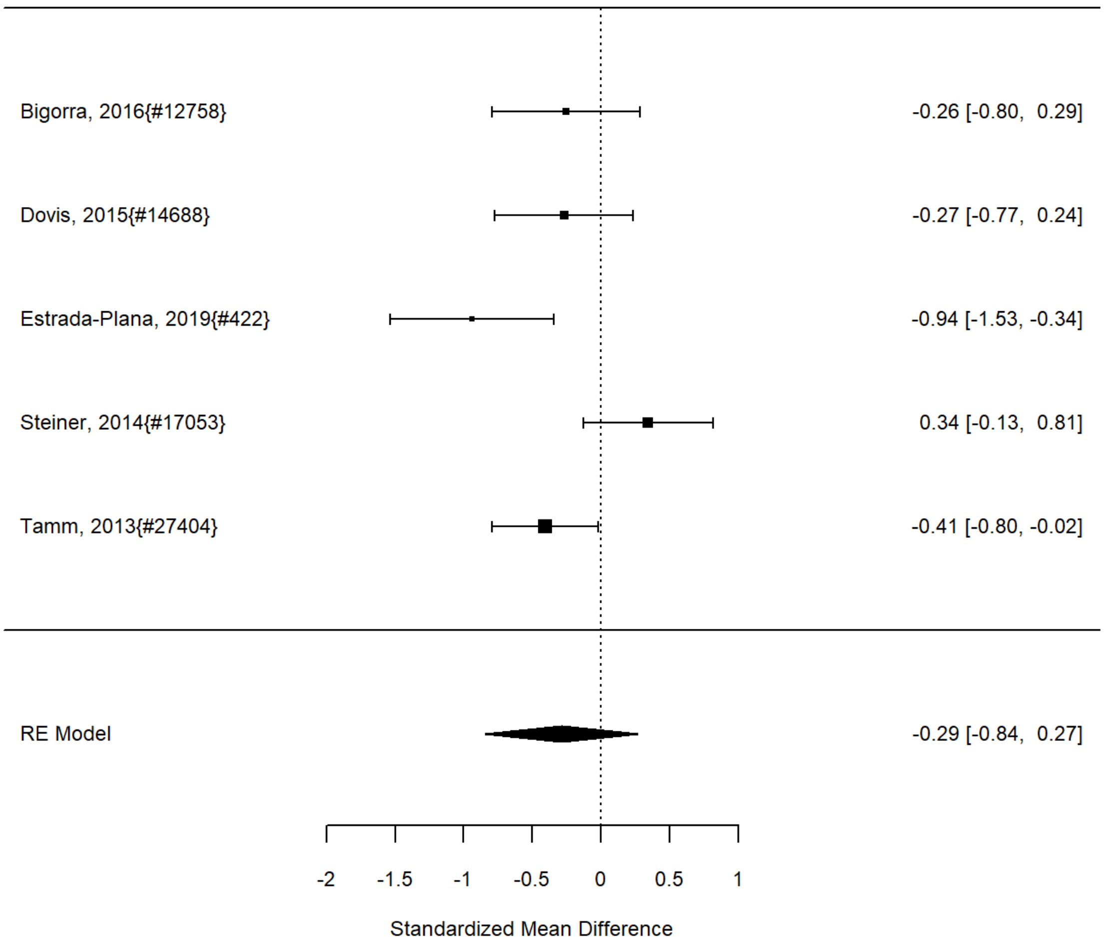
80 or higher. Over 70 percent of studies included participants with a history of stimulant medication treatment, and of those, two thirds of their ADHD cohorts had prior or ongoing stimulant treatment. Five of the studies required stimulant treatment to be discontinued at least 24-hours before undergoing cognitive training, and several required an even longer washout period. For studies that distinguished between ADHD presentations (combined, inattentive, hyperactive/impulsive), the most prevalent was ADHD-combined type. While ADHD participants with typical co-occurring disorders such as conduct disorder were not excluded from most studies, a few studies purposefully included children with concomitant learning disorders (e.g., dyslexia, language disorder).[222, 595] Race and ethnicity demographics were not mentioned in almost all studies.

Cognitive training interventions were delivered across different settings, including home-based and hospital/clinic-based programs. More than half of the studies used a computerized video game format such as the Cogmed digital working memory training program. Some studies used other non-computerized cognitive training modalities including structured, interactive games (e.g., Training Executive, Attention, and Motor Skills) and paper-and-pencil neuropsychological tasks, or they employed functional cognitive rehabilitation paradigms used in occupational therapy to improve ADHD as documented in detail in Appendix C, Table C.2. ADHD-matched control groups received treatment as usual,[56, 166, 221, 367, 456, 613] or they were randomized to a waitlist or no intervention.[139, 199, 243, 258, 313, 456, 578] Half the studies were compared to children exposed to non-adaptive/non-calibrated versions of the targeted cognitive intervention,[148, 222, 229, 372] cognitive training of a separate domain (e.g., training of working memory vs. training of inhibitory control) or sham cognitive training[227, 229, 368] or attention-matched intervention.[129, 457] Other studies reported on the comparative effects for two alternative interventions without control group.[368, 489, 595, 628]

Studies reported a variety of study-specific outcomes, such as improvement in individual cognitive tasks. In terms of pre-specified key outcomes for this review, ADHD symptom rating scale scores were most frequently reported.

Studies that reported on a problem behavior are shown in Figure 63.

Figure 63. Effects of cognitive training on behavior (SMD)

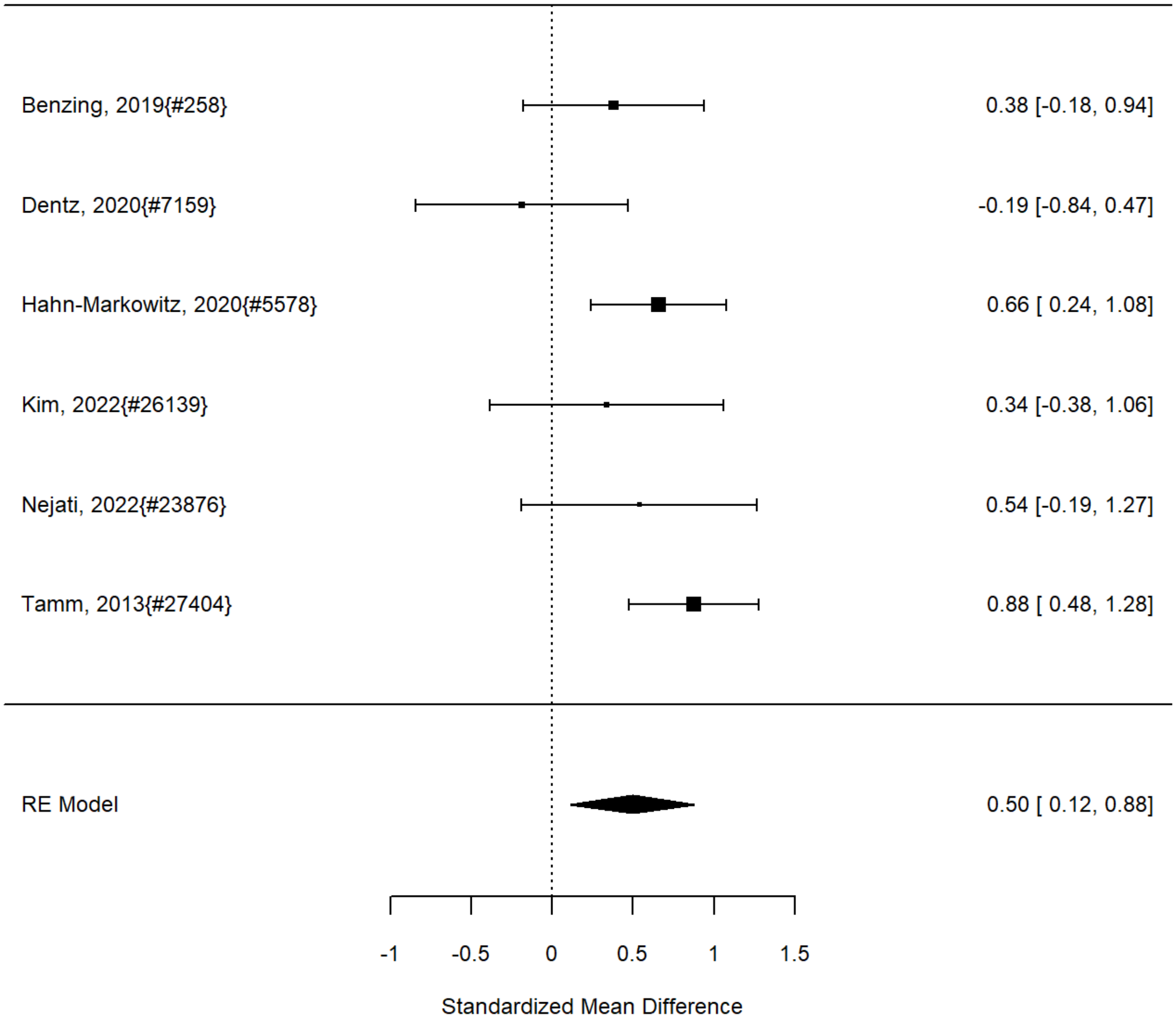


Notes: RE = random effects, SMD = standardized mean difference

Across identified studies, cognitive training had no statistically significant effect (SMD -0.29; CI -0.84, 0.27; 5 studies, n=337). This small set of studies did not detect heterogeneity or publication bias. All studies included in the analyses were RCTs. Removing two high-risk of bias RCTs resulted in a smaller estimate, but the effect was still statistically significant (SMD -0.26, CI -0.35, -0.18).

Studies reporting on broadband measure scores are documented in Figure 64.

Figure 64. Effects of cognitive training on broadband measures (SMD)

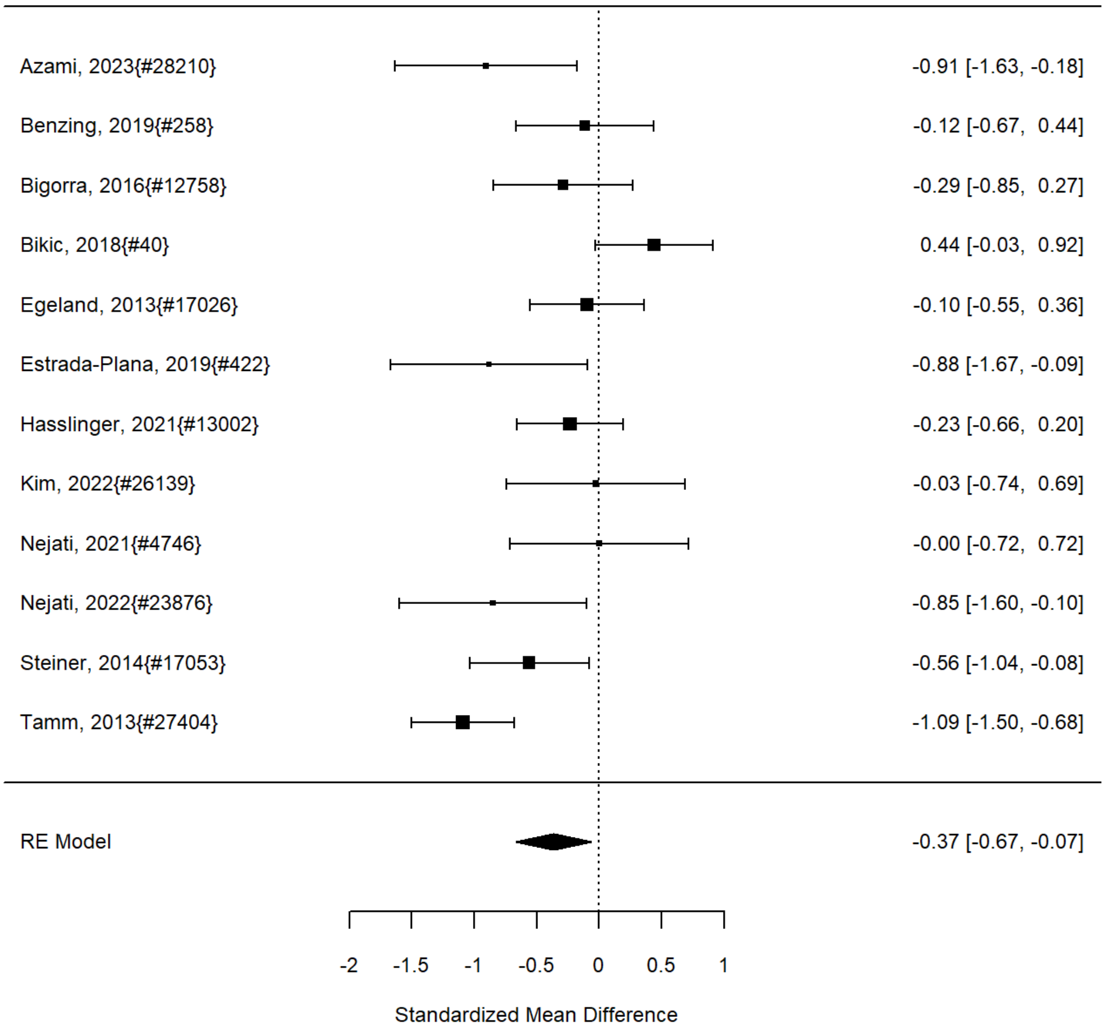


Notes: RE = random effects, SMD = standardized mean difference

The interventions were associated with a statistically significant improvement in broadband measures (SMD 0.50; CI 0.12, 0.88; 6 studies, n=344). Children included in the studies were between six and seven, and seven and ten, where reported. Heterogeneity was not remarkable (I-squared 58%) and there was no indication of publication bias. Removing high-risk of bias studies left only two studies with a smaller effect estimate that was no longer statistically significant due to wide confidence intervals (SMD 0.43; CI -0.54, 1.42). Similarly, restricting to parallel RCTs only found a smaller and not statistically significant effect (SMD 0.43; CI -0.06, 0.93). Only one study reported sufficient detail for a categorical analysis indicating no difference between groups (RR 0.96; CI 0.59, 1.55; 1 study, n=339).[372]

The studies reporting on the effect of cognitive training on ADHD symptoms are shown in Figure 65.

Figure 65. Effects of cognitive training on ADHD symptoms (SMD)

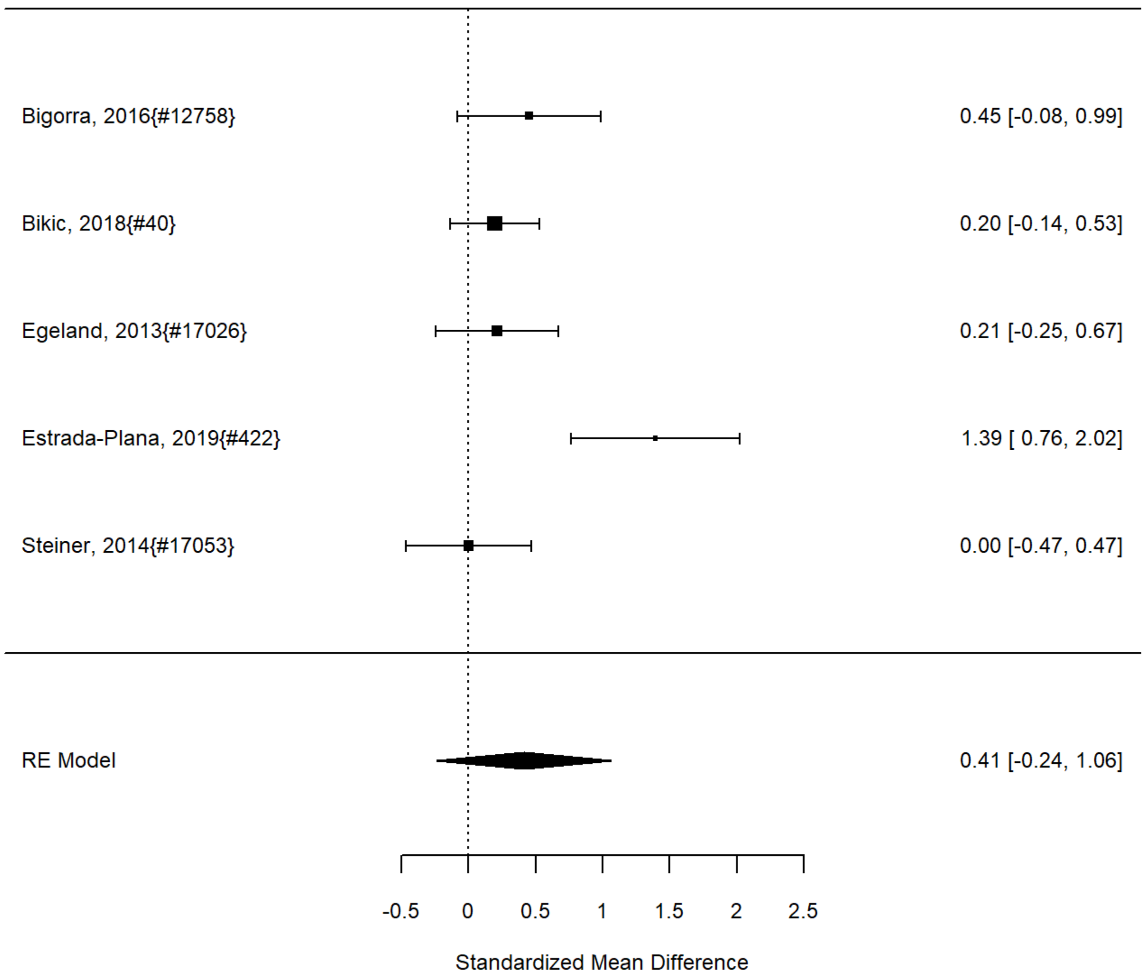


Notes: ADHD = attention deficit hyperactivity disorder, RE = random effects, SMD = standardized mean difference

Across studies, we found improvement of ADHD symptoms associated with cognitive training compared to control groups (SMD -0.37; CI -0.67, -0.07; 12 studies, n=655). The analysis did detect some heterogeneity (I-squared 65%). There was no evidence of publication bias. Removing studies with high risk of bias also indicated a lack of systematic effect (SMD -0.24; CI -0.73, 0.30) and heterogeneity was not substantially reduced. An additional study reporting on a categorical symptom outcome (number with at least 30% improvement) did not detect statistically significant differences between groups (RR 1.28; CI 0.85, 1.94; 1 study, n=337).[372]

Studies reporting on effects of cognitive training on functional impairment are shown in Figure 66.

Figure 66. Effects of cognitive training on functional impairment (SMD)



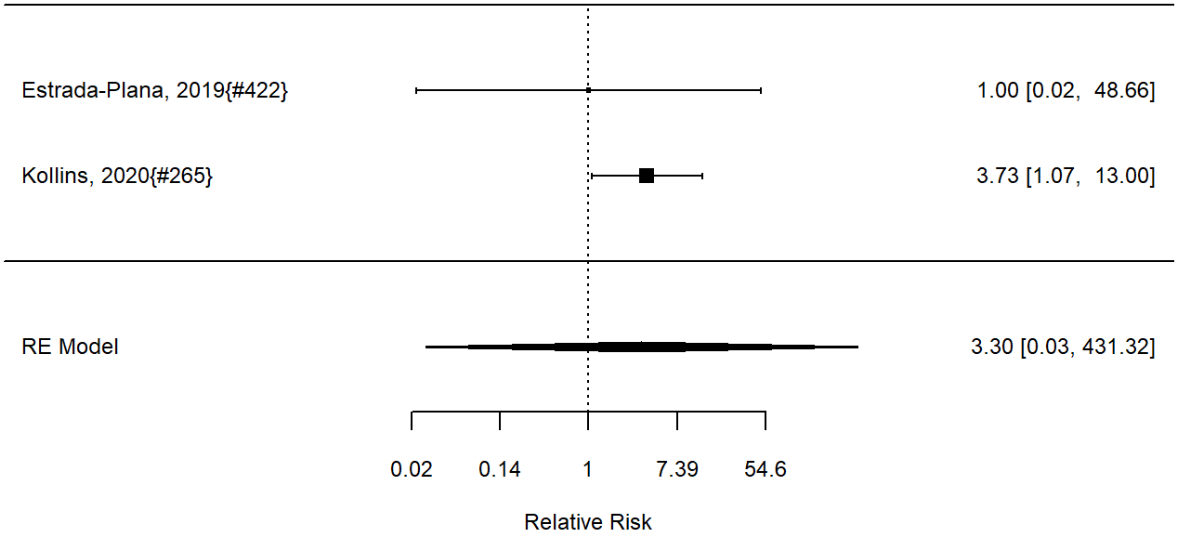
Notes: RE = random effects, SMD = standardized mean difference

Studies indicated an improvement in functional impairment, but the effect was not statistically significant (SMD 0.41; CI -0.24, 1.06; 5 studies, n=387). There was some heterogeneity and effect estimates varied somewhat (I-squared 77%). There was no indication of publication bias. Excluding three high-risk of bias studies in a sensitivity analysis (and thereby removing an outlier) did result in a smaller effect estimate that also was not statistically significant (SMD 0.27; CI -1.20, 1.74). An additional study reporting on impairment as a categorical variable did not detect differences between groups (RR 1.29; CI 1.00. 1.66, n=348).[372]

We could not compute effect estimates for treatment satisfaction in this intervention subset. Although two studies reported on an academic rating scale, estimates varied widely and we could not derive a meaningful summary estimate due to wide confidence intervals (SMD -0.72; CI -9.59, 8.15; 2 studies, n=68).[129, 222]

Appetite suppression was not assessed, but the number of participants experiencing an adverse event is shown in Figure 67.

Figure 67. Effects of cognitive training on participants with adverse events (RR)



Notes: RE = random effects, RR = relative risk

Only two studies reported clearly on the number of participants with adverse events in both treatment arms to determine the presence or absence of adverse events. Across studies, we did not detect a systematic effect of the intervention compared to a control group (RR 3.30; CI 0.03, 431.32; 2 studies, n=402). One of the studies reported no adverse events occurring in either study arm,[258] the other reported more events in the intervention group, including frustration and headache (but no serious adverse events). In this small set of studies there was no evidence of heterogeneity and publication bias could not be assessed. Removing the high risk of bias study left one estimate that suggested a higher rate of adverse events in the intervention group (RR 3.73; CI 1.01, 10.83).[372]

5.3.5.1 Cognitive Training Comparative Effects

A small number of individual studies had active comparators. One study compared structured games versus parent training.[489] The study did not report on key outcomes, but it concluded that working memory training is effective.

Four studies compared different cognitive training approaches.[229, 368, 595] A study comparing central executive training versus inhibitory control training did not report on outcomes of interest in sufficient detail to allow us to compute effect sizes, but the study concluded that the finding supported the use of central executive training.[368] Another study compared Cogmed working memory training versus a new active working memory and executive function compensatory training (paying attention in class).[595] The study reporting finding no difference in a broadband measure, but it reported insufficient details to compute effect sizes. An additional study compared executive function training with multiple targets versus working memory training or inhibition and cognitive flexibility.[229] The study did not report on key outcomes addressed in this review, but it concluded that there was no significant difference on any executive function measures. Another study compared two cognitive training batteries: ADHD executive functioning training versus general executive function training not specific to ADHD.[628] The study reported no difference for ADHD symptoms (SMD 0.08; CI -0.33, 0.48; 1 study, n=94).

5.3.5.2 Cognitive Training Summary of Findings

Table 16 shows the findings for the outcomes of interest together with the number of studies and study identifiers. Comparative effectiveness and safety results are not shown as none of the identified studies reported on the key outcomes in sufficient detail.

Table 16. KQ2 summary of findings and strength of evidence for cognitive training

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 cognitive training vs control	Behavior	4 RCTs[148, 229, 258, 578]	No systematic effect (SMD -0.29; CI -0.84, 0.27; 5 studies, n=337)	C, I	Low for no effect
KQ2 cognitive training vs control	Broadband measures	6 RCTs and CTs[139, 222, 313, 367, 372, 457]	Results favor intervention (SMD 0.50; CI 0.12, 0.88; 6 studies, n=344; RR 0.96; CI 0.59, 1.55; 1 study, n=339)	C	Low for benefit
KQ2 cognitive training vs control	ADHD symptoms	12 RCTs[56, 129, 139, 148, 221, 243, 258, 367, 372, 456, 457, 578]	Results favor intervention (SMD -0.37; CI -0.67, -0.07; 12 studies, n=655; RR 1.28; CI 0.85, 1.94; 1 study, n=337)	C	Low for benefit
KQ2 cognitive training vs control	Functional impairment	6 RCTs[56, 148, 199, 243, 258, 372]	No systematic effect (SMD 0.41; CI -0.24, 1.06; 5 studies, n=387)	C	Low for no effect
KQ2 cognitive training vs control	Acceptability of treatment	0 studies	No data	C	Insufficient
KQ2 cognitive training vs control	Academic performance	2 RCTs[129, 222]	No systematic effect but no meaningful summary estimate could be derived (SMD -0.72; CI -9.59, 8.15; 2 studies, n=68)	C	Insufficient
KQ2 cognitive training vs control	Appetite suppression	1 study[367]	No effect size data	C	Insufficient
KQ2 cognitive training vs control	Participants with adverse events	2 RCTs[258, 372]	No systematic effect, but no meaningful summary estimate could be derived (RR 3.30; CI 0.03, 431.32; 2 studies, n=402)	I	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, C = inconsistency, CI = 95% confidence interval, CT controlled trial without random assignment, I = imprecision, KQ = Key Question, RCT = randomized controlled trial, RR = relative risk, SMD = standardized mean differences, SoE = strength of evidence

Table 16 generally shows an emerging evidence base. Studies predominantly reported on specific measures rather than generally important outcomes such as ADHD symptoms. Strength of evidence was downgraded due to heterogeneity or inconsistency in direction of effects, and imprecision where no meaningful summary estimate could be derived from the available research. The evidence for multiple outcomes of interest is insufficient to date.

While different cognitive trainings have been compared in comparative effectiveness and safety evaluations, studies reported on study-specific intermediate outcomes, and it is unclear whether and which cognitive training is superior to others.

5.3.6 Neurofeedback

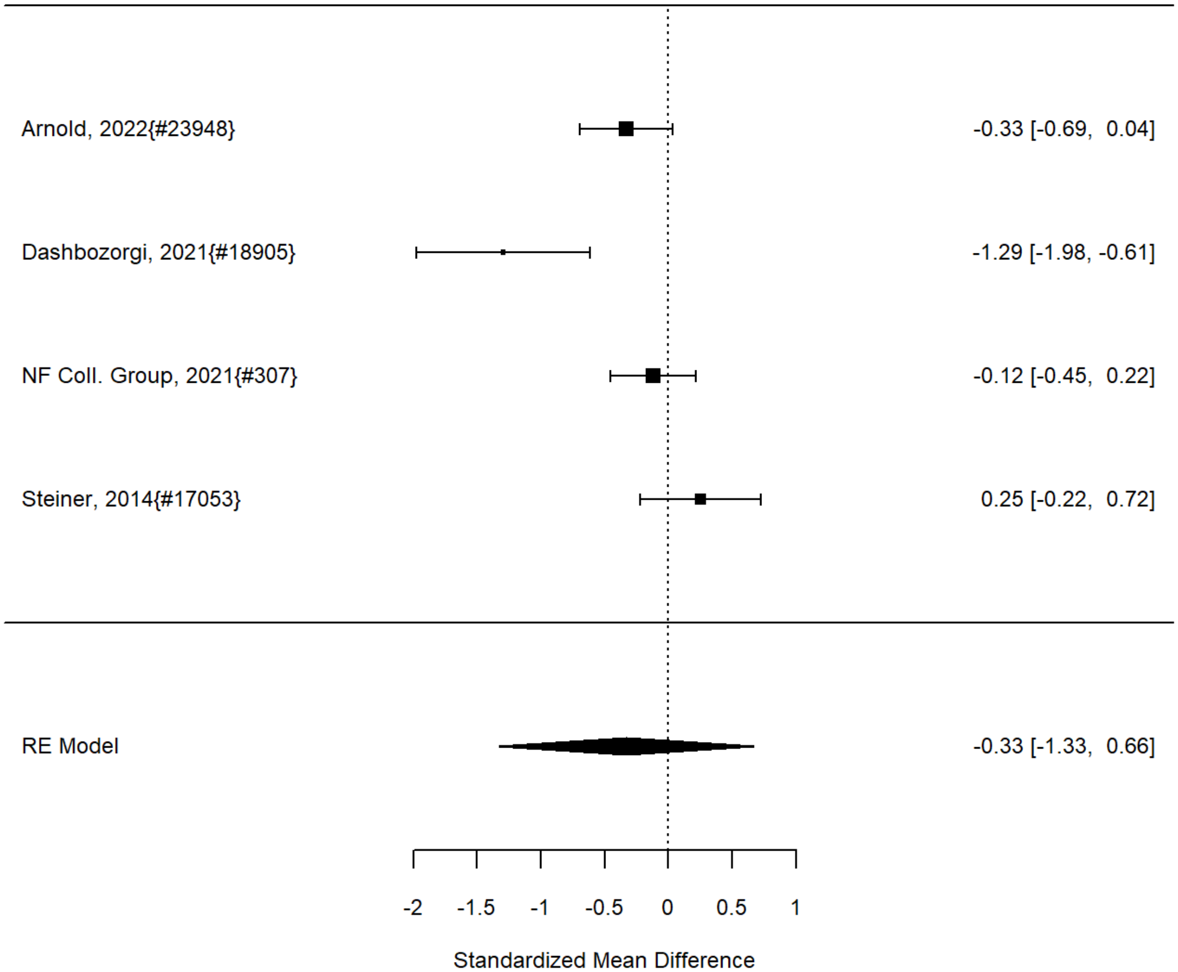
We identified 21 studies using neurofeedback.[126, 130, 156, 215, 240, 280, 291, 294, 302, 320, 375, 398, 409, 435, 458, 483, 484, 490, 492, 562, 567] The earliest identified study was published in 2003.[280] Studies came from 11 different countries, in particular Germany and the United States. Almost all studies used a randomized control trial study design, except for two non-randomized controlled studies,[156, 302] The populations studied were between the ages of 6 and 18 years. Female population proportions in mixed samples ranged from 15[398] to 37[302] percent, and three studies did not include any girls.[215, 484, 492] In nearly all studies, participants were required to demonstrate an IQ of 80 or higher. For studies that distinguished between ADHD presentations, the most prevalent type, ranging from 15[492] to 100[567] percent of ADHD participants, was the combined type. There were no reported systemic co-occurring disorders within the included study populations, though many did not exclude commonly associated co-occurring disorders within their study population. Race and ethnicity demographics were described in few of the identified studies.[458, 562]

A variety of neurofeedback protocols were tested for their efficacy in treating ADHD symptoms. Two thirds involved theta/beta electroencephalogram (EEG) marker modulation.[126, 130, 156, 172, 215, 240, 291, 294, 302, 398, 458, 492, 562] One third of protocols centered around modulation of slow cortical potentials.[294, 320, 375, 435, 567] Among the neurofeedback studies, three quarters reported on a passive control group, including attention-matched task,[215, 291] waitlisted for intervention,[398, 492] and no intervention groups.[302, 562] Several studies reported efficacy results compared to an alternative intervention, most frequently cognitive training or methylphenidate.

Studies reported a variety of often study-specific outcomes, such as improvement in individual cognitive tasks as documented in Appendix C, Table C.2. In terms of pre-specified outcomes, broadband scale scores and standardized symptom scores were the most frequently reported outcomes.

Studies reporting on reductions in problematic behaviors, such as aggression and off-task behavior at school, are shown in Figure 68.

Figure 68. Effects of neurofeedback on behavior (SMD)

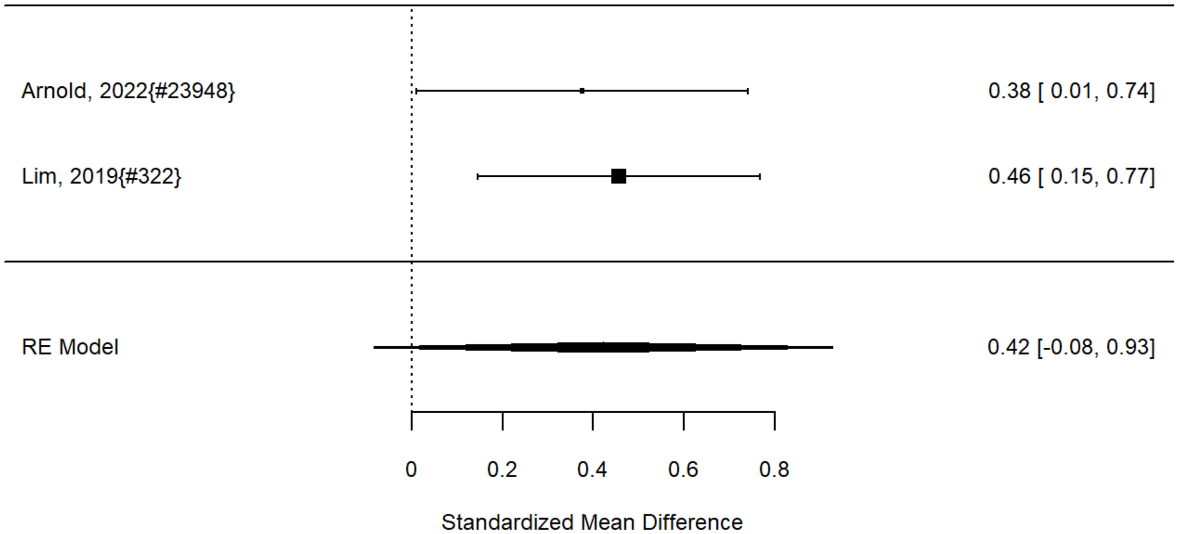


Notes: RE = random effects, SMD = standardized mean difference

Study results varied considerably, and no systematic effect was seen across studies (SMD -0.33; CI -1.33, 0.66; 4 studies, n=372). Despite the small number of studies, the analysis detected heterogeneity (I-squared 86%). There was no indication of publication bias, and removing a high-risk study did also not indicate a statistically significant effect (SMD -0.52; CI -2.00, 0.97). Two of these studies reported long-term behavior improvements, but estimates varied, and no meaningful summary estimate could be derived (SMD -0.21; CI -1.55; 1.12).[126, 458]

Two studies reported on a continuous broadband measure as shown in Figure 69.

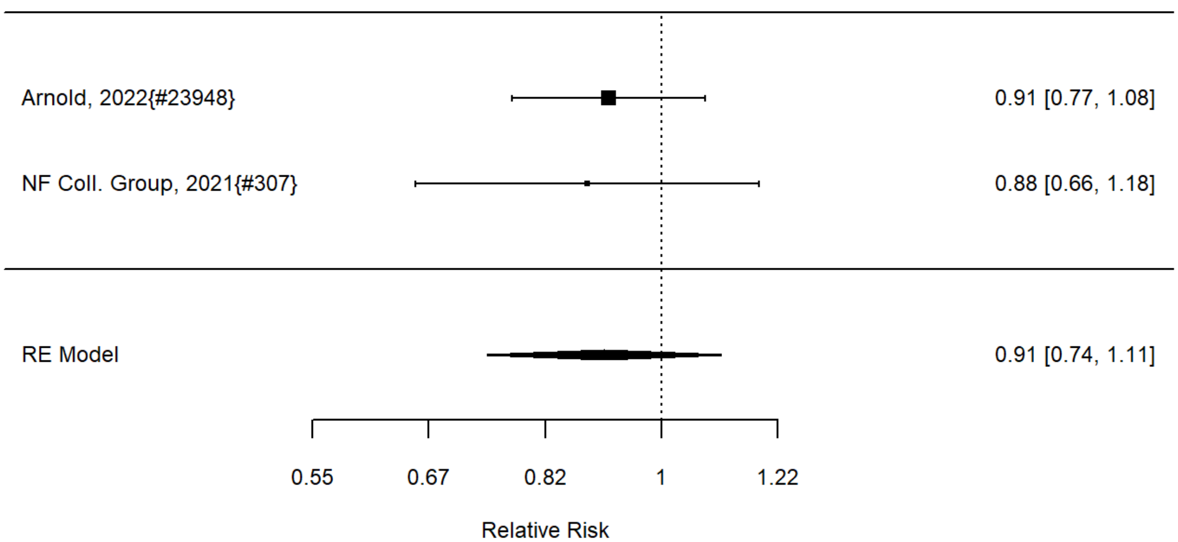
Figure 69. Effects of neurofeedback on broadband measures (SMD)



Notes: RE = random effects, SMD = standardized mean difference

Although studies reported positive effects, the summary estimate was not statistically significant (SMD 0.42; CI -0.08, 0.93; 2 studies; n=283). Heterogeneity was not detected, and there were too few studies for further analyses. Of these, one reported significant improvement[126] after 25 months (SMD 0.38; CI 0.01, 0.74).[126] The equivalent analysis for a categorical outcome is shown in Figure 70.

Figure 70. Effects of neurofeedback on broadband measures (RR)

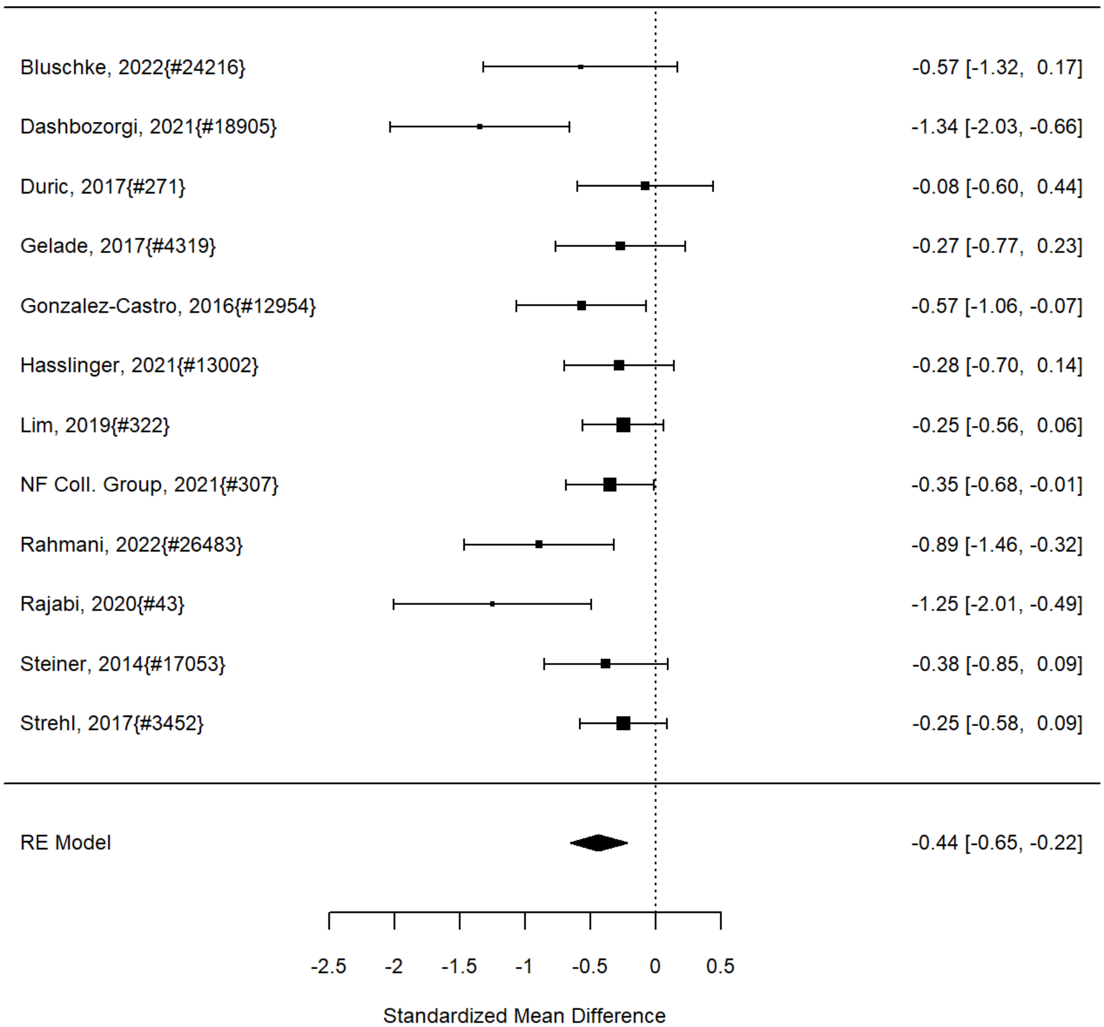


Notes: RE = random effects, SMD = standardized mean difference

Although studies reported positive effects, the individual nor the pooled studies were not statistically significant (RR 0.91; CI 0.74, 1.11; 2 studies, n=262). Both studies reported long-term outcome effects.

Results for ADHD symptoms are reported in Figure 71.

Figure 71. Effects of neurofeedback on ADHD symptoms (SMD)

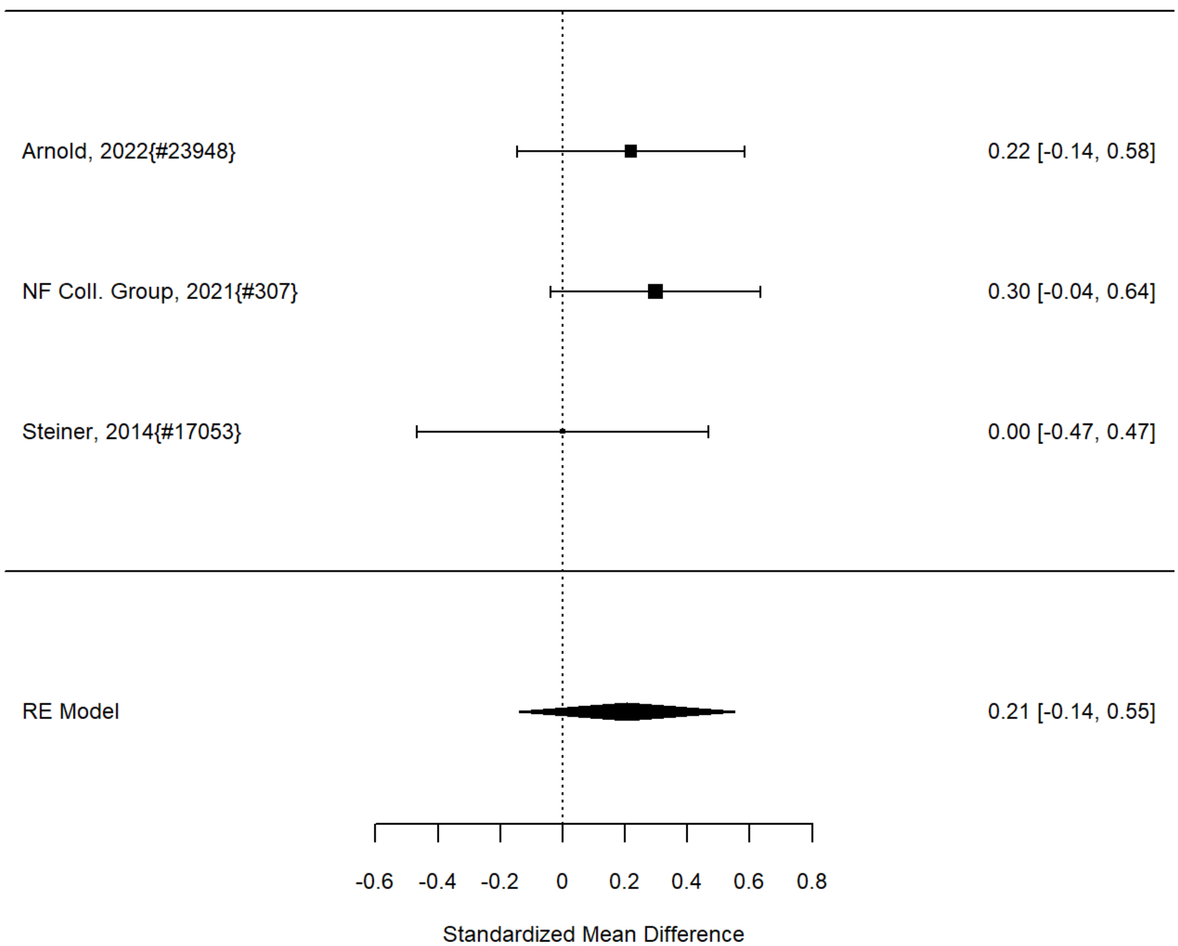


Notes: ADHD = attention deficit hyperactivity disorder, RE = random effects, SMD = standardized mean difference

Across studies, neurofeedback was associated with a statistically significant ADHD symptom reduction compared to different passive control groups (SMD -0.44; CI -0.65, -0.22; 12 studies, n=945). The youngest children included in the studies were 6 years old. The analysis detected little heterogeneity (I-squared 33%). Excluding seven high-risk of bias studies (i.e., more than half of all included studies) resulted in a similar effect estimate but also wider confidence intervals and consequently, the effect was no longer statistically significant (SMD -0.59; CI -1.25, 0.06). Similarly, restricting to sham-controlled neurofeedback studies only resulted in the same effect estimate across studies, but due to larger confidence intervals, the effect was not statistically significant (SMD -0.42; CI -1.31, 0.48). This group includes controlled trials without random assignments; restricting to the nine RCTs found the same point estimate as the overall analysis and the result remained statistically significant (SMD -0.47; CI -0.79, -0.15). Analyses also suggested the presence of publication bias (Begg p 0.01, Egger p 0.01). However, the trim and fill method did not suggest a different effect estimate (SMD -0.43; CI -0.68, -0.18). One of the included studies reported a statistically significant long-term effect (SMD 0.35; CI 0.68, 0.010) for a continuous outcome,[458] but a second study reporting categorical improvement did not (RR 0.91; CI 0.72, 1.14).[126]

Studies reporting on functional impairment outcomes are shown in Figure 72.

Figure 72. Effects of neurofeedback on functional impairment (SMD)



Notes: RE = random effects, SMD = standardized mean difference

Studies did not indicate a systematic effect of neurofeedback on functional impairment (SMD 0.21; CI -0.14, 0.55; 3 studies; n=332). Statistical heterogeneity was limited (I-squared 49%). Two of the studies reported long-term improvement, but the effect was not statistically significant (SMD 0.26; CI -0.24, 0.76).[126, 458]

We did not identify treatment satisfaction or academic performance estimates. One study reported on appetite suppression and found no systematic difference between intervention and control groups (RR 1.45; CI 0.68, 3.10; 1 study, n=142).[458] Identified studies did not report on the number of participants with adverse events.

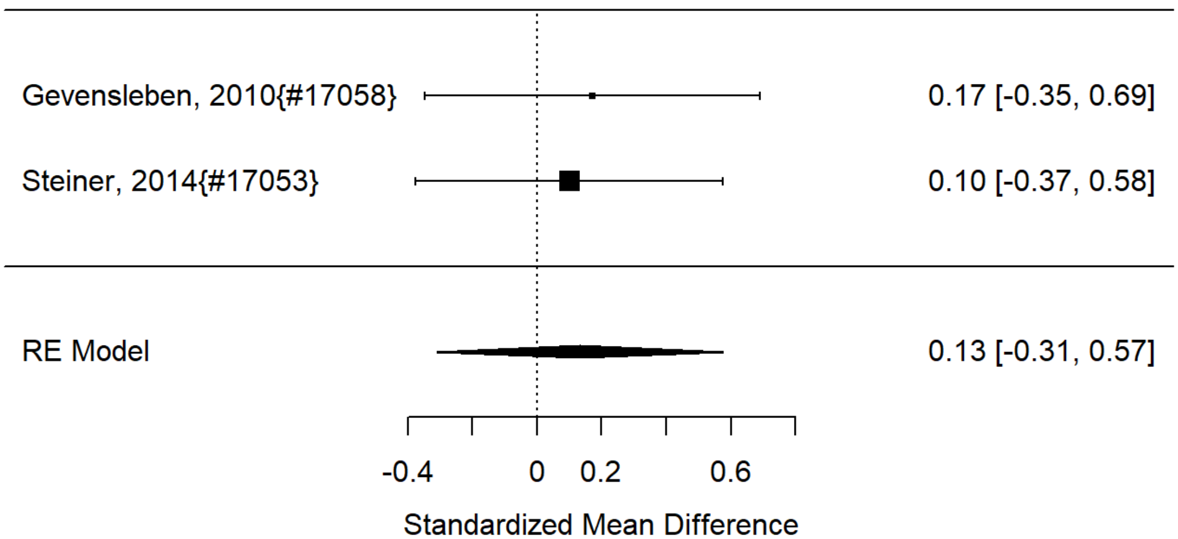
5.3.6.1 Neurofeedback Comparative Effects

Seven studies reported on active comparators, including cognitive training,[294, 320, 435, 562] medication with methylphenidate,[291, 483] and electromyographic biofeedback,[215] as documented in the next subsections.

5.3.6.1.1 Neurofeedback Versus Cognitive Training

Two studies reported on individual behaviors as documented in Figure 73.

Figure 73. Neurofeedback versus cognitive training on behaviors (SMD)



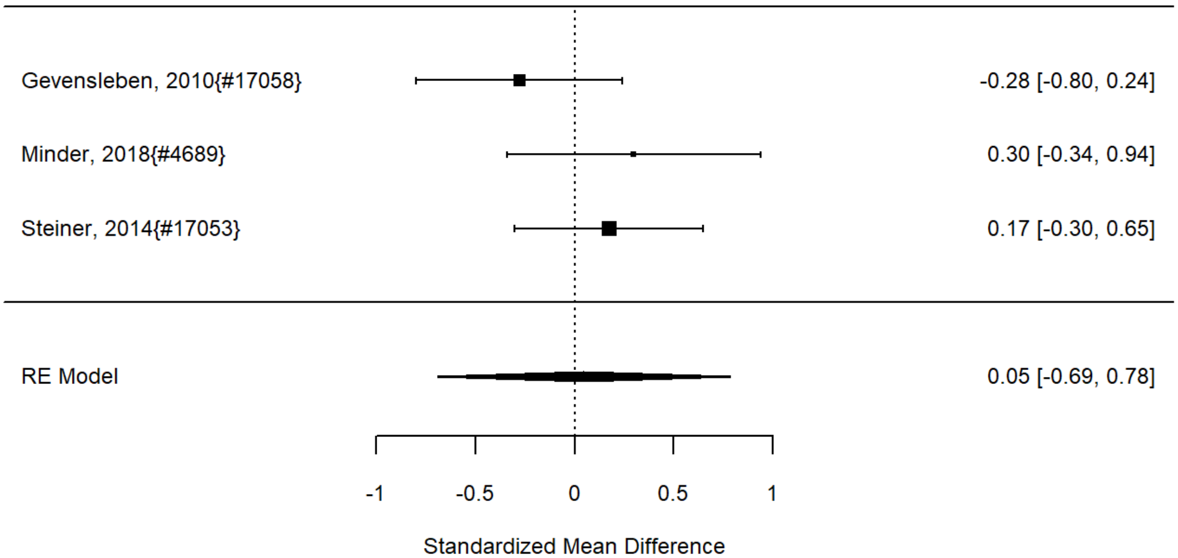
Notes: RE = random effects, SMD = standardized mean difference

Across studies, we found no statistically significant difference between neurofeedback and cognitive training, but the number of identified studies contributing to the comparison was small (SMD 0.13; CI -0.31, 0.57; 2 studies, n=129). The set did not identify heterogeneity; both studies were classified as high risk of bias.

The identified studies did not compare the effect of neurofeedback and cognitive training on broadband measures.

Results for ADHD symptoms are shown in Figure 74.

Figure 74. Neurofeedback versus cognitive training on ADHD symptoms (SMD)



Notes: ADHD = attention deficit hyperactivity disorder, RE = random effects, SMD = standardized mean difference

Across studies, we found no systematic difference between interventions (SMD 0.05; CI -0.69, 0.78; 3 studies, n=167) and little heterogeneity was detected (I-squared 15%) in this small set of studies (all judged to be high risk of bias). One study reported on a categorical outcome (number of responders) and also found no statistically significant difference (RR 1.34; CI 0.76, 2.37; 1 study; n=77).[435]

Two studies reported on a functional impairment measure. Both reported no statistically significant difference between interventions, but estimates varied, and the studies could not be combined to a meaningful effect estimate (SMD 0.10; CI -1.35, 1.56; 2 studies, n=133) given the wide confidence intervals.[294, 562] We did not identify studies that evaluated neurofeedback versus cognitive training that reported on other outcomes of interest for the review.

5.3.6.1.2 Neurofeedback Versus Stimulants

Two studies were identified that made comparisons to medication, and each one reported on some of the outcomes of interest. One study compared personalized at-home neurofeedback training versus methylphenidate.[483] The study found more improvement in broadband measures in the medication group compared to neurofeedback (RR 3.61; 2.36, 5.52; 1 study, n=149).

Both studies reported on ADHD symptom measures comparing neurofeedback versus methylphenidate.[291, 483] Both studies found more improvement associated with methylphenidate, but effect estimates differed and resulted in wide confidence intervals, precluding a meaningful effect estimate (SMD 0.52; CI -1.29, 2.34; 2 studies, n=209).[291, 483]

One of the studies reported adverse events; it found significantly fewer participants experienced adverse events in the neurofeedback versus the methylphenidate group (RR 0.23; CI 0.15, 0.35; 1 study, n=149).[483]

5.3.6.1.3 Neurofeedback Versus Other Active Comparators

One study compared neurofeedback and electromyographic biofeedback.[130] The authors reported that for ADHD symptoms, results favored neurofeedback in parent reports, but no effect estimate could be derived.

5.3.6.2 Neurofeedback Summary of Findings

Table 17 shows the findings for the outcomes of interest, together with the number of studies and study identifiers for the key outcomes. Comparative effects are shown when more than one study was identified that reported on the outcome.

Table 17. KQ2 summary of findings and strength of evidence for neurofeedback

KQ2 Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 neurofeedback vs control	Behavior	4 RCTs[126, 215, 458, 562]	No systematic effect (SMD -0.33; CI -1.33, 0.66; 4 studies, n=372)	I	Low for no effect
KQ2 neurofeedback vs control	Broadband measures	4 RCTs[126, 398, 458, 484]	No systematic effect, but estimates varied, and no meaningful summary estimate could be derived (SMD 0.42; CI -0.08, 0.93; 2 studies, n=195; RR 0.91; CI 0.74, 1.11; 2 studies, n=262)	I	Insufficient
KQ2 neurofeedback vs control	ADHD symptoms	13 RCTs[126, 215, 240, 291, 320, 398, 409, 458, 484, 490, 492, 562, 567] 2 CTs[156, 302]	Results favor intervention (SMD -0.44; CI -0.65, -0.22; 12 studies, n=945; RR 0.91; CI 0.72, 1.14; 1 study, n=120)	S, C	Low for benefit
KQ2 neurofeedback vs control	Functional impairment	4 RCTs[126, 409, 458, 562]	No systematic effect (SMD 0.21; CI -0.14, 0.55; 3 studies; n=332)	I	Low for no effect
KQ2 neurofeedback vs control	Acceptability of treatment	0 studies	No data	C	Insufficient
KQ2 neurofeedback vs control	Academic performance	0 studies	No data	C	Insufficient
KQ2 neurofeedback vs control	Appetite suppression	1 RCT[458]	No systematic effect (RR 1.45; CI 0.68, 3.10; 1 study, n=142)	C	Insufficient
KQ2 neurofeedback vs control	Participants with adverse events	0 studies	No data	C	Insufficient
KQ2 CER neurofeedback vs cognitive training	Behavior	2 RCTs[294, 562]	No systematic difference (SMD 0.13; CI -0.31, 0.57; 2 studies, n=129)	I	Low for no difference
KQ2 CER neurofeedback vs cognitive training	ADHD symptoms	3 RCTs[294, 435, 562]	No systematic difference (SMD 0.05; CI -0.69, 0.78; 3 studies, n=167)	I	Low for no difference
KQ2 CER neurofeedback vs cognitive training	Functional impairment	2 RCTs	No systematic difference but n meaningful summary estimate could be derived (SMD 0.10; CI -1.35, 1.56; 2 studies, n=133)	I	Insufficient
KQ2 CER neurofeedback vs methylphenidate	ADHD symptoms	2 RCTs[291, 483]	No systematic difference (SMD 0.05; CI -0.69, 0.78; 3 studies, n=167)	I	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, C = inconsistency, CER = Comparative Effectiveness Review, CI = 95% confidence interval, CT = controlled trial without random assignment, I = imprecision, KQ = Key Question, RCT = randomized controlled trial, RR = relative risk, SMD = standardized mean differences, S = study limitation, SoE = strength of evidence

The summary of findings table (Table 17) shows an improvement for ADHD symptom scores compared to passive control (low strength of evidence, downgraded for study limitation due to the large number of high-risk of bias studies and inconsistency in effect estimates). Results for other outcomes were less favorable or unclear. For all outcomes, we downgraded for imprecision where no summary estimate could be derived. We downgraded the strength of evidence for appetite suppression due to lack of replication (only one study reported on this outcome of interest). It should be noted that the included neurofeedback approaches varied by study, and results reported in the individual studies are shown in the evidence table in more detail.

We detected no systematic difference between neurofeedback and cognitive training in the small number of studies that reported on this comparison for the outcomes of interest. We upgraded the evidence for broadband measure scores comparing neurofeedback versus methylphenidate due to the large effect. All other comparisons were downgraded for the domain inconsistency by two (results were based on a single study, and it was not possible to determine whether another study by another author group would report an effect) and study limitation (unclear whether the study was statistically powered to detect an effect for the outcome).

5.3.7 Neurostimulation

We identified one study evaluating neurostimulation that met eligibility criteria.[517] The study was an RCT conducted in Israel. The proportion of girls was 28 percent. It included youth with inattentive, hyperactive, and combined ADHD presentation. The study evaluated a transcranial direct current stimulation protocol plus cognitive therapy compared to sham neurostimulation plus cognitive therapy.

The study did not find an effect on the CBCL (Child Behavior Checklist) total score (SMD 0.19; CI -0.60, 0.97, 1 study, n=25). There was also no statistically significant improvement in ADHD symptoms based on the Vanderbilt scale score (SMD -0.58; CI -1.39, 0.22; 1 study, n=25). The study did not report on any other outcomes of interest that allowed calculation of an effect size, but it noted that three children in the active stimulation group reported headaches resulting in withdrawal of one child and temporary suspension of the intervention for the other two children.[517]

The summary of findings table (Table 18) summarizes the findings across studies.

Table 18. KQ2 summary of findings and strength of evidence for neurostimulation

KQ2 Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 neurostimulation vs control	Behavior	0 studies	No data	C	Insufficient
KQ2 neurostimulation vs control	Broadband measures	1 RCT[517]	No systematic effect (SMD 0.19; CI -0.60, 0.97, 1 study, n=25)	S, C	Insufficient
KQ2 neurostimulation vs control	ADHD symptoms	1 RCT[517]	No systematic effect (SMD -0.58; CI -1.39, 0.22; 1 study, n=25)	S, C	Insufficient

KQ2 Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 neurostimulation vs control	Functional impairment	0 studies	No data	C	Insufficient
KQ2 neurostimulation vs control	Acceptability of treatment	0 studies	No data	C	Insufficient
KQ2 neurostimulation vs control	Academic performance	0 studies	No data	C	Insufficient
KQ2 neurostimulation vs control	Appetite suppression	0 studies	No data	C	Insufficient
KQ2 neurostimulation vs control	Participants with adverse events	0 studies	No data	C	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, C = inconsistency, CI = 95% confidence interval, I = imprecision, KQ = Key Question, RCT = randomized controlled trial, S = study limitation, SMD = standardized mean differences, SoE = strength of evidence

We downgraded all outcomes to insufficient. Although the one identified study reported on a broadband measure and ADHD symptoms, the study was small and likely not powered for the documented effect size calculation.

5.3.8 Physical Exercise

We identified seven studies reporting on physical exercise interventions that met eligibility criteria.[180, 239, 345, 353, 396, 406, 503] Studies were conducted in China, Germany and Switzerland, Korea, Taiwan, Tunisia, and Turkey. None of the studies were conducted in the U.S. The percent of female participants ranged from 10[406] to 23,[396] where reported.

Studies addressed very different interventions. Two studies evaluated a martial arts intervention.[353, 406] One study each reported on the effects of treadmill training plus whole body vibration,[239] table tennis training,[180] aerobic and neurocognitive exercise,[396] physiotherapeutic treatment,[503] and exergaming using a running or jumping board with connected screen.[345]

With one exception, the identified studies did not report on the prespecified outcomes, nor did they report on the outcomes with sufficient detail to compute effect sizes. One RCT published in 2020[239] compared treadmill training plus whole body vibration training, versus treadmill training alone, in children with ADHD. The study was conducted in Turkey; children ranged in age from seven to 11 years and were treatment naïve. Eighty percent of participants had combined type ADHD and the same percentage were male. The study reported no difference between groups (SMD 0.20; -0.51, 0.92; 1 study, n=30) for a broadband measure. Other results are shown in the evidence table in the appendix.

5.3.8.1 Exercise Comparative Effectiveness

Two of the identified studies had an active comparison group. A study evaluating physiotherapeutic treatment to train motor skills versus methylphenidate did not report sufficient detail to allow effect size calculation for any of the outcomes of interest, but the study concluded that there is no clear evidence for beneficial effects of methylphenidate or physiotherapeutic treatment on children's overall graphomotor movements.[503] A study evaluating the therapeutic effect of table tennis training compared to simulated table tennis did not also not report sufficient detail for effect size calculations; the study concluded that table tennis motor coordination activities improve executive functions and handwriting problems.

5.3.8.2 Exercise Summary of Findings

Table 19 below shows the effect estimates for the outcomes of interest.

Table 19. KQ2 summary of findings and strength of evidence for physical exercise

KQ2 Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 exercise vs control	Behavior	0 studies	No data	C	Insufficient
KQ2 exercise vs control	Broadband measures	1 RCT[239]	No systematic effect (SMD 0.20; CI -0.51, 0.92; 1 study, n=30)	C	Insufficient
KQ2 exercise vs control	ADHD symptoms	1 RCT[345]	No data	C	Insufficient
KQ2 exercise vs control	Functional impairment	0 studies	No data	C	Insufficient
KQ2 exercise vs control	Acceptability of treatment	0 studies	No data	C	Insufficient
KQ2 exercise vs control	Academic performance	0 studies	No data	C	Insufficient
KQ2 exercise vs control	Appetite suppression	0 studies	No data	C	Insufficient
KQ2 exercise vs control	Participants with adverse events	0 studies	No data	C	Insufficient

Notes: C = inconsistency, CI = 95% confidence interval, KQ = Key Question, RCT = randomized controlled trial, SMD = standardized mean differences, SoE = strength of evidence

Given the lack of studies or lack of replication of effects in more than one study, we determined evidence for all outcomes of interest to be insufficient.

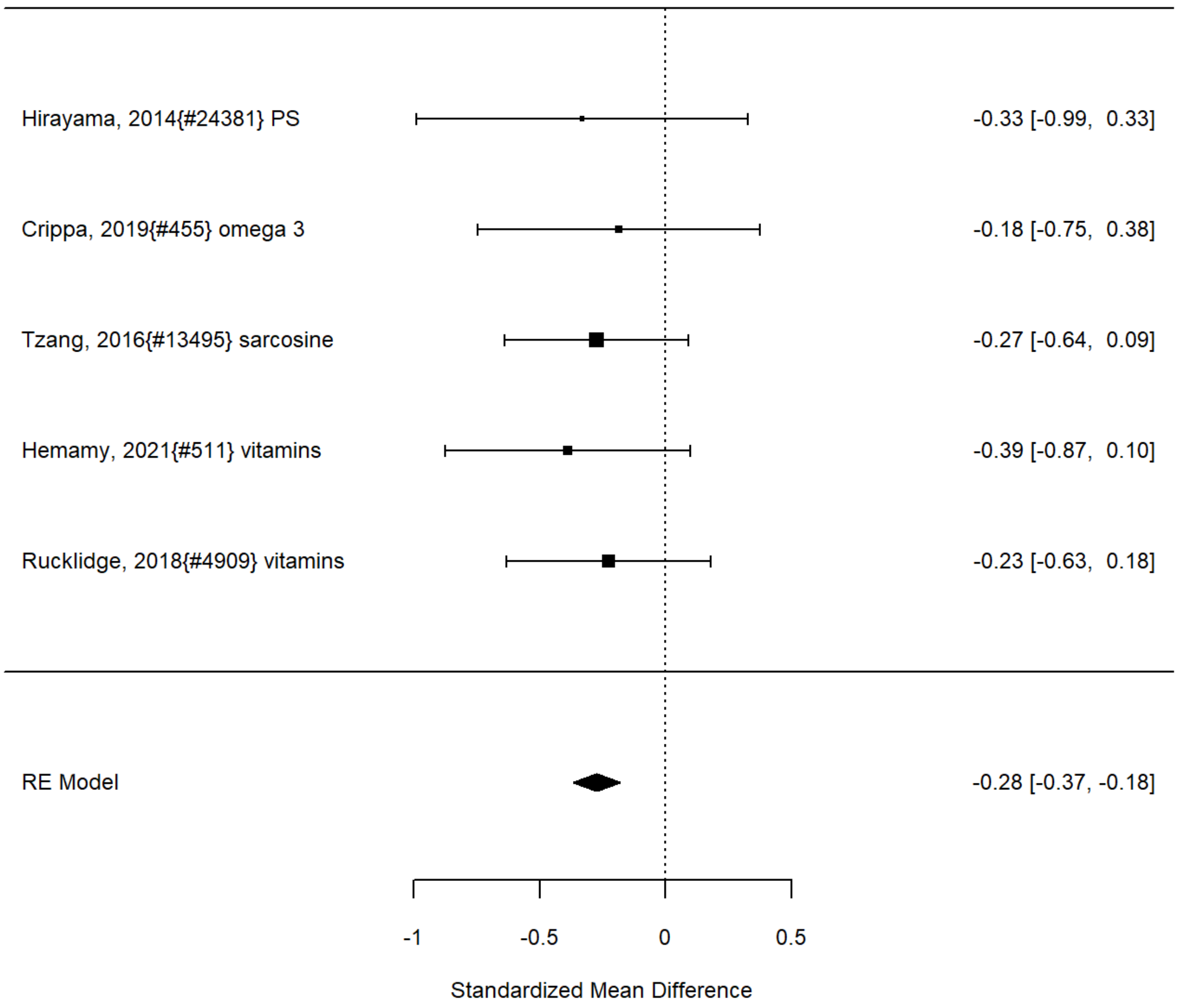
5.3.9 Nutrition and Supplements

We identified 39 studies of nutrition or supplement interventions. The vast majority were placebo-controlled studies of dietary supplements. Several evaluated nutritional supplements as augmentation to stimulant medication. The earliest eligible study was published in 2004. Only two of the identified studies were conducted in the United States.[350, 606] Most others were conducted in the Middle East or Europe and only three were conducted in the United States.[350, 601, 606] All studies but one (which included children as young as four)[472] enrolled children at least six years of age. Race and ethnicity were rarely reported, perhaps due to the racial homogeneity of the trial locations. Two studies had no females,[209, 364] while the others reported including between six and 45 percent included girls. ADHD presentations were rarely reported. Children with psychological and psychiatric co-occurring disorders were excluded from at least half the studies. One studied children with co-occurring epilepsy,[262] one study included children with chronic sleep-onset insomnia.[596] and one[478] included children with iron deficiency.

The studies assessed a wide range of dietary and supplement approaches. Omega 3 fatty acid (DHA and/or EPA) was evaluated in 13 studies.[138, 171, 178, 209, 212, 262, 310, 318, 349, 411, 441, 510, 601] Three studies evaluated vitamins.[324, 350, 505] Two studies evaluated saffron[136, 363] two evaluated zinc sulfate,[116, 149] The DASH (Dietary Approaches to Stop Hypertension) diet,[364] an individually designed restricted elimination diet,[472] and a further dietary intervention[296] were also studied. Two studies evaluate melatonin.[440, 596] The most common categories of outcomes were broadband and ADHD symptom scores. In terms of instruments, CPRS and the ADHD Rating Scale, 4th Version (ADHD RS-IV) were the most frequently reported outcome measures.

Figure 75 shows results for individual problem behavior such as teacher-reported conduct problems evaluated in individual studies; the figure is ordered by dietary supplement.

Figure 75. Effects of nutrition or supplements on behavior (SMD)

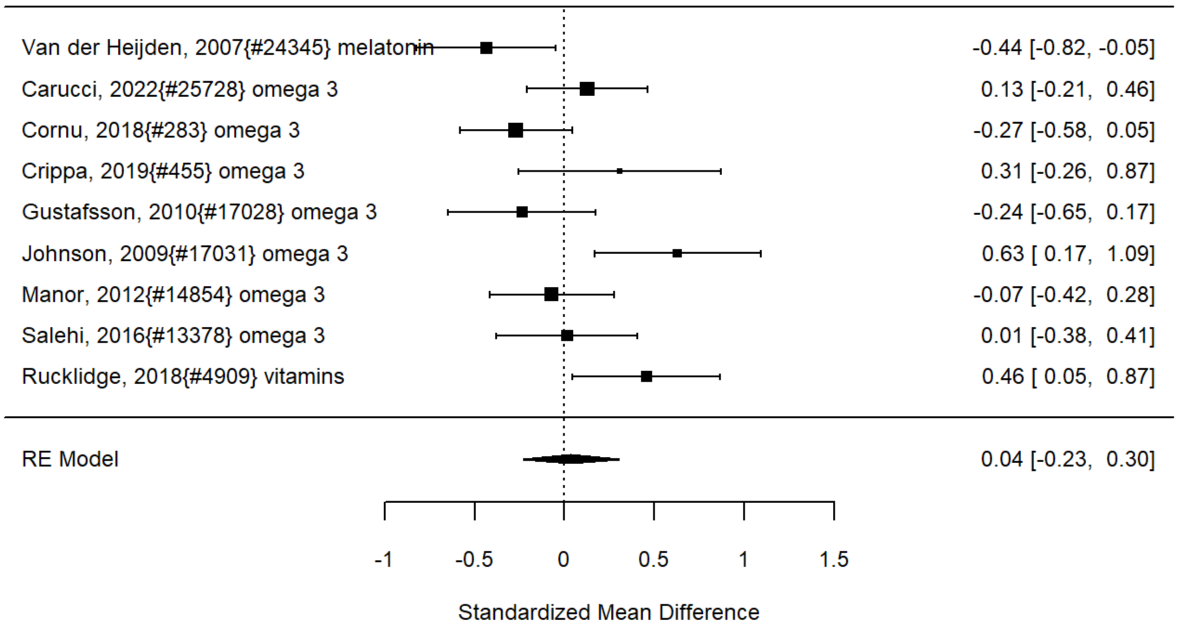


Notes: PS = phosphatidylserine, RE = random effects, SMD = standardized mean difference

Across studies, nutritional approaches (docosahexaenoic acid, phosphatidylserine, vitamins and minerals, sarcosine), were associated with improvement in problem behavior compared to control (SMD -0.28; CI -0.37, -0.18; 5 studies, n=360). None of the studies included children under six years of age. There was no evidence of heterogeneity and publication bias was not detected. All studies used random assignment to treatment groups and excluding one high risk of bias study found a similar effect (SMD -0.25; CI -0.33, -0.17). The included omega 3 study (n=49), the most commonly evaluated nutrition or supplement intervention in this subgroup, reported no statistically significant differences, and heterogeneity could not be determined (SMD 0.18; CI -0.38, 0.75).[212]

Results of nutrition and supplements on broadband measures are shown in Figure 76.

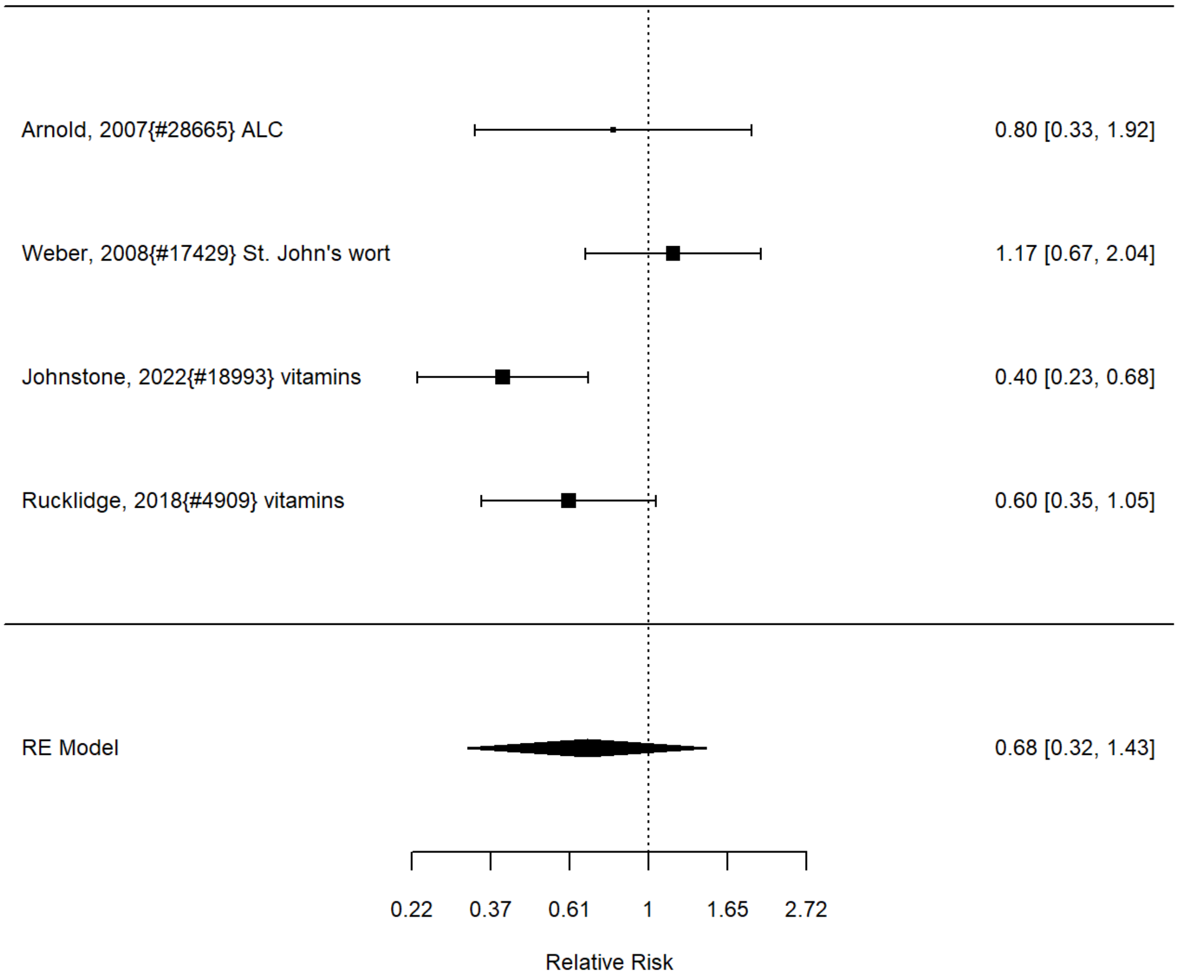
Figure 76. Effects of nutrition or supplements on broadband measures (SMD)



Notes: RE = random effects, SMD = standardized mean difference

Across studies, we did not detect a consistent effect of the intervention compared to control (SMD 0.04; CI -0.23, 0.30; 9 studies, n=953). There was some evidence of heterogeneity (I-squared 66%). Heterogeneity was not explained by risk of bias; excluding two high-risk of bias studies resulted in a very similar estimate (SMD 0.06; CI -0.31, 0.44) and heterogeneity increased. There was no evidence of publication bias. The most common supplement assessed in this category was omega 3 and when restricting to omega 3 studies, results for broadband measures were similar in not showing a systematic benefit across seven studies (n=755) and there was less heterogeneity (SMD 0.04; CI -0.24, 0.32; I-squared 54%).[171, 209, 212, 310, 349, 411, 510] A few studies assessed the number of participants that improved (categorical measure) according to a broadband measure as shown in Figure 77.

Figure 77. Effects of nutrition or supplements on broadband measures (RR)

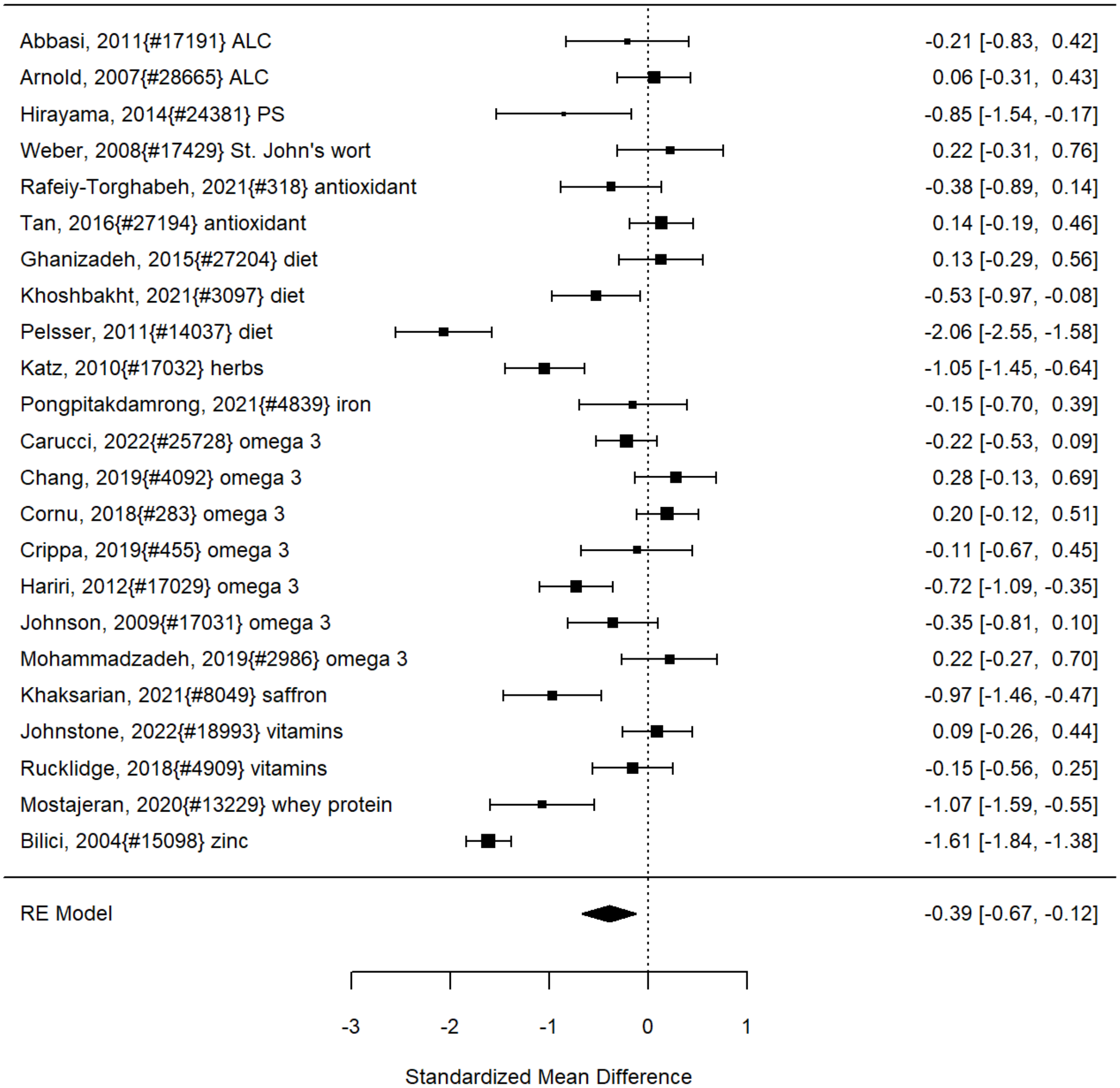


Notes: ALC = acetyl-L-carnitine, RE = random effects, RR = relative risk

Similar effects are shown for broadband measures used as a categorical variable and the analysis did not detect a systematic treatment effect (RR 0.68; CI 0.32, 1.43; 4 studies, n=385). The studies assessed different interventions, including a metabolite for energy metabolism,[125] micronutrients,[350] vitamin-mineral treatment,[505] and St. John's Wort[606] and there was some evidence of heterogeneity (I-squared 73%). None of the studies were judged to be high risk of bias. There no indication of publication bias.

All studies reporting on the effects of nutrition or supplements on ADHD symptoms are shown in Figure 78.

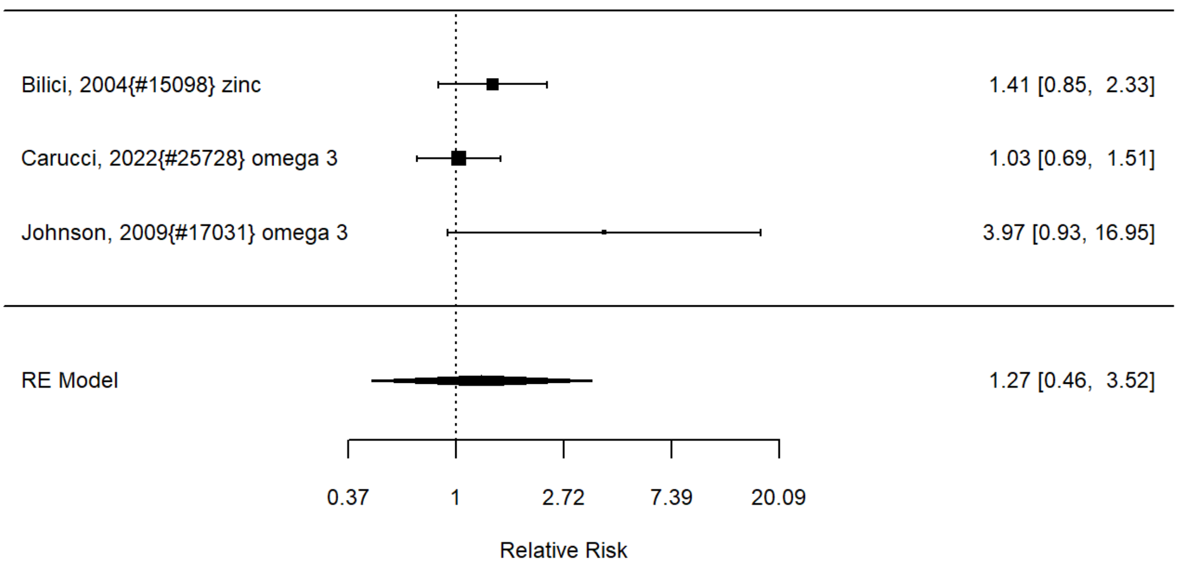
Figure 78. Effects of nutrition or supplements on ADHD symptoms (SMD)



Notes: ALC = acetyl-L-carnitine, PS = phosphatidylserine, RE = random effects, SMD = standardized mean difference

Across studies, analyses for the nutritional approaches and supplements showed a positive effect on ADHD symptoms compared to control (SMD -0.39; CI -0.67, -0.12; 23 studies, n=2357). The youngest children included in the studies were four years old. There was considerable heterogeneity (I-squared 89%) in results across studies. The largest effects were reported by a study evaluating a zinc sulfate supplement[149] and a restricted elimination diet.[472] There was no evidence of publication bias. Most identified studies were RCTs; restricting to parallel RCTs exclusively found a similar effect (SMD -0.32; CI -0.55, -0.08). Excluding four high-risk of bias studies suggested a smaller treatment estimate but the result was still statistically significant (SMD -0.26; CI -0.52, -0.01), and heterogeneity was not reduced. An omega 3 supplement was the only comparable intervention that was studied in more than one of the otherwise very diverse studies. Restricting to the seven omega 3 studies (n=719) did not find any benefits of the supplement (SMD -0.11; CI -0.45, 0.24; I-squared 71%).[171, 178, 209, 212, 318, 349, 441] The studies reporting on symptom improvement as a categorical variable (i.e., number of participants showing a treatment response) are shown in Figure 79.

Figure 79. Effects of nutrition or supplements on ADHD symptoms (RR)

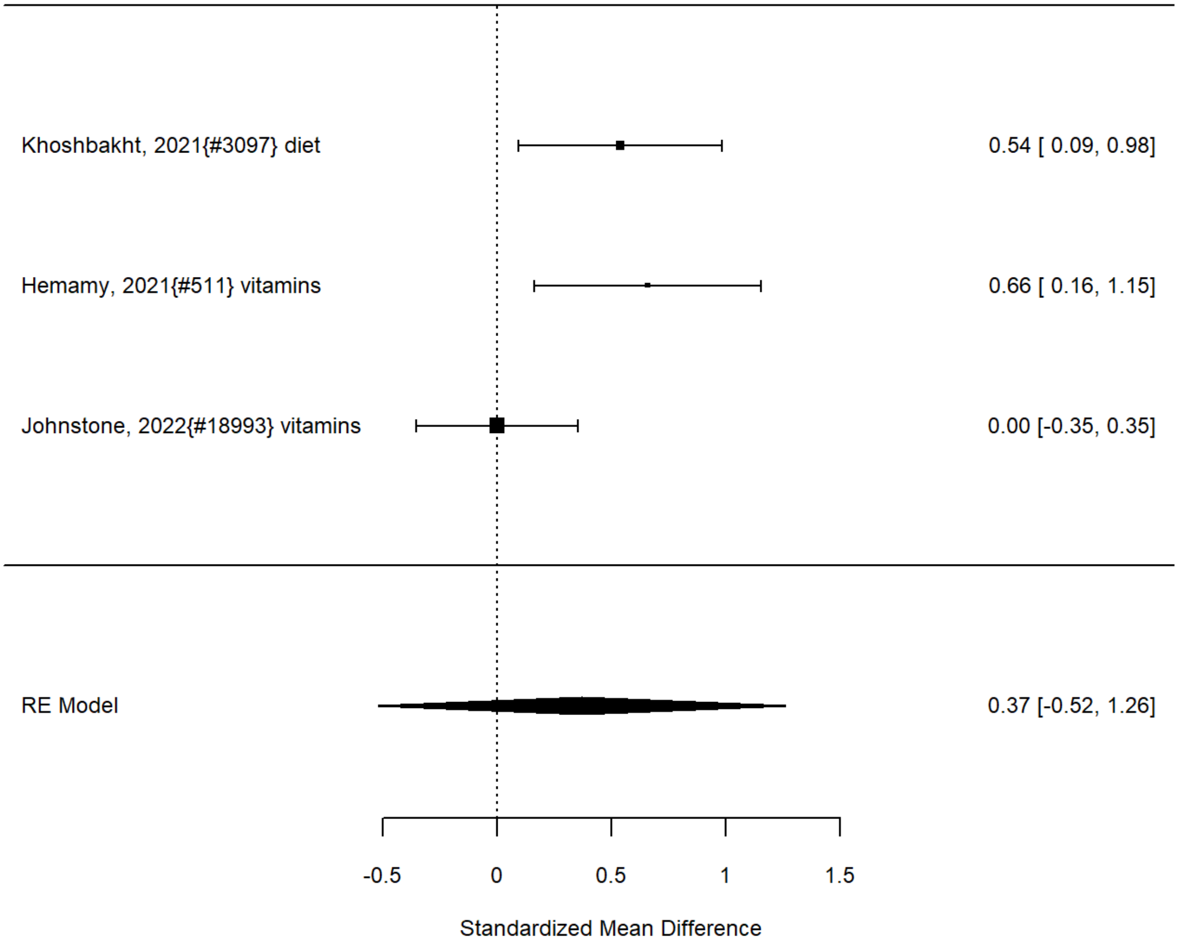


Notes: RE = random effects, RR = relative risk

Studies did not indicate a statistically significant effect of nutrition interventions on ADHD symptoms when using a categorical outcome. (RR 1.27; CI 0.46, 3.52; 3 studies, n=416). Despite the small number of studies, some heterogeneity was detected (I-squared 24%). There was no evidence of publication bias. Two studies (n=224) with a categorical ADHD symptom measure evaluated omega 3; the studies found no statistically significant effect (RR 1.67; 0.00, 6502; I-squared 68%),[171, 349] heterogeneity was not reduced, and the estimate was very imprecise.

Effects of nutrition and supplements on functional outcomes are shown in Figure 80.

Figure 80. Effects of nutrition or supplements on functional impairment (SMD)



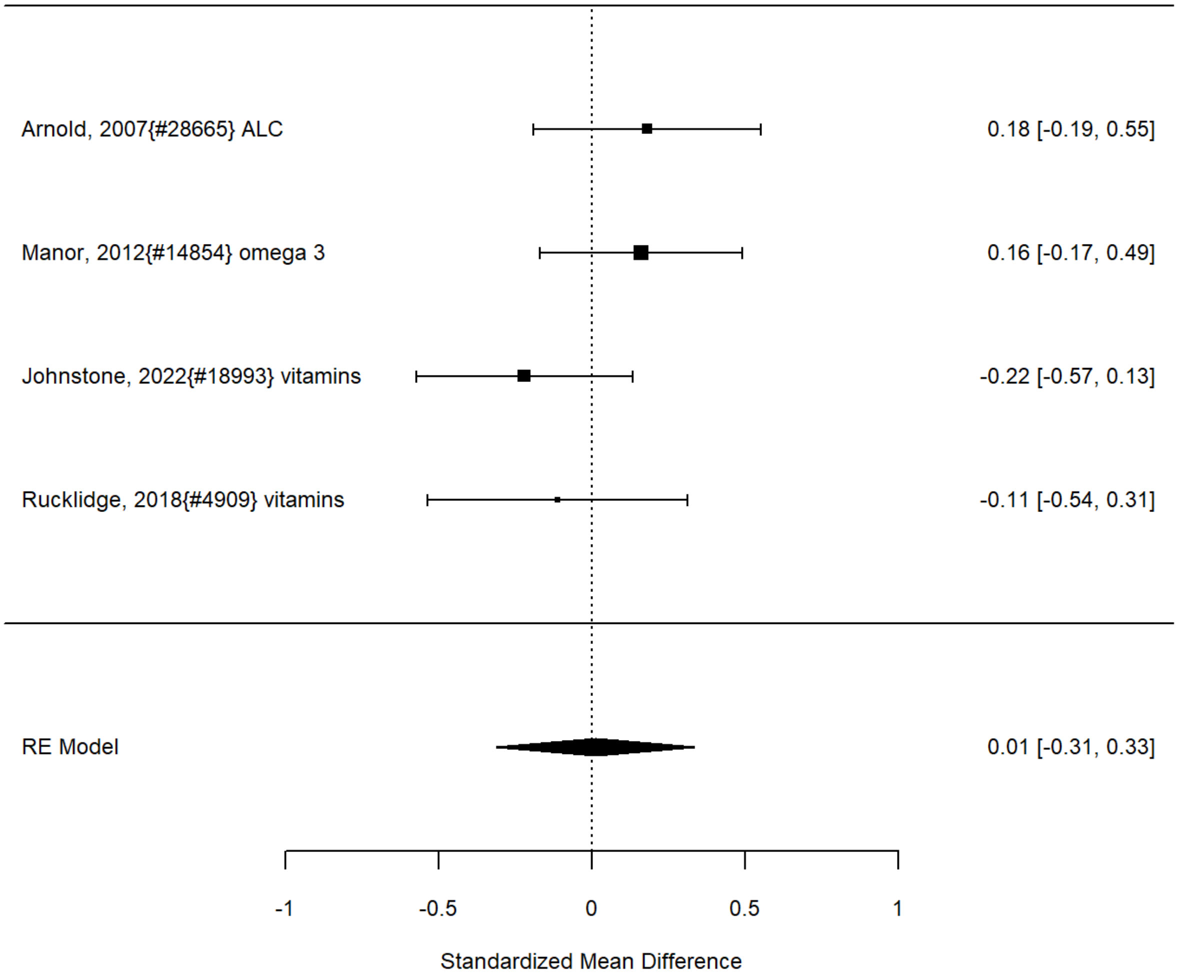
Notes: RE = random effects, SMD = standardized mean difference

Across available studies reporting sufficient detail for effect size calculations, no systematic benefit was found for functional impairment (SMD 0.37; CI -0.52, 1.26; 3 studies, n=272). Studies evaluated different interventions, including vitamin D plus magnesium,[324] micronutrients,[350] and the DASH diet.[364] Despite the small number of studies, the analysis detected heterogeneity (I-squared 65%).

There were no data for treatment acceptability or academic performance.

A few studies assessed continuous variables indicative of appetite suppression, such as height, body mass index (BMI), and weight changes as shown in Figure 81.

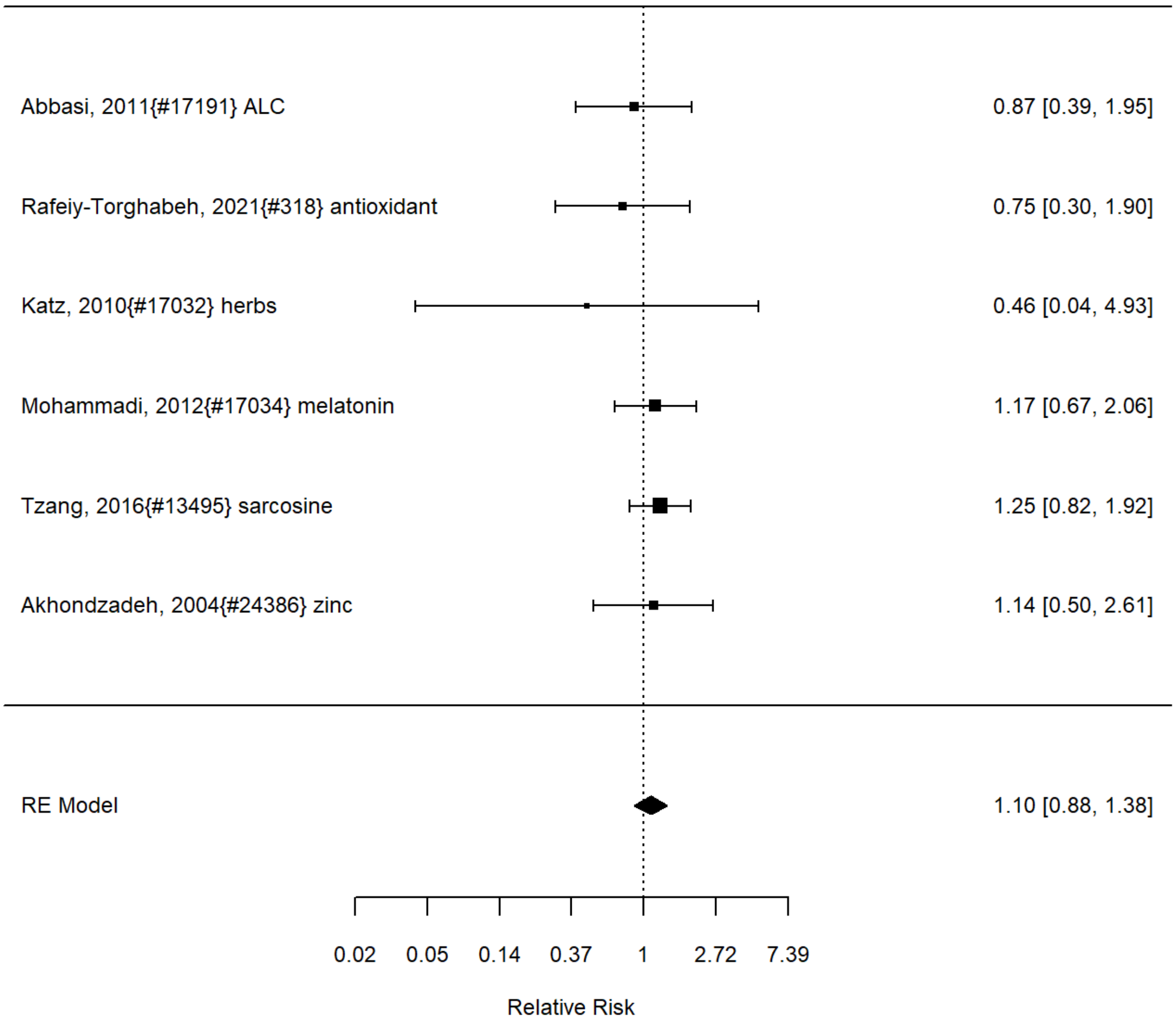
Figure 81. Effects of nutrition or supplements on appetite suppression (SMD)



Notes: ALC = acetyl-L-carnitine, RE = random effects, SMD = standardized mean difference

There were no differences between treatment arms (SMD 0.01; CI -0.31, 0.33; 4 studies, n=485) for appetite suppression measures. Heterogeneity was negligible (I-squared 19%). There was no indication of publication bias. Removing one high risk of bias study showed no effect either (SMD -0.05; CI -0.58, 0.48). One of the studies assessed omega 3 specifically (n=162); the study did not detect a statistically significant effect (SMD 0.16; CI -0.17, 0.49; I-squared 0).[411] The equivalent analysis for a categorical outcome (number of participants reporting appetite suppression) is shown in Figure 82.

Figure 82. Effects of nutrition or supplements on appetite suppression (RR)

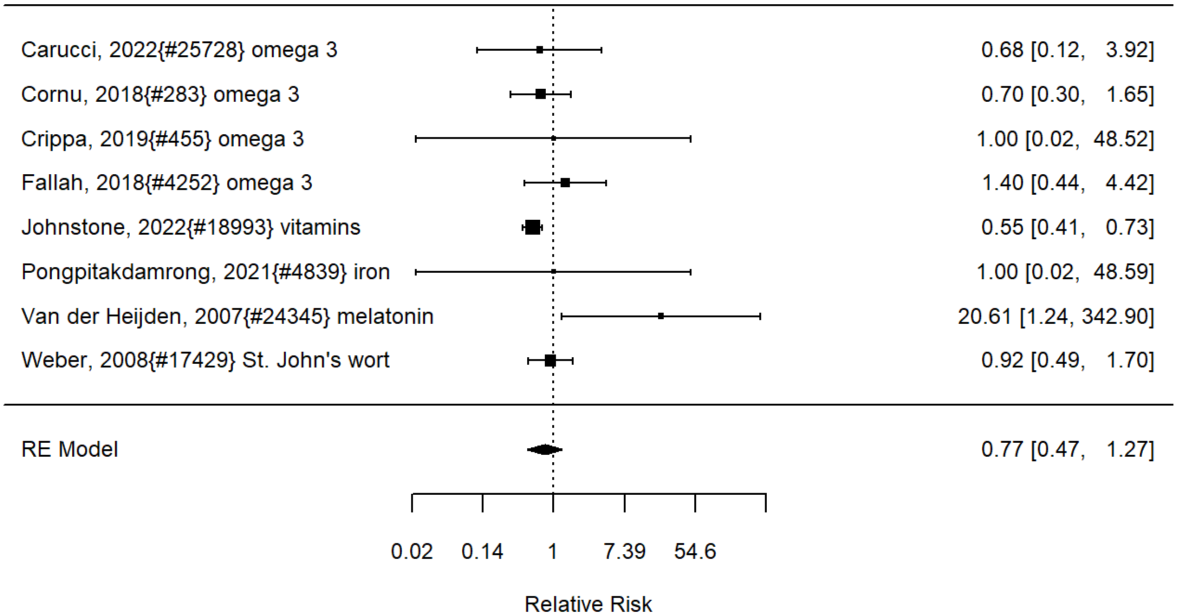


Notes: ALC = acetyl-L-carnitine, PS = phosphatidylserine, RE = random effects, RR = relative risk

The equivalent analyses for a categorical outcome came to similar conclusions and did not detect an effect on appetite suppression (RR 1.10; CI 0.88, 1.38; 6 studies, n=439). The analysis did not detect heterogeneity. There was some indication of publication bias (Begg p 0.06, Egger p 0.02). An alternative estimate using the trim and fill method also showed no systematic benefit (RR 1.16; CI 0.89, 1.51). Removing a high-risk of bias study in a sensitivity analysis found a similar effect (RR 1.14; CI 0.88, 1.48) suggesting that the result was not primarily driven by poor methodology.

Studies evaluating the effects of nutrition or supplements on adverse events are shown in Figure 83.

Figure 83. Effects of nutrition or supplements on participants with adverse events (RR)



Notes: RE = random effects, RR = relative risk

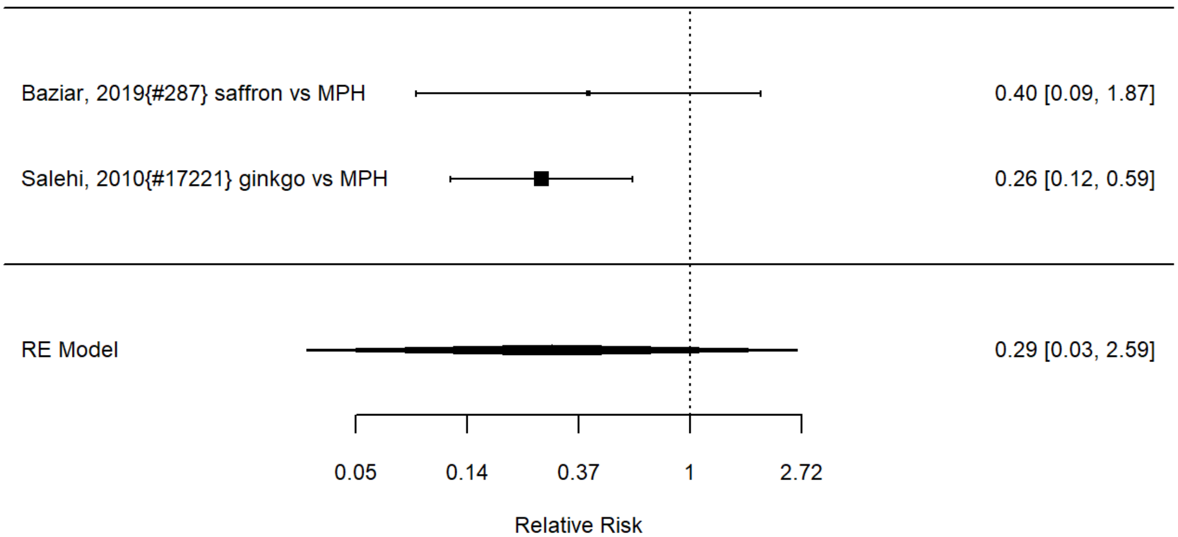
Across studies, there was no indication that the interventions were associated with a higher risk of experiencing an adverse event (RR 0.77; CI 0.47, 1.27; 8 studies, n=735). Heterogeneity was negligible (I-squared 26%), there was no evidence of publication bias, and none of the studies contributing to the effect estimate were considered high risk of bias. This analysis included four omega 3 studies. The result for this subset (n=398) was similar to the overall analysis and omega 3 was also not associated with an increased risk of experiencing adverse events (RR 0.87; CI 0.48, 1.56; I-squared 0).

5.3.9.1 Nutrition and Supplements Comparative Effects

Few of the nutrition and supplement studies used active comparators comparing the nutrition or supplement to a different intervention.

Three studies compared to methylphenidate while the intervention group received saffron,[136] sweet almond syrup,[444] or ginkgo biloba[509] Two of the studies reported on symptoms but they found conflicting results. One reported no difference between saffron versus methylphenidate groups, while one favored methylphenidate over ginkgo biloba and the studies could not be combined to a meaningful summary estimate (SMD 0.40; CI -4.80, 5.59; 2 studies, n=100). However, both studies reported also on the outcome appetite suppression as shown in Figure 84.

Figure 84. Nutrition or supplements versus methylphenidate on appetite suppression (RR)



Notes: RE = random effects, RR = relative risk

Both studies found more events in the methylphenidate groups but due to the small number of studies and differences in effect sizes, the pooled effect was not statistically significant (RR 0.29; CI 0.03, 2.59; 2 studies, n=100).

One study compared omega 3 versus zinc supplements and found no difference in a broadband measure (SMD 0.02; CI -0.37, 0.41; 1 study, n=150).[510]

5.3.9.2 Nutrition and Supplements Summary of Findings

Table 20 displays the findings for each outcome category along with the number of studies and study identifiers. The summary of findings table displays data for all outcomes of interest across all nutrition/supplements. In addition, the table shows the effects for specific supplements where more than one study reported on the particular agent for the outcome; only Omega 3 was evaluated in more than one study reporting on the same outcome. Results of the individual studies are documented in Appendix C, Table C.2.

Table 20. KQ2 summary of findings and strength of evidence for nutrition and supplements

KQ2 Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 nutrition/ supplements vs control	Behavior	6 RCTs[212, 324, 328, 505, 586, 590]	Results favor intervention across the diverse nutrition and supplement approaches (SMD -0.28; CI -0.37, -0.18; 5 studies, n=360)	S, I	Low for benefit
KQ2 nutrition/ supplements vs control	Broadband measures	14 RCTs[116, 125, 171, 209, 212, 310, 349, 350, 411, 505, 510, 586, 596, 606]	No systematic effect (SMD 0.04; CI -0.23, 0.30; 9 studies, n=953; RR 0.68; CI 0.32, 1.43; 4 studies, n=385)	C	Moderate for no effect
KQ2 Omega 3 vs control	Broadband measures	7 RCTs[171, 209, 212, 310, 349, 411, 510]	No systematic effect (SMD 0.04; CI -0.24, 0.32; 7 studies, n=755)	S	Moderate for no effect

5. Results: Treatment of ADHD

KQ2 Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 nutrition/ supplements vs control	ADHD symptoms	26 RCTs[104, 125, 138, 149, 171, 178, 209, 212, 295, 296, 318, 328, 349, 350, 360, 363, 364, 440, 441, 443, 472, 478, 488, 505, 579, 606]	Results favor intervention across the diverse nutrition and supplement approaches (SMD -0.39; CI -0.67, -0.12; 23 studies, n=2357; RR 1.27; CI 0.46, 3.52; 2 studies, n=416)	C	Low for benefit
KQ2 Omega 3 vs control	ADHD symptoms	8 RCTs[171, 178, 209, 212, 240, 318, 349, 441]	No systematic effect (SMD -0.11; CI -0.45, 0.24; 7 studies, n=719; RR 1.67; 0.00, 6502; 2 studies, n=224)	S	Low for no effect
KQ2 nutrition/ supplements vs control	Functional impairment	4 RCTs[324, 350, 364, 411]	No systematic effect (SMD 0.37; CI -0.52, 1.26; 3 studies, n=272)	S, I	Low for no effect
KQ2 nutrition/ supplements vs control	Acceptability of treatment	0 studies	No data	C	Insufficient
KQ2 nutrition/ supplements vs control	Academic performance	0 studies	No data	C	Insufficient
KQ2 nutrition/ supplements vs control	Appetite changes and growth suppression	12 RCTs[104, 116, 125, 350, 360, 411, 440, 441, 488, 505, 590, 606]	No systematic effect (SMD -0.01; CI -0.31, 0.33; RR 1.10; CI 0.88, 1.38; 6 studies, n=439)	S	Low for no effect
KQ2 nutrition/ supplements vs control	Number of participants with adverse events	1 RCTs[601]	No systematic effect (RR 0.77; CI 0.47, 1.27; 8 studies, n=735)	S	Moderate for no effect
KQ2 Omega 3 vs control	Number of participants with adverse events	5 RCTs[171, 209, 212, 262, 411]	No systematic effect (RR 0.87; CI 0.48, 1.56, 3 studies, n=398)	S	Low for no effect
KQ2 CER supplement vs methylphenidate	ADHD symptoms	2 RCTs[136, 509]	No systematic effect (SMD 0.40; CI -4.80, 5.59; 2 studies, n=100)	C	Insufficient
KQ2 CER supplement vs methylphenidate	Appetite changes and grows suppression	2 RCTs[136, 509]	No systematic effect (RR 0.29; CI 0.03, 2.59; 2 studies, n=100)	C, I	Low for favoring supplements

Notes: ADHD = attention deficit hyperactivity disorder, C = inconsistency, CER = Comparative Effectiveness Review, CI = 95% confidence interval, I = imprecision, KQ = Key Question, RCT = randomized controlled trial, RR = relative risk, S = study limitation, SMD = standardized mean differences, SoE = strength of evidence

The majority of studies reported on ADHD symptoms, and we found low strength of evidence that nutrition and supplements can show benefits. We downgraded by two for inconsistency since we only found effects for one outcome type (continuous, not categorical data) and the continuous data showed considerable heterogeneity. In addition, the evaluated supplements and dietary approaches were very diverse. And it was not possible to identify an effect of a specific intervention that has shown positive effects in more than one study. There was also a positive effect shown for individual problem behaviors, but the number of studies and samples were small, none of the individual studies reported statistically significant effects, and an additional study may change the statistical significance of the pooled effect (downgraded by two for imprecision). We found no effect on broadband measures and no statistically significant difference between study arms for functional impairment; we downgraded the strength of evidence due to heterogeneity (inconsistency). There was insufficient evidence to estimate the effect on acceptability of treatment and academic performance due to the lack of research studies. There was moderate strength evidence that nutrition and supplement interventions are just as safe as a placebo, but we downgraded for study limitation as some studies had reported adverse events but did not report on the number of participants experiencing adverse events.

The evaluated supplements and dietary approaches were very diverse but the effect of omega 3 has been assessed in multiple studies. We found no evidence that omega 3 improves behavior, broadband measure scores, or ADHD symptoms, and it was not associated with appetite suppression or experiencing adverse events. We downgraded the omega 3 evidence due to study limitations.

We found two studies that reported the comparative effectiveness of supplements versus methylphenidate. While both reported on ADHD symptoms, we determined the strength of evidence to be insufficient because of the small number of studies reporting on two different supplements (inconsistency), studies reported conflicting results (inconsistency) and no meaningful summary estimate could be derived (imprecision). There was low strength of evidence that supplements reported fewer appetite suppression events than methylphenidate (downgraded for inconsistency and imprecision). We downgraded the strength of evidence for no difference between omega 3 and zinc in broadband measures to insufficient (study limitation, downgraded by two as the single study did not let us assess inconsistency).

5.3.10 Complementary, Alternative, or Integrative Medicine

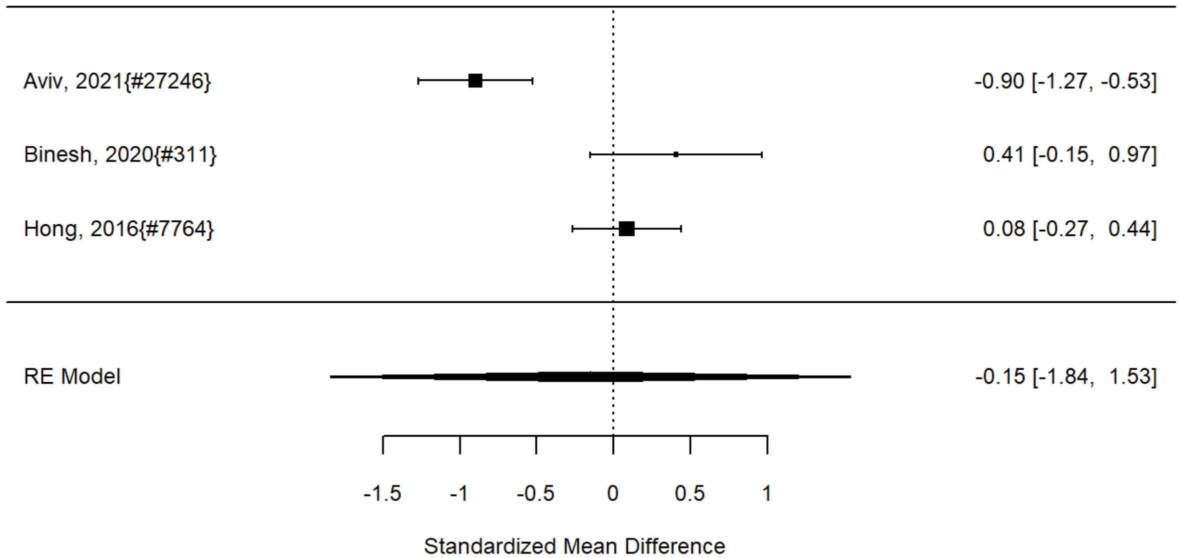
We identified six studies that evaluated complementary, alternative, or integrative medicine interventions.[128, 150, 278, 279, 332, 646] Studies were published between 2001 and 2022; they were conducted in Switzerland,[278, 279] China,[646] Iran,[150] Israel,[128] and Korea.[332] All studies included both children and adolescents and participants were predominately male. Race or ethnicity of the included study participants was not reported. ADHD presentations were also not reported. Studies evaluated acupuncture, homeopathy, and hippotherapy. Three studies compared to a passive control group (waitlist, placebo, attention-matched control).

None of the studies reported on individual problem behaviors.

Two of the identified studies reported on a broadband measure in sufficient detail to calculate an effect size, but the estimates varied greatly, and no meaningful summary estimate could be derived (SMD 0.03; CI -3.66, 3.73; 2 studies, n=218).[332, 646] One acupoint stimulation study reported a positive effect on a categorical broadband measure (RR 0.23; CI 0.07, 0.75; 1 study, n=78).[646]

The studies reporting on ADHD symptoms are shown in Figure 85.

Figure 85. Effects of complementary, alternative, or integrative medicine on ADHD symptoms (SMD)



Notes: ADHD = attention deficit hyperactivity disorder, RE = random effects, SMD = standardized mean difference

We did not detect a systematic effect of interventions (SMD -0.15; CI -1.84, 1.53; 3 studies, n=313). The studies evaluated hippotherapy, traditional acupuncture, and auricular acupuncture. The positive effect was reported by a study evaluating therapeutic horseback riding.[128] One of the studies reported on symptom improvement as a categorical variable and found auricular acupuncture improved symptoms (RR 4.26; CI 1.42, 12.77; 1 study, n=44).[150]

None of the identified studies reported sufficient detail to calculate effect estimates for the other outcomes of interest, including functional impairment, treatment satisfaction, academic performance, and appetite suppression.

One study evaluating transcutaneous electrical acupoint stimulation reported on the number of participants with adverse events. The study did not demonstrate a statistically significant effect of the intervention compared to sham treatment (RR 2.00; CI 0.19, 21.16; 1 study, n=78) and it reported that adverse events were rare and not serious.[646]

5.3.10.1 Complementary, Alternative, or Integrative Medicine Comparative Effects

One of the identified studies (n=115) compared homeopathy and methylphenidate.[279] The high risk of bias study used the CGI scale but did not provide sufficient detail to allow computation of effect sizes. The authors concluded that homeopathic treatment appears to be similar to the effect of methylphenidate.

5.3.10.2 Complementary, Alternative, or Integrative Medicine Summary of Findings

Table 21 shows the findings for the outcomes of interest together with the number of studies and study identifiers.

Table 21. KQ2 summary of findings and strength of evidence for CAM

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 CAM vs control	Behavior	0 studies	No data	C	Insufficient
KQ2 CAM vs control	Broadband measures	3 RCTs[278, 332, 646]	No systematic effect (SMD 0.03; CI -3.66, 3.73; 2 studies, n=218; RR 0.23; CI 0.07, 0.75; 1 study, n=78)	C, I	Insufficient
KQ2 CAM vs control	ADHD symptoms	3 RCTs[128, 150, 332]	No systematic effect and no meaningful summary estimate could be derived (SMD -0.15; CI -1.84, 1.53; 3 studies, n=313)	C	Insufficient
KQ2 CAM vs control	Functional impairment	0 studies	No data	C	Insufficient
KQ2 CAM vs control	Acceptability of treatment	0 studies	No data	C	Insufficient
KQ2 CAM vs control	Academic performance	0 studies	No data	C	Insufficient
KQ2 CAM vs control	Appetite suppression	0 studies	No data	C	Insufficient
KQ2 CAM vs control	Participants with adverse events	1 RCT[646]	No systematic effect (RR 2.00; CI 0.19, 21.16; 1 study, n=78)	S, C	Insufficient

Notes: C = inconsistency, CAM = Complementary, Alternative, or Integrative Medicine; CI = 95% confidence interval, I = imprecision, KQ = Key Question, RCT = randomized controlled trial, RR = relative risk, S = study limitation, SMD = standardized mean differences, SoE = strength of evidence

Very few studies reported on the key outcomes selected for the review and the conclusion for the outcomes was that the evidence base is insufficient because of lack of research, conflicting results, and lack of replication of effects for specific integrative or alternative medicine approaches. The strength of evidence was determined to be insufficient for broadband measure scores due to inconsistency and imprecision. Studies evaluated different interventions, and no meaningful summary estimate of the intervention group could be derived. The strength of evidence was determined to be insufficient for symptoms because of conflicting results across studies and lack of meaningful summary estimate; it is unclear whether complementary, alternative, or integrative medicine interventions have an effect on ADHD symptoms. Similarly, the strength of evidence was determined to be insufficient for the number of participants with adverse events. Given the variation in approaches, the identified study is unlikely a good representation of expected adverse events for this intervention group, and only one of the identified studies reported on the outcome.

Only one comparative effectiveness study was identified, and it reported insufficient details to compute effect sizes for the outcomes of interest; hence the strength of evidence was determined to be insufficient.

5.3.11 Parent Support

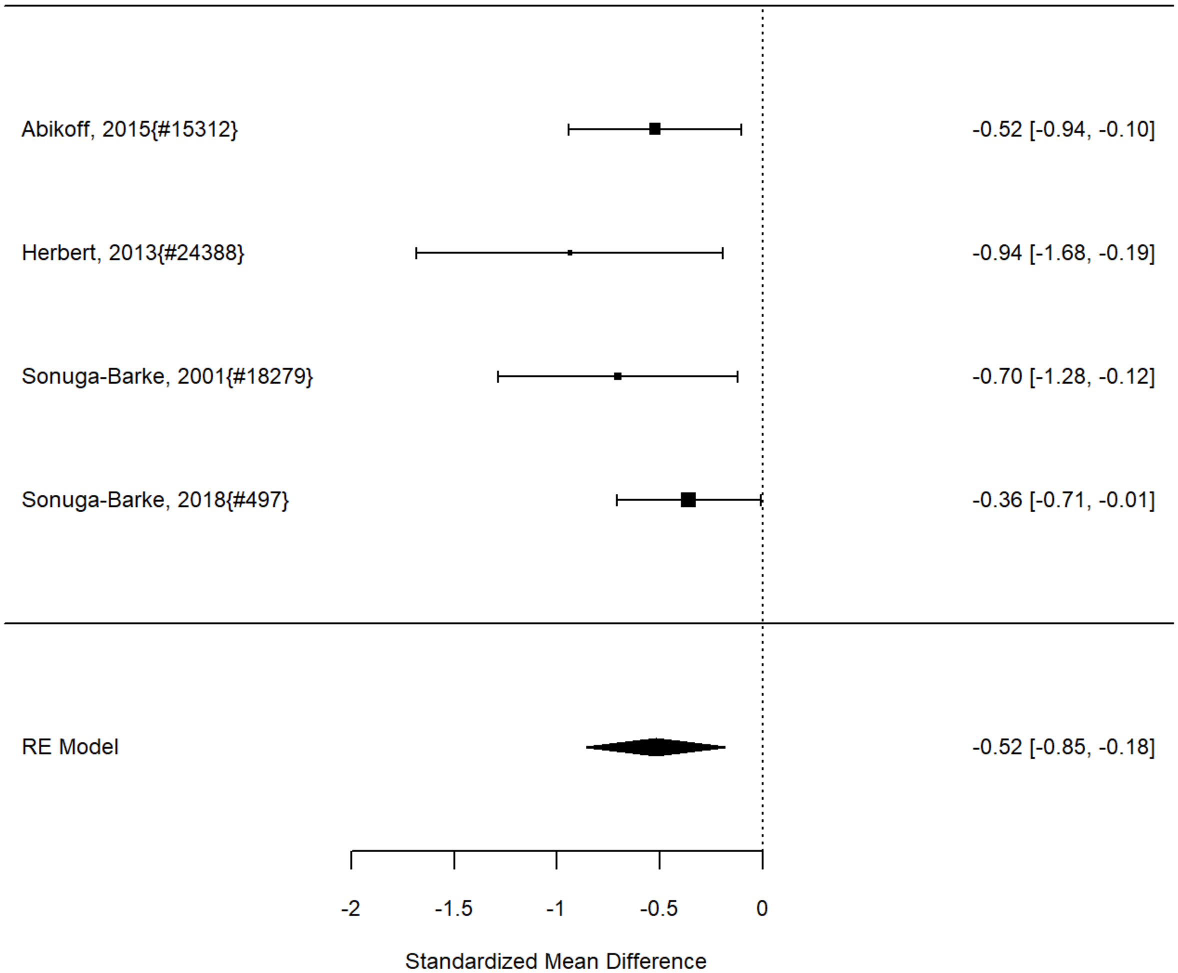
We identified 19 studies evaluating an intervention primarily targeting parents.[110, 176, 200, 228, 257, 265, 266, 325, 333, 384, 428, 520, 544, 550-552, 569, 585, 593] Some psychosocial studies presented earlier in the chapter also included a parent component, but as an addition to targeting the children and adolescents directly. The studies in this section do not mention a component directed at the youth with ADHD and instead focus on the parents. The earliest identified parent support study was published in 2001.[550] Evaluations were published in 13 different countries, primarily the United States[110, 176, 200, 325] and the UK.[266, 550-552] The populations studied were parents of children with ADHD between the ages of three and up to 18 years, but only three studies reported on parents of teenagers with ADHD.[200, 265, 266] For studies that distinguished between ADHD presentations, the most prevalent type of the ADHD participants was the combined type. While ADHD participants with co-occurring psychiatric disorders were not excluded from most of the studies, only one study purposely included specific co-occurring disorders; the study included youth with a dual diagnosis of ADHD and oppositional defiant disorder.[257] One study included children with sleep problems[428] Race and ethnicity demographics for the parents or children were not mentioned in most studies.

Interventions were diverse in terms of the approach as well as intensity and included behavioral training for parents, in-home nurse visits, group psychotherapy, telephone-assisted self help, psychoeducation, and parental friendship coaching. One intervention each targeted sleep or reading, several evaluated the New Forest Parenting Program. Of the identified studies, most reported on a control group, including attention-matched groups,[265, 290] no intervention, waitlist, or treatment as usual.[228, 266, 329, 384, 520, 551, 585] Some studies included both a control group and an alternative psychological or behavioral intervention, had only an alternative intervention as comparison, or compared parent training as stimulant augmentation to medication alone.

Although we did not restrict the type, target, or focus of the intervention (i.e., either primarily addressing the wellbeing of parents or training parents to affect change in the children with ADHD), we only included studies that reported data on the effects on the children with ADHD; studies reporting only on parental outcomes were excluded (see Table 1). Studies reported a variety of often study-specific outcomes, such as family dynamics and parental stress. In terms of pre-specified outcomes, broadband scales and symptom scores were the most frequently reported outcomes.

Figure 86 shows the effects on individual behaviors assessed in the studies, including showing physical aggression, externalizing problem behavior in the family, and observed ADHD behavior in a play situation.

Figure 86. Effects of parent support on behavior (SMD)

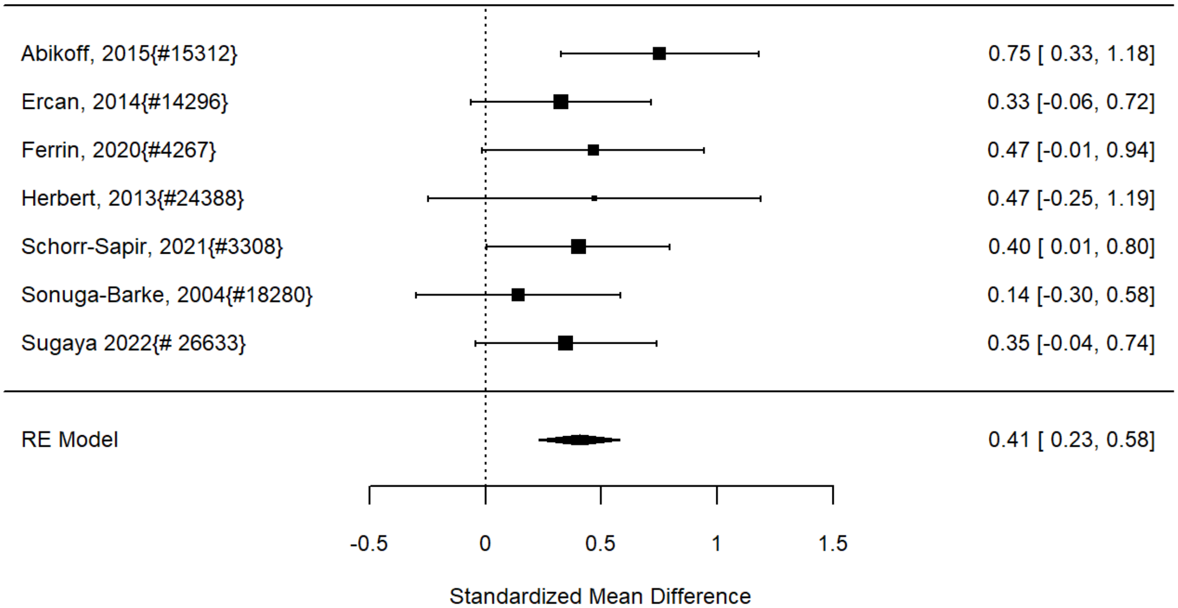


Notes: RE = random effects, SMD = standardized mean difference

Across studies parent interventions were associated with a positive effect on problem behavior (SMD -0.52; CI -0.85, -0.18; 4 studies, n=357). The analysis did not detect statistical heterogeneity. All included studies were RCTs. Removing one RCT judged to be high-risk of bias found a similar effect (SMD -0.47; CI -0.86, -0.08). There was some indication of publication bias (Begg p 0.08, Egger p 0.01). Using the trim and fill method for an alternative estimate found a smaller effect estimate (SMD -0.43; CI -0.63, -0.22), but the effect was still statistically significant.

Results for broadband measures are shown in Figure 87.

Figure 87. Effects of parent support on broadband measures (SMD)

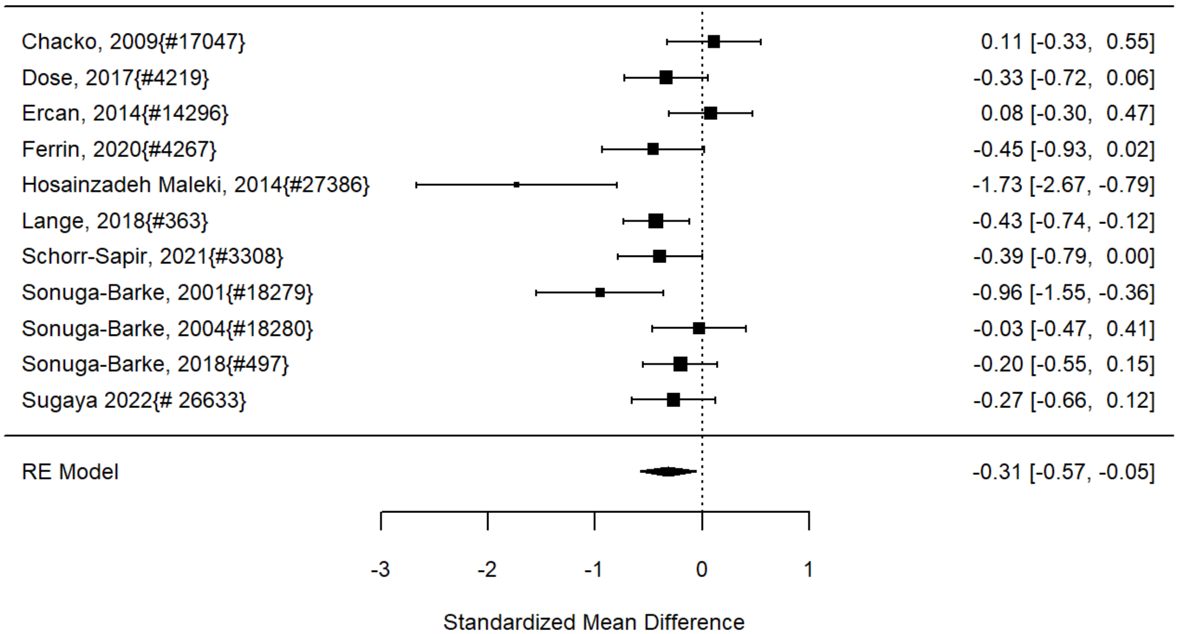


Notes: RE = random effects, SMD = standardized mean difference

Analyses found statistically significant positive effects of parent support interventions (SMD 0.41; CI 0.23, 0.58; 7 studies, n=613). The youngest children included in the studies were three years old, and the oldest were 18. The included interventions were all multi-component interventions targeting parents, but the content varied considerably. Interventions included the New Forest Parenting Package for parents of preschoolers versus wait list,[110] a combination of methylphenidate plus parental training and support versus medication alone,[257] a psychoeducation interventions versus treatment as usual,[266] parent training for mothers versus waitlist,[551] parenting strategies for preschoolers versus waitlist.[325] a non-violent resistance parent training versus wait list,[520] and a behavioral training for parents supported by methylphenidate versus parent education with methylphenidate treatment.[569] The analysis did not detect heterogeneity. There was no evidence of publications bias. Most studies used random assignment; when restricting to RCTs only, the effect estimate was unchanged (SMD 0.42; CI 0.21, 0.64). Removing four high-risk of bias studies reported a similar point estimate but the effect was no longer statistically significant (SMD 0.52; CI -0.02, 1.05). Two of the studies reported on long-term outcomes, but estimates varied, and no meaningful summary estimate for the intervention effect could be derived (SMD 0.53; CI -2.18, 3.24; 2 studies; n=221).[110, 257]

A number of studies reported on ADHD symptom measures (Figure 88).

Figure 88. Effects of parent support on ADHD symptoms (SMD)

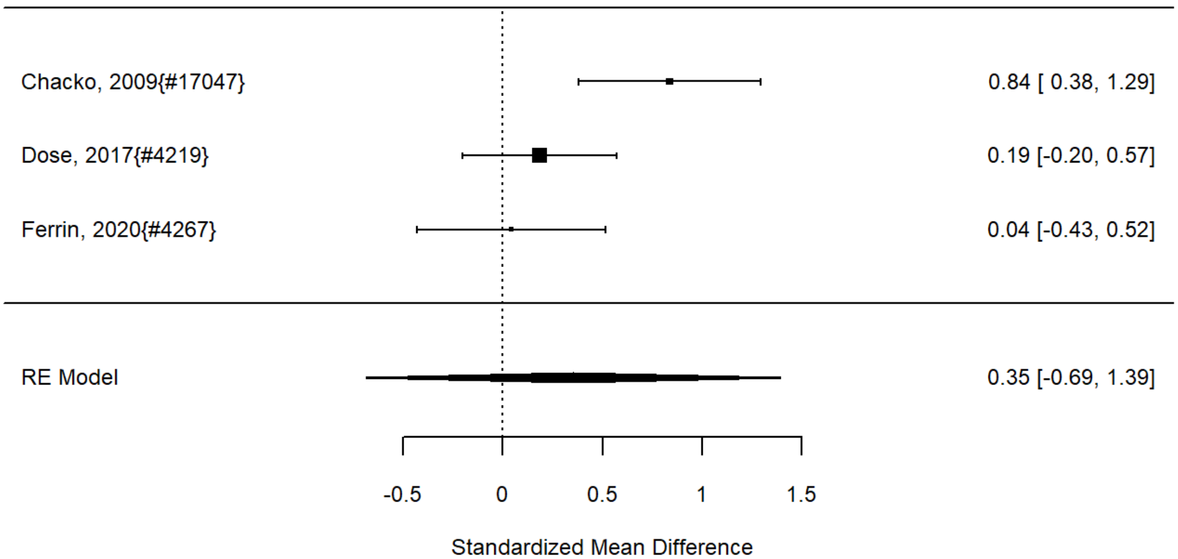


Notes: ADHD = attention deficit hyperactivity disorder, RE = random effects, SMD = standardized mean difference

Analyses indicated a benefit of the parent interventions on ADHD symptoms compared to control groups not receiving the intervention, but the effect was small, and the statistical significance was borderline (SMD -0.31; CI -0.57, -0.05; 11 studies; n=1078). The youngest children included in the studies were three years old, the oldest were 18. There was little statistical heterogeneity (I-squared 52%) in results, but the multi-component interventions varied in content and complexity. Strongest effects were shown for an education and behavior strategy program for parents of preschoolers,[550] psychoeducation for families,[266] and the New Forest Parenting Package for parents of preschoolers,[384] specifically. Most studies were RCTs; restricting exclusively to RCTs found a very similar effect estimate (SMD -0.35; CI -0.61, -0.09). Removing six high-risk of bias studies suggested a smaller, not statistically significant effect (SMD -0.31; CI -0.76, 0.14) but heterogeneity increased in this sensitivity analysis. There was some evidence of publication bias (Begg p 0.16, Egger p 0.02). Using the trim and fill method to correct for publication bias found a similar estimate (SMD -0.27; CI -0.52, -0.03), which was still statistically significant. Three studies reported outcomes at 12 months or more; there was no systematic effect across studies (SMD -0.02; CI -0.71, 0.67; 3 studies; n=324).[228, 257, 290] One study evaluating an education and behavior strategy program for parents of preschoolers reported on a categorical symptom outcome; the study found no statistically significant effect (RR 2.13; CI 0.93, 4.89; 1 study, n=50).[550]

Functional impairment outcomes were also frequently reported in identified studies, as shown in Figure 89.

Figure 89. Effects of parent support on functional impairment (SMD)



Notes: RE = random effects, SMD = standardized mean difference

Pooled effect estimates showed no systematic effect of the intervention on functional impairment (SMD 0.35; CI -0.69, 1.39; 3 studies, n=252). There was some heterogeneity (I-squared 71%). Removing one high risk of bias study reported also a non-significant effect with wide confidence intervals (SMD 0.44; CI -4.60, 5.49). There was no evidence of publication bias. One of the studies reported a long-term effect, which was not statistically significant (SMD 0.19; CI -0.20, 0.57; 1 study, n=103).[228]

There were insufficient data to calculate effects on treatment satisfaction, academic outcomes, appetite suppression, and number of participants with adverse events.

5.3.11.1 Parent Support Comparative Effectiveness

Multiple studies reported comparative effects, usually comparing two different parenting approaches.

Two studies assessed the *New Forest Parenting* program compared to an alternative approach. One study compared the *New Forest Parenting* versus an alternative comprehensive program (*Helping the Noncompliant Child*) and found no difference in aggressive behaviors (SMD 0.05; CI -0.29, 0.40; 1 study, n=164) but the CPRS ratings were lower in the *Helping the Noncompliant Child* group (SMD -0.41; CI 0.76, -0.07; 1 study, n=164). There was no difference in treatment satisfaction (SMD -0.13; CI -0.48, 0.21; 1 study, n=164).[110] One of the studies compared *Helping the Noncompliant Child* to methylphenidate treatment plus sham parent training.[569] The study found no statistically significant difference between intervention arms for a broadband measure (SMD -0.14; CI -0.53 0.25; 1 study, n=102) or ADHD symptom scale scores (SMD 0.06; CI -0.32, 0.45; 1 study, n=102). The effect estimates for appetite suppression (RR 0.78; CI 0.38, 1.62; 1 study, n=101) and the number of participants with adverse events (RR 0.97; CI 0.86, 1.10; 1 study, n=99) was also not statistically significant. One study compared the *New Forest Parenting* program with the *Incredible Years* alternative parenting program.[552] The study found no difference in ADHD symptom scores (SMD -0.09; CI -0.33, 0.15; 1 study, n=307). A study by the same author group compared a parent training focusing on education about ADHD and behavior management strategies versus a parent counseling and support intervention.[550] The study found no differences in effects on behavior in direct observations (SMD 0.36; CI -0.36, 0.88; 1 study, n=307) or broadband measure scores (RR 0.74; 0.42, 1.30; 1 study, n=307), but results statistically significantly favored the parent training when comparing the parental ratings of childhood symptom scores to assess ADHD (SMD -0.69; CI -1.22, -0.16; 1 study, n=307).

A study comparing parent psychoeducation to parent counseling found no statistically significant differences in ADHD symptom assessments (SMD -0.32; CI -0.77, 0.13; 1 study, n=81) or functional impairment (SMD 0.07; CI -0.38, 0.52; 1 study, n=81), and concluded that psychoeducation is a complementary rather than a substitute treatment.[265]

A study (n=92) evaluating a behavioral parent training for children with ADHD targeting executive function versus a consequence-based program did not report sufficient detail on our key outcomes to calculate effect sizes, but the study concluded positive effects on daily rated problem behaviors and hyperactivity-impulsivity symptoms for both interventions. Results favored the targeted behavioral training for inattention. A nursing case-management intervention working with families versus receiving a parenting book and newsletter did not report sufficient detail to assess effect sizes but the study (n=174) indicated that for broadband measures there were no significant differences between groups (while the overall evaluation was considered positive).[200] A study comparing a parental friendship coaching intervention versus psychoeducation and social support found no significant differences in aggressive behaviors in the children with ADHD (SMD 0.14; CI -0.16, 0.43; 1 study, n=172), but the study concluded that the coaching intervention showed parents providing more emotion strategies and praise.[544]

Authors comparing the STEPP (*Strategies To Enhance Positive Parenting*) program to a traditional parent training program found no differences in ADHD symptoms (SMD 0.16; CI -0.28, 0.60; 1 study, 120) but found lower functional impairment scores favoring STEPP (SMD 0.51; CI 0.07, 0.96; 1 study, n=120).[176]

One study compared behavior parent training in a group versus individual training plus education; it found no statistically significant difference in effects on ADHD symptom scores (SMD -0.24; CI -0.77, 0.28; 1 study; n=56).[593]

5.3.11.2 Parent Support Summary of Findings

Table 22 shows the findings for the outcomes of interest together with the number of studies and study identifiers.

Table 22. KQ2 summary of findings and strength of evidence for parent support

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 parent support vs control	Behavior	6 RCTs[110, 325, 384, 550, 552, 569]	Results favor intervention (SMD -0.52; CI -0.85, -0.18; 4 studies, n=357)	C	Low for no effect
KQ2 parent support vs control	Broadband measures	7 RCTs and CTs[110, 257, 266, 325, 520, 551, 569]	Results favor intervention (SMD 0.41; CI 0.23, 0.58; 7 studies, n=613)	C	Moderate for benefit
KQ2 parent support vs control	ADHD symptoms	12 RCTs and CTs[176, 228, 257, 266, 333, 384, 520, 550-552, 569, 585]	Results favor intervention (SMD -0.31; CI -0.57, -0.05; 11 studies; n=1078; RR 2.13, CI 0.93, 4.89; 1 study, n=50)	C, I	Low for benefit

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 parent support vs control	Functional impairment	3 RCTs[176, 228, 266]	No systematic effect (SMD 0.35; CI -0.69, 1.39; 3 studies, n=252)	C	Low for no effect
KQ2 parent support vs control	Acceptability of treatment	0 studies	No data	C	Insufficient
KQ2 parent support vs control	Academic performance	0 studies	No data	C	Insufficient
KQ2 parent support vs control	Appetite suppression	1 RCT[569]	No systematic effect (RR 3.27; CI 0.96, 11.16; 1 study, n=99)	C	Insufficient
KQ2 parent support vs control	Participants with adverse events	1 RCT[569]	No systematic effect (RR 0.98; CI 0.86, 1.11; 1 study, n=96)	C	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, C = inconsistency, CI = 95% confidence interval, CT = controlled trial without random assignment, I = imprecision, KQ = Key Question, RCT = randomized controlled trial, RR = relative risk, SMD = standardized mean difference, SoE = strength of evidence

Across studies, parent training interventions were associated with improvements in broadband measure scores (moderate strength of evidence, downgraded for the domain inconsistency, given the variation in intervention approaches and the lack of replication of intervention effects. Standardized ADHD symptom scores (low strength of evidence) was downgraded for imprecision, given that the pooled effect was very close to a statistically non-significant result. There was no systematic effect on individual behaviors assessed in the studies, but the existing evidence is limited (inconsistency). We found no systematic effect on functional impairment, but we downgraded for the domain inconsistency as effect estimates varied. Evidence was insufficient to determine acceptability of treatment, academic performance, appetite suppression, and participants with adverse events due to lack of research reporting on the outcome (downgraded for inconsistency as no replication could be evaluated).

The strength of evidence for comparative studies was insufficient as studies had not been replicated yet and all results were unique to the reported study and the robustness of results could not be further evaluated; in addition, it was unclear whether the study was sufficiently powered to detect a difference for the outcome examined.

5.3.12 School Interventions

We identified ten studies reporting on teacher or school environment interventions.[163, 208, 238, 259, 433, 529, 531, 577, 602, 640] The earliest study was published in 2009.[602] Interventions were evaluated in three different countries, predominantly the United States. The populations studied were most often children attending elementary through middle school between the ages of 6 and 14, with only one study including adolescents up to 17 years old.[521] In two studies, participants were required to demonstrate an IQ of 80 or higher.[163, 259] Only one study required participants to not be taking stimulant medication or to be on a stable dose with no plans of change during the study duration.[208] The majority of participants used ADHD medication at baseline. For studies that provided information on ADHD presentations, the combined type was the most prevalent presentation, followed by inattentive type. While ADHD participants with co-occurring disorders were not excluded from most of the studies, one study purposely required participants to have word-reading difficulties or reading disabilities in addition to ADHD.[577] Several studies also report on participant co-occurring disorders, with the most common conditions reported being oppositional defiant disorder, conduct disorder, and anxiety and mood disorders.[163, 529, 531, 577, 602]

More than half of the studies used a multimodal intervention strategy comprising both teacher training and parent training,[163, 529, 531, 577, 640] or included intervention components targeting the children with ADHD.[163, 238, 259, 433, 531, 577] Two studies examined teacher-specific interventions. One[208] tested a Web-based online learning modules for elementary-school teachers, while the other[602] tested two different types of ADHD consultation services for teachers to help them plan and execute classroom-based ADHD interventions for students. Most studies reported on a control group, including waitlist control, no intervention, ADHD medication only (compared to other modes of active treatment),[529, 640] and treatment as usual. Some studies reported on an alternative intervention, such a lower intensity intervention[531] or a modified version of an original intervention[259] and evaluated the comparative effectiveness of these interventions.

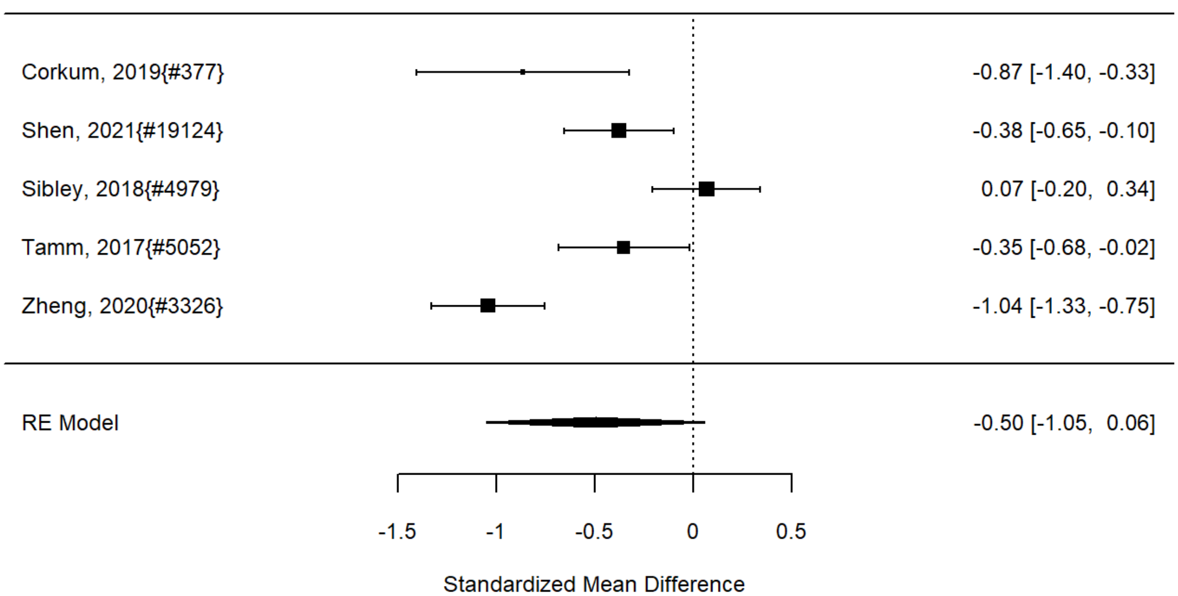
Studies reported a variety of often study-specific outcomes, such as improvement in individual cognitive tasks. In terms of pre-specified outcomes, symptom scores, functional impairment, and academic scores were the most frequently reported outcomes.

Two studies reported on individual problem behaviors, but results were conflicting and could not be combined to a meaningful summary estimate (SMD -0.01; CI -1.38, 1.36; 2 studies, n=395).[238, 531] One of these reported on a long-term outcome: an evaluation of an intensive summer program reported no differences in school disciplinary incidents compared to no intervention (SMD 0.09; CI -0.18, 0.36; 1 study, n=209) at the 12 month follow up.[531]

We did not identify studies reporting on broadband measure scores to assess the effect of a school intervention.

Studies reporting on ADHD symptoms are shown in Figure 90.

Figure 90. Effects of school interventions on ADHD symptoms (SMD)



Notes: ADHD = attention deficit hyperactivity disorder, RE = random effects, SMD = standardized mean difference

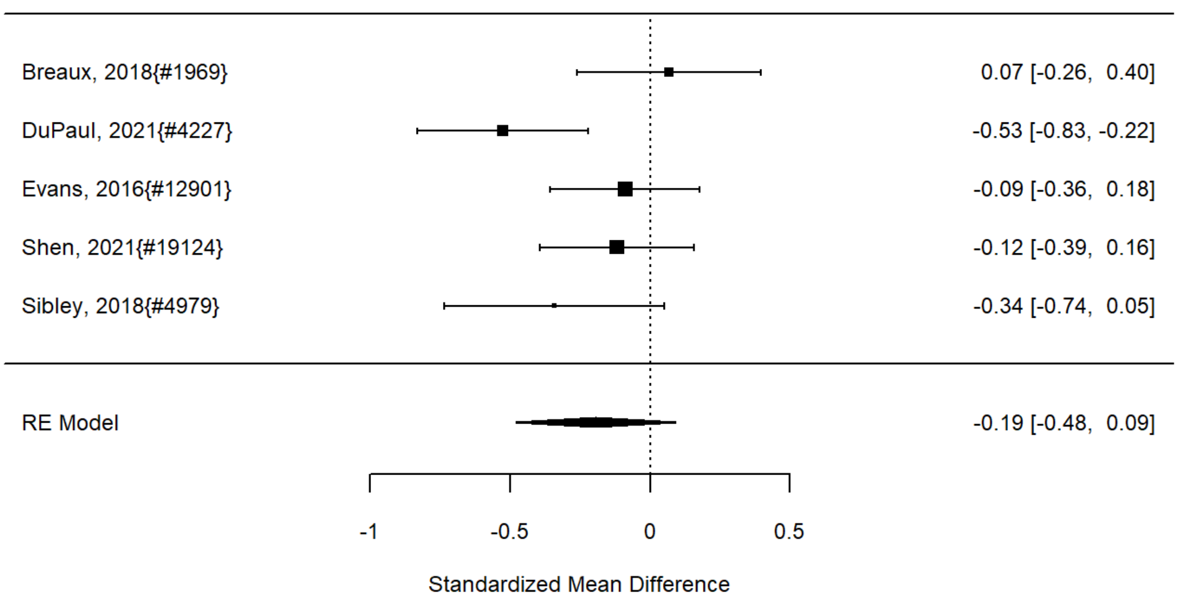
Across studies, we did not find a systematic effect of school interventions on ADHD symptoms (SMD -0.50; CI -1.05, 0.06; 5 studies, n=822). The age of the children in the included studies ranged from six to 17. There was evidence of heterogeneity (I-squared 87%). We found no indication of publication bias. Removing high-risk of bias studies in a sensitivity analysis left only three studies; the effect estimate was smaller and was also not statistically significant (SMD -0.15; CI -2.99, 2.68). Heterogeneity was only marginally reduced. One of the studies reported on a long-term outcome: an evaluation of an intensive summer program reported no differences in ADHD symptoms (SMD 0.07; CI -0.20, 0.34; 1 study, n=282) at the 12 month follow up.[531]

Two studies assessed the effects on functional outcomes, however, they reported conflicting results and could not be combined to a meaningful summary estimate (SMD 0.22; CI -4.39, 4.82; 2 studies; n=274).[208, 259] There was heterogeneity (I-squared 83%) but no further analyses could be performed due to the small number of studies. One of the studies evaluated a Web-based intervention for teachers of elementary students with ADHD[208] and reported improvements in functional impairment in the students. The other assessed a school-based training intervention program for adolescents but found no differences compared to community care in a peer relation rating scale at the 12-month follow up.[259]

Three studies reported favorable results regarding the acceptability of the treatment approach, but there was insufficient data to compute effect sizes.[208, 529, 531]

A small number of school intervention studies reported on academic performance measures as shown in Figure 91.

Figure 91. Effects of school interventions on academic performance (SMD)



Notes: RE = random effects, SMD = standardized mean difference

Although most individual studies reported some improvement, across studies, the effect was not statistically significant (SMD -0.19; CI -0.48, 0.09; 5 studies, n=854). There was little heterogeneity (I-squared 53%). We did not detect potential publication bias. Removing one high-risk of bias study found a smaller effect that was not statistically significant (SMD -0.10; CI 0.33, 0.12) and the analysis detected no heterogeneity, suggesting that methodological rigor of the studies was a source of heterogeneity. Two of the studies reported on long-term outcomes 12 and 15 months), but the estimates varied, and neither the individual nor the combined effects were statistically significant (SMD -0.17; CI -1.69, 1.35; 2 studies, n=153).[259, 531]

Identified studies did not report on the other prespecified outcomes for the review appetite suppression and participants with adverse events.

5.3.12.1 School Interventions Comparative Effects

Four of the identified school interventions also reported on a comparison to an alternative intervention, all of which were also school setting interventions.

One study assessed a dose-response question and compared a high versus a low intensity summer program. The study is shown in more detail in the appendix; briefly, the authors found no differences in school disciplinary incidents (SMD 0.01; CI -0.26, 0.28; 1 study, n=325) or ADHD symptom assessments (SMD 0.01; CI -0.26, 0.29; 1 study, n=325), and they concluded that the high intensity intervention was superior only in engagement and uptake of selected skills.[531]

Other school interventions reported on the comparison to alternative, school-based or teacher-led interventions. This included a study comparing two homework management programs, one focused on contingency management-based treatment versus a planning skill program.[163] The study found no differences in treatment acceptability (SMD 0.00; CI -0.26, 0.26; 1 study, n=222) and no statistically significant differences in GPA (grade point average) scores (SMD 0.12; CI -0.14, 0.39; 1 study, n=222) and concluded that developing a strong working alliance and engaging parents and students are key elements for school-based programs. Comparing the after-school version of the program Challenging Horizons versus the mentoring version of the program found no differences in functional impairment (SMD 0.02; CI -0.24, 0.28; 1 study, n=326) or academic performance as measured by GPA (SMD -0.19; CI -0.46, 0.07; 1 study, n=326), but the study concluded that the after school version offers more benefits for adolescents.[259]

One study compared approach of ongoing feedback for teachers that selected interventions for students on the basis of functional and academic assessment data versus a traditional data-based approach chosen by the teacher. The difference between interventions for academic performance was not statistically significant (SMD -0.26; CI -0.56, 0.05; 1 study, n=167).[602]

5.3.12.2 School Interventions Summary of Findings

Table 23 shows the findings for the outcomes of interest together with the number of studies and study identifiers.

Table 23. KQ2 summary of findings and strength of evidence for school interventions

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 school intervention vs control	Behavior	3 RCTs[238, 433, 531]	Conflicting results, no meaningful summary estimate could be derived (SMD -0.01; CI -1.38, 1.36; 2 studies, n=395)	C	Insufficient
KQ2 school intervention vs control	Broadband measures	0 studies	No data	C	Insufficient
KQ2 school intervention vs control	ADHD symptoms	6 RCTs[208, 259, 529, 531, 577, 640]	No systematic effect (SMD -0.50; CI -1.05, 0.06; 5 studies, n=822)	I	Low for no benefit

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 school intervention vs control	Functional impairment	2 RCTs[208, 259]	Conflicting results, no meaningful summary estimate could be derived (SMD 0.22; CI -4.39, 4.82; 2 studies; n=274)	C	Insufficient
KQ2 school intervention vs control	Acceptability of treatment	1 RCT[163]	Studies reported favorable results, but effect could not be estimated	I	Insufficient
KQ2 school intervention vs control	Academic performance	5 RCTs[163, 238, 259, 529, 531]	No systematic effect (SMD -0.19; CI -0.48, 0.09; 5 studies, n=854)	I	Low for no benefit
KQ2 school intervention vs control	Appetite suppression	0 studies	No data	C	Insufficient
KQ2 school intervention vs control	Participants with adverse events	0 studies	No data	C	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, C = inconsistency, CI = 95% confidence interval, I = imprecision, KQ = Key Question, RCT = randomized controlled trial, RR = relative risk, SMD = standardized mean differences, SoE = strength of evidence

Several school interventions showed favorable results for key outcomes, but the pooled effects were not statistically significant and suggested no systematic effect of school interventions in general. For behavior and functional impairment, only a small number of studies was identified and these reported conflicting results so that no meaningful effect estimate could be derived and we were not able to determine whether school interventions improve these outcomes or not. Across studies, we did not find that school interventions systematically improve ADHD symptoms and although several studies found an effect on academic performance, the pooled result was not statistically significantly different from no effect and we did not detect a clear beneficial effect. Treatment acceptability (low strength of evidence) was favorable across three identified studies reporting on the outcome, but no effect estimate could be determined (downgraded for imprecision). We did not identify studies reporting on appetite suppression or participants with adverse events and no evidence statement could be derived.

The comparative effects were all rated as insufficient as none of the identified evaluations have been replicated, and all results were unique to the reported study, the specific intervention and the specific comparator; hence the robustness of results could not be evaluated.

5.3.13 Provider Interventions

We identified nine studies[252, 254-256, 308, 371, 386, 451, 466] evaluating healthcare provider interventions or interventions changing how ADHD care is delivered. The earliest study was published in 2007.[256] All were conducted in the United States, except for one in Canada. The patient populations studied were children with ADHD; no studies included teenagers. The percent of female participants ranged from 15 to 36 percent, where reported. Only one study[386] reported ADHD presentation type; 41 percent of children were classified as inattentive, ten percent as hyperactive and 49 percent as combined presentation. No studies purposely included patients with specific co-occurring disorders. A study conducted in Philadelphia[308] reported that 46 percent of patients were African American. The majority of patients in the other studies were White.

Of the identified studies, six reported on a control group with treatment as usual.[252, 255, 256, 308, 386, 466] In one of these trials, pediatricians used titration trials to determine optimal medication dosages; doses were standardized by week, but doctors were blinded to exact dosage.[256] Another study[255] held four training sessions for providers and installed a Web portal to assist with treatment monitoring. Another combined a Web portal with an ADHD care manager.[308] One study provided office-based training in using stimulant medications to physicians and one hour of training to office staff in the use of new software.[386] Another created a Web-based platform that enabled clinicians to administer online clinical questionnaires to parents and teachers to monitor patients remotely between visits.[466] One study evaluated the effects of pharmacogenetic testing to enable genomically assisted prescribing.[252] Finally, one head to head study compared collaborative care, where a care manager delivered three or four content modules to parents and children, to enhanced usual care from a provider known to the care manager.[371]

The studies are difficult to compare and assessed unique interventions, often with multiple components and targeting different aspects of the healthcare system and healthcare delivery processes. In addition, many used study-specific evaluation measures and rarely reported on key outcomes prespecified for this review or did not report sufficient detail to compute effect sizes for outcomes of interest.

One study reported on a broadband measure and evaluated children under the care of providers that used a trigger algorithm and alert resolution process with online clinical questionnaires to monitor patients remotely between visits. The cluster RCT reported that the children in the intervention condition experience less improvement after 15 months in global functioning (SMD -0.36; CI -0.65, -0.07; 1 study, n=263) than the control group participants.[466]

Studies reported conflicting results for ADHD symptoms and no meaningful summary estimate could be derived for the intervention (SMD 0.26; CI -4.79, 5.31; 2 studies, n=537).[308, 466] This included the trigger algorithm study which did not find positive effects[466] and a study evaluating a care manager combined with an online electronic health record portal to enhance communication and shared decision making, which favored the intervention.[308]

The provider or healthcare system interventions that reported on a control group did not report on any other outcome of interest for this review. Other assessed (study-specific) outcomes are shown in evidence table C.2 in Appendix C.

5.3.13.1 Provider Interventions Comparative Effects

Two studies compared a health service intervention to an alternative model. One assessed a collaborative care model versus a referral to mental health providers in an enhanced usual care condition. The study (n=411) did not report sufficient detail to compute effect sizes but concluded that the collaborative care model improved symptoms more than the referred group.[371] A telehealth service delivery model combining pharmacotherapy and caregiver behavior training versus children remaining under the care of their primary care provider who received only a single consultation with a tele-psychiatrist who shared treatment recommendations were compared in the second study.[451] The study reported statistically significant improvement in symptom measures (SMD -0.54; CI -0.81, -0.27; RR 1.64; CI 1.09, 2.47; 1 study, n=223) as well as functional impairment (SMD 0.27; CI 0.01, 0.54; 1 study, n=223) for the telehealth group.[451]

5.3.13.2 Provider Interventions Summary of Findings

Table 24 displays the findings for the outcomes of interest together with the number of studies and study identifiers. Comparative effectiveness results are shown only for outcomes for which effect sizes could be calculated.

Table 24. KQ2 summary of findings and strength of evidence for provider interventions

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	Reasons for Downgrading	SoE
KQ2 provider interventions vs control	Behavior	0 studies	No data	C	Insufficient
KQ2 provider interventions vs control	Broadband measures	2 RCTs[252, 466]	No systematic effect (SMD -0.36; CI -0.65, -0.07; 1 study, n=263)	S, C	Insufficient
KQ2 provider interventions vs control	ADHD symptoms	4 RCTs[255, 256, 308, 386]	Conflicting results, no meaningful summary estimate could be derived (SMD 0.26; CI -4.79, 5.31; 2 studies; n=537)	I	Insufficient
KQ2 provider interventions vs control	Functional impairment	0 studies	No data	C	Insufficient
KQ2 provider interventions vs control	Acceptability of treatment	0 studies	No data	C	Insufficient
KQ2 provider interventions vs control	Academic performance	0 studies	No data	C	Insufficient
KQ2 provider interventions vs control	Appetite suppression	0 studies	No data	C	Insufficient
KQ2 provider interventions vs control	Participants with adverse events	0 studies	No data	C	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, C = inconsistency, CI = 95% confidence interval, I imprecision, KQ = Key Question, RCT = randomized controlled trial, SMD = standardized mean differences, S = study limitation, SoE = strength of evidence

Studies targeting providers or the delivery of healthcare reported on very different intervention approaches, and studies were difficult to compare. In addition, many did not report in sufficient detail (or not at all) on the outcomes of interest for this review. All studies had moderate or high risk of bias, as randomization at the provider level led to some imbalances in patient characteristics between groups. Attrition and detection bias also affected most studies. Strength of evidence was determined to be insufficient either for lack of research (behavior, functional impairment, treatment acceptability, academic performance, appetite suppression, participants with adverse events), study limitations and lack of replication (broadband measure scores), or studies reporting conflicting results making it impossible to determine whether interventions do affect the outcomes of interest (ADHD symptoms).

All effects comparing two active interventions were based on a single study without replication and therefore determined the strength of evidence to be insufficient for evidence statements.

5.4 KQ2a. How do these outcomes vary by presentation (inattentive, hyperactive/impulsive, and combined) or other co-occurring conditions?

We assessed for all key outcomes whether the impact of interventions was associated with the ADHD presentation and whether co-occurring conditions were associated with the treatment effect. Studies varied in what proportion of children with inattentive, hyperactive/impulsive, and combined presentation of ADHD were included. Some studies targeted specific presentations, e.g., evaluated an intervention in a sample with exclusively combined presentation. And while most identified studies did not exclude children with co-occurring disorders, we identified a few studies that purposefully addressed interventions for children with specific co-occurring disorders. In these studies, all children had a dual diagnosis.

5.4.1 ADHD Presentation

Most studies included a range of ADHD presentations, although we identified one study that included only youth with inattentive ADHD presentation.[476] The study evaluated an integrated psychosocial treatment approach; results are documented in Appendix C, Table C.2. A number of studies included only children with combined presentation.[104, 148, 229, 261, 295, 354, 439, 444, 508, 509, 522, 567, 636] The studies evaluated diverse interventions. Half of the studies that restricted participants to the combined ADHD presentation evaluated FDA-approved pharmacologic treatments, and other individual studies assessed the effects of a behavior intervention, nutrition intervention, psychosocial interventions, neurofeedback, cognitive training, and a new pharmacological agent.

We assessed the effect of presentation in indirect comparisons across studies and we documented results of subgroup analyses as reported by the individual authors.

5.4.1.1 Indirect Analyses ADHD Presentation

We first conducted indirect analyses across the large number of studies included in the review. For individual behavior measures, we did not find an effect of the proportion of children with inattentive (p 0.10), hyperactive (p 0.44), or combined (p 0.74) presentation on the reported effect size across all included interventions. For broadband assessments, we did not find an effect on the reported effect size for the proportion of children with inattentive presentation (continuous data p 0.52, categorical data p 0.90), hyperactive (continuous data p 0.73, categorical data p 0.92), or combined (continuous data p 0.70, categorical data p 0.96) across all included interventions.

For ADHD symptom scores in studies reporting a continuous outcome, we did not find an effect on the reported effect size for the proportion of children with inattentive presentation (p 0.18), hyperactive (p 0.65), or combined (p 0.21) across all included interventions. However, the equivalent analysis for categorical outcomes was statistically significant for inattentive presentation (p 0.03). The analysis indicated that treatment effects were lower in samples with a higher proportion of inattentive children, but the effect was very small (1 percentage point increase in the inattentive proportion was associated with a 1.3% reduction in the relative risk for symptom improvement).

None of the analysis for the outcome functional impairment were significant; results were borderline for the proportion of children with inattentive presentation (p 0.12), hyperactive (p 0.31), or combined (p 0.10), indicating a systematic effect across all included interventions. Results could not be confirmed in the analyses for categorical data as too few studies were available for the analysis. There were insufficient data to test the effect for treatment satisfaction.

For academic performance outcomes, results were borderline for the proportion of children with inattentive presentation (p 0.06), but results for hyperactive presentation (p 0.59) and combined presentation (p 0.25) were not statistically significant. Findings could not be confirmed nor refuted with categorical data due to lack of studies.

For the outcome appetite suppression, we did not find an effect of the presentation on the reported effect size, i.e., results for inattentive (p 0.39), hyperactive (p 0.24), or combined presentation (p 0.52) were not statistically significantly different across studies and interventions. We did not identify an effect of the likelihood of experiencing an adverse event based on the ADHD presentation as results for inattentive presentation (p 0.34), hyperactive presentation (p 0.42), and combined presentation (p 0.50) were not statistically significant.

We also analyzed this question within a more homogenous group of studies, the FDA-approved medications, i.e., the largest intervention group in the report. In this subgroup with likely less residual heterogeneity, we either found no effect of the ADHD presentation or there were too few studies for analyzes, with one exception: the proportion of participants with inattentive ADHD presentation reporting adverse events (p 0.01). When differentiating further between two large subsets, we found no effect of ADHD presentation within simulant studies or within non-stimulant studies, suggesting that the study composition and medication type may be confounded. It is unclear from these analyses whether the proportion of participants with inattentive, hyperactive, or combined presentation is systematically associated with differences in treatment effects.

5.4.1.2 Reported Analyses for Subgroups in ADHD Presentation

Some of the identified studies reported results stratified by ADHD presentation or reported results of a moderator analysis that evaluated the effects of the ADHD presentation on treatment effects. The studies reported on different intervention types including: FDA-approved pharmacological interventions,[108, 164, 306, 442, 538, 557] a new pharmaceutical agent,[637] psychosocial interventions;[163, 523] cognitive training;[166] nutritional supplements;[310, 349, 411, 510] and provider training,[386] respectively. The reported subgroup results were primarily for ADHD symptoms and broadband assessments.

A cognitive training intervention identified a subgroup of boys who had both a lower hyperactivity and a higher conduct disorder symptom score with significantly better planning/organizing skills than the total group of participants.[166] A study evaluating an omega-3 supplement reported that improvements were significantly more frequent in the inattentive ADHD presentation (p 0.03) than in the combined ADHD presentation (no statistically significant treatment effect).[349] One omega 3 and zinc study[510] reported the superior effect of zinc over omega-3 was only seen in the inattentive, not in the combined presentation of ADHD children (p 0.21).

All other studies did not detect systematic effects of ADHD presentation. One study[108] evaluating long-acting methylphenidate reported that inattentive and combined ADHD subgroups did not differ significantly in their improvements in the parent (p 0.61) or teacher (p 0.85) SNAP-IV ratings (Swanson, Nolan, and Pelham (SNAP) Questionnaire). A further study reported no significant treatment interaction between relapse and the ADHD presentation.[164] A study evaluating atomoxetine reported that baseline ADHD severity did not moderate treatment efficacy on response inhibition (p 0.54), sustained attention (p 0.96), or fear identification (p 0.66).[306] A study assessing the effects of omega 3[310] found a higher percentage of children who ranked below the median in hyperactivity/impulsivity on a continuous performance test improved more in ADHD symptom severity, but the difference was not statistically significant (p 0.177). Reported results for the effects of a provider intervention on ADHD Rating Scale-IV Scores and SNAP-IV Scores showed no treatment effects specific to combined ADHD presentation or ADHD inattentive presentation.[386]A study of atomoxetine[442] assessed changes from baseline of ADHD-RS-IV-Parent Total Score and did not find any interaction.

Some studies stratified by clinical severity. A study evaluating mixed amphetamine salts[557] stratified participants by low or high baseline severity on ADHD-RS-IV Scale and CGI scores. The mean reduction in ADHD severity was greater for low baseline severity in all dose groups relative to placebo (p<0.01) on the ADHD-RS-IV scale and for doses above 10mg on CGI Impression Scores (p<0.01). In a further study, evaluated efficacy and adverse effects of methylphenidate treatment for baseline ADHD severity as reported by teachers and parents found no significant effect on parent- or teacher-rated Conners ADHD index at 16 weeks (p values >0.1).[538] One study evaluating hopantenic acid[386] indicated that treatment effects were maximized in patients with the ADHD combined presentation group, but between-group differences were not statistically significant. Stratified analyses of an omega 3 intervention evaluating ADHD RS-IV Scores explored whether children rated with abnormal scores Sin at least two of the Conners' subscales showed a different treatment response. The interaction was statistically significant (p < 0.15) in four out of the eight CRS-P subscales (Parent Child Rating Scales) .[411] A behavioral sleep intervention for children with ADHD[523] reported that children with ADHD symptom severity scores above the 75th percentile were more likely to have moderate/severe sleep problems over time. ADHD symptom severity was a moderator for ADHD symptoms (p 0.04) and quality of life (p 0.04) over time, suggesting the intervention is less effective for youth who have sleep problems. All other studies did not detect an effect.

5.4.2 Effect of Co-Occurring Disorders

We abstracted the results of study-reported effects (subgroup analyses or moderator analyses) as well as indirect comparisons across studies using a meta-regression approach.

A small number of studies addressed co-occurring disorders presenting with ADHD overall. Identified studies targeting specific populations included participants with ADHD as well as oppositional defiant disorder, conduct disorder, or aggression;[151, 174, 207, 220, 226, 257, 264, 321, 432, 623] learning disabilities;[221, 480, 526, 538, 577, 602, 624] sleep conditions;[329, 428, 513, 523] mood disorders such as depression and anxiety;[132, 292, 377] tic disorders;[118, 380, 540, 556] traumatic brain injury;[383] epilepsy;[262] substance use disorder;[497] iron deficiency;[478] genetic disorders;[113] or organizational deficits;[106] respectively. Few of the studies reported statistically significant, systematic effects of co-occurring conditions and only selected studies reported effects on the key outcomes for this report.

In the MTA study, children with ADHD-only or ADHD with oppositional defiant disorder (ODD) or conduct disorder (but without anxiety disorders) responded best to MTA medication treatments (with or without behavioral treatments), while children with multiple comorbid disorders (anxiety and ODD/conduct disorder) responded optimally to combined (medication and behavioral) treatments;[343] children with comorbid anxiety, particularly those with overlapping disruptive disorder comorbidities, showed preferential benefits to the intervention;[864] no detrimental effect of anxiety on medication response for core ADHD or other outcomes in anxious or non-anxious ADHD children was demonstrated;[910] comorbid anxiety disorder did moderate outcome, in participants without anxiety, results paralleled intent-to-treat findings, for those with anxiety disorders, behavioral treatment yielded significantly better outcomes than community care (and was no longer statistically different from medication management and combined treatment) regarding ADHD symptoms;[942] comorbidity with oppositional defiant disorder or conduct disorder (54% of the sample yielded such preintervention comorbidity) significantly moderated findings, initial comorbidity with anxiety disorder served as a clear moderator of treatment response. Whereas the 66 percent of the MTA sample without anxiety at baseline displayed a response to treatment that was close to that of the overall sample, the 34 percent with comorbid anxiety showed a relatively better response to the behavioral aspects of the MTA treatments.[830] Parent-reported anxiety and ODD/CD (oppositional defiant disorder/conduct disorder) status were noted on response to treatment, indicating that children with ADHD and anxiety disorders (but no ODD/CD) were likely to respond equally well to the MTA behavioral and medication treatments, children with ADHD-only or ADHD with ODD/CD (but without anxiety disorders) responded best to MTA medication treatments (with or without behavioral treatments), while children with multiple comorbid disorders (anxiety and ODD/CD) responded optimally to combined (medication and behavioral) treatments.[863] For other functioning domains (social skills, academics, parent-child relations, oppositional behavior, anxiety/depression), results suggested slight advantages of combined over single treatments (medical management, behavior) and community care, children with parent-defined comorbid anxiety disorders, particularly those with overlapping disruptive disorder comorbidities, showed preferential benefits to the behavioral and combined interventions.[864] A further study[461] reported that youths with ADHD and comorbid ODD showed statistically significant improvement in ADHD, ODD, and quality-of-life measures following atomoxetine treatment; treatment response was similar in youths with and without ODD, except that the comorbid group showed improvement compared with placebo at 1.8 mg/kg/day but not 1.2 mg/kg/day. In contrast, youths without ODD showed improvement at 1.2 mg/kg/day and no incremental benefit at 1.8 mg/kg/day. A third study reported that children with ODD did not benefit as much from the atomoxetine than other children.[133] One study enrolled children with ADHD and aggressive behavior and titrated stimulant treatment to identify patients with inadequate reductions in aggressive behavior. The study concluded that rigorous titration of stimulant medication and concurrent behavioral therapy may avert the need for additional medications.[151] All other studies did not detect treatment effect differences associated with co-occurring conditions or reported on other outcomes such as ODD scores as documented in Appendix C, Table C.3.

5.4.2.1 Indirect Analyses, Co-Occurring Disorders

We assessed whether the subgroup influences the impact of the interventions for the key outcomes in indirect comparisons. For the outcome behavior, we did not find a systematic effect across any of the evaluated subgroups that provided sufficient data for the analysis (sleep p 0.99). For broadband scale scores, we also found no systematic effect (sleep p 0.07). Symptom scores provided the most data for the comparisons; however, the analysis did not detect systematic effects (sleep p 0.50). For functional outcomes, results were also not statistically significant (sleep p 0.93). Treatment satisfaction could not be evaluated due to the small number of studies. Appetite suppression was not significant (learning disability p 0.41), nor was adverse events (sleep p 0.68).

Within the more homogenous subgroup of FDA-approved medications, stimulants alone, and non-stimulants alone, there were insufficient data for analyses for all outcomes of interest.

We did not detect evidence indicating a differential effect associated with co-occurring disorders. However, based on the small number of studies and the indirect nature of effect analysis, the results have to be interpreted with caution.

5.6 KQ2b. What is the risk of diversion of pharmacologic treatment?

Only two studies met inclusion criteria for KQ2b.[455, 497] One was an RCT evaluating either 200 or 400 mg viloxazine vs placebo and found no evidence for misuse.[455] Viloxazine, however, is a non-stimulant (NRI) medication with low abuse potential.

The other study was a double-blind RCT of OROS (Osmotic-Release Oral System) methylphenidate plus cognitive behavioral therapy (CBT) versus placebo plus CBT in adolescents with ADHD and a co-occurring substance use disorder .[497] Rates of misuse or diversion in the stimulant group (2.1%-4.8%) were approximately double the rates in the placebo group, though the differences did not reach statistical significance. Findings are difficult to generalize to non-substance-use ADHD populations, as misuse and diversion rates may be higher in this subpopulation than in ADHD adolescents without substance use disorder. However, nearly doubled rates of misuse may be clinically relevant, given that participants were blinded to treatment assignment, and rates were systematically higher in the stimulant group.

5.7 Summary of Findings KQ2a and KQ2b

Table 25 documents the results across studies.

Table 25. KQ2a summary of findings and strength of evidence for ADHD interventions

Intervention and Comparison	Outcome	Number of Studies; Study	Findings	Reasons for Downgrading	SoE
KQ2a effect modifier ADHD presentation	Behavior	N/A	Indirect comparisons did not suggest an effect	D	Low for no effect
KQ2a effect modifier ADHD presentation	Broadband measures	N/A	Indirect comparisons did not suggest an effect	D	Low for no effect
KQ2a effect modifier ADHD presentation	ADHD symptoms	N/A	Indirect comparisons did not suggest an effect	D	Low for no effect
KQ2a effect modifier ADHD presentation	Functional impairment	N/A	Indirect comparisons did not suggest an effect	D	Low for no effect
KQ2a effect modifier ADHD presentation	Acceptability of treatment	N/A	Indirect comparisons did not suggest an effect	D	Low for no effect
KQ2a effect modifier ADHD presentation	Academic performance	N/A	Indirect comparisons did not suggest an effect	D	Low for no effect
KQ2a effect modifier ADHD presentation	Appetite suppression	N/A	Indirect comparisons did not suggest an effect	D	Low for no effect
KQ2a effect modifier ADHD presentation	Participants with adverse events	N/A	Indirect comparisons reported conflicting results	D, C	Insufficient

Intervention and Comparison	Outcome	Number of Studies; Study	Findings	Reasons for Downgrading	SoE
KQ2a effect modifiers co-occurring disorders	Behavior	N/A	Indirect comparisons did not detect effects, but few studies addressed co-occurring disorders systematically	D, C	Insufficient
KQ2a effect modifiers presentation and co-occurring disorders	Broadband measures	N/A	Indirect comparisons did not detect effects, but few studies addressed co-occurring disorders systematically	D, C	Insufficient
KQ2a effect modifiers presentation and co-occurring disorders	ADHD symptoms	N/A	Indirect comparisons did not detect effects, but few studies addressed co-occurring disorders systematically	D, C	Insufficient
KQ2a effect modifiers presentation and co-occurring disorders	Functional impairment	N/A	Indirect comparisons did not detect effects, but few studies addressed co-occurring disorders systematically	D, C	Insufficient
KQ2a effect modifiers presentation and co-occurring disorders	Acceptability of treatment	N/A	Indirect comparisons did not detect effects, but few studies addressed co-occurring disorders systematically	D, C	Insufficient
KQ2a effect modifiers presentation and co-occurring disorders	Academic performance	N/A	Indirect comparisons did not detect effects, but few studies addressed co-occurring disorders systematically	D, C	Insufficient
KQ2a effect modifiers presentation and co-occurring disorders	Appetite suppression	N/A	Indirect comparisons did not detect effects, but few studies addressed co-occurring disorders systematically	D, C	Insufficient
KQ2a effect modifiers presentation and co-occurring disorders	Participants with adverse events	N/A	Indirect comparisons did not detect effects but few studies addressed co-occurring disorders systematically	D, C	Insufficient
KQ2b diversion	Misuse	2 studies[455, 497]	Did not indicate any issues	D, C	Insufficient

Notes: ADHD = attention deficit hyperactivity disorder, C = inconsistency, D = indirectness, KQ = Key Question, N/A = not applicable, SoE = strength of evidence

Across identified studies, we either detected no evidence of effect modifiers or the research base was insufficient for any evidence statements. We downgraded results for indirectness given that the comparison was indirect, across studies. In several instances, we also downgraded for the domain inconsistency because consistency could not be assessed or could not be assumed because the identified studies did not cover the entire range of possible variables (e.g., a small number of studies only addressed co-occurring disorders systematically).

We identified only a small number of studies that systematically addressed co-occurring disorders, and evidence is insufficient for concrete evidence statements. Only two studies reported on diversion, and it was therefore not possible to quantify the risk of diversion of pharmacological treatment.

6. Results: Monitoring ADHD

6.1 Key Question (KQ) 3 ADHD Monitoring Key Points

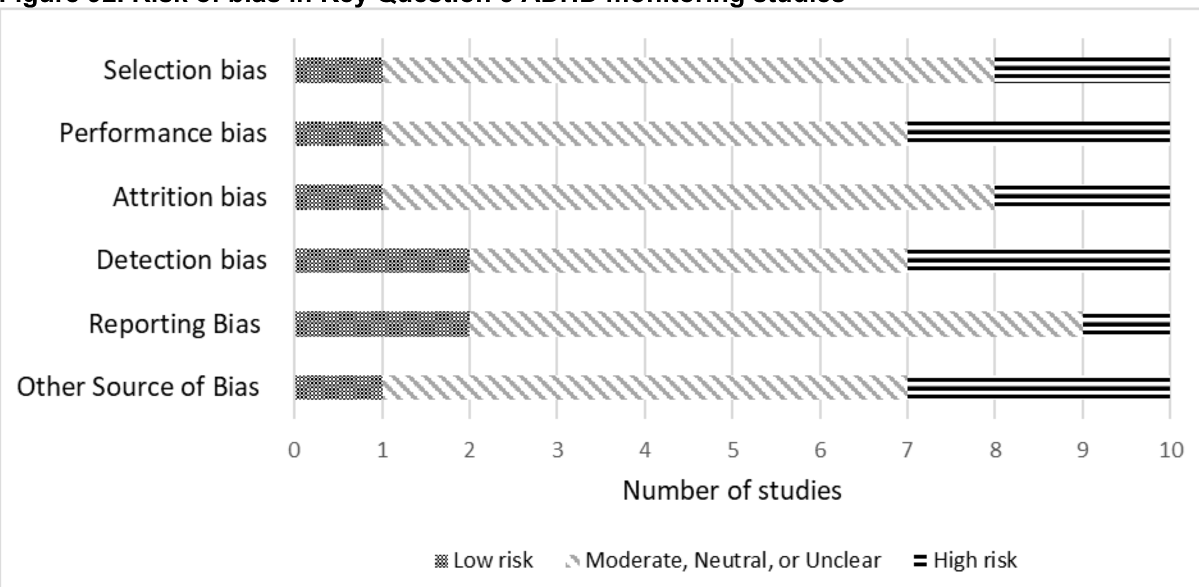
- Very few monitoring studies have been reported and more research is needed on how youth with attention deficit hyperactivity disorder (ADHD) should be monitored over time.
- Different assessment modalities may provide valid but different perspectives and more than a single assessment modality may be required for comprehensive and effective monitoring of ADHD outcomes over time.

6.2 KQ 3 ADHD Monitoring Summary of Findings

We identified a small number of studies addressing a monitoring strategy.[173, 203, 255, 256, 268, 274, 466, 545, 609, 629] Results of the individual studies are shown in Appendix D, Table D.3. However, studies did not provide information on the predefined key outcomes.

The potential for risk of bias in the KQ3 studies is documented in Figure 92. The critical appraisal for the individual studies is in Appendix D.

Figure 92. Risk of bias in Key Question 3 ADHD monitoring studies

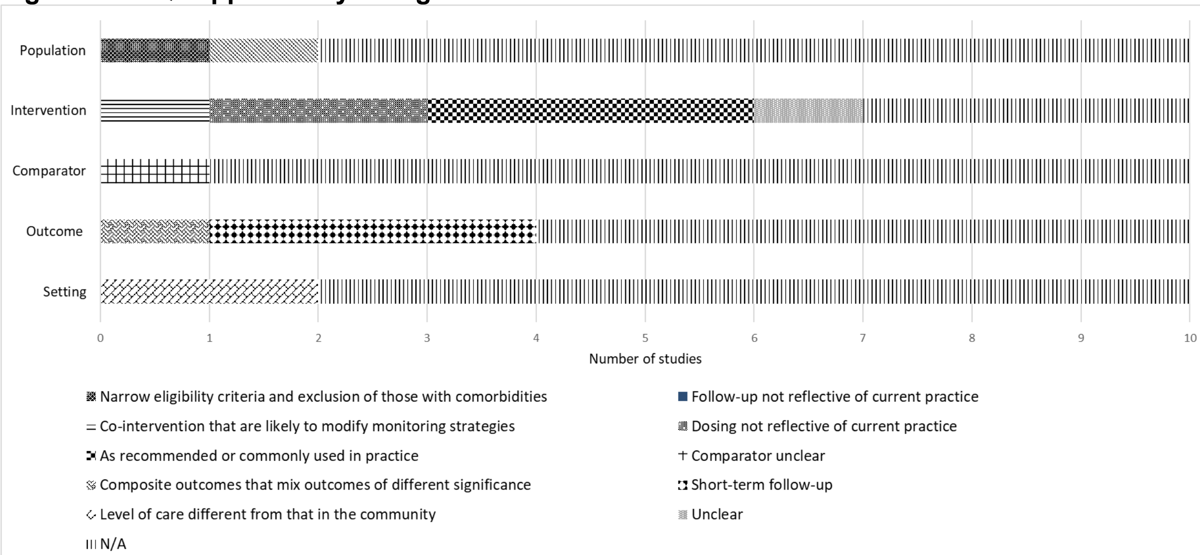


Notes: ADHD = attention deficit hyperactivity disorder

Across studies, selection bias was likely present in two studies.[274, 466] Performance bias was present in two studies.[268, 274] Attrition bias was also present in two of the identified studies.[173, 203] Detection bias was determined to be present in three studies.[173, 274, 466] Reporting bias was likely in one study.[545] In the small set of studies, a third were rated as high risk of bias for other sources.[255, 268, 629]

Figure 93 shows the distribution of applicability issues in KQ3 studies. The applicability for the individual studies is in Appendix D.

Figure 93. KQ3 applicability rating



Notes: KQ = Key Question, N/A = not available

Given the small number of available studies, results of the different monitoring strategies are documented in Table 26. More details can be found in Appendix Table C.3.

Table 26. KQ3 monitoring strategies evidence

Study: Author, Year; Location	Intervention, Analysis, Follow Up	Results
Cedergren, 2021[173] Sweden	Open-label monitoring consisting of 5 follow-up visits in 12 months using a continuous performance test (QbTest) and investigator rating on the ADHD-RS. Qualitative comparison of change in ADHD-RS and QbTest scores over 12 months Naturalistic follow up, with medication administered according to clinician judgement of need.	Bonferroni-adjusted pairwise comparisons showed statistically significant reductions in QbTest and ADHD-RS scores over the 12-month study. Both measures appear to capture symptom change over time, but weak correlations between the measures suggest that their role in medical follow-up might be complementary rather than interchangeable.
Cohen, 1989[203] United States	Randomized, double-blind, placebo-controlled crossover study of the use of monitoring ADHD symptoms – before and during treatment with methylphenidate – using the ADD-H Comprehensive Teacher Rating Scale, Conners parent rating scale, and the Gordon Diagnostic System (a computerized continuous performance task assessing vigilance and impulse control). Group differences in change in symptom scores over time. Naturalistic follow up, before and during treatment with fixed-dose (5mg for children weighing less than 30kg, 10mg for children weighing 30kg or more), short-acting methylphenidate administered twice daily for 1 month, with measures collected at baseline, 1 month (the time of crossover), and 2 months (endpoint).	Both rating scales demonstrated significant change in symptoms (inattention and hyperactivity on the ADD-H scale; hyperactivity on the Conners scale) during treatment with methylphenidate compared with placebo, whereas the Gordon task did not demonstrate change. Rating scales, but not this continuous performance task, appear helpful in monitoring the short-term effects of stimulant treatment.

6. Results: Monitoring of ADHD

Study: Author, Year; Location	Intervention, Analysis, Follow Up	Results
Epstein, 2007[256] United States	12 pediatric practices were randomly assigned to receive access to collaborative consultative services or a control group. In the collaborative consultation services, pediatricians were encouraged and assisted to use rating scales for symptom monitoring and titration trials to determine optimal medication dosages. Physicians were taught to prescribe 4 different doses of methylphenidate during a titration trial (placebo, 18 mg, 36 mg, 54 mg); the order of week-long dosing was blinded but standardized across patients (week 1, 18 mg; week 2, placebo; week 3, 36 mg; week 4, 54 mg) to determine optimal dosing for each patient. Parents and teachers completed weekly behavioral ratings (Conners Global Index) & side effect rating scales. Data were returned to Duke Univ psychiatrist to determine the best starting medication dose; a report describing the titration results was faxed back to pediatricians. Patients in control group practices received treatment as usual, without access to consultative services. Assessed Conners Global Index & side effect rating scales. Monthly follow up with Conners and side effect rating scales for 12 months, sent to Duke U psychiatrists for interpretatin, with recommendations returned to the pediatrician	Use of symptom ratings did not differ significantly by group, nor did the change in symptoms over time. Pediatrician compliance with the collaborative consultation service was poor (pediatricians for 29 of 59 patients in the consultation group received a titration trial and 13/59 participated in monthly medication monitoring). Preliminary secondary analyses indicated that those children whose pediatricians complied with titration had significantly better outcomes compared with those who did not and TAU controls (group x time P<.01) Children in the collaborative consultation service–complier group had a 27% reduction in symptom scores compared with 18% reduction in the TAU controls and 13% reduction in consultation non-compliers.
Epstein, 2016[255] United States	Cluster randomized controlled trial of either a technology-assisted quality improvement (QI) intervention or TAU control. QI intervention consisted of 4 training sessions, office flow modification, guided QI, and an ADHD Internet portal to assist with treatment monitoring versus TAU control practices Assessed intervention effects on parent- and teacher-rated ADHD severity using on the Vanderbilt ADHD total symptom score. 12 months follow up	Intent-to-treat analyses examining outcomes (parent ratings of ADHD severity) in all 577 children assessed for ADHD were not significant (b=-1.97, P=0.08), but among the 373 children prescribed ADHD medication, a significant intervention effect on reducing parent-rated symptom severity (b=-2.42, P=0.04) but not teacher-rated symptoms was observed. Prescriber compliance with treatment guidelines was poor, as only 373 of the 577 patients received medication at any time in the 1-year follow-up, and many who did receive it were prescribed sub-optimal doses. Compared with the usual care group, providers in the intervention group had 25% more patient contacts (d=.38, p=.0008) and collected 4.6 (d=.57, p<.0001) and 9.9 (d=.54, p<.0001) times more parent and teacher ratings, respectively. However, providers in the intervention group collected parent ratings in only half and teacher ratings in a quarter of their patients during the initial year of medication treatment.
Fiks, 2017[268] United States	Cluster-randomized open label trial at the practice level (9 intervention, 10 control sites) for 3-component quality-improvement program that	Differences between intervention arms were not statistically significant, though clinicians in both study arms were

6. Results: Monitoring of ADHD

Study: Author, Year; Location	Intervention, Analysis, Follow Up	Results
	employs distance learning: (1) 3 15-minute Web-based presentations on evidence-based practices for managing ADHD in primary care; (2) optional collaborative consultation with ADHD experts via a health system online networking site or private email/telephone conversation; (3) and performance feedback reports or calls every 2 months informing them of their rates of sending and receiving ADHD rating scales from parents and teachers and allowed them to compare their results to results of the entire group; feedback reports were discussed during four, 1-hour conference calls). Participation qualified for Maintenance of Certification credit from the American Board of Pediatrics. Collection of rating scales was facilitated via an electronic application linked to the electronic health record versus waitlist control Number of parent and teacher rating scales sent out and received back assessed	significantly more likely to administer and receive parent and teacher rating scales compared to an 8-month baseline period. Intervention clinicians who participated in at least one performance feedback call were more likely to send out parent rating scales than intervention clinicians who did not participate (relative difference of 14.2 percentage points, 95% CI: 0.6, 27.7. For all study outcomes, practices with the highest rates of clinician participation in the study (≥ 80%), were not superior to practices with lower rates of involvement (< 80%). Participation was low (105 of 166 invited); 42 of 53 in the intervention group completed all 3 education presentations; 30 (57%) participated in at least one feedback call, and 19 (36%) participated in all 3 components of the intervention.
Florida International University, 2010[274] United States	Randomized to receive either osmotic release oral system-methylphenidate alone (78%) or behavioral therapy alone (22%). After 6 months, children with a decline in body mass index >0.5 z-units were randomized to 1 of 3 weight recovery treatments: (1) monthly height/weight monitoring plus daily medication; (2) drug holidays on non-school days (with monthly monitoring); or (3) daily caloric supplements (with daily medication and monthly monitoring). Standardized body weight and height assessed 18 follow-up visits over 30 months	All groups significantly increased their weight gain. Drug holidays + monitoring, caloric supplementation + monitoring, and monitoring alone all led to increased weight velocity in children taking CNS stimulants, but with no differences between groups, and no intervention led to increased height velocity. When analyzed by what parents did (versus what they were assigned to), caloric supplementation ($p<0.01$) and drug holidays ($p<0.05$) increased weight velocity more than monitoring of height and weight. Over the entire study, participants declined in standardized weight (-0.44 z-units) and height (-0.20 z-units).
Oppenheimer, 2019[466] United States	Naturalistic study of a Web-based platform enabling clinicians to administer online monthly clinical questionnaires to parents and teachers for monitoring of patients remotely between visits. Trigger algorithm alerts clinicians to clinically actionable events that are documented in the medical record versus non-alert group Patients were the unit of analysis. Parent and teacher reports of current medication, medication side effects inventory, Vanderbilt ADHD Parent Rating Scale, Clinical Global Impression-Severity (CGI-S) scale, and Clinical Global Impression-Improvement (CGI-I) scale 15 months follow up	Trigger algorithms produced alerts requiring immediate review in 8% of the parent reports. Clinicians perceived 74% of alerts to be significant enough to prompt urgent follow-up with parents, suggesting a low rate of false positive alerts. Patients who generated alerts compared to those who did not had more severe ADHD symptoms (beta = 5.8, 95% CI: 3.5–8.1 [$p < 0.001$] in the 90 days prior to an alert, further supporting validity of the alerts.
Smith, 2000[545] United States	A assessed the reliability, validity, and unique contributions of self-reports by adolescents receiving treatment for ADHD in a summer	Average reliability for the adolescent self-report across all measures was .78 (range .74-.83), similar to the reliability of .82 for counselors (range .78-.85), and

6. Results: Monitoring of ADHD

Study: Author, Year; Location	Intervention, Analysis, Follow Up	Results
	treatment program that included self-monitoring as a treatment component. Self-reported IOWA Conners Inattention/Overactivity and Oppositional/Defiant subscales, ratings of interactions with peers and staff. Assessed changes in reliability during a placebo-controlled, cross-over study of 30 mg of methylphenidate. Observed frequencies of negative behavior, rating from parents and teachers	significantly better than the teacher reliability of .60 (range .51-.68). Teacher and counselor ratings on the Conners changed significantly during stimulant treatment whereas adolescent self-ratings did not. The findings suggest that adolescents can provide reliable information on their symptoms, but not beyond what parents can provide. Adolescents may also be poor sources of information about the change in ADHD symptoms, but a good source of information about improved interactions with others in response to treatment.
Weisman, 2018[609] Israel	Mobile app allows patients or their parents to report their clinical status following initiation of prescription or after changing medication dosage; purpose of the app is to facilitate communication with MD; app includes questions on severity of ADHD symptoms and potential side effects and can also function as a medication reminder Treatment as usual, without app	CGI-Severity no significant difference No significant difference on ADHD-RS, possibly due to inadequate power, Significant difference (p= 0 .008) favoring intervention group on the Clinician Rating Scale (CRS). Intervention group had significantly better adherence, as measured by pill count (p < .015).
Yang, 2012[629] Korea	Naturalistic study of symptom monitoring and medication adherence assessed using the Medication Event Monitoring System, a bottle cap with a microprocessor that records all instances and times that the bottle is opened Patient self-report, clinician rating, pill count assessed; measure of adherence 8 weeks follow up	The rate of non-adherence was 46.2%, higher than patient self-report of 17.9%, clinician rating of 31.7%, and pill count of 12.8%. Pill count and monitoring system concordance was 0.249 (95% CI: 0.102-0.386). Self-report concordance was 0.237 (95% CI: -0.024-0.468). Non-adherent patients had more severe symptoms at baseline and inferior improvement compared with adherent patients.

Notes: ADD-H = attention deficit disorder with hyperactivity, ADHD = attention deficit hyperactivity disorder, ADHD-RS = ADH rating scale, CI = 95% confidence interval, CGI-I = Clinical Global Impression-Improvement scale, CNS = central nervous system stimulants, CRS = clinician rating scale, GGI-S = (Clinical Global Impression-Severity scale, KQ = Key Question, MD = medical doctor, QB test = quantified behavioral test, RR = relative risk, TAU = treatment as usual

We identified 10 studies addressing some type of monitoring strategy for ADHD.[173, 203, 255, 256, 268, 274, 466, 545, 609, 629] Three studies of ADHD rating scales and/or a computerized continuous performance task assessed their reliability and sensitivity to detect symptom change over time. The studies reported a relatively poor correlation between these measures over time, whether the correlations were between different raters on the same rating scale[545] or between assessment modalities (e.g., rating scale vs computerized performance test).[173, 203] Both subjective assessment modalities (e.g., self-report, parent, teacher, and clinician rating scales)[173, 203, 545] and more objective measurement modalities (e.g., continuous performance task)[173] may be sensitive to clinical change in response to treatment, but one study suggested that subjective measures may be more sensitive to detecting treatment-associated changes in ADHD symptom severity and other functional outcomes.[203]

Three studies assessed the impact on ADHD symptoms of interventions that target medication prescriber training to improve either symptom monitoring or adherence to treatment guidelines. One study assessed the impact of collaborative consultative services,[256] and two assessed the impact of a quality improvement intervention on outcome monitoring[268, 710] or ADHD symptoms.[710] Collectively, the studies showed that medication prescribers (mostly pediatricians) exhibited poor compliance in attending training programs for quality improvement in treating ADHD.[256, 268] Even when they did participate in those traininigs, pediatrician compliance with treatment guidelines was poor, as the pediatricians rarely acquired ratings of symptom severity from either parents or, even less often, from teachers,[256, 268] even when the intervention increased the collection of ratings compared with waitlist controls.[268] Moreover, pediatricians often did not prescribe stimulant medication for youth who met diagnostic criteria for ADHD,[255, 256] and when they did prescribe, the doses were sub-optimal,[255] even when provided intensive advice and support services from mental health specialists.[256] Youth whose prescribers participated in the consultative services from specialists, however, had greater reductions in ADHD symptom severity.[256] One study assessed the validity of alerts generated by a computer algorithm based on ratings from monthly monitoring of ADHD symptom severity. Alerts were then sent to prescribers notifying them of putatively actionable clinical events.[466] Prescribers deemed the alerts to be generally valid, suggesting that computerized algorithms applied to symptom ratings combined with automated clinican alerts may have clinical utility.

One study of youth who had stimulant-induced weight loss compared the effects of (1) height and weight monitoring alone, with (2) caloric supplementation plus monitoring, and (3) medication holidays plus monitoring on the trajectory of weight gain.[274] All three interventions increased weight significantly, suggesting that monitoring of height and weight during medication administration may be efficacious in attenuating stimulant-induced weight loss, though the study did not include the no-intervention control that would have been needed to prove this. Intent-to-treat analyses showed that the addition of caloric supplementation or medication holidays did not provide significant incremental benefit on attenuating weight loss when compared with monitoring alone, though per-protocol analyses suggested that the use of these additional interventions yielded significant additional benefits.

One study used a mobile app to allow patients or their parents to continuously report their clinical status. The study only reported on eight weeks of follow up after initiating the intervention.[609] One study continuously assessed patients and evaluated the use of an electronic bottle cap for stimulant medication to monitor treatment adherence.[629] Non-adherence was shown to be higher when monitored with this bottle cap compared with patient report, clinician rating, and pill count. The methods used to assess adherence correlated weakly with one another. Non-adherent patients had more severe symptoms at baseline and inferior improvement compared with adherent patients, providing evidence for the validity of the bottle cap method for monitoring adherence. If the bottle cap is considered the gold-standard, then self-reports, clinician impressions, and even pill counts would be deemed unreliable measures of medication adherence.

7. Discussion

We identified a large body of evidence contributing to the knowledge base on attention deficit hyperactivity disorder (ADHD) diagnostic tools, treatment outcomes, and monitoring strategies. We included studies dating back to 1980, marking the advent of modern diagnostic criteria for ADHD and the introduction of long-acting forms of stimulant medication. The questions addressed in our review were informed by Key Informants and supported by a Technical Expert Panel. A dedicated systematic review team with content experts conducted a detailed synthesis of existing research, including over 500 studies in this systematic review.

Despite the large number of publications included, our review has limitations in its scope due, in part, to decisions about which studies to include in the review. For example, we required intervention studies to treat participants for at least four weeks to ensure that the studies assessed sustained, and not merely temporary, effects on outcomes. This decision excluded some early studies of ADHD treatment that have contributed to the development of the field. We also required studies to be either large or to report a power analysis to ensure that they were sufficiently powered to detect effects. This criterion ensured the reader would not be left guessing whether a study was either underpowered to show effects or genuinely showed the absence of evidence of an effect. This criterion, however, also excluded studies that have contributed historically to the evidence base. We furthermore limited treatment studies to youth with a clinical diagnosis of ADHD, which excluded studies that evaluated interventions in broader populations. Finally, we restricted publications to the English language, which may have excluded other important studies that have contributed to the evidence base.

Findings in Relation to the Decisional Dilemma(s)

The following text discusses findings in the context of the decisional dilemmas the review set out to address.

Diagnostic Approaches for ADHD

Studies of diagnostic approaches most commonly report sensitivity (true positive rate) and specificity (true negative rate) for a given diagnostic threshold applied to the measure being assessed. Sensitivity and specificity, however, depend on the diagnostic threshold selected, and their values are inherently a trade-off, such that varying the diagnostic threshold to increase either sensitivity or specificity reduces the other. Interpreting diagnostic performance in terms of sensitivity and specificity is therefore difficult. Investigators instead often report performance for sensitivity and specificity in terms of Receiver Operating Characteristics (ROC) curves because the area under the curve (AUC) provides an overall, single index of performance that does not depend on the diagnostic threshold for the tool being assessed. AUC values range from 0.5 (corresponding to the y=x diagonal of the ROC curve, and indicating that the tool provides no information above chance for classification) to 1.0 (corresponding to the x=0 vertical line, which indicates that the test can correctly classify all participants as having ADHD, and all non-ADHD participants as not having it – a perfect test). AUC values are commonly interpreted as follows: 90 to 100 represents *excellent* performance; 80 to 90 *good*; 70 to 80 *fair*; 60 to 70 *poor*; and 50 to 60 indicates *failed* performance. Our assessment of performance of the various tools was specifically for clinical diagnosis compared with a diagnosis made by expert mental health clinicians, distinct from any other clinical utility the tools may have.

7. Discussion

Many diagnostic studies in this review aimed to distinguish ADHD youth from neurotypical controls, which is of limited clinical relevance: in clinically referred youth, most parents, teachers, and clinicians are reasonably confident that something is wrong, but they are unsure whether the cause of their concern is ADHD. The more clinically relevant and difficult question, therefore, is how well the measures distinguish ADHD youth from youth who have other emotional and behavioral problems. Moreover, studies that simply discriminate ADHD youth from neurotypical controls cannot discern whether diagnostic performance is determined by the presence of ADHD or by the presence of any other characteristics that accompany clinical "caseness," such as the presence of comorbid illnesses or effects of chronic stress or current or past treatment.

Overall, AUCs for parent rating scales ranged widely from poor[339] to excellent,[632] with a low strength of evidence due to imprecision and study limitations. Analyses restricted to the Child Behavioral Checklist (CBCL) (the most commonly evaluated scale) yielded more consistent good AUCs differentiating youth with ADHD from others in clinical samples, but the number of studies contributing data was small. One study reported moderate rater agreement between mothers and fathers for inattention, hyperactivity, and impulsivity. Internal consistency for rating scale items was generally high across most rating scales. Reported test-retest reliability was substantial, but only two studies reported on the measure.

AUCs for teacher rating scales ranged from failed performance (distinguishing ADHD from either neurotypical controls or other patients[491]) to good (distinguishing ADHD from either neurotypical controls or clinic patients[359]) with a low strength of evidence, primarily due to imprecision. The internal consistency for scale items was generally high. Teacher ratings demonstrated very low rater agreement with the corresponding parent rating scales, suggesting either a problem with the instruments or a large variability in symptom presentation that depended on environmental context (home or school).

Clinicians likely need ratings from both parents and teachers to yield a more complete representation of symptom expression across informants or settings. We found only two studies, however, that formally combined ratings from parents and teachers to diagnose ADHD, with one study reporting limited specificity when using the Conners to distinguish ADHD from other clinically referred youth,[18] and a machine learning study reporting excellent diagnostic accuracy when using the Behavior Rating Inventory of Executive Function (BRIEF) to distinguish ADHD youth from typically developing controls.[467]

Though data are limited, self-reports from youth seem to perform less well than corresponding parent and teacher reports, with AUCs ranging from failed for Child Behavioral Checklist/Achenbach System of Empirically Based Assessment (CBCL/ASEBA) distinguishing ADHD from other patients[491] to good for the Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Scale (SWAN) distinguishing ADHD from neurotypical controls.[168, 297]

Studies employing combined approaches, such as integrating diagnostic aids with clinician impressions, were limited. One study reported increased sensitivity and specificity when an initial clinician diagnosis was combined with an electroencephalogram (EEG) biomarker for that patient (the reference standard was a consensus diagnosis from a panel of ADHD experts).[27] These findings were not independently replicated, and no test-retest reliability was reported.

AUCs for all blood biomarkers ranged from 0.68 (serum miRNAs)[635] to excellent (erythropoietin and erythropoietin receptors levels)[309] in differentiating ADHD from neurotypical youth, but with a low strength of evidence. None have been independently replicated, and no test-retest reliability was reported.

Diagnostic Accuracy for Youth Younger Than 7 Years of Age

We found only a small number of studies in youth younger than seven year of age. Only three of the studies assessed the performance of rating scales: the CBCL ADHD Problems Scale to distinguish ADHD (co-occurring with a disruptive behavior disorder) from a disruptive behavior disorder alone with "good" AUC;[167] or the total score for the Disruptive Behavior Diagnostic Observation Schedule to distinguish ADHD (with or without a comorbid disruptive behavior disorder) from typically developing youth also with "good" AUC;[167] or the BRIEF to distinguish ADHD from typically developing controls (average diagnostic accuracy was excellent). The other studies assessed imaging or EEG measures, with AUCs ranging from fair to excellent. The findings provide very little evidence for the utility of any diagnostic approach in youth younger than age seven, though the two studies of rating scales suggest that performance may be comparable to performance of similar scales in youth older than seven.

Comparative Diagnostic Accuracy of EEG, Imaging, or Executive Function Measures for Youth Aged 7 Through 17

Most studies used machine learning for classification based on EEG measures. AUCs ranged from poor[197] to excellent in differentiating ADHD youth from neurotypical controls.[412] Strength of evidence is low due to large variations in diagnostic performance across studies, and often the methods for classification were not well described. The intraclass correlation coefficient (ICC) for the Theta/Beta ratio, based on repeated measures on two different visits, was 0.83.[27]

In the neuroimaging studies, AUCs ranged from "poor" for distinguishing ADHD youth without co-occurring disorders from healthy controls[1188] to "excellent" for distinguishing ADHD youth from healthy controls.[581] Most studies relied on machine learning to develop the diagnostic algorithms, and none assessed test-retest reliability or the independent reproducibility of findings.

Many machine learning studies have been reported to date. Machine learning has usually been applied retrospectively to pre-existing datasets or repositories. AUCs generally were not reported for machine learning studies. Using EEG data, sensitivity ranged from 80 percent (with equal specificity)[179] to 98 percent (also with high corresponding specificity).[157, 172] Using MRI data, sensitivity showed a wider range from 61 percent (with a corresponding specificity of 68%)[1188] to almost perfect sensitivity and specificity.[581] Most studies attempted to discriminate ADHD youth from healthy controls retrospectively in pre-existing datasets, not from other clinical populations and not prospectively. In addition, reporting of final mathematical models or algorithms differentiating the diagnostic groups was limited. The overall strength of evidence is low.

Most of the EEG and imaging studies have employed leave-one-out cross validation and have rarely assessed performance in independent samples not contributing to generation of the diagnostic algorithm -- a serious overall weakness. No independent replication studies using the same marker/measure have been conducted, and very few have assessed test-retest or inter-rater reliability. No clinical effectiveness studies have been performed using these measures or diagnostic algorithms in the real world. Thus, biomarker, EEG, imaging, and machine learning algorithms do not seem remotely close to being ready for clinical application.

Studies evaluating neuropsychological tests yielded AUCs ranging from poor[24, 263] to excellent[140] in differentiating ADHD youth from both neurotypical controls and other patients, with a low strength of evidence. Many studies used idiosyncratic combinations of cognitive measures, including various measures from continuous performance tests (e.g., errors of omission, errors of commission, response time, response time variability, and detectability) to differentiate ADHD from control participants. These idiosyncratic combinations make the results of meta-analyses difficult to interpret. Extracting specific, comparable measures of inattention and impulsivity from continuous performance tests yielded diagnostic performance ranging from poor to excellent in differentiating ADHD youth from neurotypical controls, and fair in differentiating from other patients.[21, 24, 162] Only one diagnostic study assessed test-retest reliability, which was poor. No studies provided an independent replication of diagnosis using the same measure. Strength of evidence for continuous performance tasks (CPT) measures was low; thus, despite the widespread use of neuropsychological testing in the evaluation of youth suspected as having ADHD, often at considerable expense, indirect comparisons of AUCs suggest that the performance of neuropsychological test measures in the diagnosis of ADHD is comparable to the diagnostic performance of ADHD rating scales from a single informant, and the overall strength of evidence for estimates of that diagnostic performance is low. Moreover, in head-to-head comparisons, the diagnostic accuracy of parent rating scales is typically better than neuropsychological test measures.[467, 732]

Variation in Diagnostic Accuracy by Clinical Setting or Patient Subgroup

We did not identify studies that directly compared diagnostic accuracy in head-to-head comparisons across different clinical settings. Instead, we had to compare performance indirectly, across studies. In addition, the reporting of diagnostic accuracy data was limited, and therefore analyses had to be performed on estimates as reported by the original authors, precluding meta-analytic modeling. Indirect comparisons nevertheless indicated that the setting is an effect modifier for diagnostic performance. The range of reported diagnostic sensitivities was narrower in non-clinical samples, indicating that the detection of true positive cases was more consistent across studies in the community when compared to clinical settings, perhaps because ADHD youth identified in community samples are much less complex and less heterogeneous in their presentations than those presenting in clinical settings. We also found that specificity (the rate of identifying true negatives) was significantly lower when diagnosing ADHD youth in community settings compared with clinical settings. A lower true negative rate indicated that youth in the community who did not have ADHD were mistakenly diagnosed as having ADHD, perhaps because they had symptoms that were confused with those of ADHD. We also found that diagnostic specificity was significantly lower when differentiating ADHD youth from other patients than from neurotypical controls, likely because patients with other clinical problems have symptoms that overlap those of ADHD. Thus, the diagnostic group being differentiated from ADHD – whether it is neurotypical "healthy" controls, or youth who have a different emotional/behavioral/psychiatric disorder – and the setting in which the diagnostic tool is being applied has a critical role in diagnostic performance. We also found some indication that diagnostic performance was better for youth who were older compared with younger than 7 years of age (Figure 14), but effects were not statistically significant. Hence, we analyzed studies of mixed samples together and reported on the diagnostic performance by diagnostic test modality, rather than by age group.

Adverse Effects of Being Labeled Correctly or Incorrectly as Having ADHD

We did not identify any study that addressed the consequence of correctly or incorrectly receiving a diagnosis of ADHD.

Safety and Effectiveness of Pharmacologic and Nonpharmacologic Treatments

Analyses that included studies of all therapeutic interventions, regardless of treatment modality, provided strong evidence for the significant efficacy of treatments in improving ADHD outcomes. We conducted extensive analyses to understand which classes of interventions produced significant therapeutic responses in various clinical outcome domains. We can compare the magnitude of those therapeutic responses (effect sizes) across interventions, as well as within and across outcome measures, using the standardized mean difference (SMD) for the active compared with control intervention. SMD values of 0.2 to 0.5 are considered small, 0.5 to 0.8 medium, and above 0.8 are large. We will use the descriptive terms in summarizing the magnitude of treatment responses here, but the precise numerical values can be found in the Results section.

We note that many of the studies for psychosocial interventions, parent support, neurofeedback, and nutritional and supplement therapies, compared the active intervention against either wait list controls, treatment as usual, or another passive intervention group, and therefore they did not adequately control for the effects of parent or therapist attention and other non-specific effects of therapy. In addition, many of these studies were unable to blind either the youth undergoing treatment, their patents, the treating clinician, or study assessors to treatment assignment and study hypotheses,[1195, 1196] predisposing assessment of outcomes to reporter bias, particularly as parents and teachers often have an allegiance to non-medication interventions.[1197, 1198] These limitations in study design considerably undermines the strength of evidence for psychosocial, parent, neurofeedback, and nutritional interventions.

With these caveats noted, numerous classes of intervention yielded significant effects on measures of *ADHD symptom severity*. These included: Food and Drug Administration (FDA)-approved medications collectively; stimulant medications collectively, and methylphenidate and amphetamines separately; nonstimulant medications collectively, and norepinephrine reuptake inhibitors (NRIs) and alpha agonists separately; psychosocial treatment collectively; neurofeedback; nutrition or supplements; and parent support. All had small to medium effect sizes, except stimulants, which had large effect sizes, especially amphetamines, which also had highly variable effect sizes. Augmentation of ongoing stimulant treatment with non-stimulant medication (alpha agonists) yielded small but statistically significant improvements in ADHD symptoms compared to augmentation with placebo. Half the neurofeedback studies were at high risk of bias, and when those studies were excluded, effects on ADHD symptoms were no longer significant. Seven omega 3 studies, a subset of nutritional supplements, did not yield significant effects on ADHD symptoms or other outcomes. A newer stimulant medication (not approved for ADHD treatment), modafinil, produced significant improvement in ADHD symptoms in each of four studies, though in aggregate the medium effect size for improvement was not statistically significant due to effect size heterogeneity. The strength of evidence for effects on ADHD symptoms is high for FDA-approved medications collectively and for stimulant and non-stimulant medications separately; strength of evidence is moderate for psychosocial interventions, and low for neurofeedback, parent support, the group of nutritional interventions, and non-stimulant augmentation of ongoing stimulant therapy.

For *broadband measures*, FDA-approved medications and stimulants collectively yielded significant, medium-sized effects, with comparable effects for amphetamine and methylphenidate derivatives, though amphetamines yielded much more variable effects across studies. Only one stimulant study included children younger than six years of age.[109] Non-stimulants collectively, and NRIs and alpha agonists separately, also improved broadband scale scores, with a moderate effect size. Only one non-stimulant study included children younger than six years old.[378] Parent support had significant small effects across a small number of studies and low strength of evidence, and cognitive training had medium effects across an equally small number of studies with low strength of evidence. For *disruptive behaviors*, significant improvement was observed with FDA-approved medications and parent support, with moderate effect size, and with cognitive training and nutrition or supplements, both with small effect sizes and low strength of evidence. For *functional impairments*, only FDA-approved medications, as well as stimulant and non-stimulant medications collectively yielded significant improvement, with effect sizes that were medium, large, and small, respectively. No treatment modality yielded significant meta-analytic effects on *academic performance*, though only nine studies (3 psychological, 1 stimulant, 1 combined psychological plus stimulant, and 4 school interventions) assessed this as a treatment outcome. One study assessed the effectiveness of an FDA-approved medication in improving academic performance and found large, significant, and positive effects; all other individual studies yielded nonsignificant improvements of small effect size. We found only one neuromodulation study (direct current stimulation), a small number of studies assessing the effects of exercise, or the effects of complementary and alternative medicines that met our inclusion criteria; none yielded significant improvement in any ADHD outcome domains. Thus, the large number of studies combined with their medium-to-large effect sizes allow us to conclude with a high strength of evidence that FDA-approved medications collectively improve ADHD clinical outcomes in all domains we assessed – in ADHD symptom severity, broadband measures, disruptive problem behaviors, and functional impairment.

Medication therapies were associated with adverse events, including *appetite suppression*, with a high strength of evidence. Stimulants were associated with an increased number of *participants reporting adverse events* compared with placebo, with a similar but nonsignificant effect of methylphenidate and a similar though significant effect of amphetamines. Stimulants were associated with appetite suppression compared to placebo, with somewhat smaller effects for methylphenidate than for amphetamines. Non-stimulants compared with placebo were associated with an increased number of participants reporting adverse events, with comparable rates in NRI studies and alpha agonists. Non-stimulants were also associated with suppressed appetite compared to placebo, with significant appetite suppression from NRIs but weaker and non-significant effects from alpha agonists. Studies of non-pharmacological therapies rarely reported the systematic assessment of adverse effects.

The most common head-to-head comparison between two alternative medication treatment types was atomoxetine versus different methylphenidate medications, which did not detect significant differences in effects on ADHD symptoms, broadband measures, behavioral problems, functional impairment, appetite suppression, or the number of patients experiencing adverse events, though the direction of effects consistently favored methylphenidate medications. Indirect comparison of studies evaluating stimulants and non-stimulants compared to control groups showed larger reported effect sizes for stimulants providing greater improvement for

ADHD symptoms and broadband measures while functional impairment, appetite suppression, and the number of participants reporting adverse events were comparable. We identified only one head-to-head comparisons of NRIs versus alpha agonists that met eligibility criteria. It reported significantly greater improvement in ADHD symptoms from the alpha agonist guanfacine over the NRI atomoxetine, with a small effect size, though indirect comparisons did not find a significant difference between alpha agonists and NRIs in their effects on any outcome domains.

We found little evidence that youth-directed psychosocial and medication interventions are better in improving ADHD outcomes when delivered in combination than as monotherapies. Most of these studies, however, compared the effects of combination therapy against the effects of medication alone, which is a high bar to surpass. Combination compared with monotherapy yielded an improvement in ADHD symptoms with a small effect size at a trend-level of statistical significance, but no evidence for improvement in other outcome domains. Furthermore, our findings suggest that combined medication and youth-directed psychosocial therapies do not improve ADHD symptoms better than either medication or behavioral therapy alone. We note, however, that few combinations have been evaluated and these analyses do not consider the possibility that exact sequencing of psychological and medication therapies may produce differential effects on outcomes.[204, 471]

Very few studies have evaluated the long-term effectiveness of any treatment modality for any ADHD outcome domains. For example, only one study of an FDA-approved medication (atomoxetine)[164] that met our inclusion criteria evaluated effects on long-term outcomes. It found significant improvement in broadband measures, with a very large effect size, but no effects on ADHD symptoms or functional impairment, and significantly more adverse events and less weight gain, compared with placebo. Two studies of psychosocial interventions (behavioral therapy and attention training and a sleep intervention in sleep-disordered youth) produced evidence for significant long-term improvement in ADHD symptoms, with a moderate effect size;[334, 523] one also evaluated *treatment satisfaction*, finding a small and nonsignificant effect. Three studies of parent support found negligible and non-significant long-term effects on ADHD symptoms,[228, 257, 290] two studies found nonsignificant long-term effects on broadband measures[110, 257] and one on functional impairment.[228] Two neurofeedback studies reported long-term effects on problem behaviors and functional impairment that were small and not significant.[126, 458] One of these studies reported a small but significant long-term improvement in ADHD symptoms,[458] whereas the other reported small nonsignificant effects.[126] Two studies of school-based interventions assessed effects on long-term outcomes.[259, 531] One (a study of an intensive summer program) found no improvement in ADHD symptoms or school disciplinary problems compared to no intervention.[531] The other (a school-based training intervention) found no significant improvement in impaired peer relations for ADHD youth.[259] Neither intervention improved long-term academic performance. More studies assessed the long-term effects of combined pharmacological (stimulant) and behavioral treatment on ADHD outcomes; however, only one assessed long-term effects on ADHD symptoms and functional impairment, finding small, nonsignificant effects for each.[343] Two assessed long-term effects on problem behaviors, with conflicting results.[107, 343] One study reported small, nonsignificant long-term effects on broadband measures.[107] Thus, with few exceptions, the body of evidence suggests that most interventions, including combined medication and psychological treatment, yield no significant long-term improvement in most ADHD outcomes.

Variation in Outcomes by Clinical Presentation

We found little evidence that treatment outcomes varied by ADHD presentation but available data were limited.

Risk of Medication Diversion

We found only one study that assessed the risk of medication diversion in the treatment of ADHD. It was a double-blind randomized controlled trial comparing stimulant plus cognitive behavioral therapy (CBT) vs placebo plus CBT in treating adolescents who had ADHD with comorbid substance use disorder (SUD). The stimulant arm had twice the self-reported rate of diversion than the placebo arm which, though not statistically significant, suggests that further studies of diversion and stimulant misuse is warranted, particularly in ADHD youth with SUD. Caution is indicated when prescribing stimulants to ADHD youth who have comorbid SUD.

ADHD Monitoring

We identified only 10 studies pertaining to the assessment of monitoring strategies for ADHD outcomes.

Several of the studies indicated that monitoring measures correlated poorly over time, whether the correlations were between different raters using the same rating scale[545] or between different assessment modalities (e.g., rating scale with computerized performance test).[173, 203] These findings suggest that assessment modalities may be more complementary than interchangeable, and that more than a single assessment modality may be required for comprehensive and effective monitoring of ADHD outcomes.[173, 545] One study suggested that subjective outcome measures, such as rating scales, may be more sensitive than more objective measures, such as the continuous performance task, for detecting treatment-induced changes in ADHD.[203]

Three studies assessed the effects on ADHD symptoms of interventions that train pediatricians to improve either their symptom monitoring or their adherence to treatment guidelines.[255, 256, 268] Despite very extensive training efforts, and even when expert support and consultation was available,[256] pediatricians exhibited poor compliance in attending training programs for treating ADHD,[256, 268] and even when they did attend, pediatrician compliance with treatment guidelines was poor, both in terms of monitoring treatment response and in following dosing guidelines. Use of expert consultative services and compliance with recommendations was poor.[256]

One study suggested that monitoring height and weight, combined with either medication holidays or caloric supplementation, may be helpful for attenuating stimulant-associated weight loss but not slowing of height velocity.[274] Another study suggested that use of an electronic bottle cap may be more accurate and valid than patient reports, clinician impression, or pill counts for monitoring of medication adherence.[629]

Findings in Relation to Existing Research Syntheses and Practice Guidelines

The conclusions and clinical recommendations of this review are generally consistent with those of the two prior Agency for Healthcare Research and Quality reviews on ADHD.[11, 53] The Key Questions of the 2011 review focused primarily on long-term (> 1 year) treatment effectiveness and adverse effects, whereas the three Key Questions of the 2018 review were nearly identical to ours. The 2018 review served as an important resource for development of the 2019 clinical practice guidelines for the evaluation and treatment of ADHD from the American Academy of Pediatrics (AAP),[1199] which in turn was the primary source for the recommendations from the U.S. Center for Disease Control for the diagnosis and treatment of ADHD.[1200]

Our findings for diagnostic tools suggest that the clinical diagnosis of ADHD likely benefits from ratings of ADHD symptoms from multiple informants, which is consistent with the AAP guidelines that advise documentation of symptoms and impairment in more than one setting (such as home and school), with information obtained from parents, school personnel, and mental health clinicians. To these informants we would add that inquiring about symptoms from both parents, and directly from the youth, can also be helpful. The 2018 review did not assess the diagnostic performance of ADHD rating scales. That review concluded, however, that brain imaging and EEG had insufficient evidence to support their use as diagnostic tools, consistent with our conclusions, and despite the FDA approval of one EEG measure as a purported diagnostic aid.[26, 27] To those conclusions we add that neuropsychological tests (including measures from continuous performance tests) and blood biomarkers also do not yet have sufficient evidence to serve as diagnostic tools.

Our treatment findings concluded that FDA-approved stimulant and non-stimulant medications had the greatest strength of evidence across all interventions for significantly improving ADHD symptoms and other outcomes. Thirty-five papers that met criteria for inclusion in the current review assessed treatment effectiveness for more than a year, which was the focus of the 2011 review. That 2011 review concluded with a low strength of evidence that methylphenidate and atomoxetine were both effective long-term, though the average effect sizes after a year were somewhat lower than those for the short-term studies included in the present review. The 2018 review did not restrict the time frame for treatment, but nevertheless found insufficient evidence to modify conclusions for the effectiveness of FDA-approved medications. The present review adds to these prior reviews by providing mean effect sizes for comparisons of FDA-approved medication with placebo on improving not only ADHD symptoms, but a range of other important outcomes as well, at least for short-term outcomes. The current review also showed that stimulant and most non-stimulant medications yielded comparable effects on key effectiveness outcomes when these medications were compared head-to-head. Clinical guidelines advise starting treatment for youth older than six years of age with FDA-approved medications, which the findings of this review support.

The current review did not find that combination therapies of medication plus psychosocial therapies produce better results than medication alone. Moreover, we found that the effect sizes for parent therapies tended to be smaller than those for other interventions in improving ADHD outcomes. The 2011 review found larger effect sizes than we found for parent training for preschool youth with ADHD or disruptive behavioral disorders, but the prior review included studies that did not meet criteria for inclusion in our review. The 2018 review also found that parent training improved ADHD symptoms, but the review did not provide a mean effect size. Neither of the prior reviews assessed the effectiveness of combination treatment. The AAP clinical guidelines for preschool children advise treatment with parent training and/or classroom behavioral interventions as the first line of treatment, if available. These recommendations remain supported by the present review, particularly given the paucity of prior medication studies for preschool children. The guidelines also recommend the combination of parent training, classroom interventions, or behavioral interventions with medication therapy for older youth with ADHD, though no evidence suggests that this combination of therapies is better than monotherapy, and some evidence from head-to-head comparison studies suggests that the combination is not better than monotherapy.

The 2018 review found some evidence that cognitive training, and insufficient evidence that neurofeedback, improve ADHD symptoms. Our report includes substantially more studies and we found low strength of evidence that cognitive training does not improve ADHD symptoms, and some evidence that neurofeedback does, although the strength of evidence is low. We also found, with low strength of evidence, that the group of nutritional supplements and dietary interventions improve ADHD symptoms and problem behaviors. However, the approaches were very diverse, and approaches assessed in more than one study did not show an effect. The evidence for specific nutritional or supplement interventions is still too low to suggest their routine use.

The 2018 review found no papers pertaining to the assessment of monitoring strategies for youth with ADHD, whereas our current review identified ten such papers. The APA and Centers for Disease Control and Prevention (CDC) clinical guidelines do not include recommendations for monitoring strategies.

Implications

Our review points to the complementary nature of rating scales from multiple informants – from both parents if possible and from teachers, and even from the youth as well – since the scores tend to correlate poorly with one another and because ADHD symptoms in the same child can vary across settings. No single informant is a gold-standard. Multiple informants will provide a more complete clinical picture for how symptoms are expressed and perceived in different settings, and they will accordingly inform clinical judgement when making a diagnosis. Similarly, neuropsychological test measures of executive functioning, such as the CPT, may help inform a clinical diagnosis, but they are not definitive either in ruling in or ruling out a diagnosis of ADHD. Rating scales and neuropsychological tests are more helpful in diagnosis when the clinical question is whether a youth has ADHD or is healthy, rather than when the clinical question is whether a youth had ADHD or another mental health or behavioral problem, which tends to incorrectly identify youth with other clinical conditions as having ADHD. Biomarkers, EEG, and magnetic resonance imaging (MRI) are not yet close to being ready to aid clinical diagnosis. Ultimately, a valid and reliable diagnosis of ADHD requires the judgment of a clinician who is experienced in the evaluation of youth with and without ADHD, with the aid of standardized rating scales and input from multiple informants across multiple settings, including parents, teachers, and the youth themselves.

An increasing number of treatment modalities have been shown to significantly improve ADHD symptoms, and with comparable effect sizes when delivered as monotherapies. These include stimulant medications (methylphenidate and amphetamine), non-stimulant medications (particularly the NRIs atomoxetine and viloxazine, as well as the alpha agonists clonidine and guanfacine), individual psychosocial treatments, neurofeedback, and nutritional interventions, though very few of the non-medication studies have employed precisely the same interventions, which precluded an assessment of which specific interventions within each of these treatment categories were most effective. Psychosocial interventions, parent support, neurofeedback, and nutrition and supplements may exert considerably weaker effects on ADHD symptoms than the other interventions. Strength of evidence is high for medications and moderate for the other treatment modalities. The absence of head-to-head studies comparing the effectiveness of these monotherapies precludes recommendations regarding which is most likely to be helpful and should be tried first. Stimulant and NRI medications, separately and in head-to-head comparisons, have shown effectiveness and similar rates of side effects, including appetite suppression. The combination of treatment modalities, including combined medication plus psychosocial therapy, has minimal evidence for improving ADHD outcomes, and in fact a moderate strength of evidence indicates that combined therapy is no better than monotherapy. Treatment guidelines that recommend combination therapy[1199, 1201, 1202] should consider that successful combinations showing clear superiority still need to be explored and identified. A further finding of this review is that only FDA-approved medications have been shown to statistically significantly improve broadband symptoms and functional impairment.

Findings from studies that attempted to train pediatricians in better adherence to ADHD monitoring and treatment guidelines suggest that training established pediatricians to adhere more closely to the guidelines does not work and that either much stronger incentives are needed for established pediatricians (such as including training and demonstrated compliance in criteria for maintenance of board certification), or else demonstrable guideline adherence should be included in pediatric residency training programs.

Strengths and Limitations

A major strength of this review is its inclusiveness, incorporating publications from 1980 and yielding more than 500 separate studies that informed our findings. Other strengths include: a review of evidence for the utility of biomarkers, EEG, and neuroimaging measures in the diagnosis of ADHD; parsing of non-pharmacological therapies by the target of the therapy (the youth, parent, or school); and the parsing of ADHD outcome measures to provide more clarity on the functional domains that treatments affect.

Despite the large number of included studies, we restricted this review to studies that reported on children with a clinically confirmed diagnosis of ADHD, excluding studies with broader samples (such as evaluations of psychosocial programs that were not specific to youth with a clinical diagnosis). In addition, although studies of children of all ages were eligible for inclusion in the report, the number of studies exclusively addressing younger children with ADHD were relatively few. The median minimum age in included studies was six years old. Samples were predominantly male, and the median number of girls included in the studies was only 25 percent. Furthermore, smaller studies were not included unless they demonstrated a power analysis, which may have excluded studies of more intensive treatments. We also excluded studies documenting very short-term treatment effects by requiring studies to report on a minimum treatment duration of four weeks. This requirement may have excluded relevant brief interventions, or very intense psychosocial interventions delivered in a short time period. Furthermore, this synthesis was focused on outcomes selected with the help of an expert panel, and it should be noted that individual interventions may show effects on other outcomes. Because few studies compared treatment effects in direct, head-to-head comparisons, we had to explore modifiers indirectly, across studies. Finally, despite a very comprehensive search, few monitoring studies were available to inform this report.

Future Research

One of the most important potential uses of this systematic review would be the identification of effect modifiers for both the performance of diagnostic tools and therapeutic interventions – for example, determining whether a diagnostic tool performs better or worse, or a treatment is more or less effective, in one patient subgroup than another (Key Question [KQ] 1c and KQ2a), such as in younger or older patients, in ethnic minorities, in those experiencing material hardship, in patients with a comorbid illness, or in those with a specific ADHD presentation. These analyses are essential for improving clinical assessments and treatment planning. Future studies of ADHD should more systematically address the modifier effects of these patient characteristics. More research is needed on the performance of diagnostic tools, the consequences of being misdiagnosed as either having or not having ADHD, the real-world effectiveness and long-term outcomes of medication and other therapies, and effectiveness of monitoring strategies. Much more research is needed on the diagnosis and treatment of preschool children who have ADHD.

Future Research on ADHD Diagnosis

Future studies of diagnostic tools should include assessment of how well the tools distinguish ADHD youth not simply from typically developing youth, but especially from youth who have other emotional and behavioral problems. They should also assess the potential adverse consequences of youth being incorrectly diagnosed with or without ADHD. Research is needed to identify consensus algorithms that combine rating scale data from multiple informants to improve the clinical diagnosis of ADHD, which at present is unguided, ad hoc, and suboptimal.

Despite the theoretical promise and a large number of prior studies of the use of continuous performance tests, EEG, or imaging to diagnose ADHD, conclusions about these potential diagnostic tools was severely limited by the use of different diagnostic measures within each test modality, differing diagnostic thresholds applied to those measures across studies, and differing algorithms that combine those variables to reach a diagnostic decision, and the frequent failure to clearly report those study elements in the publication. Therefore, to support future efforts at synthetic analyses, diagnostic studies should report sufficient detail of their measures and diagnostic algorithms -- precise operational definitions and measurements of the variable(s) used for diagnosis, any diagnostic algorithm employed, the chosen statistical cut-offs, and the number of false positives and false negatives the diagnostic tool yields.

Studies of diagnostic tools should include ROC analyses to support comparison of test performance across studies that are independent of diagnostic threshold for the tool. Studies should also include assessment of test-retest reliability to help discern whether variability in measures and test performance across settings is a function of setting or is a consequence of measurement variability across time. Future studies should address the role of co-occurring disorders in the diagnostic process and their influences on their performance of the diagnostic tools. In addition, more studies are needed that compare the diagnostic accuracy of different test modalities head-to-head.

Making available in public repositories the raw, individual-level data, as well as the algorithms or computer code, for diagnostic tools is important to aid future efforts at replication, synthesis, and new discovery. Independent replication of performance measures of diagnostic tools in real-world settings is essential prior to FDA approval and before recommendations for widespread clinical use.

Finally, the "diagnostic tests” that are most often used clinically, usually at considerable financial expense, are neuropsychological measures of “executive functioning”. These include, among others, measures of working memory and errors of omission on continuous performance tests (thought to represent the clinical construct of inattention) and measures of impulsive responding on continuous performance tests (thought to represent the clinical construct of impulsivity). These and other objective, quantitative neuropsychological test measures of executive functioning notoriously correlate only weakly with the clinical constructs of inattention, impulsivity, and hyperactivity that are based on observation of real-world behavior and that define ADHD.[173] Many youth with ADHD have normal executive functioning profiles on neuropsychological testing, and many who have impaired executive functioning on neuropsychological tests do not have ADHD.[1203] A major open question for future research is how these two constructs—neuropsychological test measures of executive functioning and the real-world functional problems that define ADHD—map on to one another, and how the correspondence of that mapping can be improved.

Future Research on ADHD Treatment

More trials are needed that compare alternative interventions head-to-head or that compare combination treatments with monotherapy. Future studies of psychosocial and parent interventions should employ study designs that support more valid causal inferences and higher strength of evidence for the effectiveness of the interventions assessed, including active attention comparator conditions and effective blinding of participants and assessors to study interventions and hypotheses.[1195, 1196] More and higher quality studies with independent replication are needed to assess the effectiveness of individual complementary and alternative therapies, as well as exercise. Much more research is needed to assess long-term treatment compliance, long-term treatment effectiveness across a wide array of interventions, patient-centered outcomes beyond ADHD symptom improvement, medication diversion, and adverse effects associated with treatment (including non-pharmacological interventions).

Studies evaluating ADHD interventions should address the role of patient characteristics as modifiers of treatment effects. This effort will help to identify which treatments are most effective for which patients, to aid in the development of personalized treatments for youth with ADHD. To aid discovery and confirmation of these modifiers, future treatment studies should make publicly available all individual-level demographic, clinical, comorbidity, treatment, and all available outcome data (not only the primary outcomes), together with a detailed data dictionary. Patient-centered outcomes that assess functional domains other than ADHD symptoms, such as functional impairment and academic performance, should be acquired in clinical trials and shared publicly.

Future Research on ADHD Monitoring

Much more research is needed that compares the utility of various strategies for monitoring outcomes and tracking response to treatment over time in ADHD youth. The temporal stability of outcome measures and their sensitivity to change in response to treatment should be assessed to support ADHD monitoring strategies.

Future synthetic studies should also consider reviewing studies of long-term outcomes in ADHD youth, even if not in the context of comparing monitoring strategies, as the findings will be of interest to patients, parents, and clinicians and will critically inform treatment decisions.

Applicability

Several included studies reported multiple exclusions for eligible participants, which limited the generalizability of findings. Diagnostic performance, as well as treatment effects in clinical practice, may not translate from the favorable effects shown in the documented research to real world practice. In addition, the number of girls included in the identified studies was small and several studies did not include any female participants, potentially limiting the applicability of the findings.

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Abbreviations and Acronyms

AAP	American Academy of Pediatrics
ACAC	Association for Child and Adolescent Counseling
ADD-H	attention deficit disorder with hyperactivity
ADHD	attention deficit hyperactivity disorder
ADHD-RS-IV	ADHD Rating Scale Version IV
AHDD	attention hyperactivity deficit disorder
AHRQ	Agency for Healthcare Research and Quality
APA	American Psychological Association
ASD	autism spectrum disorder
AUC	area under the curve
BASC-2	Behavior Assessment System for Children, Second Edition
BMI	body mass index
BRIEF2	Behavior Rating Inventory of Executive Function, Second Edition
CAM	complementary, alternative, or integrative medicine
CBCL	Child Behavior Checklist
CBT	cognitive-behavioral therapy
CHADD	Children and Adults with ADHD
CHAOS	Conduct-Hyperactive-Attention Problem-Oppositional Symptom
CGI	Clinical Global Impression
CGI-I	Clinical Global Impression-Improvement
CGI-S	Clinical Global Impression-Severity
CI	confidence intervals
CNS	central nervous system
CPRS	Conners Parent Rating Scale
CPT	Continuous Performance Test
DASH	Dietary Approaches to Stop Hypertension
DBDRS	Disruptive Behavior Disorder Ratings Scale
DHA	Docosahexaenoic acid
DIPA-L	Diagnostic Infant and Preschool Assessment, Likert version
DS-ADHD	diagnosis-supported attention deficit hyperactivity disorder
DSM	Diagnostic and Statistical Manual of Mental Disorders
DSM-III	Diagnostic and Statistical Manual of Mental Disorders, Third Edition
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
EEG	electroencephalogram/electroencephalography
EHC	Effective Health Care
EKG	electrocardiogram

EPA	Eicosapentaenoic acid
EPC	Evidence-based Practice Center
FDA	Food and Drug Administration
GPA	Grade Point Average
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GIRK	G protein-coupled inward-rectifying potassium channel
ICC	Intraclass Correlation Coefficient
ICD-11	International Classification of Diseases, Eleventh Edition
ID	identification
IQ	Intelligence quotient
KQ1	Key Question 1
KQ2	Key Question 2
KQ3	Key Question 3
MEMS	Medication Event Monitoring System
mg	milligram
MPH	Methylphenidate
MTA	Multimodal Treatment Study of Children with ADHD
MRI	magnetic resonance imaging
N	sample size
N/A	not applicable
NRI	norepinephrine reuptake inhibitor
ODD	oppositional defiant disorder
OROS	osmotic-release oral system
p	probability
PCORI	Patient-Centered Outcomes Research Institute
PICOTSO	Population, Intervention, Comparator, Outcome, Timing, Setting, Study Design, and Other limiters
PSC	Pediatric Symptom Checklist
QbTest	continuous performance test
QI	quality improvement
QUADAS 2	Quality Assessment of Diagnostic Accuracy Studies
RCT	randomized controlled trial
RoB 2	Risk-of-Bias tool for randomized trials, version 2
RTI-B	Response to Intervention – Behavioral
RR	relative risk
SEADS	Submit Supplemental Evidence and Data for Systematic Reviews
SMART	Sequential Multiple Assignment Randomized Trial
SMD	standardized mean difference

SNAP-IV	Swanson, Nolan, and Pelham (SNAP) Questionnaire
SoE	strength of evidence
SPN-812	viloxazine extended release
SRDR	Systematic Review Data Repository
SUD	substance use disorder
SWAN	Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Rating Scale
TAU	treatment-as-usual
TOO	Task Order Officer
TRF	Teacher Report Form
UK	United Kingdom

Appendix A. Methods

Search Strategies

Search Strategy KQ1

PubMed

1
"Attention Deficit Disorder with Hyperactivity"[Mesh] OR "attention deficit hyperactivity disorder"[tiab] OR "ADHD"[tiab] OR "attention deficit disorder"[tiab]
2
"Pediatrics"[Mesh] OR "Adolescent"[Mesh] OR "Infant"[Mesh] OR "Child"[Mesh] OR child[tiab] OR children[tiab] OR infant[tiab] OR infants[tiab] OR preschool[tiab] OR preschooler[tiab] OR pediatric [tiab] OR teenager[tiab] OR teenagers[tiab] OR teenaged[tiab] OR teen[tiab] OR teens[tiab] OR adolescent[tiab] OR adolescents[tiab] OR adolescence[tiab] OR youth[tiab] OR paediatric[tiab] OR youths[tiab]
3
"Attention Deficit and Disruptive Behavior Disorders/diagnosis"[Majr] OR mass screening[mesh] OR questionnaires[mesh] OR Interviews as Topic[Mesh] OR Psychometrics[Mesh] OR Psychiatric Status Rating Scales[Mesh] OR diagnosis[mesh:noexp] OR "Diagnostic Techniques and Procedures"[Mesh] OR "Referral and Consultation"[Mesh] OR questionnaire[tiab] OR questionnaires[tiab] OR screening[tiab] OR screen[tiab] OR scale[tiab] OR instrument[tiab] OR instruments[tiab] OR interview[tiab] OR interviews[tiab] OR diagnosis[tiab] OR diagnostic[tiab] OR diagnosed[tiab] OR Measure [tiab] OR test[tiab] OR tests[tiab] OR testing[tiab] OR "Attention Deficit Disorder with Hyperactivity/diagnostic imaging"[Majr]
4
"Sensitivity and Specificity"[Mesh] OR "Diagnostic Errors"[Mesh] OR sensitivity[tiab] OR specificity[tiab] OR (accura*[tiab] AND (diagnos*[tiab] OR classif*[tiab])) OR misdiagnos*[tiab] OR "ROC curve"[tiab] OR "positive predictive value"[tiab] OR "negative predictive value"[tiab] OR "false positive"[tiab] OR "false negative"[tiab] OR "likelihood ratio"[tiab] OR systematic review [tiab]
5
Editorial[ptyp] OR Letter[pt] OR Case Reports[pt] OR Comment[pt] address[pt] OR "autobiography"[pt] OR "bibliography"[pt] OR "biography"[pt] OR "case report"[tw] OR "case reports"[tw] OR "case series"[tw] OR "comment on"[All Fields] OR congress[pt] OR "dictionary"[pt] OR "directory"[pt] OR "festschrift"[pt] OR "historical article"[pt] OR lecture[pt] OR "legal case"[pt] OR "legislation"[pt] OR "news"[pt] OR "newspaper article"[pt] OR "patient education handout"[pt] OR "periodical index"[pt]
6
animals[mh]
7
English[la]
8
#1 AND #2 AND #3 AND #4 NOT #5 NOT #6 AND #7

PUBLICATION DATE RANGE: 2016 to date

PsycINFO (Proquest)

(SU ("Attention Deficit Disorder with Hyperactivity") OR TI ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder") OR AB ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder"))
"AND"
(AGE (childhood OR adolescence) OR SU ("Pediatrics") OR TI (child OR children OR infant OR infants OR preschool OR preschooler OR pediatric OR teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth) OR AB (child OR children OR infant OR infants OR preschool OR preschooler OR pediatric OR teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth))
"AND"
(SU ("Screening") OR SU ("Health Screening") OR SU ("Questionnaires") OR SU ("Screening Tests") OR SU ("Psychological Screening Inventory") OR SU ("Psychiatric Evaluation") OR SU ("Psychodiagnosis") OR SU ("Psychodiagnostic Interview") OR SU ("Psychometrics" OR SU "Rating Scales") OR SU ("Diagnosis") OR SU ("Professional Referral") OR SU ("Diagnostic Interview Schedule") OR SU ("Behavioral Assessment") OR TI (questionnaire OR questionnaires OR screening OR screen OR scale OR instrument OR instruments OR interview OR interviews OR diagnosis OR diagnostic OR diagnosed OR "diagnostic interview schedule for children" OR "diagnostic inventory for screening children") OR AB (questionnaire OR questionnaires OR screening OR screen OR scale OR instrument OR instruments OR interview OR interviews OR diagnosis OR diagnostic OR diagnosed))
"AND"
SU ("Misdiagnosis") OR TI (sensitivity OR specificity OR (accura* AND (diagnos* OR classif*)) OR misdiagnos*) OR AB (sensitivity OR specificity OR accuracy OR misdiagnos*)

AND
Record Type: peer reviewed journal
AND
yr(2016-2023)
AND
English language

ERIC (EBSCOhost)

S1
"attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder"
S2
Screening OR "Health Screening" OR Questionnaires OR "Screening Tests" OR "Psychological Screening Inventory" OR "Psychiatric Evaluation" OR "Psychodiagnosis" OR "Psychodiagnostic Interview" OR "Psychometrics" OR "Rating Scales" OR "Diagnosis" OR "Professional Referral" OR "Diagnostic Interview Schedule" OR "Behavioral Assessment" OR questionnaire OR questionnaires OR screening OR screen OR scale OR instrument OR instruments OR interview OR interviews OR diagnosis OR diagnostic OR diagnosed

S3
“Misdiagnosis" OR sensitivity OR specificity OR (accura* AND (diagnos* OR classif*)) OR misdiagnos*
S4
S1 AND S2 AND S3

Filter:
Publication date range: 2016-2023

EMBASE
#1
'attention deficit disorder'/exp OR 'attention deficit disorder' OR 'attention deficit hyperactivity disorder':ab,ti OR 'adhd':ab,ti OR 'attention deficit disorder':ab,ti
#2
'pediatrics'/exp OR 'adolescent'/exp OR 'infant'/exp OR 'child'/exp OR child:ab,ti OR children:ab,ti OR infant:ab,ti OR infants:ab,ti OR preschool:ab,ti OR preschooler:ab,ti OR pediatric:ab,ti OR teenager:ab,ti OR teenagers:ab,ti OR teenaged:ab,ti OR teen:ab,ti OR teens:ab,ti OR adolescent:ab,ti OR adolescents:ab,ti OR adolescence:ab,ti OR youth:ab,ti
#3
'attention deficit disorder'/exp/mj/dm_di OR 'screening'/exp OR 'questionnaire'/exp OR 'interview'/exp OR 'psychometry'/exp OR 'psychological rating scale'/exp OR 'diagnosis'/exp OR 'assessment of humans'/exp OR 'checklist'/exp OR 'clinical assessment tool'/exp OR 'clinical observation'/exp OR 'patient referral'/exp OR questionnaire:ab,ti OR questionnaires:ab,ti OR screening:ab,ti OR screen:ab,ti OR scale:ab,ti OR instrument:ab,ti OR instruments:ab,ti OR interview:ab,ti OR interviews:ab,ti OR diagnosis:ab,ti OR diagnostic:ab,ti OR diagnosed:ab,ti
#4
('sensitivity and specificity'/exp OR 'predictive value'/exp OR 'diagnostic error'/exp OR sensitivity:ab,ti OR specificity:ab,ti OR accuracy:ab,ti OR accurate:ab,ti OR accurately:ab,ti OR misdiagnos*:ab,ti)
NOT ('case report'/exp OR 'case study'/exp OR 'editorial'/exp OR 'letter'/exp OR 'note'/exp)
#5
#1 AND #2 AND #3 AND #4
#6
#5 AND [embase]/lim NOT [medline]/lim
#7
#6 AND [humans]/lim AND [2016-2023]/py

Cochrane Reviews
#1
MeSH descriptor: [Attention Deficit Disorder with Hyperactivity] explode all trees
#2
("attention deficit hyperactivity disorder" OR "ADHD" OR "attention deficit disorder"):ti,ab,kw
(Word variations have been searched)
#3
#1 OR #2
#4

MeSH descriptor: [Pediatrics] explode all trees
#5
MeSH descriptor: [Adolescent] explode all trees
#6
MeSH descriptor: [Infant] explode all trees
#7
MeSH descriptor: [Child] explode all trees
#8
#4 OR #5 OR #6 OR #7
#9
#3 OR #8
#10
MeSH descriptor: [Mass Screening] explode all trees
#11
MeSH descriptor: [Surveys and Questionnaires] explode all trees
#12
MeSH descriptor: [Interviews as Topic] explode all trees
#13
MeSH descriptor: [Psychometrics] explode all trees
#14
MeSH descriptor: [Psychiatric Status Rating Scales] explode all trees
#15
MeSH descriptor: [Diagnosis] explode all trees
#16
MeSH descriptor: [Diagnostic Techniques and Procedures] explode all trees
#17
MeSH descriptor: [Referral and Consultation] explode all trees
#18
#1 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17
#19
(questionnaire OR questionnaires OR screening OR screen OR scale OR instrument OR instruments OR interview OR interviews OR diagnosis OR diagnostic OR diagnosed):ti,ab,kw (Word variations have been searched)
#20
#18 OR #19
#21
#3 AND #9 AND #20
Limited to 2016-2023 and Cochrane Reviews

KQ2

PubMed
1
"Attention Deficit Disorder with Hyperactivity"[Mesh] OR "attention deficit hyperactivity disorder"[tiab] OR "ADHD"[tiab] OR "attention deficit disorder"[tiab]

2
"Pediatrics"[Mesh] OR "Adolescent"[Mesh] OR "Infant"[Mesh] OR "Child"[Mesh] OR child[tiab] OR children[tiab] OR infant[tiab] OR infants[tiab] OR preschool[tiab] OR preschooler[tiab] OR pediatric[tiab] OR teenager[tiab] OR teenagers[tiab] OR teenaged[tiab] OR teen[tiab] OR teens[tiab] OR adolescent[tiab] OR adolescents[tiab] OR adolescence[tiab] OR youth[tiab]
3
(randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR Clinical trial[pt] OR "clinical trial"[tiab] OR "clinical trials"[tiab] OR "evaluation studies"[pt] OR "evaluation studies as topic"[MeSH] OR "evaluation study"[tiab] OR "evaluation studies"[tiab] OR "intervention studies"[MeSH] OR "intervention study"[tiab] OR "intervention studies"[tiab] OR "case-control studies"[MeSH] OR "case-control"[tiab] OR "cohort studies"[MeSH] OR cohort[tiab] OR "longitudinal"[tiab] OR longitudinally[tiab] OR "prospective"[tiab] OR prospectively[tiab] OR "comparative study"[pt] OR "comparative study"[tiab] OR systematic[sb] OR "meta-analysis"[pt] OR "meta-analysis as topic"[MeSH] OR "meta-analysis"[tiab] OR "metaanalyses"[tiab])
4
Editorial[ptyp] OR Letter[pt] OR Case Reports[pt] OR Comment[pt]
5.
animals[mh]
6
English[la]
7
#1 AND #2 AND #3 NOT #4 NOT #5 AND #6
PUBLICATION DATE RANGE: 1980 to date

PsycInfo

S1
("Attention Deficit Disorder with Hyperactivity") OR SU "Attention Deficit Disorder with Hyperactivity" OR TI ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder") OR AB ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder")
S2
AG (adolescence) OR TI (teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth) OR AB (teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth) OR AG (childhood) OR DE "Pediatrics" OR TI (child OR children OR infant OR infants OR preschool OR preschooler OR pediatric OR teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth) OR AB (child OR children OR infant OR infants OR preschool OR preschooler OR pediatric OR teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth)
S3
SU (intervention OR treatment OR therapy OR counseling OR training OR education OR medication OR drug OR psychostimulant OR "Psychotherapy") OR TI (intervention OR treatment OR therapy OR counseling OR training OR education OR medication OR drug OR

psychostimulant OR "Psychotherapy" OR Medicine OR program) OR AB (intervention OR treatment OR therapy OR counseling OR training OR education OR medication OR drug OR psychostimulant OR “Psychotherapy” OR Medicine)
S4
ZC “longitudinal study” OR ZC “empirical study” OR ZC “followup study” OR ZC “longitudinal study” OR ZC “prospective study” OR ZC “systematic review” OR ZC “treatment outcome/clinical trial” OR DE “Clinical Trials” OR DE “Cohort Analysis” OR DE “Followup Studies” OR DE “Longitudinal Studies” OR DE “Prospective Studies” OR TI (randomized OR randomised OR randomization OR randomisation OR randomly OR trial OR groups OR trials OR “evaluation study” OR evaluation studies OR “intervention study” OR “intervention studies” OR “case-control” OR cohort OR longitudinal OR longitudinally OR prospective OR prospectively OR “comparative study”) OR AB (randomized OR randomization OR randomly OR trial OR groups OR trials OR “evaluation study” OR evaluation studies OR “intervention study” OR “intervention studies” OR “case-control” OR cohort OR longitudinal OR longitudinally OR prospective OR prospectively OR “comparative study”)
S5
1 AND 2 AND 3 AND 4

AND
Record Type: peer reviewed journal
AND
yr(2016-2023)
AND
English language

S1
MAINSUBJECT.EXACT("Attention Deficit Disorder with Hyperactivity") OR SU "Attention Deficit Disorder with Hyperactivity" OR TI ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder") OR AB ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder")
S2
AG (adolescence) OR TI (teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth) OR AB (teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth)
S3
(MAINSUBJECT.EXACT("Attention Deficit Disorder with Hyperactivity") OR SU "Attention Deficit Disorder with Hyperactivity" OR TI ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder") OR AB ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder")) AND (AG (adolescence) OR TI (teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth) OR AB (teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth))
S4
DE "CNS Stimulating Drugs" OR DE "Methylphenidate" OR DE "Dextroamphetamine" OR DE "Amphetamine" OR DE "Clonidine" OR DE "Serotonin Norepinephrine Reuptake

Inhibitors" OR DE "Atomoxetine" OR DE "Tricyclic Antidepressant Drugs" OR DE "Desipramine" OR DE "Nortriptyline" OR DE "Bupropion" OR DE "Serotonin Norepinephrine Reuptake Inhibitors" OR DE "Venlafaxine" OR DE "Monoamine Oxidase Inhibitors" OR DE "Amantadine" OR TI (Azstarys OR Cotempla XR-ODT OR Desoxyn OR "Alpha agonist" OR psychostimulants OR "CNS stimulating" OR "Central Nervous System stimulants" OR methylphenidate OR Dexmethylphenidate OR Dextroamphetamine OR lisdexamfetamine OR Amphetamine OR aptensio OR concerta OR Ritalin OR methylin OR medikinet OR equasym OR quillivant OR metadate OR daytrana OR focalin OR Dexedrine OR dextrostat OR procentra OR zenzedi OR Adderall OR vyvanse OR elvanse OR tyvense OR dyanavel OR evekeo OR "alpha-2 agonists" OR guanfacine OR intuniv OR tenex OR estulic OR afken OR clonidine OR catapres OR clophelin OR kapvay OR nexiclon OR duraclon OR "Serotonin Norepinephrine Reuptake Inhibitors" OR Strattera OR atomoxetine OR "Tricyclic Antidepressants " OR "Desipramine" OR "Nortriptyline" OR norpramin OR pertofrane OR pamelor OR "dopamine reuptake inhibitors" OR modanifil OR Provigil OR alertec OR modavigil OR modiodal OR modalert OR armodafinil OR nuvigil OR "norepinephrine-dopamine reuptake inhibitors" OR bupropion OR Wellbutrin OR zyban OR forfivo OR "Serotonin Norepinephrine Reuptake Inhibitors" OR duloxetine OR Cymbalta OR "serotonin norepinephrine dopamine reuptake inhibitors" OR "Venlafaxine" OR Effexor OR trevilor OR (Monoamine Oxidase AND Inhibitors) OR selegiline OR eldepryl OR emsam OR selgene OR zelapar OR "n methyl d aspartate receptor agonists" OR "Amantadine" OR symmetrel OR memantine OR Namenda) OR AB (Azstarys OR Cotempla XR-ODT OR Desoxyn OR "Alpha agonist" OR psychostimulants OR "CNS stimulating" OR "Central Nervous System stimulants" OR methylphenidate OR Dexmethylphenidate OR Dextroamphetamine OR lisdexamfetamine OR Amphetamine OR aptensio OR concerta OR Ritalin OR methylin OR medikinet OR equasym OR quillivant OR metadate OR daytrana OR focalin OR Dexedrine OR dextrostat OR procentra OR zenzedi OR Adderall OR vyvanse OR elvanse OR tyvense OR dyanavel OR evekeo OR "alpha-2 agonists" OR guanfacine OR intuniv OR tenex OR estulic OR afken OR clonidine OR catapres OR clophelin OR kapvay OR nexiclon OR duraclon OR "Serotonin Norepinephrine Reuptake Inhibitors" OR Strattera OR atomoxetine OR "Tricyclic Antidepressants " OR "Desipramine" OR "Nortriptyline" OR norpramin OR pertofrane OR pamelor OR "dopamine reuptake inhibitors" OR modanifil OR Provigil OR alertec OR modavigil OR modiodal OR modalert OR armodafinil OR nuvigil OR "norepinephrinedopamine reuptake inhibitors" OR bupropion OR Wellbutrin OR zyban OR forfivo OR "Serotonin Norepinephrine Reuptake Inhibitors" OR duloxetine OR Cymbalta OR "serotonin norepinephrine dopamine reuptake inhibitors" OR "Venlafaxine" OR Effexor OR trevilor OR (Monoamine Oxidase AND Inhibitors) OR selegiline OR eldepryl OR emsam OR selgene OR zelapar OR "n methyl d aspartate receptor agonists" OR "Amantadine" OR symmetrel OR memantine OR Namenda)

S5

DE "Psychotherapy" OR DE "Adolescent Psychotherapy" OR DE "Multisystemic Therapy" OR DE "Behavior Therapy" OR DE "Dialectical Behavior Therapy" OR DE "Brief Psychotherapy" OR DE "Child Psychotherapy" OR DE "Play Therapy" OR DE "Client Centered Therapy" OR DE "Cognitive Behavior Therapy" OR DE "Group Psychotherapy" OR DE "Therapeutic Community" OR DE "Integrative Psychotherapy" OR DE "Psychotherapeutic Counseling" OR DE "Family Therapy" OR DE "Supportive Psychotherapy" OR DE "Cognitive Therapy" OR DE "Parent Training" OR DE "Parent Child Relations" OR DE "Time Management" OR DE "Mindfulness" OR DE "School Based Intervention" OR DE "Memory Training" OR DE

"Biofeedback Training" OR DE "Biofeedback" OR DE "Computer Assisted Instruction" OR DE "Intelligent Tutoring Systems" OR DE "Diets" OR DE "Dietary Supplements" OR DE "Food Additives" OR DE "Fatty Acids" OR DE "Acupuncture" OR DE "Remedial Education" OR DE "Early Intervention" OR DE "Alternative Medicine" OR TI (Monarch external Trigeminal Nerve Stimulation OR eTNS OR "EndeavorRx" OR ((classroom OR school OR schools) AND (behavior intervention OR behavior interventions)) OR "peer intervention" OR (("organization skills") AND (training OR intervention)) OR "psychosocial therapy" OR "psychosocial intervention" OR "psychosocial interventions" OR "psychosocial approach" OR "psychosocial approaches" OR "psychosocial treatment" OR "psychosocial support" OR "psychoeducation" OR "nonpharmacologic therapy" OR "nondrug therapy" OR "non-drug therapy" OR "Play Therapy" OR "cognitive behavioral therapy" OR "cognitive behavior therapy" OR "cognitive behavioural therapy" OR "cognitive behaviour therapy" OR Mindfulness OR complementary OR "alternative medicine" OR "alternative therapy" OR "alternative therapies" OR "Interpersonal skills training" OR "Parent-Child Interaction Therapy" OR "parent training" OR "parent engagement" OR "parent management" OR "parenting skills" OR "parenting intervention" OR "parenting interventions" OR "Barkley's defiant child" OR "Teacher-Child Interaction Training" OR "Incredible Years" OR "New Forest Parenting" OR "Triple P" OR "Helping the Noncompliant Child" OR "child life and attention skills" OR "clas" OR PCIT OR "parent child interaction therapy" OR "Summer Treatment Program" OR "Daily Report Card" OR "organization skills" OR "organizational skills" OR "time management" OR "homework intervention" OR braintrain OR "memory training" OR "Captain's log mindpower builder" OR "memory gyms" OR "attention gym" OR "smartdriver plus" OR "smartmind pro" OR "RoboMemo" OR "play attention" OR metronome OR brainmaster OR mindmed OR "attention lab" OR (activate AND c8) OR "attention training" OR "CogniPlus" OR cogmed OR "working memory training" OR biofeedback OR neurofeedback OR neuroagility OR neuroptimal OR acupuncture OR "vision training" OR "visual training" OR "vision therapy" OR "education intervention" OR "cognitive remediation" OR neurotherapy OR "elimination diet" OR "diet therapy" OR (("low carb" OR "low carbohydrate" OR "low carbohydrates" OR "gluten free") AND diet) OR "feingold diet" OR "red dye" OR ((vitamin OR vitamins) AND (supplement OR supplements)) OR "herbal supplement" OR "herbal supplements" OR probiotics OR "omega 3" OR "slow cortical potentials" OR "few foods diet" OR "oligoantigenic diet" OR "restriction diet" OR "food intolerance" OR "food allergy" OR "food allergies" OR "food sensitivity" OR "food sensitivities" OR "multimodal treatment" OR homeopathy OR homeopathic OR chiropractic OR chiropractor) OR AB (Monarch external Trigeminal Nerve Stimulation OR eTNS OR "EndeavorRx" OR ((classroom OR school OR schools) AND (behavior intervention OR behavior interventions)) OR "peer intervention" OR (("organization skills") AND (training OR intervention)) OR"psychosocial therapy" OR "psychosocial intervention" OR "psychosocial interventions" OR "psychosocial approach" OR "psychosocial approaches" OR "psychosocial treatment" OR "psychosocial support" OR "psychoeducation" OR "nonpharmacologic therapy" OR "nondrug therapy" OR "non-drug therapy" OR "Play Therapy" OR "cognitive behavioral therapy" OR "cognitive behavior therapy" OR "cognitive behavioural therapy" OR "cognitive behaviour therapy" OR Mindfulness OR complementary OR "alternative medicine" OR "alternative therapy" OR "alternative therapies" OR "Interpersonal skills training" OR "Parent-Child Interaction Therapy" OR "parent training" OR "parent engagement" OR "parent management" OR "parenting skills" OR "parenting intervention" OR "parenting interventions" OR "Barkley's defiant child" OR "Teacher-Child Interaction Training" OR 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S6

(DE "CNS Stimulating Drugs" OR DE "Methylphenidate" OR DE "Dextroamphetamine" OR DE "Amphetamine" OR DE "Clonidine" OR DE "Serotonin Norepinephrine Reuptake Inhibitors" OR DE "Atomoxetine" OR DE "Tricyclic Antidepressant Drugs" OR DE "Desipramine" OR DE "Nortriptyline" OR DE "Bupropion" OR DE "Serotonin Norepinephrine Reuptake Inhibitors" OR DE "Venlafaxine" OR DE "Monoamine Oxidase Inhibitors" OR DE "Amantadine" OR TI (Azstarys OR Cotempla XR-ODT OR Desoxyn OR "Alpha agonist" OR psychostimulants OR "CNS stimulating" OR "Central Nervous System stimulants" OR methylphenidate OR Dexmethylphenidate OR Dextroamphetamine OR lisdexamfetamine OR Amphetamine OR aptensio OR concerta OR Ritalin OR methylin OR medikinet OR equasym OR quillivant OR metadate OR daytrana OR focalin OR Dexedrine OR dextrostat OR procentra OR zenzedi OR Adderall OR vyvanse OR elvanse OR tyvense OR dyanavel OR evekeo OR "alpha-2 agonists" OR guanfacine OR intuniv OR tenex OR estulic OR afken OR clonidine OR catapres OR clophelin OR kapvay OR nexiclon OR duraclon OR "Serotonin Norepinephrine Reuptake Inhibitors" OR Strattera OR atomoxetine OR "Tricyclic Antidepressants " OR "Desipramine" OR "Nortriptyline" OR norpramin OR pertofrane OR pamelor OR "dopamine reuptake inhibitors" OR modanifil OR Provigil OR alertec OR modavigil OR modiodal OR modalert OR armodafinil OR nuvigil OR "norepinephrine-dopamine reuptake inhibitors" OR bupropion OR Wellbutrin OR zyban OR forfivo OR "Serotonin Norepinephrine Reuptake Inhibitors" OR duloxetine OR Cymbalta OR "serotonin norepinephrine dopamine reuptake inhibitors" OR "Venlafaxine" OR Effexor OR trevilor OR (Monoamine Oxidase AND Inhibitors) OR selegiline OR eldepryl OR emsam OR selgene OR zelapar OR "n methyl d aspartate receptor agonists" OR "Amantadine" OR symmetrel OR memantine OR Namenda) OR AB (Azstarys OR Cotempla XR-ODT OR Desoxyn OR "Alpha agonist" OR psychostimulants OR "CNS stimulating" OR "Central Nervous System stimulants" OR methylphenidate OR Dexmethylphenidate OR Dextroamphetamine OR lisdexamfetamine OR Amphetamine OR aptensio OR concerta OR Ritalin OR methylin OR medikinet OR equasym OR quillivant OR metadate OR daytrana OR focalin OR Dexedrine OR dextrostat OR procentra

OR zenzedi OR Adderall OR vyvanse OR elvanse OR tyvense OR dyanavel OR evekeo OR "alpha-2 agonists" OR guanfacine OR intuniv OR tenex OR estulic OR afken OR clonidine OR catapres OR clophelin OR kapvay OR nexiclon OR duraclon OR "Serotonin Norepinephrine Reuptake Inhibitors" OR Strattera OR atomoxetine OR "Tricyclic Antidepressants " OR "Desipramine" OR "Nortriptyline" OR norpramin OR pertofrane OR pamelor OR "dopamine reuptake inhibitors" OR modanifil OR Provigil OR alertec OR modavigil OR modiodal OR modalert OR armodafinil OR nuvigil OR "norepinephrinedopamine reuptake inhibitors" OR bupropion OR Wellbutrin OR zyban OR forfivo OR "Serotonin Norepinephrine Reuptake Inhibitors" OR duloxetine OR Cymbalta OR "serotonin norepinephrine dopamine reuptake inhibitors" OR "Venlafaxine" OR Effexor OR trevilor OR (Monoamine Oxidase AND Inhibitors) OR selegiline OR eldepryl OR emsam OR selgene OR zelapar OR "n methyl d aspartate receptor agonists" OR "Amantadine" OR symmetrel OR memantine OR Namenda)) OR (DE "Psychotherapy" OR DE "Adolescent Psychotherapy" OR DE "Multisystemic Therapy" OR DE "Behavior Therapy" OR DE "Dialectical Behavior Therapy" OR DE "Brief Psychotherapy" OR DE "Child Psychotherapy" OR DE "Play Therapy" OR DE "Client Centered Therapy" OR DE "Cognitive Behavior Therapy" OR DE "Group Psychotherapy" OR DE "Therapeutic Community" OR DE "Integrative Psychotherapy" OR DE "Psychotherapeutic Counseling" OR DE "Family Therapy" OR DE "Supportive Psychotherapy" OR DE "Cognitive Therapy" OR DE "Parent Training" OR DE "Parent Child Relations" OR DE "Time Management" OR DE "Mindfulness" OR DE "School Based Intervention" OR DE "Memory Training" OR DE "Biofeedback Training" OR DE "Biofeedback" OR DE "Computer Assisted Instruction" OR DE "Intelligent Tutoring Systems" OR DE "Diets" OR DE "Dietary Supplements" OR DE "Food Additives" OR DE "Fatty Acids" OR DE "Acupuncture" OR DE "Remedial Education" OR DE "Early Intervention" OR DE "Alternative Medicine" OR TI (Monarch external Trigeminal Nerve Stimulation OR eTNS OR "EndeavorRx" OR ((classroom OR school OR schools) AND (behavior intervention OR behavior interventions)) OR "peer intervention" OR (("organization skills") AND (training OR intervention)) OR "psychosocial therapy" OR "psychosocial intervention" OR "psychosocial interventions" OR "psychosocial approach" OR "psychosocial approaches" OR "psychosocial treatment" OR "psychosocial support" OR "psychoeducation" OR "nonpharmacologic therapy" OR "nondrug therapy" OR "non-drug therapy" OR "Play Therapy" OR "cognitive behavioral therapy" OR "cognitive behavior therapy" OR "cognitive behavioural therapy" OR "cognitive behaviour therapy" OR Mindfulness OR complementary OR "alternative medicine" OR "alternative therapy" OR "alternative therapies" OR "Interpersonal skills training" OR "Parent-Child Interaction Therapy" OR "parent training" OR "parent engagement" OR "parent management" OR "parenting skills" OR "parenting intervention" OR "parenting interventions" OR "Barkley's defiant child" OR "Teacher-Child Interaction Training" OR "Incredible Years" OR "New Forest Parenting" OR "Triple P" OR "Helping the Noncompliant Child" OR "child life and attention skills" OR "clas" OR PCIT OR "parent child interaction therapy" OR "Summer Treatment Program" OR "Daily Report Card" OR "organization skills" OR "organizational skills" OR "time management" OR "homework intervention" OR braintrain OR "memory training" OR "Captain's log mindpower builder" OR "memory gyms" OR "attention gym" OR "smartdriver plus" OR "smartmind pro" OR "RoboMemo" OR "play attention" OR metronome OR brainmaster OR mindmed OR "attention lab" OR (activate AND c8) OR "attention training" OR "CogniPlus" OR cogmed OR "working memory training" OR biofeedback OR neurofeedback OR neuroagility OR neuroptimal OR acupuncture OR "vision training" OR "visual training"

OR "vision therapy" OR "education intervention" OR "cognitive remediation" OR neurotherapy OR "elimination diet" OR "diet therapy" OR (("low carb" OR "low carbohydrate" OR "low carbohydrates" OR "gluten free") AND diet) OR "feingold diet" OR "red dye" OR ((vitamin OR vitamins) AND (supplement OR supplements)) OR "herbal supplement" OR "herbal supplements" OR probiotics OR "omega 3" OR "slow cortical potentials" OR "few foods diet" OR "oligoantigenic diet" OR "restriction diet" OR "food intolerance" OR "food allergy" OR "food allergies" OR "food sensitivity" OR "food sensitivities" OR “multimodal treatment” OR homeopathy OR homeopathic OR chiropractic OR chiropractor) OR AB (Monarch external Trigeminal Nerve Stimulation OR eTNS OR "EndeavorRx" OR ((classroom OR school OR schools) AND (behavior intervention OR behavior interventions)) OR "peer intervention” OR (("organization skills") AND (training OR intervention)) OR"psychosocial therapy" OR "psychosocial intervention" OR "psychosocial interventions" OR "psychosocial approach" OR "psychosocial approaches" OR "psychosocial treatment" OR "psychosocial support" OR "psychoeducation" OR "nonpharmacologic therapy" OR "nondrug therapy" OR "non-drug therapy" OR "Play Therapy" OR "cognitive behavioral therapy" OR "cognitive behavior therapy" OR "cognitive behavioural therapy" OR "cognitive behaviour therapy" OR Mindfulness OR complementary OR "alternative medicine" OR "alternative therapy" OR "alternative therapies" OR "Interpersonal skills training" OR "Parent-Child Interaction Therapy" OR "parent training" OR "parent engagement" OR "parent management" OR "parenting skills" OR "parenting intervention" OR "parenting interventions" OR "Barkley's defiant child" OR "Teacher-Child Interaction Training" OR "Incredible Years" OR "New Forest Parenting" OR "Triple P" OR "Helping the Noncompliant Child" OR "child life and attention skills" OR "clas" OR PCIT OR "parent child interaction therapy" OR "Summer Treatment Program" OR "Daily Report Card" OR "organization skills" OR "organizational skills" OR "time management" OR "homework intervention" OR braintrain OR "memory training" OR "Captain's log mindpower builder" OR "memory gyms" OR "attention gym" OR "smartdriver plus" OR "smartmind pro" OR “RoboMemo” OR "play attention" OR metronome OR brainmaster OR mindmed OR "attention lab" OR (activate AND c8) OR "attention training" OR “CogniPlus” OR cogmed OR "working memory training" OR biofeedback OR neurofeedback OR neuroagility OR neuroptimal OR acupuncture OR "vision training" OR "visual training" OR "vision therapy" OR "education intervention" OR "cognitive remediation" OR neurotherapy OR "elimination diet" OR "diet therapy" OR (("low carb" OR "low carbohydrate" OR "low carbohydrates" OR "gluten free") AND diet) OR "feingold diet" OR "red dye" OR ((vitamin OR vitamins) AND (supplement OR supplements)) OR "herbal supplement" OR "herbal supplements" OR probiotics OR "omega 3" OR "slow cortical potentials" OR "few foods diet" OR "oligoantigenic diet" OR "restriction diet" OR "food intolerance" OR "food allergy" OR "food allergies" OR "food sensitivity" OR "food sensitivities" OR “multimodal treatment” OR homeopathy OR homeopathic OR chiropractic OR chiropractor))

S7

((MAINSUBJECT.EXACT("Attention Deficit Disorder with Hyperactivity") OR SU "Attention Deficit Disorder with Hyperactivity" OR TI ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder") OR AB ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder")) AND (AG (childhood OR adolescence) OR DE "Pediatrics" OR TI (child OR children OR infant OR infants OR preschool OR preschooler OR pediatric OR teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth) OR AB (child OR children OR infant

OR infants OR preschool OR preschooler OR pediatric OR teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth))) AND ((DE "CNS Stimulating Drugs" OR DE "Methylphenidate" OR DE "Dextroamphetamine" OR DE "Amphetamine" OR DE "Clonidine" OR DE "Serotonin Norepinephrine Reuptake Inhibitors" OR DE "Atomoxetine" OR DE "Tricyclic Antidepressant Drugs" OR DE "Desipramine" OR DE "Nortriptyline" OR DE "Bupropion" OR DE "Serotonin Norepinephrine Reuptake Inhibitors" OR DE "Venlafaxine" OR DE "Monoamine Oxidase Inhibitors" OR DE "Amantadine" OR TI (Azstarys OR Cotempla XR-ODT OR Desoxyn OR "Alpha agonist" OR psychostimulants OR "CNS stimulating" OR "Central Nervous System stimulants" OR methylphenidate OR Dexmethylphenidate OR Dextroamphetamine OR lisdexamfetamine OR Amphetamine OR aptensio OR concerta OR Ritalin OR methylin OR medikinet OR equasym OR quillivant OR metadate OR daytrana OR focalin OR Dexedrine OR dextrostat OR procentra OR zenzedi OR Adderall OR vyvanse OR elvanse OR tyvense OR dyanavel OR evekeo OR "alpha-2 agonists" OR guanfacine OR intuniv OR tenex OR estulic OR afken OR clonidine OR catapres OR clophelin OR kapvay OR nexiclon OR duraclon OR "Serotonin Norepinephrine Reuptake Inhibitors" OR Strattera OR atomoxetine OR "Tricyclic Antidepressants " OR "Desipramine" OR "Nortriptyline" OR norpramin OR pertofrane OR pamelor OR "dopamine reuptake inhibitors" OR modanifil OR Provigil OR alertec OR modavigil OR modiodal OR modalert OR armodafinil OR nuvigil OR "norepinephrine-dopamine reuptake inhibitors" OR bupropion OR Wellbutrin OR zyban OR forfivo OR "Serotonin Norepinephrine Reuptake Inhibitors" OR duloxetine OR Cymbalta OR "serotonin norepinephrine dopamine reuptake inhibitors" OR "Venlafaxine" OR Effexor OR trevilor OR (Monoamine Oxidase AND Inhibitors) OR selegiline OR eldepryl OR emsam OR selgene OR zelapar OR "n methyl d aspartate receptor agonists" OR "Amantadine" OR symmetrel OR memantine OR Namenda) OR AB (Azstarys OR Cotempla XR-ODT OR Desoxyn OR "Alpha agonist" OR psychostimulants OR "CNS stimulating" OR "Central Nervous System stimulants" OR methylphenidate OR Dexmethylphenidate OR Dextroamphetamine OR lisdexamfetamine OR Amphetamine OR aptensio OR concerta OR Ritalin OR methylin OR medikinet OR equasym OR quillivant OR metadate OR daytrana OR focalin OR Dexedrine OR dextrostat OR procentra OR zenzedi OR Adderall OR vyvanse OR elvanse OR tyvense OR dyanavel OR evekeo OR "alpha-2 agonists" OR guanfacine OR intuniv OR tenex OR estulic OR afken OR clonidine OR catapres OR clophelin OR kapvay OR nexiclon OR duraclon OR "Serotonin Norepinephrine Reuptake Inhibitors" OR Strattera OR atomoxetine OR "Tricyclic Antidepressants " OR "Desipramine" OR "Nortriptyline" OR norpramin OR pertofrane OR pamelor OR "dopamine reuptake inhibitors" OR modanifil OR Provigil OR alertec OR modavigil OR modiodal OR modalert OR armodafinil OR nuvigil OR "norepinephrinedopamine reuptake inhibitors" OR bupropion OR Wellbutrin OR zyban OR forfivo OR "Serotonin Norepinephrine Reuptake Inhibitors" OR duloxetine OR Cymbalta OR "serotonin norepinephrine dopamine reuptake inhibitors" OR "Venlafaxine" OR Effexor OR trevilor OR (Monoamine Oxidase AND Inhibitors) OR selegiline OR eldepryl OR emsam OR selgene OR zelapar OR "n methyl d aspartate receptor agonists" OR "Amantadine" OR symmetrel OR memantine OR Namenda)) OR (DE "Psychotherapy" OR DE "Adolescent Psychotherapy" OR DE "Multisystemic Therapy" OR DE "Behavior Therapy" OR DE "Dialectical Behavior Therapy" OR DE "Brief Psychotherapy" OR DE "Child Psychotherapy" OR DE "Play Therapy" OR DE "Client Centered Therapy" OR DE "Cognitive Behavior Therapy" OR DE "Group Psychotherapy" OR DE "Therapeutic Community" OR DE "Integrative Psychotherapy" OR DE "Psychotherapeutic

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"psychosocial support" OR "psychoeducation" OR "nonpharmacologic therapy" OR "nondrug therapy" OR "non-drug therapy" OR "Play Therapy" OR "cognitive behavioral therapy" OR "cognitive behavior therapy" OR "cognitive behavioural therapy" OR "cognitive behaviour therapy" OR Mindfulness OR complementary OR "alternative medicine" OR "alternative therapy" OR "alternative therapies" OR "Interpersonal skills training" OR "Parent-Child Interaction Therapy" OR "parent training" OR "parent engagement" OR "parent management" OR "parenting skills" OR "parenting intervention" OR "parenting interventions" OR "Barkley's defiant child" OR "Teacher-Child Interaction Training" OR "Incredible Years" OR "New Forest Parenting" OR "Triple P" OR "Helping the Noncompliant Child" OR "child life and attention skills" OR "clas" OR PCIT OR "parent child interaction therapy" OR "Summer Treatment Program" OR "Daily Report Card" OR "organization skills" OR "organizational skills" OR "time management" OR "homework 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"food allergies" OR "food sensitivity" OR "food sensitivities" OR "multimodal treatment" OR homeopathy OR homeopathic OR chiropractic OR chiropractor) OR AB (Monarch external Trigeminal Nerve Stimulation OR eTNS OR "EndeavorRx" OR ((classroom OR school OR schools) AND (behavior intervention OR behavior interventions)) OR "peer intervention" OR (("organization skills") AND (training OR intervention)) OR"psychosocial therapy" OR "psychosocial intervention" OR "psychosocial interventions" OR "psychosocial approach" OR "psychosocial approaches" OR "psychosocial treatment" OR "psychosocial support" OR "psychoeducation" OR "nonpharmacologic therapy" OR "nondrug therapy" OR "non-drug therapy" OR "Play Therapy" OR "cognitive behavioral therapy" OR "cognitive behavior therapy" OR "cognitive behavioural therapy" OR "cognitive behaviour therapy" OR Mindfulness OR complementary OR "alternative medicine" OR "alternative therapy" OR "alternative therapies" OR "Interpersonal skills training" OR 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acupuncture OR "vision training" OR "visual training" OR "vision therapy" OR "education intervention" OR "cognitive remediation" OR neurotherapy OR "elimination diet" OR "diet therapy" OR (("low carb" OR "low carbohydrate" OR "low carbohydrates" OR "gluten free") AND diet) OR "feingold diet" OR "red dye" OR ((vitamin OR vitamins) AND (supplement OR supplements)) OR "herbal supplement" OR "herbal supplements" OR probiotics OR "omega 3" OR "slow cortical potentials" OR "few foods diet" OR "oligoantigenic diet" OR "restriction diet" OR "food intolerance" OR "food allergy" OR "food allergies" OR "food sensitivity" OR "food sensitivities" OR “multimodal treatment” OR homeopathy OR homeopathic OR chiropractic OR chiropractor)))

S8

ZC "longitudinal study" OR ZC "empirical study" OR ZC "followup study" OR ZC "longitudinal study" OR ZC "meta analysis" OR ZC "prospective study" OR ZC "retrospective study" OR ZC "systematic review" OR ZC "treatment outcome/clinical trial"OR DE "Clinical Trials" OR DE "Cohort Analysis" OR DE "Followup Studies" OR DE "Longitudinal Studies" OR DE "Prospective Studies" OR DE "Meta Analysis" OR TI (randomized OR randomised OR randomization OR randomisation OR randomly OR trial OR groups OR trials OR "evaluation study" OR evaluation studies OR "intervention study" OR "intervention studies" OR "case-control" OR cohort OR longitudinal OR longitudinally OR prospective OR prospectively OR retrospective OR "comparative study" OR "meta-analysis" OR "meta-analyses") OR AB (randomized OR randomised OR randomization OR randomisation OR randomly OR trial OR groups OR trials OR "evaluation study" OR evaluation studies OR "intervention study" OR "intervention studies" OR "case-control" OR cohort OR longitudinal OR longitudinally OR prospective OR prospectively OR retrospective OR "comparative study" OR "meta-analysis" OR "meta-analyses") AND (ZZ "journal article")

S9

(((MAINSUBJECT.EXACT("Attention Deficit Disorder with Hyperactivity") OR SU "Attention Deficit Disorder with Hyperactivity" OR TI ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder") OR AB ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder")) AND (AG (childhood OR adolescence) OR DE "Pediatrics" OR TI (child OR children OR infant OR infants OR preschool OR preschooler OR pediatric OR teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth) OR AB (child OR children OR infant OR infants OR preschool OR preschooler OR pediatric OR teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth))) AND ((DE

"CNS Stimulating Drugs" OR DE "Methylphenidate" OR DE "Dextroamphetamine" OR DE "Amphetamine" OR DE "Clonidine" OR DE "Serotonin Norepinephrine Reuptake Inhibitors" OR DE "Atomoxetine" OR DE "Tricyclic Antidepressant Drugs" OR DE "Desipramine" OR DE "Nortriptyline" OR DE "Bupropion" OR DE "Serotonin Norepinephrine Reuptake Inhibitors" OR DE "Venlafaxine" OR DE "Monoamine Oxidase Inhibitors" OR DE "Amantadine" OR TI (Azstarys OR Cotempla XR-ODT OR Desoxyn OR "Alpha agonist" OR psychostimulants OR "CNS stimulating" OR "Central Nervous System stimulants" OR methylphenidate OR Dexmethylphenidate OR Dextroamphetamine OR lisdexamfetamine OR Amphetamine OR aptensio OR concerta OR Ritalin OR methylin OR medikinet OR equasym OR quillivant OR metadate OR daytrana OR focalin OR Dexedrine OR dextrostat OR procentra OR zenzedi OR Adderall OR vyvanse OR elvanse OR tyvense OR dyanavel OR evekeo OR "alpha-2 agonists" OR guanfacine OR intuniv OR tenex OR estulic OR afken OR clonidine OR catapres OR clophelin OR kapvay OR nexiclon OR duraclon OR "Serotonin Norepinephrine Reuptake Inhibitors" OR Strattera OR atomoxetine OR "Tricyclic Antidepressants " OR "Desipramine" OR "Nortriptyline" OR norpramin OR pertofrane OR pamelor OR "dopamine reuptake inhibitors" OR modanifil OR Provigil OR alertec OR modavigil OR modiodal OR modalert OR armodafinil OR nuvigil OR "norepinephrine-dopamine reuptake inhibitors" OR bupropion OR Wellbutrin OR zyban OR forfivo OR "Serotonin Norepinephrine Reuptake Inhibitors" OR duloxetine OR Cymbalta OR "serotonin norepinephrine dopamine reuptake inhibitors" OR "Venlafaxine" OR Effexor OR trevilor OR (Monoamine Oxidase AND Inhibitors) OR selegiline OR eldepryl OR emsam OR selgene OR zelapar OR "n methyl d aspartate receptor agonists" OR "Amantadine" OR symmetrel OR memantine OR Namenda) OR AB (Azstarys OR Cotempla XR-ODT OR Desoxyn OR "Alpha agonist" OR psychostimulants OR "CNS stimulating" OR "Central Nervous System stimulants" OR methylphenidate OR Dexmethylphenidate OR Dextroamphetamine OR lisdexamfetamine OR Amphetamine OR aptensio OR concerta OR Ritalin OR methylin OR medikinet OR equasym OR quillivant OR metadate OR daytrana OR focalin OR Dexedrine OR dextrostat OR procentra OR zenzedi OR Adderall OR vyvanse OR elvanse OR tyvense OR dyanavel OR evekeo OR "alpha-2 agonists" OR guanfacine OR intuniv OR tenex OR estulic OR afken OR clonidine OR catapres OR clophelin OR kapvay OR nexiclon OR duraclon OR "Serotonin Norepinephrine Reuptake Inhibitors" OR Strattera OR atomoxetine OR "Tricyclic Antidepressants " OR "Desipramine" OR "Nortriptyline" OR norpramin OR pertofrane OR pamelor OR "dopamine reuptake inhibitors" OR modanifil OR Provigil OR alertec OR modavigil OR modiodal OR modalert OR armodafinil OR nuvigil OR "norepinephrinedopamine reuptake inhibitors" OR bupropion OR Wellbutrin OR zyban OR forfivo OR "Serotonin Norepinephrine Reuptake Inhibitors" OR duloxetine OR Cymbalta OR "serotonin norepinephrine dopamine reuptake inhibitors" OR "Venlafaxine" OR Effexor OR trevilor OR (Monoamine Oxidase AND Inhibitors) OR selegiline OR eldepryl OR emsam OR selgene OR zelapar OR "n methyl d aspartate receptor agonists" OR "Amantadine" OR symmetrel OR memantine OR Namenda)) OR (DE "Psychotherapy" OR DE "Adolescent Psychotherapy" OR DE "Multisystemic Therapy" OR DE "Behavior Therapy" OR DE "Dialectical Behavior Therapy" OR DE "Brief Psychotherapy" OR DE "Child Psychotherapy" OR DE "Play Therapy" OR DE "Client Centered Therapy" OR DE "Cognitive Behavior Therapy" OR DE "Group Psychotherapy" OR DE "Therapeutic Community" OR DE "Integrative Psychotherapy" OR DE "Psychotherapeutic Counseling" OR DE "Family Therapy" OR DE "Supportive Psychotherapy" OR DE "Cognitive Therapy" OR DE "Parent Training" OR DE "Parent Child Relations" OR DE "Time

Management" OR DE "Mindfulness" OR DE "School Based Intervention" OR DE "Memory Training" OR DE "Biofeedback Training" OR DE "Biofeedback" OR DE "Computer Assisted Instruction" OR DE "Intelligent Tutoring Systems" OR DE "Diets" OR DE "Dietary Supplements" OR DE "Food Additives" OR DE "Fatty Acids" OR DE "Acupuncture" OR DE "Remedial Education" OR DE "Early Intervention" OR DE "Alternative Medicine" OR TI (Monarch external Trigeminal Nerve Stimulation OR eTNS OR "EndeavorRx" OR ((classroom OR school OR schools) AND (behavior intervention OR behavior interventions)) OR "peer intervention" OR (("organization skills") AND (training OR intervention)) OR "psychosocial therapy" OR "psychosocial intervention" OR "psychosocial interventions" OR "psychosocial approach" OR "psychosocial approaches" OR "psychosocial treatment" OR "psychosocial support" OR "psychoeducation" OR "nonpharmacologic therapy" OR "nondrug therapy" OR "non-drug therapy" OR "Play Therapy" OR "cognitive behavioral therapy" OR "cognitive behavior therapy" OR "cognitive behavioural therapy" OR "cognitive behaviour therapy" OR Mindfulness OR complementary OR "alternative medicine" OR "alternative therapy" OR "alternative therapies" OR "Interpersonal skills training" OR "Parent-Child Interaction Therapy" OR "parent training" OR "parent engagement" OR "parent management" OR "parenting skills" OR "parenting intervention" OR "parenting interventions" OR "Barkley's defiant child" OR "Teacher-Child Interaction Training" OR "Incredible Years" OR "New Forest Parenting" OR "Triple P" OR "Helping the Noncompliant Child" OR "child life and attention skills" OR "clas" OR PCIT OR "parent child interaction therapy" OR "Summer Treatment Program" OR "Daily Report Card" OR "organization skills" OR "organizational skills" OR "time management" OR "homework intervention" OR braintrain OR "memory training" OR "Captain's log mindpower builder" OR "memory gyms" OR "attention gym" OR "smartdriver plus" OR "smartmind pro" OR "RoboMemo" OR "play attention" OR metronome OR brainmaster OR mindmed OR "attention lab" OR (activate AND c8) OR "attention training" OR "CogniPlus" OR cogmed OR "working memory training" OR biofeedback OR neurofeedback OR neuroagility OR neuroptimal OR acupuncture OR "vision training" OR "visual training" OR "vision therapy" OR "education intervention" OR "cognitive remediation" OR neurotherapy OR "elimination diet" OR "diet therapy" OR (("low carb" OR "low carbohydrate" OR "low carbohydrates" OR "gluten free") AND diet) OR "feingold diet" OR "red dye" OR ((vitamin OR vitamins) AND (supplement OR supplements)) OR "herbal supplement" OR "herbal supplements" OR probiotics OR "omega 3" OR "slow cortical potentials" OR "few foods diet" OR "oligoantigenic diet" OR "restriction diet" OR "food intolerance" OR "food allergy" OR "food allergies" OR "food sensitivity" OR "food sensitivities" OR "multimodal treatment" OR homeopathy OR homeopathic OR chiropractic OR chiropractor) OR AB (Monarch external Trigeminal Nerve Stimulation OR eTNS OR "EndeavorRx" OR ((classroom OR school OR schools) AND (behavior intervention OR behavior interventions)) OR "peer intervention" OR (("organization skills") AND (training OR intervention)) OR"psychosocial therapy" OR "psychosocial intervention" OR "psychosocial interventions" OR "psychosocial approach" OR "psychosocial approaches" OR "psychosocial treatment" OR "psychosocial support" OR "psychoeducation" OR "nonpharmacologic therapy" OR "nondrug therapy" OR "non-drug therapy" OR "Play Therapy" OR "cognitive behavioral therapy" OR "cognitive behavior therapy" OR "cognitive behavioural therapy" OR "cognitive behaviour therapy" OR Mindfulness OR complementary OR "alternative medicine" OR "alternative therapy" OR "alternative therapies" OR "Interpersonal skills training" OR "Parent-Child Interaction Therapy" OR "parent training" OR "parent engagement" OR "parent management" OR "parenting skills" OR "parenting intervention" OR "parenting 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OR "diet therapy" OR (("low carb" OR "low carbohydrate" OR "low carbohydrates" OR "gluten free") AND diet) OR "feingold diet" OR "red dye" OR ((vitamin OR vitamins) AND (supplement OR supplements)) OR "herbal supplement" OR "herbal supplements" OR probiotics OR "omega 3" OR "slow cortical potentials" OR "few foods diet" OR "oligoantigenic diet" OR "restriction diet" OR "food intolerance" OR "food allergy" OR "food allergies" OR "food sensitivity" OR "food sensitivities" OR “multimodal treatment” OR homeopathy OR homeopathic OR chiropractic OR chiropractor)))) AND (ZC "longitudinal study" OR ZC "empirical study" OR ZC "followup study" OR ZC "longitudinal study" OR ZC "meta analysis" OR ZC "prospective study" OR ZC "retrospective study" OR ZC "systematic review" OR ZC "treatment outcome/clinical trial"OR DE "Clinical Trials" OR DE "Cohort Analysis" OR DE "Followup Studies" OR DE "Longitudinal Studies" OR DE "Prospective Studies" OR DE "Meta Analysis" OR TI (randomized OR randomised OR 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S10

(((MAINSUBJECT.EXACT("Attention Deficit Disorder with Hyperactivity") OR SU "Attention Deficit Disorder with Hyperactivity" OR TI ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder") OR AB ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder")) AND (AG (childhood OR adolescence) OR DE "Pediatrics" OR TI (child OR children OR infant OR infants OR preschool OR preschooler OR pediatric OR teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth) OR AB (child OR children OR infant OR infants OR preschool OR preschooler OR pediatric OR teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth))) AND ((DE "CNS Stimulating Drugs" OR DE "Methylphenidate" OR DE "Dextroamphetamine" OR DE "Amphetamine" OR DE "Clonidine" OR DE "Serotonin Norepinephrine Reuptake Inhibitors" OR DE "Atomoxetine" OR DE "Tricyclic Antidepressant Drugs" OR DE "Desipramine" OR

DE "Nortriptyline" OR DE "Bupropion" OR DE "Serotonin Norepinephrine Reuptake Inhibitors" OR DE "Venlafaxine" OR DE "Monoamine Oxidase Inhibitors" OR DE "Amantadine" OR TI (Azstarys OR Cotempla XR-ODT OR Desoxyn OR "Alpha agonist" OR psychostimulants OR "CNS stimulating" OR "Central Nervous System stimulants" OR methylphenidate OR Dexmethylphenidate OR Dextroamphetamine OR lisdexamfetamine OR Amphetamine OR aptensio OR concerta OR Ritalin OR methylin OR medikinet OR equasym OR quillivant OR metadate OR daytrana OR focalin OR Dexedrine OR dextrostat OR procentra OR zenzedi OR Adderall OR vyvanse OR elvanse OR tyvense OR dyanavel OR evekeo OR "alpha-2 agonists" OR guanfacine OR intuniv OR tenex OR estulic OR afken OR clonidine OR catapres OR clophelin OR kapvay OR nexiclon OR duraclon OR "Serotonin Norepinephrine Reuptake Inhibitors" OR Strattera OR atomoxetine OR "Tricyclic Antidepressants " OR "Desipramine" OR "Nortriptyline" OR norpramin OR pertofrane OR pamelor OR "dopamine reuptake inhibitors" OR modanifil OR Provigil OR alertec OR modavigil OR modiodal OR modalert OR armodafinil OR nuvigil OR "norepinephrine-dopamine reuptake inhibitors" OR bupropion OR Wellbutrin OR zyban OR forfivo OR "Serotonin Norepinephrine Reuptake Inhibitors" OR duloxetine OR Cymbalta OR "serotonin norepinephrine dopamine reuptake inhibitors" OR "Venlafaxine" OR Effexor OR trevilor OR (Monoamine Oxidase AND Inhibitors) OR selegiline OR eldepryl OR emsam OR selgene OR zelapar OR "n methyl d aspartate receptor agonists" OR "Amantadine" OR symmetrel OR memantine OR Namenda) OR AB (Azstarys OR Cotempla XR-ODT OR Desoxyn OR "Alpha agonist" OR psychostimulants OR "CNS stimulating" OR "Central Nervous System stimulants" OR methylphenidate OR Dexmethylphenidate OR Dextroamphetamine OR lisdexamfetamine OR Amphetamine OR aptensio OR concerta OR Ritalin OR methylin OR medikinet OR equasym OR quillivant OR metadate OR daytrana OR focalin OR Dexedrine OR dextrostat OR procentra OR zenzedi OR Adderall OR vyvanse OR elvanse OR tyvense OR dyanavel OR evekeo OR "alpha-2 agonists" OR guanfacine OR intuniv OR tenex OR estulic OR afken OR clonidine OR catapres OR clophelin OR kapvay OR nexiclon OR duraclon OR "Serotonin Norepinephrine Reuptake Inhibitors" OR Strattera OR atomoxetine OR "Tricyclic Antidepressants " OR "Desipramine" OR "Nortriptyline" OR norpramin OR pertofrane OR pamelor OR "dopamine reuptake inhibitors" OR modanifil OR Provigil OR alertec OR modavigil OR modiodal OR modalert OR armodafinil OR nuvigil OR "norepinephrinedopamine reuptake inhibitors" OR bupropion OR Wellbutrin OR zyban OR forfivo OR "Serotonin Norepinephrine Reuptake Inhibitors" OR duloxetine OR Cymbalta OR "serotonin norepinephrine dopamine reuptake inhibitors" OR "Venlafaxine" OR Effexor OR trevilor OR (Monoamine Oxidase AND Inhibitors) OR selegiline OR eldepryl OR emsam OR selgene OR zelapar OR "n methyl d aspartate receptor agonists" OR "Amantadine" OR symmetrel OR memantine OR Namenda)) OR (DE "Psychotherapy" OR DE "Adolescent Psychotherapy" OR DE "Multisystemic Therapy" OR DE "Behavior Therapy" OR DE "Dialectical Behavior Therapy" OR DE "Brief Psychotherapy" OR DE "Child Psychotherapy" OR DE "Play Therapy" OR DE "Client Centered Therapy" OR DE "Cognitive Behavior Therapy" OR DE "Group Psychotherapy" OR DE "Therapeutic Community" OR DE "Integrative Psychotherapy" OR DE "Psychotherapeutic Counseling" OR DE "Family Therapy" OR DE "Supportive Psychotherapy" OR DE "Cognitive Therapy" OR DE "Parent Training" OR DE "Parent Child Relations" OR DE "Time Management" OR DE "Mindfulness" OR DE "School Based Intervention" OR DE "Memory Training" OR DE "Biofeedback Training" OR DE "Biofeedback" OR DE "Computer Assisted Instruction" OR DE "Intelligent Tutoring Systems" OR DE "Diets" OR DE "Dietary

Supplements" OR DE "Food Additives" OR DE "Fatty Acids" OR DE "Acupuncture" OR DE "Remedial Education" OR DE "Early Intervention" OR DE "Alternative Medicine" OR TI (Monarch external Trigeminal Nerve Stimulation OR eTNS OR "EndeavorRx" OR ((classroom OR school OR schools) AND (behavior intervention OR behavior interventions)) OR "peer intervention" OR (("organization skills") AND (training OR intervention)) OR "psychosocial therapy" OR "psychosocial intervention" OR "psychosocial interventions" OR "psychosocial approach" OR "psychosocial approaches" OR "psychosocial treatment" OR "psychosocial support" OR "psychoeducation" OR "nonpharmacologic therapy" OR "nondrug therapy" OR "non-drug therapy" OR "Play Therapy" OR "cognitive behavioral therapy" OR "cognitive behavior therapy" OR "cognitive behavioural therapy" OR "cognitive behaviour therapy" OR Mindfulness OR complementary OR "alternative medicine" OR "alternative therapy" OR "alternative therapies" OR "Interpersonal skills training" 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OR acupuncture OR "vision training" OR "visual training" OR "vision therapy" OR "education intervention" OR "cognitive remediation" OR neurotherapy OR "elimination diet" OR "diet therapy" OR (("low carb" OR "low carbohydrate" OR "low carbohydrates" OR "gluten free") AND diet) OR "feingold diet" OR "red dye" OR ((vitamin OR vitamins) AND (supplement OR supplements)) OR "herbal supplement" OR "herbal supplements" OR probiotics OR "omega 3" OR "slow cortical potentials" OR "few foods diet" OR "oligoantigenic diet" OR "restriction diet" OR "food intolerance" OR "food allergy" OR "food allergies" OR "food sensitivity" OR "food sensitivities" OR "multimodal treatment" OR homeopathy OR homeopathic OR chiropractic OR chiropractor) OR AB (Monarch external Trigeminal Nerve Stimulation OR eTNS OR "EndeavorRx" OR ((classroom OR school OR schools) AND (behavior intervention OR behavior interventions)) OR "peer intervention" OR (("organization skills") AND (training OR intervention)) OR"psychosocial therapy" OR "psychosocial intervention" OR "psychosocial interventions" OR "psychosocial approach" OR "psychosocial approaches" OR "psychosocial treatment" OR "psychosocial support" OR "psychoeducation" OR "nonpharmacologic therapy" OR "nondrug therapy" OR "non-drug therapy" OR "Play Therapy" OR "cognitive behavioral therapy" OR "cognitive behavior therapy" OR "cognitive behavioural therapy" OR "cognitive behaviour therapy" OR Mindfulness OR complementary OR "alternative medicine" OR "alternative therapy" OR "alternative therapies" OR "Interpersonal skills training" OR "Parent-Child Interaction Therapy" OR "parent training" OR "parent engagement" OR "parent management" OR "parenting skills" OR "parenting intervention" OR "parenting interventions" OR "Barkley's defiant child" OR "Teacher-Child Interaction Training" OR "Incredible Years" OR "New Forest Parenting" OR "Triple P" OR "Helping the Noncompliant Child" OR "child life and attention skills" OR "clas" OR PCIT OR "parent child interaction therapy" OR "Summer Treatment Program" OR "Daily Report Card" OR "organization skills" OR "organizational skills" OR "time management" OR "homework intervention" OR braintrain OR "memory training" OR "Captain's log mindpower builder" OR "memory gyms" OR "attention gym" OR "smartdriver plus" OR "smartmind pro" OR “RoboMemo” OR "play attention" OR metronome OR brainmaster OR mindmed OR "attention lab" OR (activate AND c8) OR "attention training" OR “CogniPlus” OR cogmed OR "working memory training" OR biofeedback OR neurofeedback OR neuroagility OR neuroptimal OR acupuncture OR "vision training" OR "visual training" OR "vision therapy" OR "education intervention" OR "cognitive remediation" OR neurotherapy OR "elimination diet" OR "diet therapy" OR (("low carb" OR "low carbohydrate" OR "low carbohydrates" OR "gluten free") AND diet) OR "feingold diet" OR "red dye" OR ((vitamin OR vitamins) AND (supplement OR supplements)) OR "herbal supplement" OR "herbal supplements" OR probiotics OR "omega 3" OR "slow cortical potentials" OR "few foods diet" OR "oligoantigenic diet" OR "restriction diet" OR "food intolerance" OR "food allergy" OR "food allergies" OR "food sensitivity" OR "food sensitivities" OR “multimodal treatment” OR homeopathy OR homeopathic OR chiropractic OR chiropractor)))) AND (ZC "longitudinal study" OR ZC "empirical study" OR ZC "followup study" OR ZC "longitudinal study" OR ZC "meta analysis" OR ZC "prospective study" OR ZC "retrospective study" OR ZC "systematic review" OR ZC "treatment outcome/clinical trial"OR DE "Clinical Trials" OR DE "Cohort Analysis" OR DE "Followup Studies" OR DE "Longitudinal Studies" OR DE "Prospective Studies" OR DE "Meta Analysis" OR TI (randomized OR randomised OR randomization OR randomisation OR randomly OR trial OR groups OR trials OR "evaluation study" OR evaluation studies OR "intervention study" OR "intervention studies" OR "case-control" OR cohort OR longitudinal OR longitudinally OR prospective OR prospectively OR retrospective OR "comparative study" OR "meta-analysis" OR "meta-analyses") OR AB (randomized OR randomised OR randomization OR randomisation OR randomly OR trial OR groups OR trials OR "evaluation study" OR evaluation studies OR "intervention study" OR "intervention studies" OR "case-control" OR cohort OR longitudinal OR longitudinally OR prospective OR prospectively OR retrospective OR "comparative study" OR "meta-analysis" OR "meta-analyses") AND (ZZ "journal article")) AND yr(1980-2011)

ERIC

S1

DE “Attention Deficit Hyperactivity Disorder” OR SU “Attention Deficit Hyperactivity Disorder” OR (“attention deficit hyperactivity disorder” OR ADHD OR “attention deficit disorder”)

S2

Child OR children OR pediatric OR adolescence OR teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth

S3

intervention OR treatment OR therapy OR counseling OR training OR education OR medication OR drug OR psychostimulant OR “Psychotherapy” OR Medicine OR program

S4

“longitudinal study” OR “empirical study” OR “followup study” OR “longitudinal study” OR “prospective study” OR “systematic review” OR “treatment outcome/clinical trial” OR “Clinical Trials” OR “Cohort Analysis” OR “Followup Studies” OR “Longitudinal Studies” OR

“Prospective Studies” OR randomized OR andomizat OR randomization OR andomization OR randomly OR trial OR groups OR trials OR “evaluation study” OR evaluation studies OR “intervention study” OR “intervention studies” OR “case-control” OR cohort OR longitudinal OR longitudinally OR prospective OR prospectively OR “comparative study”
S5
S1 AND S2 AND S3 AND S4
Publication Date Range: 2016-2023; Publication Type: Scholarly (Peer Reviewed) Journals

S1
DE "Attention Deficit Hyperactivity Disorder" OR SU "Attention Deficit Hyperactivity Disorder" OR ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder")
S2
adolescence OR teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth
S3
S1 AND S2
S4
("CNS Stimulating Drugs" OR "Methylphenidate" OR "Dextroamphetamine" OR "Amphetamine" OR "Clonidine" OR "Serotonin Norepinephrine Reuptake Inhibitors" OR "Atomoxetine" OR "Tricyclic Antidepressant Drugs" OR "Desipramine" OR "Nortriptyline" OR "Bupropion" OR "Serotonin Norepinephrine Reuptake Inhibitors" OR "Venlafaxine" OR "Monoamine Oxidase Inhibitors" OR "Amantadine") OR (Azstarys OR Cotempla XR-ODT OR Desoxyn OR "Alpha agonist" OR psychostimulants OR "CNS stimulating" OR "Central Nervous System stimulants" OR methylphenidate OR Dexmethylphenidate OR Dextroamphetamine OR lisdexamfetamine OR Amphetamine OR aptensio OR concerta OR Ritalin OR methylin OR medikinet OR equasym OR quillivant OR metadate OR daytrana OR focalin OR Dexedrine OR dextrostat OR procentra OR zenzedi OR Adderall OR vyvanse OR elvanse OR tyvense OR dyanavel OR evekeo OR "alpha-2 agonists" OR guanfacine OR intuniv OR tenex OR estulic OR afken OR clonidine OR catapres OR clophelin OR kapvay OR nexiclon OR duraclon OR "Serotonin Norepinephrine Reuptake Inhibitors" OR Strattera OR atomoxetine OR "Tricyclic Antidepressants " OR "Desipramine" OR "Nortriptyline" OR norpramin OR pertofrane OR pamelor OR "dopamine reuptake inhibitors" OR modanifil OR Provigil OR alertec OR modavigil OR modiodal OR modalert OR armodafinil OR nuvigil OR "norepinephrine-dopamine reuptake inhibitors" OR bupropion OR Wellbutrin OR zyban OR forfivo OR "Serotonin Norepinephrine Reuptake Inhibitors" OR duloxetine OR Cymbalta OR "serotonin norepinephrine dopamine reuptake inhibitors" OR "Venlafaxine" OR Effexor OR trevilor OR (Monoamine Oxidase AND Inhibitors) OR selegiline OR eldepryl OR emsam OR selgene OR zelapar OR "n methyl d aspartate receptor agonists" OR "Amantadine" OR symmetrel OR memantine OR Namenda)
S5
"Psychotherapy" OR "Adolescent Psychotherapy" OR "Multisystemic Therapy" OR "Behavior Therapy" OR "Dialectical Behavior Therapy" OR "Brief Psychotherapy" OR "Child Psychotherapy" OR "Play Therapy" OR "Client Centered Therapy" OR "Cognitive Behavior Therapy" OR "Group Psychotherapy" OR "Therapeutic Community" OR "Integrative Psychotherapy" OR "Psychotherapeutic Counseling" OR "Family Therapy" OR "Supportive

Psychotherapy" OR "Cognitive Therapy" OR "Parent Training" OR "Parent Child Relations" OR "Time Management" OR "Mindfulness" OR "School Based Intervention" OR "Memory Training" OR "Biofeedback Training" OR "Biofeedback" OR "Computer Assisted Instruction" OR "Intelligent Tutoring Systems" OR "Diets" OR "Dietary Supplements" OR "Food Additives" OR "Fatty Acids" OR "Acupuncture" OR "Remedial Education" OR "Early Intervention" OR "Alternative Medicine" OR Monarch external Trigeminal Nerve Stimulation OR eTNS OR "EndeavorRx" OR ((classroom OR school OR schools) AND (behavior intervention OR behavior interventions)) OR "peer intervention" OR (("organization skills") AND (training OR intervention)) OR "psychosocial therapy" OR "psychosocial intervention" OR "psychosocial interventions" OR "psychosocial approach" OR "psychosocial approaches" OR "psychosocial treatment" OR "psychosocial support" OR "psychoeducation" OR "nonpharmacologic therapy" OR "nondrug therapy" OR "non-drug therapy" OR "Play Therapy" OR "cognitive behavioral therapy" OR "cognitive behavior therapy" OR "cognitive behavioural therapy" OR "cognitive behaviour therapy" OR Mindfulness OR complementary OR "alternative medicine" OR "alternative therapy" OR "alternative therapies" OR "Interpersonal skills training" OR "Parent-Child Interaction Therapy" OR "parent training" OR "parent engagement" OR "parent management" OR "parenting skills" OR "parenting intervention" OR "parenting interventions" OR "Barkley's defiant child" OR "Teacher-Child Interaction Training" OR "Incredible Years" OR "New Forest Parenting" OR "Triple P" OR "Helping the Noncompliant Child" OR "child life and attention skills" OR "clas" OR PCIT OR "parent child interaction therapy" OR "Summer Treatment Program" OR "Daily Report Card" OR "organization skills" OR "organizational skills" OR "time management" OR "homework intervention" OR braintrain OR "memory training" OR "Captain's log mindpower builder" OR "memory gyms" OR "attention gym" OR "smartdriver plus" OR "smartmind pro" OR “RoboMemo” OR "play attention" OR metronome OR brainmaster OR mindmed OR "attention lab" OR (activate AND c8) OR "attention training" OR “CogniPlus” OR cogmed OR "working memory training" OR biofeedback OR neurofeedback OR neuroagility OR neuroptimal OR acupuncture OR "vision training" OR "visual training" OR "vision therapy" OR "education intervention" OR "cognitive remediation" OR neurotherapy OR "elimination diet" OR "diet therapy" OR (("low carb" OR "low carbohydrate" OR "low carbohydrates" OR "gluten free") AND diet) OR "feingold diet" OR "red dye" OR ((vitamin OR vitamins) AND (supplement OR supplements)) OR "herbal supplement" OR "herbal supplements" OR probiotics OR "omega 3" OR "slow cortical potentials" OR "few foods diet" OR "oligoantigenic diet" OR "restriction diet" OR "food intolerance" OR "food allergy" OR "food allergies" OR "food sensitivity" OR "food sensitivities" OR “multimodal treatment” OR homeopathy OR homeopathic OR chiropractic OR chiropractor

S6

S4 OR S5

S7

S3 AND S6

S8

"longitudinal study" OR "empirical study" OR "followup study" OR "longitudinal study" OR "meta analysis" OR "prospective study" OR "retrospective study" OR "systematic review" OR "treatment outcome/clinical trial" OR "Clinical Trials" OR "Cohort Analysis" OR "Followup Studies" OR "Longitudinal Studies" OR "Prospective Studies" OR "Meta Analysis" OR randomized OR randomised OR randomization OR randomisation OR randomly OR trial OR

groups OR trials OR "evaluation study" OR evaluation studies OR "intervention study" OR "intervention studies" OR "case-control" OR cohort OR longitudinal OR longitudinally OR prospective OR prospectively OR retrospective OR "comparative study" OR "meta-analysis" OR "meta-analyses"
S9 S7 AND S8
Publication Date Range: 1980-2011; Publication Type: Journal Articles

EMBASE

1
'attention deficit disorder'/exp OR 'attention deficit disorder' OR 'attention deficit hyperactivity disorder':ab,ti OR 'adhd':ab,ti OR 'attention deficit disorder':ab,ti
2
'child'/exp OR 'pediatric'/exp OR 'adolescent'/exp
OR child:ab,ti OR children:ab,ti OR pediatrics:ab,ti OR teenager:ab,ti OR teenagers:ab,ti OR teenaged:ab,ti OR teen:ab,ti OR teens:ab,ti OR adolescent:ab,ti OR adolescents:ab,ti OR adolescence:ab,ti OR youth:ab,ti
3
#1 AND #2
4
'intervention':ab,ti OR 'treatment':ab,ti OR 'therapy':ab,ti OR 'counseling':ab,ti OR 'training':ab,ti OR 'education':ab,ti OR 'medication':ab,ti OR 'drug':ab,ti OR 'psychostimulant':ab,ti OR 'Psychotherapy':ab,ti OR 'Medicine':ab,ti OR 'program':ab,ti
5
#3 AND #4
6
('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR random*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR ((cross NEAR/1 over*):ab,ti) OR placebo*:ab,ti OR ((doubl* NEAR/1 blind*):ab,ti) OR ((singl* NEAR/1 blind*):ab,ti) OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR 'clinical study'/exp OR 'clinical trial':ti,ab OR 'clinical trials':ti,ab OR 'controlled study'/exp OR 'evaluation'/exp OR 'evaluation study':ab,ti OR 'evaluation studies':ab,ti OR 'intervention study':ab,ti OR 'intervention studies':ab,ti OR 'case control':ab,ti OR 'cohort analysis'/exp OR cohort:ab,ti OR longitudinal*:ab,ti OR prospective:ab,ti OR prospectively:ab,ti OR 'follow up'/exp OR 'follow up':ab,ti OR 'comparative effectiveness'/exp OR 'comparative study'/exp OR 'comparative study':ab,ti OR 'comparative studies':ab,ti OR 'evidence based medicine'/exp OR 'systematic review':ab,ti) NOT ('case report'/exp OR 'case study'/exp OR 'editorial'/exp OR 'letter'/exp OR 'note'/exp)
7
#5 AND #6
8
#7 AND [embase]/lim NOT [medline]/lim
9
#8 AND [humans]/lim AND [2016-2023]/py

1

'attention deficit disorder'/exp OR 'attention deficit disorder' OR 'attention deficit hyperactivity disorder':ab,ti OR 'adhd':ab,ti OR 'attention deficit disorder':ab,ti

2

'adolescent'/exp OR teenager:ab,ti OR teenagers:ab,ti OR teenaged:ab,ti OR teen:ab,ti OR teens:ab,ti OR adolescent:ab,ti OR adolescents:ab,ti OR adolescence:ab,ti OR youth:ab,ti

3

#1 AND #2

4

'azstarys':ab,ti OR 'cotempla xr-odt':ab,ti OR 'desoxyn':ab,ti OR 'alpha agonist':ab,ti OR 'attention deficit disorder'/exp/mj/dm_dt OR 'central stimulant agent'/exp OR 'psychostimulant agent'/exp OR 'guanfacine'/exp OR 'adrenergic receptor affecting agent'/exp OR 'atomoxetine'/exp OR 'antidepressant agent'/exp OR 'n methyl dextro aspartic acid receptor'/exp OR 'memantine'/exp OR 'amantadine'/exp OR 'dopamine uptake inhibitor'/exp OR 'central nervous system stimulants':ab,ti OR 'psychostimulant':ab,ti OR 'methylphenidate':ab,ti OR 'methylphenidate hydrochloride':ab,ti OR 'aptensio':ab,ti OR 'concerta':ab,ti OR 'ritalin':ab,ti OR 'ritalin la':ab,ti OR 'medikinet':ab,ti OR 'equasym':ab,ti OR 'quillivant':ab,ti OR 'metadate':ab,ti OR 'daytrana':ab,ti OR 'dexmethylphenidate':ab,ti OR 'dexmethylphenidate hydrochloride':ab,ti OR 'focalin':ab,ti OR 'dextroamphetamine':ab,ti OR 'dexedrine':ab,ti OR 'dextrostat':ab,ti OR 'procentra':ab,ti OR 'zenzedi':ab,ti OR 'mixed amphetamine salts':ab,ti OR 'adderall':ab,ti OR 'lisdexamfetamine':ab,ti OR 'lisdexamfetamine dimesylate':ab,ti OR 'vyvanse':ab,ti OR 'venvanse':ab,ti OR 'elvanse':ab,ti OR 'tyvense':ab,ti OR 'dyanavel':ab,ti OR 'evekeo':ab,ti OR 'guanfacine':ab,ti OR 'sympatholytics':ab,ti OR 'central alpha-2 adrenergic agonist':ab,ti OR 'clonidine':ab,ti OR 'intuniv':ab,ti OR 'estulic':ab,ti OR 'tenex':ab,ti OR 'catapres':ab,ti OR 'clophelin':ab,ti OR 'kapvay':ab,ti OR 'nexiclon':ab,ti OR 'duraclon':ab,ti OR 'norepinephrine reuptake inhibitors':ab,ti OR 'selective norepinephrine reuptake inhibitors':ab,ti OR 'adrenergic uptake inhibitors':ab,ti OR 'atomoxetine':ab,ti OR 'strattera':ab,ti OR 'tricyclic antidepressants':ab,ti OR 'desipramine':ab,ti OR 'norpramin':ab,ti OR 'nortriptyline':ab,ti OR 'pamelor':ab,ti OR 'dopamine reuptake inhibitors':ab,ti OR 'modafinil':ab,ti OR 'provigil':ab,ti OR 'armodafinil':ab,ti OR 'norepinephrine-dopamine reuptake inhibitors':ab,ti OR 'bupropion':ab,ti OR 'wellbutrin':ab,ti OR 'forfivo':ab,ti OR 'venlafaxine':ab,ti OR 'reboxetine':ab,ti OR 'monoamine oxidase type b inhibitors':ab,ti OR 'selegiline':ab,ti OR 'nmda receptors':ab,ti OR 'n-methyl-d-aspartate receptor antagonists':ab,ti OR 'amantadine':ab,ti OR 'memantine':ab,ti OR 'pertofrane':ab,ti OR 'nuvigil':ab,ti OR 'cymbalta':ab,ti OR 'duloxetine':ab,ti OR 'effexor':ab,ti OR 'eldepryl':ab,ti OR 'emsam':ab,ti OR 'trevilor':ab,ti OR 'symmetrel':ab,ti OR 'namenda':ab,ti OR 'zelapar':ab,ti

5

'monarch external trigeminal nerve stimulation':ab,ti OR etns:ab,ti OR ((classroom:ab,ti OR school:ab,ti OR schools:ab,ti) AND ('behavior intervention':ab,ti OR 'behavior interventions':ab,ti)) OR 'peer intervention':ab,ti OR ('organization skills':ab,ti AND (training:ab,ti OR intervention:ab,ti)) OR 'attention deficit disorder'/exp/mj/dm_rh,dm_dm OR 'psychotherapy'/exp OR 'child psychiatry'/exp OR 'child parent relation'/exp OR 'time management'/exp OR 'feedback system'/exp OR 'teaching'/exp OR 'adaptive behavior'/exp OR 'diet therapy'/exp OR 'omega 3 fatty acid'/exp OR 'vitamin'/exp/dd_do,dd_dt,dd_ad OR 'food additive'/exp/dd_ae OR 'probiotic agent'/exp OR 'acupuncture'/exp OR 'early childhood intervention'/exp OR 'alternative medicine'/exp OR 'psychosocial therapy':ab,ti OR 'psychosocial intervention':ab,ti OR 'psychosocial interventions':ab,ti OR 'psychosocial approach':ab,ti OR 'psychosocial approaches':ab,ti OR 'psychosocial treatment':ab,ti OR 'psychosocial support':ab,ti OR 'psychoeducation':ab,ti OR 'nonpharmacologic therapy':ab,ti OR 'nondrug therapy':ab,ti OR 'non-drug therapy':ab,ti OR 'play therapy':ab,ti OR 'cognitive behavioral therapy':ab,ti OR 'cognitive behavior therapy':ab,ti OR 'cognitive behavioural therapy':ab,ti OR 'cognitive behaviour therapy':ab,ti OR mindfulness:ab,ti OR complementary:ab,ti OR 'alternative medicine':ab,ti OR 'alternative therapy':ab,ti OR 'alternative therapies':ab,ti OR 'interpersonal skills training':ab,ti OR 'parent-child interaction therapy':ab,ti OR 'parent training':ab,ti OR 'parent engagement':ab,ti OR 'parent management':ab,ti OR 'parenting skills':ab,ti OR 'parenting intervention':ab,ti OR 'parenting interventions':ab,ti OR 'barkleys defiant child':ab,ti OR 'teacher-child interaction training':ab,ti OR 'incredible years':ab,ti OR 'new forest parenting':ab,ti OR 'triple p':ab,ti OR 'helping the noncompliant child':ab,ti OR 'child life and attention skills':ab,ti OR 'clas':ab,ti OR pcit:ab,ti OR 'parent child interaction therapy':ab,ti OR 'summer treatment program':ab,ti OR 'daily report card':ab,ti OR 'organization skills':ab,ti OR 'organizational skills':ab,ti OR 'time management':ab,ti OR 'homework intervention':ab,ti OR braintrain:ab,ti OR 'memory training':ab,ti OR 'captains log mindpower builder':ab,ti OR 'memory gyms':ab,ti OR 'attention gym':ab,ti OR 'smartdriver plus':ab,ti OR 'smartmind pro':ab,ti OR 'robomemo':ab,ti OR 'play attention':ab,ti OR metronome:ab,ti OR brainmaster:ab,ti OR mindmed:ab,ti OR 'attention lab':ab,ti OR (activate:ab,ti AND c8:ab,ti) OR 'attention training':ab,ti OR 'cogniplus':ab,ti OR cogmed:ab,ti OR 'working memory training':ab,ti OR biofeedback:ab,ti OR neurofeedback:ab,ti OR neuroagility:ab,ti OR neuroptimal:ab,ti OR acupuncture:ab,ti OR 'vision training':ab,ti OR 'visual training':ab,ti OR 'vision therapy':ab,ti OR 'education intervention':ab,ti OR 'cognitive remediation':ab,ti OR neurotherapy:ab,ti OR 'elimination diet':ab,ti OR 'diet therapy':ab,ti OR (('low carb' OR 'low carbohydrate' OR 'low carbohydrates':ab,ti OR 'gluten free') AND diet:ab,ti) OR 'feingold diet':ab,ti OR 'red dye':ab,ti OR ((vitamin:ab,ti OR vitamins:ab,ti) AND (supplement:ab,ti OR supplements:ab,ti)) OR 'herbal supplement':ab,ti OR 'herbal supplements':ab,ti OR probiotics:ab,ti OR 'omega 3':ab,ti OR 'slow cortical potentials':ab,ti OR 'few foods diet':ab,ti OR 'oligoantigenic diet':ab,ti OR 'restriction diet':ab,ti OR 'food intolerance':ab,ti OR 'food allergy':ab,ti OR 'food allergies':ab,ti OR 'food sensitivity':ab,ti OR 'food sensitivities':ab,ti OR 'multimodal treatment':ab,ti OR homeopathy:ab,ti OR homeopathic:ab,ti OR chiropractic:ab,ti OR chiropractor:ab,ti

6

#4 OR #5

7

#3 AND #6

8

('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR random*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR ((cross NEAR/1 over*):ab,ti) OR placebo*:ab,ti OR ((doubl* NEAR/1 blind*):ab,ti) OR ((singl* NEAR/1 blind*):ab,ti) OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR 'clinical study'/exp OR 'clinical trial':ti,ab OR 'clinical trials':ti,ab OR 'controlled study'/exp OR 'evaluation'/exp OR 'evaluation study':ab,ti OR 'evaluation studies':ab,ti OR 'intervention study':ab,ti OR 'intervention studies':ab,ti OR 'case control':ab,ti OR 'cohort analysis'/exp OR cohort:ab,ti OR longitudinal*:ab,ti OR prospective:ab,ti OR prospectively:ab,ti OR retrospective:ab,ti OR 'follow up'/exp OR 'follow up':ab,ti OR 'comparative effectiveness'/exp OR 'comparative study'/exp OR 'comparative study':ab,ti OR

'comparative studies':ab,ti OR 'evidence based medicine'/exp OR 'systematic review':ab,ti OR 'meta-analysis':ab,ti OR 'meta-analyses':ab,ti) NOT ('case report'/exp OR 'case study'/exp OR 'editorial'/exp OR 'letter'/exp OR 'note'/exp)
9
#7 AND #8
10
#9 AND [embase]/lim NOT [medline]/lim
11
#10 AND [humans]/lim AND [1980-2011]/py

Cochrane Reviews
#1
[mh "Attention Deficit Disorder with Hyperactivity"] OR attention deficit hyperactivity disorder:ab,ti OR "ADHD":ab,ti OR "attention deficit disorder":ab,ti
#2
[mh Adolescent] OR Child:ab,ti OR children:ab,ti OR pediatric:abti OR teenager:ab,ti OR teenagers:ab,ti OR teenaged:ab,ti OR teen:ab,ti OR teens:ab,ti OR adolescent:ab,ti OR adolescents:ab,ti OR adolescence:ab,ti OR youth:ab,ti
#3
[mh "Attention Deficit Disorder with Hyperactivity"/DT] OR 'intervention':ab,ti OR 'treatment':ab,ti OR 'therapy':ab,ti OR 'counseling':ab,ti OR 'training':ab,ti OR 'education':ab,ti OR 'medication':ab,ti OR 'drug':ab,ti OR 'psychostimulant':ab,ti OR 'Psychotherapy':ab,ti OR 'Medicine':ab,ti OR 'program':ab,ti
#4
#1 AND #2 AND #3
Limited to 2016-2023 and Cochrane Reviews

#1
[mh "Attention Deficit Disorder with Hyperactivity"]
#2
attention deficit hyperactivity disorder:ab,ti OR "ADHD":ab,ti OR "attention deficit disorder":ab,ti
#3
#1 OR #2
#4
[mh Adolescent]
#5
teenager:ab,ti OR teenagers:ab,ti OR teenaged:ab,ti OR teen:ab,ti OR teens:ab,ti OR adolescent:ab,ti OR adolescents:ab,ti OR adolescence:ab,ti OR youth:ab,ti
#6
#4 OR #5
#7
[mh "Attention Deficit Disorder with Hyperactivity"/DT] OR [mh "Central Nervous System Stimulants"] OR [mh Methylphenidate] OR [mh Dexmethylphenidate] OR [mh Dextroamphetamine] OR [mh Amphetamine] OR [mh Guanfacine] OR [mh Sympatholytics] OR [mh Clonidine] OR [mh “Adrenergic Uptake Inhibitors”] OR [mh “alpha-2 Adrenergic

Receptors”] OR [mh “Adrenergic alpha-Agonists”] OR [mh "Adrenergic alpha-2 Receptor Agonists"] OR [mh "Tricyclic Antidepressive Agents"] OR [mh Desipramine] OR [mh "Dopamine Uptake Inhibitors"] OR [mh Sympathomimetics] OR [mh "Serotonin Uptake Inhibitors"] OR [mh "Monoamine Oxidase Inhibitors"] OR [mh "Monoamine Oxidase"] OR [mh Selegiline] OR [mh Bupropion] OR [mh "N-Methyl-D-Aspartate Receptors"] OR [mh Memantine] OR [mh Amantadine]
#8
“Azstarys”:ab,ti OR “Cotempla XR-ODT”:ab,ti OR “Desoxyn”:ab,ti OR "Alpha agonist":ab,ti OR “psychostimulants”:ab,ti OR "CNS stimulating":ab,ti OR "Central Nervous System Stimulants":ab,ti OR “psychostimulant”:ab,ti OR “Methylphenidate”:ab,ti OR "Methylphenidate Hydrochloride":ab,ti OR “Aptensio”:ab,ti OR “Concerta”:ab,ti OR “Ritalin”:ab,ti OR “Ritalin LA”:ab,ti OR “Medikinet”:ab,ti OR “Equasym”:ab,ti OR “Quillivant”:ab,ti OR “Metadate”:ab,ti OR “Daytrana”:ab,ti OR "Dexmethylphenidate":ab,ti OR “Dexmethylphenidate Hydrochloride”:ab,ti OR “Focalin”:ab,ti OR “Dextroamphetamine”:ab,ti OR “Dexedrine”:ab,ti OR “Dextrostat”:ab,ti OR “ProCentra”:ab,ti OR “Zenzedi”:ab,ti OR “mixed amphetamine salts”:ab,ti OR "Adderall":ab,ti OR “lisdexamfetamine”:ab,ti OR “lisdexamfetamine dimesylate”:ab,ti OR “Vyvanse”:ab,ti OR "Venvanse":ab,ti OR "Elvanse":ab,ti OR "Tyvense":ab,ti OR "Dyanavel":ab,ti OR “Evekeo”:ab,ti OR "Guanfacine":ab,ti OR "Sympatholytics":ab,ti OR “Central alpha-2 Adrenergic Agonist”:ab,ti OR “Clonidine”:ab,ti OR "Intuniv":ab,ti OR "Estulic":ab,ti OR “Tenex”:ab,ti OR “Catapres”:ab,ti OR “Clophelin”:ab,ti OR "Kapvay":ab,ti OR “Nexiclon”:ab,ti OR "Duraclon":ab,ti OR “Norepinephrine Reuptake Inhibitors”:ab,ti OR “Selective Norepinephrine Reuptake Inhibitors”:ab,ti OR Adrenergic Uptake Inhibitors:ab,ti OR "atomoxetine":ab,ti OR "Strattera":ab,ti OR "Tricyclic antidepressants":ab,ti OR "Desipramine":ab,ti OR "Norpramin":ab,ti OR "Nortriptyline":ab,ti OR "Pamelor":ab,ti OR Dopamine Reuptake Inhibitors:ab,ti OR "modafinil":ab,ti OR “Provigil”:ab,ti OR Armodafinil:ab,ti OR Norepinephrine-dopamine Reuptake Inhibitors:ab,ti OR "Bupropion":ab,ti OR “Wellbutrin”:ab,ti OR “Forfivo”:ab,ti OR “Cymbalta”:ab,ti OR "venlafaxine":ab,ti OR “reboxetine”:ab,ti OR Monoamine Oxidase Type B inhibitors:ab,ti OR "Selegiline":ab,ti OR “Eldepryl”:ab,ti OR “Zelapar”:ab,ti OR “NMDA receptors”:ab,ti OR N-Methyl-D-aspartate receptor Antagonists:ab,ti OR "Amantadine":ab,ti OR "Memantine":ab,ti OR “Pertofrane”:ab,ti OR “Nuvigil”:ab,ti OR “Cymbalta”:ab,ti OR "duloxetine":ab,ti OR "Effexor":ab,ti OR "Eldepryl":ab,ti OR "Emsam":ab,ti OR "Trevilor":ab,ti OR "Symmetrel":ab,ti OR "Namenda":ab,ti OR "Zelapar":ab,ti
#9
#7 OR #8
#10
'monarch external trigeminal nerve stimulation':ab,ti OR etns:ab,ti OR ((classroom:ab,ti OR school:ab,ti OR schools:ab,ti) AND ('behavior intervention':ab,ti OR 'behavior interventions':ab,ti)) OR 'peer intervention':ab,ti OR ('organization skills':ab,ti AND (training:ab,ti OR intervention:ab,ti)) OR [mh "Attention Deficit Disorder with Hyperactivity"/DH] OR [mh "Attention Deficit Disorder with Hyperactivity"/RH] OR [mh Psychotherapy] OR [mh "Behavior Therapy"] OR [mh "Parent-Child Relations"] OR [mh "Play Therapy"] OR [mh "Cognitive Therapy"] OR [mh "Time Management"] OR [mh "Computer-Assisted Instruction"] OR [mh "Diet Therapy"] OR [mh "Omega-3 Fatty Acids"/TU] OR [mh Vitamins/AD] OR [mh Vitamins/TU] OR [mh "Food Additives"/AE] OR [mh Probiotics/TU]

OR [mh "Acupuncture Therapy"] OR [mh "Remedial Teaching"] OR [mh "Early Intervention (Education)"] OR [mh "Complementary Therapies"] OR [mh "Combined Modality Therapy"]
#11
psychosocial therapy:ab,ti OR "psychosocial intervention":ab,ti OR "psychosocial interventions":ab,ti OR "psychosocial approach":ab,ti OR "psychosocial approaches":ab,ti OR "psychosocial treatment":ab,ti OR "psychosocial support":ab,ti OR "psychoeducation":ab,ti OR "nonpharmacologic therapy":ab,ti OR "nondrug therapy":ab,ti OR "non-drug therapy":ab,ti OR "Play Therapy":ab,ti OR "cognitive behavioral therapy":ab,ti OR "cognitive behavior therapy":ab,ti OR "cognitive behavioural therapy":ab,ti OR "cognitive behaviour therapy":ab,ti OR Mindfulness:ab,ti OR complementary:ab,ti OR "alternative medicine":ab,ti OR "alternative therapy":ab,ti OR "alternative therapies":ab,ti OR "Interpersonal skills training":ab,ti OR "Parent-Child Interaction Therapy":ab,ti OR "parent training":ab,ti OR "parent engagement":ab,ti OR "parent management":ab,ti OR "parenting skills":ab,ti OR "parenting intervention":ab,ti OR "parenting interventions":ab,ti OR "Barkley's defiant child":ab,ti OR "TeacherChild Interaction Training":ab,ti OR "Incredible Years":ab,ti OR "New Forest Parenting":ab,ti OR "Triple P":ab,ti OR "Helping the Noncompliant Child":ab,ti OR "child life and attention skills":ab,ti OR "clas":ab,ti OR PCIT:ab,ti OR "parent child interaction therapy":ab,ti OR "Summer Treatment Program":ab,ti OR "Daily Report Card":ab,ti OR "organization skills":ab,ti OR "organizational skills":ab,ti OR "time management":ab,ti OR "homework intervention":ab,ti OR braintrain:ab,ti OR "memory training":ab,ti OR "Captain's log mindpower builder":ab,ti OR "memory gyms":ab,ti OR "attention gym":ab,ti OR "smartdriver plus":ab,ti OR "smartmind pro":ab,ti OR “RoboMemo”:ab,ti OR "play attention":ab,ti OR metronome:ab,ti OR brainmaster:ab,ti OR mindmed:ab,ti OR "attention lab":ab,ti OR (activate:ab,ti AND c8:ab,ti) OR "attention training":ab,ti OR “CogniPlus”:ab,ti OR cogmed:ab,ti OR "working memory training":ab,ti OR biofeedback:ab,ti OR neurofeedback:ab,ti OR neuroagility:ab,ti OR neuroptimal:ab,ti OR acupuncture:ab,ti OR "vision training":ab,ti OR "visual training":ab,ti OR "vision therapy":ab,ti OR "education intervention":ab,ti OR "cognitive remediation":ab,ti OR neurotherapy:ab,ti OR "elimination diet":ab,ti OR "diet therapy":ab,ti OR (("low carb" OR "low carbohydrate" OR "low carbohydrates":ab,ti OR "gluten free") AND diet:ab,ti) OR "feingold diet":ab,ti OR "red dye":ab,ti OR ((vitamin:ab,ti OR vitamins:ab,ti) AND (supplement:ab,ti OR supplements:ab,ti)) OR "herbal supplement":ab,ti OR "herbal supplements":ab,ti OR probiotics:ab,ti OR "omega 3":ab,ti OR "slow cortical potentials":ab,ti OR "few foods diet":ab,ti OR "oligoantigenic diet":ab,ti OR "restriction diet":ab,ti OR "food intolerance":ab,ti OR "food allergy":ab,ti OR "food allergies":ab,ti OR "food sensitivity":ab,ti OR "food sensitivities":ab,ti OR “multimodal treatment”:ab,ti OR homeopathy:ab,ti OR homeopathic:ab,ti OR chiropractic:ab,ti OR chiropractor:ab,ti
#12
#10 OR #11
#13
#12 OR #9
#14
#3 AND #6 AND #13
with Cochrane Library publication date Between Jan 1980 and Dec 2011, in Cochrane Reviews
#15
#3 AND #6
in Cochrane Reviews

KQ3

PubMed
1
"Attention Deficit Disorder with Hyperactivity"[Mesh] OR "attention deficit hyperactivity disorder"[tiab] OR "ADHD"[tiab] OR "attention deficit disorder"[tiab]
2
"Pediatrics"[Mesh] OR "Adolescent"[Mesh] OR "Infant"[Mesh] OR "Child"[Mesh] OR child[tiab] OR children[tiab] OR infant[tiab] OR infants[tiab] OR preschool[tiab] OR preschooler[tiab] OR pediatric[tiab] OR teenager[tiab] OR teenagers[tiab] OR teenaged[tiab] OR teen[tiab] OR teens[tiab] OR adolescent[tiab] OR adolescents[tiab] OR adolescence[tiab] OR youth[tiab]
3
monitor[tiab] OR monitored[tiab] OR monitoring[tiab] OR "follow up"[tiab] OR "followed up"[tiab] OR visit[tiab] OR visits[tiab] OR session[tiab] OR sessions[tiab] OR appointment[tiab] OR appointments[tiab]
4
(randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR Clinical trial[pt] OR "clinical trial"[tiab] OR "clinical trials"[tiab] OR "evaluation studies"[pt] OR "evaluation studies as topic"[MeSH] OR "evaluation study"[tiab] OR "evaluation studies"[tiab] OR "intervention studies"[MeSH] OR "intervention study"[tiab] OR "intervention studies"[tiab] OR "case-control studies"[MeSH] OR "case-control"[tiab] OR "cohort studies"[MeSH] OR cohort[tiab] OR "longitudinal"[tiab] OR longitudinally[tiab] OR "prospective"[tiab] OR prospectively[tiab] OR "retrospective"[tiab] OR "comparative study"[pt] OR "comparative study"[tiab] OR systematic[sb] OR "meta-analysis"[pt] OR "meta-analysis as topic"[MeSH])
5
Editorial[ptyp] OR Letter[pt] OR Case Reports[pt] OR Comment[pt]
6
animals[mh]
7
humans[mh]
8
English[la]
9
#1 AND #2 AND #3 AND #4 NOT #5 NOT #6 NOT #7 AND #8
Publication Date Range: 1980 to date

PsycINFO
#1
SU "Attention Deficit Disorder with Hyperactivity" OR TI ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder") OR AB ("attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder")
#2

AGE (childhood OR adolescence) OR SU "Pediatrics" OR TI (child OR children OR infant OR infants OR preschool OR preschooler OR pediatric OR teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth) OR AB (child OR children OR infant OR infants OR preschool OR preschooler OR pediatric OR teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth)
#3
TI(monitor OR monitored OR monitoring OR ("follow up" OR "followed up" OR visit OR visits OR session OR sessions OR appointment OR appointments) AND (schedule* OR strategy*) OR "longitudinal" OR longitudinally OR "long term") OR AB(monitor OR monitored OR monitoring OR ("follow up" OR "followed up" OR visit OR visits OR session OR sessions OR appointment OR appointments) AND (schedule* OR strategy*) OR "longitudinal" OR longitudinally OR "long term")
#4
"longitudinal study" OR "empirical study" OR "followup study" OR "longitudinal study" OR "meta analysis" OR "prospective study" OR "retrospective study" OR "systematic review" OR "treatment outcome/clinical trial"OR "Clinical Trials" OR "Cohort Analysis" OR "Followup Studies" OR "Longitudinal Studies" OR "Prospective Studies" OR "Meta Analysis" OR TI (randomized OR randomised OR randomization OR randomisation OR randomly OR trial OR groups OR trials OR "evaluation study" OR evaluation studies OR "intervention study" OR "intervention studies" OR "case-control" OR cohort OR longitudinal OR longitudinally OR prospective OR prospectively OR retrospective OR "comparative study" OR "meta-analysis" OR "meta-analyses") OR AB (randomized OR randomised OR randomization OR randomisation OR randomly OR trial OR groups OR trials OR "evaluation study" OR evaluation studies OR "intervention study" OR "intervention studies" OR "case-control" OR cohort OR longitudinal OR longitudinally OR prospective OR prospectively OR retrospective OR "comparative study" OR "meta-analysis" OR "meta-analyses")
#5
#1 AND #2 AND #3 AND #4

AND
Record Type: peer reviewed journal
AND
yr(1980-2023)
AND
English language

ERIC
#1
"Attention Deficit Disorder with Hyperactivity" OR TI/AB "attention deficit hyperactivity disorder" OR ADHD OR "attention deficit disorder"
#2
childhood OR adolescence OR "Pediatrics" OR TI/AB (child OR children OR infant OR infants OR preschool OR preschooler OR pediatric OR teenager OR teenagers OR teenaged OR teen OR teens OR adolescent OR adolescents OR adolescence OR youth)
#3

TI/AB monitor OR monitored OR monitoring OR ((“follow up” OR “followed up” OR visit OR visits OR session OR sessions OR appointment OR appointments) AND (schedule* OR strategy*)) OR longitudinal OR longitudinally OR “long term”
#4
“longitudinal study” OR “empirical study” OR “followup study” OR “longitudinal study” OR “meta analysis” OR “prospective study” OR “retrospective study” OR “systematic review” OR “treatment outcome/clinical trial” OR “Clinical Trials” OR “Cohort Analysis” OR “Followup Studies” OR “Longitudinal Studies” OR “Prospective Studies” OR “Meta Analysis” OR TI/AB (randomized OR llocate t OR randomization OR llocate tion OR randomly OR trial OR groups OR trials OR “evaluation study” OR
evaluation studies OR “intervention study” OR “intervention studies” OR “case-control” OR cohort OR longitudinal OR longitudinally OR prospective OR prospectively OR retrospective OR “comparative study” OR “meta-analysis” OR “meta-analyses”)
#5
#1 AND #2 AND #3 AND #4

Publication Date Range: 1980-2023; Publication Type: Scholarly (Peer Reviewed) Journals

EMBASE
#1
‘attention deficit disorder’/exp OR “attention deficit hyperactivity disorder”:ab,ti OR “ADHD”:ab,ti OR “attention deficit disorder”:ab,ti
#2
‘pediatrics’/exp OR ‘adolescent’/exp OR ‘infant’/exp OR ‘child’/exp OR child:ab,ti OR children:ab,ti OR infant:ab,ti OR infants:ab,ti OR preschool:ab,ti OR preschooler:ab,ti OR pediatric:ab,ti OR teenager:ab,ti OR teenagers:ab,ti OR teenaged:ab,ti OR teen:ab,ti OR teens:ab,ti OR adolescent:ab,ti OR adolescents:ab,ti OR adolescence:ab,ti OR youth:ab,ti
#3
monitor:ab,ti OR monitored:ab,ti OR monitoring:ab,ti OR ((‘follow up’:ab,ti OR ‘followed up’:ab,ti OR visit:ab,ti OR visits:ab,ti OR session:ab,ti OR sessions:ab,ti OR appointment:ab,ti OR appointments:ab,ti) AND (schedule* OR strategy*)) OR ‘longitudinal’:ab,ti OR longitudinally:ab,ti OR ‘long term’:ab,ti
#4
(‘randomized controlled trial’/exp OR ‘crossover procedure’/exp OR ‘double blind procedure’/exp OR ‘single blind procedure’/exp OR random*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR (cross NEAR/1 over*):ab,ti OR placebo*:ab,ti OR (doubl* NEAR/1 blind*):ab,ti OR (singl* NEAR/1 blind*):ab,ti OR assign*:ab,ti OR llocate*:ab,ti OR volunteer*:ab,ti OR ‘clinical study’/exp OR ‘clinical trial’:ti,ab OR ‘clinical trials’:ti,ab OR ‘controlled study’/exp OR ‘evaluation’/exp OR ‘evaluation study’:ab,ti OR ‘evaluation studies’:ab,ti OR ‘intervention study’:ab,ti OR ‘intervention studies’:ab,ti OR ‘case control’:ab,ti OR ‘cohort analysis’/exp OR cohort:ab,ti OR longitudinal*:ab,ti OR prospective:ab,ti OR prospectively:ab,ti OR retrospective:ab,ti OR ‘follow up’/exp OR ‘follow up’:ab,ti OR ‘comparative effectiveness’/exp OR ‘comparative study’/exp OR ‘comparative study’:ab,ti OR ‘comparative studies’:ab,ti OR ‘evidence based medicine’/exp OR ‘systematic review’:ab,ti OR ‘meta-analysis’:ab,ti OR ‘meta-analyses’:ab,ti) NOT (‘case report’/exp OR ‘case study’/exp OR ‘editorial’/exp OR ‘letter’/exp OR ‘note’/exp)

#5
#1 AND #2 AND #3 AND #4
#6
#5 AND [embase]/lim NOT [medline]/lim
#7
#6 AND [humans]/lim AND [1980-2023]/py

Cochrane Reviews
#1
[mh "Attention Deficit Disorder with Hyperactivity"]

#2
attention deficit hyperactivity disorder:ab,ti OR ADHD:ab,ti OR attention deficit disorder:ab,ti
#3
#1 OR #2
#4
[mh Pediatrics] OR [mh Adolescent] OR [mh Infant] OR [mh Child]
#5
child:ab,ti OR children:ab,ti OR infant:ab,ti OR infants:ab,ti OR preschool:ab,ti OR preschooler:ab,ti OR pediatric:ab,ti OR teenager:ab,ti OR teenagers:ab,ti OR teenaged:ab,ti OR teen:ab,ti OR teens:ab,ti OR adolescent:ab,ti OR adolescents:ab,ti OR adolescence:ab,ti OR youth:ab,ti
#6
#4 OR #5
#7
monitor:ab,ti OR monitored:ab,ti OR monitoring:ab,ti OR ((“follow up”:ab,ti OR “followed up”:ab,ti OR visit:ab,ti OR visits:ab,ti OR session:ab,ti OR sessions:ab,ti OR appointment:ab,ti OR appointments:ab,ti) AND (schedule* OR strategy*)) OR longitudinal:ab,ti OR longitudinally:ab,ti OR “long term”:ab,ti
#8
#6 OR #7
#9
#3 AND #6 AND #8
Limited to 1980-2023 and Cochrane Reviews

ClinicalTrials.gov
Conditions: ADHD OR attention deficit
Recruitment: Completed studies
Study Results: All studies
Study type: Interventional studies
Age group: Child
Phase: Phase 2, Phase 3, Phase 4
2016-2023

Appendix B. List of Excluded and Background Studies

This appendix shows the list of excluded studies with reasons for exclusion. We only recorded one reason per publication.

Excluded Studies

1. Use of methylphenidate for attention deficit hyperactivity disorder. Mental Health Committee, Canadian Paediatric Society. Cmaj. 1990 Apr 15;142(8):817-8. PMID: 2322913. *Design*

2. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. The MTA Cooperative Group. Multimodal Treatment Study of Children with ADHD. Arch Gen Psychiatry. 1999 Dec;56(12):1073-86. doi: 10.1001/archpsyc.56.12.1073. PMID: 10591283. *Duplicate*

3. National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: changes in effectiveness and growth after the end of treatment. Pediatrics. 2004 Apr;113(4):762-9. doi: 10.1542/peds.113.4.762. PMID: 15060225. *Duplicate*

4. Randomized, controlled, crossover trial of methylphenidate in pervasive developmental disorders with hyperactivity. Arch Gen Psychiatry. 2005 Nov;62(11):1266-74. doi: 10.1001/archpsyc.62.11.1266. PMID: 16275814. *Population*

5. The pharmacological treatment of attention-deficit hyperactivity disorder (ADHD) in adolescents is effective and relatively safe. Drugs and Therapy Perspectives. 2007;23(11):9-12. doi: 10.2165/00042310-200723110-00003. *Design*

6. Guanfacine effective for attention-deficit/hyerpactivity disorder, but side effects are significant. Journal of the National Medical Association. 2008;100(5):579-80. doi: 10.1016/S0027-9684(15)31311-0. *Design*

7. ADHD medications may be linked to sudden unexplained death. Formulary. 2009;44(7):192. *Design*

8. St John's wort and ADHD in children and adolescents. Australian Journal of Pharmacy. 2009;90(1066):79. *Design*

9. Increasing prevalence of parent-reported attention-deficit/hyperactivity disorder among children --- United States, 2003 and 2007. MMWR Morb Mortal Wkly Rep. 2010 Nov 12;59(44):1439-43. doi: mm5944a3 [pii]. PMID: 21063274. *Outcome*

10. Corrigendum: Cigarette Smoking Progression Among Young Adults Diagnosed With ADHD in Childhood: A 16-year Longitudinal Study of Children With and Without ADHD. Nicotine Tob Res. 2019 Sep 19;21(10):1449. doi: 10.1093/ntr/nty260. PMID: 30615186. *Intervention*

11. Effect of Vergence/Accommodative Therapy on Attention in Children with Convergence Insufficiency: A Randomized Clinical Trial. Optom Vis Sci. 2021 Mar 1;98(3):222-33. doi: 10.1097/opx.0000000000001659. PMID: 33771952. *Population*

12. Azstarys (serdexmethylphenidate/dexmethylphenidate) for ADHD. Med Lett Drugs Ther. 2021 Oct 4;63(1634):157-9. PMID: 34550957. *Design*

13. Psychiatry Update 2022 Spring Abstract. Annals of Clinical Psychiatry. 2022;34(3). *Design*

14. (CIHR) IHCCIoHR. Strongest Families Finland Canada: Family-based Prevention and Treatment Program of Early Childhood Disruptive Behavior. 2011. *Outcome*

15. (NIMH) MGHNIoMH. Effectiveness of Atomoxetine in Treating ADHD Symptoms in Children and Adolescents With Autism. 2007. *Population*

16. Aaronson B, Glick SN, Kirk CJ, et al. Assessment of Feasibility of Face Covering in School-Aged Children With Autism Spectrum Disorders and Attention-Deficit/Hyperactivity Disorder. JAMA Netw Open. 2021 May 3;4(5):e2110281. doi: 10.1001/jamanetworkopen.2021.10281. PMID: 33999167. *Intervention*

17. Abadi MS, Madgaonkar J, Venkatesan S. Effect of yoga on children with attention deficit/hyperactivity disorder. Psychological Studies. 2008;53:154-9. *Power*

18. Abbas AK, Azemi G, Amiri S, et al. Effective connectivity in brain networks estimated using EEG signals is altered in children with ADHD. Comput Biol Med. 2021 Jul;134:104515. doi: 10.1016/j.compbiomed.2021.104515. PMID: 34126282. *Intervention*

19. Abbas R, Palumbo D, Walters F, et al. Single-dose Pharmacokinetic Properties and Relative Bioavailability of a Novel Methylphenidate Extended-release Chewable Tablet Compared With Immediate-release Methylphenidate Chewable Tablet. Clin Ther. 2016 May;38(5):1151-7. doi: 10.1016/j.clinthera.2016.02.026. PMID: 27021606. *Population*

20. Abbasi S-H, Heidari S, Mohammadi M-R, et al. Acetyl-L-Carnitine as an Adjunctive Therapy in the Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents: A Placebo-Controlled Trial. Child Psychiatry and Human Development. 2011 06/01/;42(3):367-75. PMID: EJ923317. *Duplicate*

21. Abbey McClemont SF. Racial Disparities in Teacher Ratings of ADHD Symptoms and Behavior: A Systematic Review. PROSPERO 2020 CRD42020194385. 2020. https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=194385. *Outcome*

22. Abdekhodaie Z, Tabatabaei SM, Gholizadeh M. The investigation of ADHD prevalence in kindergarten children in northeast Iran and a determination of the criterion validity of Conners' questionnaire via clinical interview. Res Dev Disabil. 2012 Mar-Apr;33(2):357-61. doi: 10.1016/j.ridd.2011.10.006. PMID: 22119681. *Language*

23. Abdel Ghaffar HMGED, Abdelghaffar NK, Ahmed HH, et al. Study of serum neopterin in children with attention deficit hyperactivity disorder and autistic spectrum disorder: Fayoum Governorate, Egypt. Egyptian Journal of Neurology, Psychiatry and Neurosurgery. 2022;58(1). doi: 10.1186/s41983-022-00448-y. *Intervention*

24. Abdel Kader AA, Mohamed NA, El Sayed BB, et al. Continuous performance task in attention deficit hyperactivity disorder children. Egyptian Journal of Neurology, Psychiatry and Neurosurgery. 2016;53(1):19-22. doi: 10.4103/1110-1083.176340. *Intervention*

25. Abdollahian E, Mokhber N, Balaghi A, et al. The effectiveness of cognitive-behavioural play therapy on the symptoms of attention-deficit/hyperactivity disorder in children aged 7-9 years. Atten Defic Hyperact Disord. 2013 Mar;5(1):41-6. doi: 10.1007/s12402-012-0096-0. PMID: 23179507. *Power*

26. Abdulhay E, Abdelhay A, Kilani A, et al. Development of arduino based low cost neuro-feedback applied to ADHD. Biomedical Research (India). 2016;2016:S31-S7. *Intervention*

27. Abed M, Mansureh HH, Masoud GL, et al. Construction of Meta-Thinking Educational Program Based on Mental-Brain Simulation (MTMBS) and Evaluating its Effectiveness on Executive Functions, Emotion Regulation, and Impulsivity in Children With ADHD: A Resting-State Functional MRI Study. J Atten Disord. 2023 Feb 26:10870547231155436. doi: 10.1177/10870547231155436. PMID: 36843348. *Power*

28. Abernethy LJ, Palaniappan M, Cooke RW. Quantitative magnetic resonance imaging of the brain in survivors of very low birth weight. Arch Dis Child. 2002 Oct;87(4):279-83. doi: 10.1136/adc.87.4.279. PMID: 12243993. *Intervention*

29. Abhijit Dutta PFSGSSMK. Homeopathy in the treatment of attention deficit hyperactivity disorder: a systematic review and meta-analysis. PROSPERO 2020 CRD42020156564. 2020. https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=156564. *Design*

30. Abigail Russell DMASBDRHJKES-BLPTF. Synthesising the existing evidence for non-pharmacological interventions targeting outcomes relevant to young people with ADHD in the school setting: systematic review protocol. PROSPERO 2021 CRD42021233924. 2021. https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=233924. *Design*

31. Abikoff H, Arnold LE, Newcorn JH, et al. Emergency/Adjunct services and attrition prevention for randomized clinical trials in children: the MTA manual-based solution. J Am Acad Child Adolesc Psychiatry. 2002 May;41(5):498-504. doi: 10.1097/00004583-200205000-00006. PMID: 12014781. *Design*

32. Abikoff H, McGough J, Vitiello B, et al. Sequential pharmacotherapy for children with comorbid attention-deficit/hyperactivity and anxiety disorders. J Am Acad Child Adolesc Psychiatry. 2005 May;44(5):418-27. doi: 10.1097/01.chi.0000155320.52322.37. PMID: 15843763. *Intervention*

33. Abikoff HB, Thompson M, Laver-Bradbury C, et al. Parent training for preschool ADHD: a randomized controlled trial of specialized and generic programs. J Child Psychol Psychiatry. 2015 Jun;56(6):618-31. doi: 10.1111/jcpp.12346. PMID: 25318650. *Duplicate*

34. Abikoff HB, Thompson M, Laver-Bradbury C, et al. Parent training for preschool ADHD: a

randomized controlled trial of specialized and generic programs. J Child Psychol Psychiatry. 2015 Jun;56(6):618-31. doi: 10.1111/jcpp.12346. PMID: 25318650. *Duplicate*

35. Abo Elella E, Hassan GAM, Sabry W, et al. Trait emotional intelligence in a sample of Egyptian children with attention deficit hyperactivity disorder. Child Adolesc Ment Health. 2017 Nov;22(4):216-23. doi: 10.1111/camh.12236. PMID: 32680413. *Intervention*

36. Abou-Abdallah T, Guilé JM, Menusier C, et al. Cognitive and relationship correlates associated with Attention-Deficit-Disorders with/without hyperactivity. Neuropsychiatrie de l'Enfance et de l'Adolescence. 2010;58(5):293-7. doi: 10.1016/j.neurenf.2009.07.001. *Intervention*

37. Abrantes AM, Strong DR, Ramsey SE, et al. Substance use disorder characteristics and externalizing problems among inpatient adolescent smokers. J Psychoactive Drugs. 2005 Dec;37(4):391-9. doi: 10.1080/02791072.2005.10399812. PMID: 16480166. *Intervention*

38. Ackermann S, Halfon O, Fornari E, et al. Cognitive Working Memory Training (CWMT) in adolescents suffering from Attention-Deficit/Hyperactivity Disorder (ADHD): A controlled trial taking into account concomitant medication effects. Psychiatry Res. 2018 Nov;269:79-85. doi: 10.1016/j.psychres.2018.07.036. PMID: 30145306. *Power*

39. Acland EL, Jambon M, Malti T. Children's emotion recognition and aggression: A multi-cohort longitudinal study. Aggress Behav. 2021 Aug 9. doi: 10.1002/ab.21989. PMID: 34369593. *Intervention*

40. Adamis D, Tatlow-Golden M, Gavin B, et al. General practitioners' (GP) attitudes and knowledge about attention deficit hyperactivity disorder (ADHD) in Ireland. Ir J Med Sci. 2019 Feb;188(1):231-9. doi: 10.1007/s11845-018-1804-3. PMID: 29654530. *Population*

41. Adamou M, Jones SL, Marks L, et al. Efficacy of Continuous Performance Testing in Adult ADHD in a Clinical Sample Using QbTest. J Atten Disord. 2022 Sep;26(11):1483-91. doi: 10.1177/10870547221079798. PMID: 35255743. *Population*

42. Adams CD, Kelly ML, McCarthy M. The Adolescent Behavior Checklist: development and initial psychometric properties of a self-report measure for adolescents with ADHD. J Clin Child Psychol. 1997 Mar;26(1):77-86. doi: 10.1207/s15374424jccp2601_8. PMID: 9118178. *Outcome*

43. Adams W. Lack of behavioral effects from Feingold diet violations. Percept Mot Skills. 1981 Feb;52(1):307-13. doi: 10.2466/pms.1981.52.1.307. PMID: 7232091. *Intervention*

44. Adhvaryu KP, Karthikbabu S, Rao PT. Motor performance of children with attention deficit hyperactivity disorder: focus on the Bruininks-Oseretsky Test of Motor Proficiency. Clinical and Experimental Pediatrics. 2022;65(11):510-8. doi: 10.3345/cep.2021.00962. *Intervention*

45. Adisetiyo V, Gray KM. Neuroimaging the neural correlates of increased risk for substance use disorders in attention-deficit/hyperactivity disorder-A systematic review. Am J Addict. 2017 Mar;26(2):99-111. doi: 10.1111/ajad.12500. PMID: 28106934. *Intervention*

46. Adisetiyo V, Gray KM, Jensen JH, et al. Brain iron levels in attention-deficit/hyperactivity disorder normalize as a function of psychostimulant treatment duration. Neuroimage Clin. 2019;24:101993. doi: 10.1016/j.nicl.2019.101993. PMID: 31479897. *Intervention*

47. Adjei AL, Chaudhary I, Kollins SH, et al. A Pharmacokinetic Study of Methylphenidate Hydrochloride Multilayer Extended-Release Capsules (Aptensio XR(®)) in Preschool-Aged Children with Attention-Deficit/Hyperactivity Disorder. Paediatr Drugs. 2020 Oct;22(5):561-70. doi: 10.1007/s40272-020-00409-z. PMID: 32776159. *Timing*

48. Adler CM, Delbello MP, Mills NP, et al. Comorbid ADHD is associated with altered patterns of neuronal activation in adolescents with bipolar disorder performing a simple attention task. Bipolar Disord. 2005 Dec;7(6):577-88. doi: 10.1111/j.1399-5618.2005.00257.x. PMID: 16403183. *Outcome*

49. Adler LA, Childress A, Cloutier M, et al. ED4 Economic Burden of Attention-Deficit/Hyperactivity Disorder (ADHD) Among Children and Adolescents in the United States (US): A Societal Perspective. Value in Health. 2021;24:S6-S7. doi: 10.1016/j.jval.2021.04.034. *Design*

50. Adler LA, Dirks B, Deas PF, et al. Lisdexamfetamine dimesylate in adults with attention-deficit/ hyperactivity disorder who report clinically significant impairment in executive function: results from a randomized, double-blind, placebo-controlled study. J Clin Psychiatry. 2013 Jul;74(7):694-702. doi: 10.4088/JCP.12m08144. PMID: 23945447. *Population*

51. Adler LA, Goodman DW, Kollins SH, et al. Double-blind, placebo-controlled study of the efficacy and safety of lisdexamfetamine dimesylate in adults with attention-deficit/hyperactivity disorder. J Clin Psychiatry. 2008 Sep;69(9):1364-73. doi: 10.4088/jcp.v69n0903. PMID: 19012818. *Population*

52. Adler LA, Liebowitz M, Kronenberger W, et al. Atomoxetine treatment in adults with attention-deficit/hyperactivity disorder and comorbid social anxiety disorder. Depress Anxiety. 2009;26(3):212-21. doi: 10.1002/da.20549. PMID: 19194995. *Population*

53. Adler LA, Lynch LR, Shaw DM, et al. Medication adherence and symptom reduction in adults treated with mixed amphetamine salts in a randomized crossover study. Postgrad Med. 2011 Sep;123(5):71-9. doi: 10.3810/pgm.2011.09.2461. PMID: 21904088. *Population*

54. Adler LA, Orman C, Starr HL, et al. Long-term safety of OROS methylphenidate in adults with attention-deficit/hyperactivity disorder: an open-label, dose-titration, 1-year study. J Clin Psychopharmacol. 2011 Feb;31(1):108-14. doi: 10.1097/JCP.0b013e318203ea0a. PMID: 21192153. *Population*

55. Adra N, Cao A, Makris N, et al. Sensory Modulation Disorder and its Neural Circuitry in Adults with ADHD: A Pilot Study. Brain Imaging Behav. 2021 Apr;15(2):930-40. doi: 10.1007/s11682-020-00302-w. PMID: 32770315. *Population*

56. Adriani W, Romano E, Pucci M, et al. Potential for diagnosis versus therapy monitoring of attention deficit hyperactivity disorder: A new epigenetic biomarker interacting with both genotype and auto-immunity. European Child & Adolescent Psychiatry. 2018 Feb 2018;27(2):241-52. *Intervention*

57. Aduen PA, Kofler MJ, Bradshaw CP, et al. The role of top-down attentional control and attention-deficit/hyperactivity disorder symptoms in predicting future motor vehicle crash risk. Neuropsychology. 2020 Nov;34(8):894-905. doi: 10.1037/neu0000707. PMID: 33197201. *Population*

58. Aduen PA, Kofler MJ, Sarver DE, et al. ADHD, depression, and motor vehicle crashes: A prospective cohort study of continuously-monitored, real-world driving. J Psychiatr Res. 2018 Jun;101:42-9. doi: 10.1016/j.jpsychires.2018.02.026. PMID: 29547761. *Population*

59. Aebi M, Kuhn C, Banaschewski T, et al. The contribution of parent and youth information to identify mental health disorders or problems in adolescents. Child and Adolescent Psychiatry and Mental Health. 2017;11(1). doi: 10.1186/s13034-017-0160-9. *Population*

60. Aebi M, Winkler Metzke C, Steinhausen HC. Accuracy of the DSM-oriented attention problem scale of the child behavior checklist in diagnosing attention-deficit hyperactivity disorder. J Atten Disord. 2010 Mar;13(5):454-63. doi: 10.1177/1087054708325739. PMID: 19372495. *Language*

61. Aevi Genomic Medicine L, a Cerecor company, Inc C. PART A: Efficacy and Safety of AEVI-001 in Children and Adolescents With ADHD and With mGluR Mutations. 2017. *Power*

62. Aflalo J, Caldani S, Acquaviva E, et al. Pilot study to explore poor visual searching capabilities in children with ADHD: a tablet-based computerized test battery study. Nord J Psychiatry. 2023 Jan 4:1-7. doi: 10.1080/08039488.2022.2162122. PMID: 36598162. *Outcome*

63. Agarwal V, Sitholey P, Kumar S, et al. Double-blind, placebo-controlled trial of clonidine in hyperactive children with mental retardation. Ment Retard. 2001 Aug;39(4):259-67. doi: 10.1352/0047-6765(2001)039<0259:Dbpcto>2.0.Co;2. PMID: 11448249. *Power*

64. Aggarwal SS, Ott SD, Padhye NS, et al. Clinical and demographic predictors of concussion resolution in adolescents: A retrospective study. Appl Neuropsychol Child. 2019 Jan-Mar;8(1):50-60. doi: 10.1080/21622965.2017.1381099. PMID: 29058480. *Intervention*

65. Aggarwal SS, Ott SD, Padhye NS, et al. Sex, race, ADHD, and prior concussions as predictors of concussion recovery in adolescents. Brain Inj. 2020 May 11;34(6):809-17. doi: 10.1080/02699052.2020.1740942. PMID: 32200661. *Intervention*

66. Aggensteiner PM, Albrecht B, Strehl U, et al. Can Neurophysiological Markers of Anticipation and Attention predict ADHD severity and Neurofeedback Outcomes? Biol Psychol. 2021 Aug 17:108169. doi: 10.1016/j.biopsycho.2021.108169. PMID: 34416347. *Intervention*

67. Agha SS, Zammit S, Thapar A, et al. Maternal psychopathology and offspring clinical outcome: A four-year follow-up of boys with ADHD. European Child & Adolescent Psychiatry. 2017 Feb 2017;26(2):253-62. *Intervention*

68. Aghaee MH, Tarkhan M. A comparative study of effectiveness of medicinal therapy and combined therapy (cognitive–behavioral and drug) of students

diagnosed with attention deficit hyperactivity disorder (ADHD). Bali Med J. 2017;6(1):82–9. *Power*

69. Aghebati A, Gharraee B, Hakim Shoshtari M, et al. Triple p-positive parenting program for mothers of ADHD children. Iran J Psychiatry Behav Sci. 2014 Spring;8(1):59-65. PMID: 24995031. *Power*

70. Agnew-Blais JC, Belsky DW, Caspi A, et al. Polygenic Risk and the Course of Attention-Deficit/Hyperactivity Disorder From Childhood to Young Adulthood: Findings From a Nationally Representative Cohort. J Am Acad Child Adolesc Psychiatry. 2021 Sep;60(9):1147-56. doi: 10.1016/j.jaac.2020.12.033. PMID: 33440202. *Intervention*

71. Agnew-Blais JC, Polanczyk GV, Danese A, et al. Evaluation of the Persistence, Remission, and Emergence of Attention-Deficit/Hyperactivity Disorder in Young Adulthood. JAMA Psychiatry. 2016 Jul 1;73(7):713-20. doi: 10.1001/jamapsychiatry.2016.0465. PMID: 27192174. *Population*

72. Agnew-Blais JC, Polanczyk GV, Danese A, et al. Young adult mental health and functional outcomes among individuals with remitted, persistent and late-onset ADHD. Br J Psychiatry. 2018 Sep;213(3):526-34. doi: 10.1192/bjp.2018.97. PMID: 29957167. *Intervention*

73. Agnew-Blais JC, Polanczyk GV, Danese A, et al. Are changes in ADHD course reflected in differences in IQ and executive functioning from childhood to young adulthood? Psychol Med. 2020 Dec;50(16):2799-808. doi: 10.1017/s0033291719003015. PMID: 31718730. *Design*

74. Agnew-Blais JC, Wertz J, Arseneault L, et al. Mother's and children's ADHD genetic risk, household chaos and children's ADHD symptoms: A gene-environment correlation study. J Child Psychol Psychiatry. 2022 Oct;63(10):1153-63. doi: 10.1111/jcpp.13659. PMID: 35833717. *Intervention*

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Appendix C. Evidence Tables

Table C.1. KQ1 evidence table

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Abramov, 2019[111] Case series N = 39 Brazil Setting: N/A	**Target:** Boys with ADHD and without a history of chronic diseases, no suspicion of psychiatric disorders other than ADHD, no use of any psychotropic medicines for at least 30 days, IQ equal or lower than 80, no less than 6 hours of regular sleep, no report of somnolence **Other:** Typically developing boys **ADHD presentation:** N/A **Diagnosed by:** Researcher **Comorbidity:** N/A **Female:** 0% **Age mean:** 11.52 **Min age:** 10 **Max age:** 13 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Classified as ADHD in accordance with the DSM-IV-TR Timing: Prior diagnosis	**Index test:** EEG EEG EP Attentional Network Test with recordings of event-related potentials from themid-frontal,mid-parietal, right frontal, and central scalp areas (C3-C4, F8, F4, Fz, Pz) for a biological classification using the clustering of variables method. 80/20 train/test split repeated 100 times Sensitivity: 89 Specificity: 75 Accuracy: 82	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Adams, 2009[112] Case series N = 35 US Setting: Specialty care	**Target:** Boys diagnosed with ADHD recruited through newspaper advertising, children with comorbidities excluded **Other:** Children volunterred from local elementary and middle schools recruited by sending a letter home to parents **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 0% **Age mean:** 10.1 (1.74) for the ADHD group, 10.5 (0.89) for the control group **Min age:** 8 **Max age:** 14 **Ethnicity:** % White : 100 **Reference standard:** Clinical diagnosis Diagnoses provided by licensed mental health professionals or pediatric physicians and parents provided consent to have medical records reviewed for confirmation of diagnosis, Behavior Assessment System for children (BASC) Monitor parent rating Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT Virtual Classroom, virtual reality continuous performance test including visualand/or auditory distracters; logistic regression with percent correct as the predictor (difference between ADHD and control groups trended toward significance) Sensitivity: 50 Specificity: 88 Accuracy: 68	**Index test 2:** Neuropsychological,CPT The Vigil continuous performance test; logistic regression with percent correct as the predictor (no statistically significant difference between ADHD and control groups) Sensitivity: 50 Specificity: 69 Accuracy: 59	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Ahmadi, 2021[115] Case series N = 40 Iran Setting: Specialty care	**Target:** Right handed children with ADHD and no history of any neurofeedback, any other neuro-modulation treatment, or treatment with methylphenidate **Other:** Healthy children **ADHD presentation:** inattentive : 48,combined : 52 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 36% **Age mean:** ADHD-C 8.5 (0.7), ADHD-I 8.75 (0.65), control 8.92 (1.38) **Min age:** 6 **Max age:** 11 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Swanson, Nolan, and Pelham IV questionnaire parent and teacher ratings. The child behavior checklist completed by parents. The final diagnosis of the children was independently performed by a child psychologist and a child psychiatrist who both were blinded to the previous findings. Timing: Prior diagnosis	**Index test:** EEG EEG eyes open resting-state; spatial and frequency band feature extraction andclassification done using deep convolutional neural network; combination of beta 1, beta 2, and gamma bands used for classification. 5 times 5-fold cross validation Sensitivity: 99 Specificity: 99 Accuracy: 99 Rater agreement: Comparison of model accuracy with expected accuracy (chance level) 0.99	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Algorta, 2016[117] Case series N = 18,232 UK Setting: Other	**Target:** Children with ADHD; data from The British Child and Adolescent Mental Health Survey 1999 **Other:** Children without ADHD **ADHD presentation:** inattentive : 27,hyperactive : 8,combined : 65 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 18% **Age mean:** Mean and SD reported by subtype - ADHD-C= 10.02 (3.09) / ADHD- I = 10.07 (2.81) / ADHD-H = 9.32 (2.92) **Min age:** 5 **Max age:** 15 **Ethnicity:** % White : 89 **Reference standard:** Clinical diagnosis Trained child and adolescent psychiatrists reviewed both the verbatim accounts and the answers to the Development and Well-Being Assessment; unmodified DSM-IV current rather than life-time diagnostic criteria used Timing: Later diagnosis	**Index test:** Parent rating SDQ (Strengths and Difficulties Questionnaire) Range 0.81-0.96 for hyperactivity/inattention, conduct problems and total difficulties scales in male and female subsamples and at different age ranges	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Alloway, 2009[119] Case series N = 91 UK Setting: School	**Target:** Children who score in the normal range on the Developmental, Diagnosticand Dimensional Interview, a computerized assessment for autistic spectrum disorders; all receiving stimulants but were taken off 24 hours prior to testing **Other:** Healthy typically developing children and children with low working memory; age-matched to within 60 days (plus or minus 30 days) of children in the ADHD group **ADHD presentation:** combined : 100 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 13% **Age mean:** 9.75 (1.0) for the ADHD group, 9.91 (0.92) for the working memory-impared group, 9.91 (0.92) for the typically developing group **Min age:** 8 **Max age:** 11 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Comprehensive clinical diagnostic assessment by pediatric psychiatrists and community pediatricians Timing: Concurrent	**Index test:** Teacher rating scale CTRS (Conners' Teacher Rating Scale) short form; discriminant function analysis ADHD index Sensitivity: 72 Specificity: 95	**Index test 2:** Teacher rating scale BRIEF (Behavior Rating Inventory of Executive Function) teacher rating; discriminant function analysis all three indices Sensitivity: 78 Specificity: 90	**Index test 3:** Teacher rating scale WMRS (Working Memory Rating Scale) teacher rating; discriminant function analysis Sensitivity: 82 Specificity: 100	**Index text 4:** Neuropsycholog ical,CPT,EF Conners K test (Conners' Continuous Performance Test) to assess performance on a vigilance task, discriminant function analysis Sensitivity: 41 Specificity: 65

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Altınkaynak, 2020[120] Case series N = 46 Turkey Setting: Specialty care	**Target:** ADHD referrals from university hospital psychiatry department, drug-naïve, without neurological conditions or hearing problems, right-handed **Other:** Healthy controls with no neurological, endocrine or psychiatric illness, and normal hearing function **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 30.4% **Age mean:** 9.09 (1.62) for ADHD group, 9.13 (1.63) for control group **Min age:** 7 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Psychiatrists used DSM-IV to diagnose patients with ADHD Timing: Prior diagnosis	**Index test:** EEG EEG time and frequency analysis of Event Related Potentials (ERP) obtained from EEGsignals while participants performed an auditory oddball task; multilayer Perception classifier, leave-one out cross validation Sensitivity: 91 Specificity: 91 Accuracy: 91 AUC: 0.91 Rater agreement: Inter-rater reliability for the classifier ICC 0.82	**Index test 2:** EEG EEG time and frequency analysis of Event Related Potentials (ERP) obtained from EEGsignals while participants performed an auditory oddball task; support vector machine (SVM) classifier, leave-one out cross validation Sensitivity: 95 Specificity: 82 Accuracy: 89 AUC: 0.89 Rater agreement: Inter-rater reliability for the classifier ICC 0.78	**Index test 3:** EEG EEG time and frequency analysis of Event Related Potentials (ERP) obtained from EEGsignals while participants performed an auditory oddball task; naïve Bayes classifier, leave-one out cross validation Sensitivity: 86 Specificity: 86 Accuracy: 87 AUC: 0.94	**Index text 4:** EEG EEG time and frequency analysis of Event Related Potentials (ERP) obtained from EEGsignals while participants performed an auditory oddball task; k-nearest neighbor classifier, leave-one out cross validation Sensitivity: 91 Specificity: 82 Accuracy: 87 AUC: 0.89 Inter-rater reliability for the classifier Kappa: 0.73

Amado-Caballero, 2020[121] Case series N = 148 Spain Setting: N/A	**Target:** Participants diagnosed with combined ADHD according to the DSM-5, none have taken medication **Other:** Healthy children **ADHD presentation:** combined : 100 **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** % N/A **Age mean:** N/A **Min age:** 6 **Max age:** 15 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Clinicians diagnosis using DSM-5 Timing: Prior diagnosis	**Index test:** Clinician tool,Activity ActiGraph GT3x device placed in wrist of patient, data of physical activity and sedentary activity in a 24 hour period used to develop Convolutional Neural Network (CNN) able to diagnose combined ADHD from actigraphic record. 70/30 train/test split used for validation. Sensitivity: 98 70%/30% train/test with 300 second window size Specificity: 100 70%/30% train/test with 300 second window size Accuracy: 99 70%/30% train/test with 300 second window size AUC: 0.9993 70%/30% train/test with 300 second window size PPV: 100 70%/30% train/test with 300 second window size NPV: 98 70%/30% train/test with 300 second window size LR+: 21 LR-: 0.0238 70%/30% train/test with 300 second window size	N/A	N/A	N/A
Arjona, 2023[124] Arjona Valladares, 2020[662] Case series N = 63 Spain Setting: N/A	**Target:** Participants from two different clinical services; stopped taking medication 48 hours before testing **Other:** Recruited from public schools; parents or tutors did not report any neurological disease or psychological impairment **ADHD presentation:** inattentive : 35,hyperactive : 3,combined : 62	**Index test:** EEG Combination of EEG recorded during delayed match-to-sample task, Event-Related Spectral Perturbation(ERSP) values; behavioral data, early Theta, and late Alpha Event-Related Synchronization (ERS) included in model, linear discriminant	**Index test 2:** EEG EEG recorded during delayed match-to-sample task, Event-Related Spectral Perturbation (ERSP) values; early Theta and late Alpha Event-Related	**Index test 3:** EEG EEG recorded during delayed match-to-sample task, Event-Related Spectral Perturbation (ERSP) values;	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Diagnosed by: Specialist **Comorbidity:** N/A **Female:** 24% **Age mean:** 10.89 (3.43) for the ADHD group, 10.8 (3.01) for the normodevelopment group **Min age:** 6 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Only those patients with a diagnostic agreement between the filled-by parents or tutors DuPaul questionnaire and the clinical interview were included in the study; diagnosis was supported by the Conners Rating Scale and Nesplora Aula Timing: Prior diagnosis	analysis, ADHD vs normodevelopmental, leave-one-out cross validation Sensitivity: 76 Specificity: 74	Synchronization (ERS) included in model, linear discriminant analysis, ADHD vs normodevelopmental, leave-one-out cross validation Sensitivity: 76 Specificity: 59	behavioral data (Reaction Time, Standard Deviation of Reaction Time, and Correct Responses) included in model, linear discriminant analysis, ADHD vs normodevelopmental, leave-one-out cross validation Sensitivity: 66 Specificity: 65	

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Bansal, 2012[28] Case series N = 83 US Setting: Specialty care	**Target:** Children with no lifetime diagnosis of Obsessive Compulsive Disorder, Tourette Syndrome, or Tic disorder, and no premature birth (gestation=<36 weeks); recruited through the general outpatient clinic at the Yale Child Study Center or through advertisements with a local chapter of Children with Attention Deficit Disorder **Other:** Healthy children with no lifetime or current DSM-IV Axis 1 or 2 disorder; IQ>=80 **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 19.5% **Age mean:** 12.6 (3.18) for ADHD group, 10.5 (2.43) healthy children **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed with ADHD, diagnostic assessments were supplemented using the Conners ADHD Parent, Teacher Rating Scales, and the DuPaul-Barkley ADHD rating scale Timing: Prior diagnosis	**Index test:** Imaging sMRI brain imaging; semi-supervised: applied leave-one-out cross validation to select a set of features that differed significantly between groups of individuals who were already clinically diagnosed and hierarchical clustering to the feature vectors to discover naturalistic groupings of individuals in the dataset; 10 independent split-half replication analyses and leave-one-out cross-validation Sensitivity: 94 ADHD children from healthy children Specificity: 89 ADHD children from healthy children	N/A	N/A	N/A

Bard, 2013[134] Case series N = 587 US Setting: School	**Target:** Participants were urban, suburban, and rural students; all high screening in Vanderbilt ADHD Diagnostic Teacher Rating Scale **Other:** Participants were initially recruited from 41 elementary schools in 5 Oklahoma school districts including urban, suburban, and rural students; only a probability proportional-by-size subsample of low-screen (Vanderbilt ADHD Diagnostic Teacher Rating Scale **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** % 29% female in entire sample **Age mean:** **Min age:** 5 **Max age:** 15 **Ethnicity:** % Hispanic or Latino : 9 % Black/African American : 15 % American Indian or Alaska Native : 8 % White : 64 Other : 4 **Reference standard:** Clinical diagnosis ADHD Case Definition required a Diagnostic Interview Schedule for Children-IV (DISC-IV-P) diagnostic indication of ADHD, 4+ inattention, or 4+ hyperactive/impulsive symptoms from the Vanderbilt ADHD Diagnostic Teacher Rating Scale (VADTRS) teacher screen, and 1+ impairment symptoms from the VADTRS Timing: Concurrent	**Index test:** Parent rating VADPRS (Vanderbilt ADHD Diagnostic Parent Rating Scale) Sensitivity: 80 Specificity: 75 PPV: 19 NPV: 98 Rater agreement: A kappa coefficient of agreement between risk classifiers (>5 symptoms for inattention and for hyperactive) Pearson correlation: VADPRS counts versus DISC-IV-P counts; inattention r=0.69 (95% CI: 0.61, 0.77), hyperactive/impulsive r=0.66 (95% CI: 0.52, 0.80) Kappa: Subtype risk kappa inattention 0.75 (95% CI: 0.48, 1.00), hyperactive/impulsive 0.82 (95% CI: 0.59, 1.00) Internal consistency: Cronbach's alpha: Inattention 0.94 (95% CI: 0.93, 0.96), Hyperactive/impulsive 0.93 (95% CI: 0.92, 0.95) Alpha: A second VADPRS was collected from a small subset of the parents interviewed, the majority of these second screens (24 of the 28) were collected from parents whose children obtained high teacher screening scores on the Vanderbilt ADHD Diagnostic Teacher R Test-retest: Correlations in a high risk sample were .91 for inattention, .92 for hyperactive/impulsive, .95 for conduct/oppositional, .87 for	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
		anxiety/depression, .82 for performance subscales			

Barkley, 1994[135] Case series N = 47 US Setting: Mixed	**Target:** Children recruited from consecutive referrals to the outpatient clinics of the Departments of Psychiatry and Pediatrics with complaints of short attention span, impulsivity, and overactivity at school as reported by mothers, a duration of these problems of 6 months, and an age of onset of these problems before 7 years; IQ>=80; not on medication or stopped medication 48 hours prior to testing **Other:** Children with learning disabilities obtained either from referrals to a Learning Problems Clinic in the Department of Pediatrics or from newspaper ads soliciting families with children in school programs for children with LD; neurotypical developing child **ADHD presentation:** inattentive : 50,combined : 50 **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 0% **Age mean:** 9.2 (1.3) for the ADD with hyperactivity group, 9.1 (1.4) for the ADD without hyperactivity group, 9.9 (1.5) for the learning disabled group, 9.1 (1.4) for the neurotypical group **Min age:** 6 **Max age:** 11 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Teacher ratings on the Child Attention Profile and parent ratings on the Child Behavior Checklist, clinical diagnosis using DSM-III-R criteria Timing: Concurrent	**Index test:** Neuropsychological,CPT Continuous Performance Test number correct, cutoff score 36, ADD groups combined PPV: 92 NPV: 63	**Index test 2:** Neuropsychological,EF Controlled Oral Word Association verbal fluency F-A-S test, cutoff score 13, ADD groups combined PPV: 90 NPV: 59	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Berger, 2010[141] Hadassah Medical Organization, 2008[810] Case series N = 58 Israel Setting: Specialty care	**Target:** Children were drug naïve; no mental retardation, chronic condition other than ADHD, chronic use of medications, or diagnosis of depression, anxiety or psychosis **Other:** Healthy children without any symptoms or signs of ADHD **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 29% **Age mean:** 9.86 (1.89) in the ADHD group, 10.50 (1.81) in the control group **Min age:** 6 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD diagnosis was established by a certified pediatric neurologist based on DSM-IV-TR criteria Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT Computerized continuous performance functions test, which includes a multi-task approach Sensitivity: 100 Test of reliability, percentage of true positive results amont the 45 children with ADHD Accuracy: 95	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Berger, 2017[140] Case series N = 798 US Setting: N/A	**Target:** Participants referred to the outpatient pediatric clinics of a neurocognitive center; drug-naïve; no intellectual disability, other chronic condition, chronic use of medications, or primary psychiatric diagnosis **Other:** Randomly recruited typically developed children who study in regular classes at primary schools **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 39.5% **Age mean:** 9.27 (1.65) in ADHD group, 9.71 (1.64) in control group **Min age:** 7 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Child met the criteria for ADHD according to DSM- IV- TR, as assessed by a certified pediatric neurologist Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT MOXO-Continuous Performance Test (CPT) Total Score including 4 indices: attention, timing, hyperactivity, and impulsivity for all age groups AUC: 0.92 0.91-0.96 over the 6 age groups	**Index test 2:** Neuropsychological MOXO-Continuous Performance Test (CPT) Total Score including 4 indices: attention, timing, hyperactivity, and impulsivity for 12 year old participants AUC: 0.92 (0.85, 0.98)	**Index test 3:** Neuropsychological MOXO-Continuous Performance Test (CPT) Timing for 12 year old participants; number of correct responses given while the target stimulus is still presented on the screen AUC: 0.80 (0.71, 0.89)	**Index text 4:** MOXO-Continuous Performance Test (CPT) Hyperactivity for 12 year old participants; the number of all types of commission responses that are not coded as impulsive responses AUC: 0.82 (0.73, 0.91)

Bergeron, 2017[142] Case series N = 447 Canada Setting: Mixed	**Target:** Adolescents living in the Montreal urban area selected in regular classrooms from 4 secondary schools reflecting heterogeneous socioeconomic levels and adolescents from youth centers, specialised psychiatric clinics, inpatient units, and day treatment centers **Other:** Adolescents living in the Montreal urban area selected in regular classrooms from 4 secondary schools reflecting heterogeneous socioeconomic levels and adolescents from youth centers, specialised psychiatric clinics, inpatient units, and day treatment cen **ADHD presentation:** N/A **Diagnosed by:** Researcher **Comorbidity:** N/A **Female:** % 44% in the school subsample and 57% in the clinical subsample **Age mean:** **Min age:** 12 **Max age:** 15 **Ethnicity:** N/A **Reference standard:** Other Interview supported by Schedule for Affective Disorders and Schizophrenia for School-Aged Children (KIDDIE-SADS) Timing: Concurrent	**Index test:** Teen/child self report DIA-R (Dominic Interactive for Adolescents-Revised, ADHD scale 18 items, cutoff >=10 Sensitivity: 86 (62, 100) Specificity: 70 (65, 74) AUC: 0.85 (0.78, 0.92) LR+: 2.8 (2.0, 3.6) Internal consistency: Cronbach's alpha: >0.80 for the total sample Evaluated twice, 7 to 15 days apart (mean = 9.5, SD = 3.28) Test-retest: Total sample ICC 0.84 (95% CI 0.81, 0.87); school subsample ICC 0.84 (95% CI 0.80, 0.87); clinical subsample ICC 0.82 (95% CI 0.77, 0.86) Temporal stability:	N/A	N/A	N/A
Beriha, 2018[143] Case series N = 297 India Setting: School	**Target:** Children diagnosed with ADHD **Other:** Children with anxiety, depression, or conduct disorder,and neurotypical children from same recruitement process as ADHD group **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A	**Index test:** EEG EEG recording during visual attention and mental task, extraction of 4 non-linearfeatures combined with symptoms important for differentiation of psychiatric disorders, particle swarm optimization tuned back propagation neural network (PSO-BPNN) classifier	**Index test 2:** EEG EEG recording during visual attention and mental task, extraction of four non-linear features combined with symptoms important for differentiation of psychiatric disorders, particle swarm	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Female: % N/A **Age mean:** N/A **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Eexperts used the DSM-V to determine diagnosis ADHD, anxiety, depression, conduct disorder, and control Timing: Prior diagnosis	Sensitivity: 100 Specificity: 100 Accuracy: 100	optimization tunedradial basis function (PSO-RBF) classifier Sensitivity: 90 Specificity: 89 Accuracy: 97		

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Bledsoe, 2020[152] Case series N = 35 US Setting: N/A	**Target:** Participants with ADHD without other psychiatric or psychological disorder, IQ>=80, 24- to 48-hr washout period prior to testing and not taking any other medications during testing **Other:** Healthy age and IQ matched typically developing children.; all participants were recruited from a diversity of socioeconomic status (SES) and ethnic backgrounds to control for potential group differences **ADHD presentation:** combined : 100 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 26% **Age mean:** N/A **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Participants were diagnosed with ADHD-C using the Diagnostic Interview Schedule for Children–IV–Parent Version (DISC-IV-P) with agreement between two investigators Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT Support vector machine classification using Conners Global Index-Restless/ Impulsivecomposite score and d2 Test of Attention/Concentration total score; leave-one-(participant)-out cross-validation Sensitivity: 100 After leave-one-(participant)-out cross-validation Specificity: 100 After leave-one-(participant)-out cross-validation Accuracy: 100 After leave-one-(participant)-out cross-validation	**Index test 2:** Neuropsychological,CPT Support vector machine classification using Behavior Assessment System for Children- 2nd edition hyperactivity scale and d2 Test of Attention/Concentration total score. Leave-one-(participant)-out cross-validation. Sensitivity: 100 After leave-one-(participant)-out cross-validation Specificity: 96 After leave-one-(participant)-out cross-validation Accuracy: 97 After leave-one-(participant)-out cross-validation	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Bloch, 2012[153] Case series N = 34 Israel Setting: Specialty care	**Target:** Children referred by a neurologist or a child psychiatrist for a neurocognitive evaluation for ADHD; no known diagnosis of mental retardation or major psychopathology **Other:** Children referred by a neurologist or a child psychiatrist for a neurocognitive evaluation in order to substantiate a possible diagnosis of ADHD; for 7 patients, the diagnosis of ADHD was excluded (patients were subsequently diagnosed, two with dysthymia, **ADHD presentation:** N/A **Diagnosed by:** Researcher **Comorbidity:** N/A **Female:** 44% **Age mean:** 11.5 **Min age:** 7 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Clinical diagnosis of ADHD was based on consensus between the research team based on SNAP–IV, DAWBA, and clinical interview all based on DSM-IV criteria. Timing: Concurrent	**Index test:** Neuropsychological,CPT TOVA (Test of Variables of Attention) Sensitivity: 63 Specificity: 85 PPV: 94 NPV: 37	**Index test 2:** Neuropsychological,EF Subtests of The Cambridge Neuropsychological Test Automated Battery (CANTAB) Sensitivity: 57% for Working Memory, Spatial Working Memory, 71% for Stocking of Cambridge, and 71% for Cognitive Set-Shifting-Intradimensional/ Extradimensional Shift subtests Specificity: 22% for Working Memory, Spatial Working Memory, 11% for Stocking of Cambridge, and 7% for Cognitive Set-Shifting-Intradimensional/ Extradimensional Shift subtests	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Boroujeni, 2019[157] Case series N = 76 Iran Setting: Specialty care	**Target:** Children who had come to doctor Mohammad Behdad (neurologist) clinic for EEG signal recording **Other:** Typically developing children **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 26% **Age mean:** **Min age:** 4 **Max age:** 15 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis confirmed by neurologist using DSM-IV criteria Timing: Concurrent	**Index test:** EEG Combination of EEG signals obtained during eyes open, eyes closed, and a Continuous PerformanceTest (CPT), combination of non-linear features, support vector machine (SVM) classification, 70/30 training/testing split. Best results obtained from combination of correlation dimension and fractal dimension in FP2 channel, and correlation dimension and sample entropy in Fz channel. Sensitivity: 98 Specificity: 92 Accuracy: 96	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Boucugnani, 1989[159] Case series N = 56 US Setting: N/A	**Target:** Children with ADHD and free of medication at least 16 hours before testing **Other:** Age and gender-matched neurotypical developing children; identified by teacher report as achieving on grade level or above and as experiencing no significant behavioral or attentional problems in the classroom **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 14% **Age mean:** **Min age:** 7 **Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis made by a psychologist, physician, or psychiatrist using DSM-III criteria and Child Behavior Checklist Inattentive subscale, Bristol Social Adjustment Guides Inconsequence scale, and the Connors Rating Scale Hyperativity Index parent or teacher rating	**Index test:** Neuropsychological,EF Variables in multivariate linear equation included Trail-Making test- Part B and the Wisconsin Card Sorting Test perseverative responses, failure to maintain set, and perseverative errors; stepwise discriminant function analysis Accuracy: 79	N/A	N/A	N/A

Breaux, 2016[162] Case series N = 168 US Setting: Primary Care	**Target:** Children presenting with elevated levels of externalizing problems at age 3 and were diagnosed with ADHD or ADHD+ODD at age 6; no intellectual disability, deafness, blindness, language delay, cerebral palsy, epilepsy, autism, and/or psychosis **Other:** Children presenting with elevated levels of externalizing problems at age 3 who were not not diagnosed with ADHD at age 6; 13% of participants diagnosed with ODD only **ADHD presentation:** inattentive : 8,hyperactive : 17,combined : 75 **Diagnosed by:** Other (specify) Graduate student **Comorbidity:** N/A **Female:** 38.67% 16 ADHD only, 13 ADHD + ODD **Age mean:** NA **Min age:** 3 **Max age:** 6 **Ethnicity:** % Hispanic or Latino : 22.6,Other : predominately Puerto Rican % Black/African American : 10.1 % White : 53.6 % Multiracial : 13.7 **Reference standard:** Clinical diagnosis Trained psychology graduate students assigned diagnoses of ADHD and ODD based on measures administered at age 6: Diagnostic Interview Schedule for Children–IV (NIMH DISC-IV), BASC (for mother, father, and teacher), and Disruptive Behavior Rating Scale (for mother and father) Timing: Concurrent	**Index test:** Neuropsychological,CPT,EF Battery of measures including NEPSY Statue, Present task, and the Conners Kiddie Continuous Performance Test ADHD Confidence Index plus hyperactivity/impulsivity and inattention symptoms at age 3 Sensitivity: 64 Specificity: 75 Accuracy: 70 AUC: PPV: 67 NPV: 72	**Index test 2:** CPT,EF Battery of measures including NEPSY Statue, Present task, and the Conners Kiddie Continuous Performance Test ADHD Confidence Index Sensitivity: 65 Specificity: 69 Accuracy: 67 PPV: 63 NPV: 71	**Index test 3:** Neuropsychological Delay Aversion: Present task Sensitivity: 55 Specificity: 66 PPV: 57 NPV: 64	**Index text 4:** Neuropsychological,CPT Inhibition/Attention: K-CPT ADHD Confidence Index; produced by a discriminant function analysis consisting of percent omissions, gender, age, standard error by ISI, hit reaction time, response style, attentiveness, and reaction time by block Sensitivity: 62 Specificity: 68 PPV: 61 NPV: 69

Bunte, 2013[167] Case series N = 251 Netherlands Setting: N/A	**Target:** Preschool children with externalizing behavioral problems and diagnosed with ADHD or disruptive behavior disorder plus ADHD; IQ>=70; no current medications **Other:** Typically developing children recruited from regular elementary schools and daycare centers **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** Other : sample with disruptive behavior or ADHD **Female:** 24% **Age mean:** mean 55 months (SD 7.8) **Min age:** 3.5 **Max age:** 5.5 **Ethnicity:** % Black/African American : 2 % Asian : 0.5 % White : 86 % Multiracial : 12,Other : Turkish/Moroccan **Reference standard:** Clinical diagnosis Clinical diagnosis made by child psychiatrist and child psychologist Timing: Prior diagnosis	**Index test:** Clinician tool,Observation DB-DOS (Disruptive Behavior Diagnostic Observation Schedule) observational assessment method, differentiates examiner and parent context, coding system for behavior problems consists of problems in the domains of Behavior Regulation (15 items) and Anger Modulation (6 items); Competence scale not used Sensitivity: 87 Specificity: 79 AUC: 0.92 (0.88, 0.96) Rater agreement: Interrater reliability between researchers administering test range 0.88–0.95 across domains and range 0.86–0.97 across contexts ICC: 0.92 Internal consistency: range 0.77–0.91 across domains and 0.69–0.94 across contexts Alpha: 0.82 ICC; children retested after 8 weeks Test-retest: 0.64 Temporal stability: range.059–0.71 across domains and 0.52–0.80 across contexts	N/A	N/A	N/A
Burton, 2019[168] Case series N = 15560 Canada Setting: Mixed	**Target:** Population-based sample with reported diagnosis of ADHD, ADHD clinic sample children and adolescents diagnosed with ADHD by a psychiatrist and clinical psychologist and IQ>=80 **Other:** Population-based sample: did not report a diagnosis of ADHD. Clinic sample (validation sample): children	**Index test:** Parent rating zSWAN (standarized Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Rating Scale) parent rating, optimal cut-point >0.74. Cut-point created using population-based sample tested using validation sample,	**Index test 2:** Teen/child self report zSWAN (standardized Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Rating Scale) self report, optimal cut-point >0.81, self-	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	and adolescents not diagnosed with ADHD, IQ>=80 **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 26.23% 21.43% in validation sample **Age mean:** 11.0 (2.8) 9.1 (2.2) in validation sample **Min age:** 6 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis The Validation ADHD Group diagnoses were based on consensus between a psychiatrist and clinical psychologist following assessment; in the community sample the group was previously diagnosed with ADHD Timing: Prior diagnosis	standardized for age, gender, and respondent Sensitivity: 82 84% in clinical validation sample Specificity: 81 92% in clinical validation sample AUC: 0.88 Internal consistency: Alpha: 0.95	reports done by adolescents ages 13-17 from population-based sample only standardized for age, gender, and respondent Sensitivity: 57 Specificity: 81 AUC: 0.71 Alpha: 0.88		

Bussing, 1998[169] Case series N = 499 US Setting: School	**Target:** Total special education population in one school district with 70% participation rate **Other:** Other special ed students. (See above). **ADHD presentation:** inattentive : 18,hyperactive : 14,combined : 40 **Diagnosed by:** Researcher **Comorbidity:** Learning disability : Special education students,N/A **Female:** 28% **Age mean:** 9.7 (1.0) **Min age:** 7 **Max age:** 12 **Ethnicity:** % White : 51 Other : 49% "non-white" **Reference standard:** Clinical diagnosis ADHD per DSM IV diagnosis Timing: Concurrent	**Index test:** Parent rating ADDES (Attention Deficit Disorders Evaluation Scale), parent rating (data for 15th percentile) Sensitivity: When administered two months before DISC for DSM IV, sensitivity was 58% (SE 3.8%) to discriminate from other special ed students. Specificity: When administered two months before DISC for DSM IV, specificity was 82% (SE 1.9%) to discriminate from other special ed students. Accuracy: 73 "Efficiency" = 73% at 2 months before DSM-IV administered. Data is for 15th percentile on ADDES PPV: When administered two months before DISC for DSM IV, PPV was 64% (SE 0,5%) to discriminate from other special ed students. NPV: When administered two months before DISC for DSM IV, NPV was 77% (SE 3.4%) to discriminate from other special ed students.	**Index test 2:** Parent rating ASQ (Conners Abbreviated Symptom Questionnaire), parent ratingData abstracted for60 T score Sensitivity: When administered simultaneous with DSM IV, sensitivity was 84% (SE 3%) to discriminate from other special ed students. Specificity: When administered simultaneous with DISC for DSM IV, specificity was 71% (SE2.2%) %) to discriminate from other special ed students. Accuracy: 76% "efficiency" when administered simultaneous with DISC for DSM IV, 76% "efficiency" to discriminate from other special ed students. PPV: When administered simultaneous with DISC for DSM IV, PPV was 61% (SE 4%) to discriminate from other special ed students. NPV: When administered simultaneous with DISC for DSM IV, NPV was 89% (SE 3%) to discriminate from other special ed students.	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Canivez, 2016[170] Case series N = 40 US Setting: School	**Target:** Children with ADHD **Other:** Control group children randomly selected and attempted matching of sex, age, race, and special education classification **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 20% **Age mean:** 6.60 (1.14) for ADHD group, 7.45(0.51) for control group **Min age: Max age:** **Ethnicity:** % Hispanic or Latino : 2.5 % White : 77.5 % Multiracial : 15 Other : 5% No response for race/ethnicity **Reference standard:** Clinical diagnosis Diagnostic and Statistical Manual of Mental Disorders (4th ed., text rev.; DSM- IV-TR) criteria for ADHD Timing: Prior diagnosis	**Index test:** Neuropsychological,EF DN:CAS (Das–Naglieri Cognitive Assessment System), a test of cognitive abilities basedon the Planning, Attention, Simultaneous, and Successive Theory Sensitivity: 80 Specificity: 75 Accuracy: 78 AUC: 0.846 (0.722, 0.970) PPV: 76 NPV: 79 Rater agreement: Cognitive Assessment System discriminant function analysis classifications versus a priori diagnosis Kappa: 0.550	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Catherine Joy, 2021[172] Case series N = 10 India Setting: N/A	**Target:** Children specifically identified by professional psychiatrists **Other:** Children without ADHD from the same age group **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % N/A **Age mean:** N/A **Min age:** 7 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD identified by psychiatrists, using patient history and Vanderbilt ADHD assessment rating scale Timing: Prior diagnosis	**Index test:** EEG EEG eyes-open and eyes-closed resting state EEG, permutation entropy feature extractionand artificial neural network (ANN) classifier. Leave-one-out cross validation Sensitivity: 98 Specificity: 99 Accuracy: 99.82	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Caudal, 2011[260] Case series N = 112 France Setting: N/A	**Target:** Participants with ADHD, had to be without a parent who had a neurological disorder, excluded if the clinician decided that the child was clinically unsuitable as a candidate and/or if there were any contraindications to use the EIS system **Other:** Children without ADHD symptoms **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 26.92% **Age mean:** 8 **Min age:** 3 **Max age:** 18 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed with ADHD according to the DSM-IV and further examinations Timing: Prior diagnosis	**Index test:** Other (e.g., ECG) : Electro interstitial scans (EIS) Electro interstitial scans to measure bioimpedance Sensitivity: 80 Cutoff 7.4 micro Siemens Specificity: 98 Cutoff 7.4 micro Siemens AUC: 0.876 (0.823, 0.918)	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Chan, 2022[177] Case series N = 188 China Setting: Other	**Target:** Participants diagnosed with ADHD **Other:** Age- and gender-matched typically developing children without any reported diagnosis of developmental disorders, psychiatric disorders, and subjective complaints from parents on children's difficulty in attention or self-control; recruited through posting **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 28% **Age mean:** 9.55 (2.01) for the ADHD group, 9.56 (2.52) for the typically developing group **Min age:** 5 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed by a psychiatrist, pediatrician, or clinical psychologist at the Child Assessment Centre or at private clinics Timing: Prior diagnosis	**Index test:** Neuropsychological,EF Online assessment consisting of two temporal-order judgment tasks: one task used tone pairs presented with two interstimulus intervals (ISI) and the other task used pairs of consonant-vowel (CV) syllables with 20 varying ISI levels, participants were asked to determine the sequence of the sound pairs; hierarchical binary logistic regression using accuracy in ISI 40ms in the tone task and ISI passing threshold in the CV task, ROC analysis Sensitivity: 76 Specificity: 51 AUC: 0.67 (0.59, 0.75)	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Chang, 2019[179] Case series N = 60 Taiwan Setting: Specialty care	**Target:** Male participants with IQ > 80, did not receive any medication for ADHD testing, no history of epilepsy, mental retardation, drug abuse, head injury, or psychotic disorders **Other:** Age-matched controls **ADHD presentation:** combined : 100 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 0% **Age mean:** 8.4 (1.9) for ADHD group, 8.4 (1.7) for control group **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Swanson, Nolan, and Pelham (SNAP-IV) Teacher and Parent Rating Scale. Examined by a pediatric neurologist or psychiatrist. Timing: Prior diagnosis	**Index test:** EEG EEG quantitative EEG (qEEG), eyes closed, 21 electrodes for 20 minutes at a samplingrate of 256 Hz, electrodes arranged based on the international 10-20 system. Support vector machine (SVM) classification with 8 features, 10 fold cross validiation. Sensitivity: 80 Specificity: 80 AUC: 0.8778	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Chang, 2022[182] Case series N = 60 Taiwan Setting: Specialty care	**Target:** Participants had IQ>80, right-handedness, no history of brain injury, no known neurological or psychiatric conditions or comorbidities **Other:** IQ>80, right-handedness, no history of brain injury, no known neurological or psychiatric conditions or comorbidities **ADHD presentation:** N/A **Diagnosed by:** Provider **Comorbidity:** N/A **Female:** 20% **Age mean:** 6.7 (1.8) for the ADHD group, 6.4 (1.8) for the neurotypical group **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD assessed and confirmed by at least two pediatricians in clinical settings Timing: Prior diagnosis	**Index test:** EEG EEG signals recorded during eyes-open resting state and CPT (Conners K-CPT 2 or 3); EEG data segments including a period containing a fusion of resting state and cognitive execution used; long short-term memory (LSTM) network that utilizes deep learning techniques with learning the cognitive state transition to discriminate between ADHD and neurotypical children; leave-one-subject out and 10-fold cross validation Sensitivity: 90 Specificity: 91 Accuracy: 91	**Index test 2:** EEG EEG signals recorded during eyes-open resting state and CPT (Conners K-CPT 2 or 3); beta band, O2 electrode feature applied to the long short-term memory (LSTM) model with transition data; leave-one-subject out and 10-fold cross validation Accuracy: 86	**Index test 3:** EEG EEG signals recorded during eyes-open resting state and CPT (Conners K-CPT 2 or 3); beta band, O1 electrode feature applied to the long short-term memory (LSTM) model with transition data; leave-one-subject out and 10-fold cross validation Accuracy: 78	**Index text 4:** EEG EEG signals recorded during eyes-open resting state and CPT (Conners K-CPT 2 or 3); theta/beta ratio, Cz electrode feature applied to the long short-term memory (LSTM) model with transition data; leave-one-subject out and 10-fold cross validation

Chang, 2023[181] Case series N = 62 Taiwan Setting: Specialty care	**Target:** Children from a pediatric neurology clinical; unmedicated prior to the examination **Other:** Pediatric neurology clinical sample; patients without ADHD were diagnosed as having headache (11 patients), epilepsy (10 patients), dizziness (six patients), and tic disorders (four patients); age and sex-matched to ADHD patients **ADHD presentation:** inattentive : 26,combined : 74 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 48% **Age mean:** 7.7 (2.3) in the ADHD group, 7.8 (2.3) in the non-ADHD group **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Examined by a pediatric neurologist or psychiatrist, ADHD was diagnosed according to the DSM-V criteria, and ADHD severity was evaluated using the Swanson, Nolan, and Pelham Questionnaire, Fourth Edition (SNAP-IV) Timing: Concurrent	**Index test:** Clinician tool,Activity Smart chair containing piezoelectric material connected to a recording device to measure the movements of participants; recordings were performed during a routine visit; variance and zero-crossing rate with XGBoost classifier Sensitivity: 93 Highest performance among all combinations of feature set + classifier	**Index test 2:** Clinician tool,Activity Smart chair containing piezoelectric material connected to a recording device to measure the movements of participants; recordings were performed during a routine visit; variance, zero-crossing rate, and high energy rate with KNN classifier Sensitivity: Specificity: 95 Highest performance among all combinations of feature set + classifier Accuracy: 92 Highest performance among all combinations of feature set + classifier	**Index test 3:** Clinician tool,Activity Smart chair containing piezoelectric material connected to a recording device to measure the movements of participants; recordings were performed during a routine visit; variance with support vector machine classifier AUC: 0.98 Highest performance among all combinations of feature set + classifier	**Index text 4:** Sensitivity: Specificity: Accuracy: AUC: PPV: NPV: Rater agreement: Kappa: Internal consistency:
Charach, 2009[183] Case series N = 1,038 Canada Setting: Specialty care	**Target:** School children consecutively referred for diagnostic assessment of ADHD between May 1996 and February 2006 to an outpatient specialty clinic in a large pediatric hospital in Toronto; children taking stimulants stopped medication during 2 day teacher observation and 1 day clinician observation	**Index test:** Teacher rating scale CTRS-R (Conners' Teacher Rating Scale–Revised); T scores >=60 on the total symptoms subscale compared to clinical diagnosis Sensitivity: 82 (79, 85) Specificity: 48 (42, 54) LR+: 1.58 (1.41, 1.77)	**Index test 2:** Teacher rating scale CTRS-R (Conners' Teacher Rating Scale–Revised); T scores >=60 on the total symptoms subscale compared to having 6 inattentive and 6 hyperactive symptoms	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Other: Children not diagnosed with ADHD from the same referral process as the ADHD children **ADHD presentation:** inattentive : 43,hyperactive : 27,combined : 17 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 24.5% female in entire sample **Age mean:** 8.8 (2.1) **Min age:** 6 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Telephone Teacher Interview using DSM-IV criteria used as comparison to assess diagnostic accuracy of the CTRS-R. Children also received a diagnostic evaluation including the Parent Interview for Child Symptoms, the Wechsler Intelligence Scale for Children-III and -IV, Clinical Evaluation of Language Fundamentals-3, and the Wide Range Achievement Test-3 Timing: Later diagnosis	LR-: 0.37 (0.30, 0.45)	on the Telephone Teacher Interview Sensitivity: 94 (89, 96) Specificity: 32 (29, 35) LR+: 1.37 (1.29, 1.46) LR-: 0.20 (0.11, 0.36)		

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Chelune, 1986[184] Case series N = 48 US Setting: N/A	**Target:** Participants medication free for at least 16 hours prior to testing **Other:** Normal controls from previous study; matched for age, sex, and both maternal and paternal educational backgrounds **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 29% **Age mean:** 9.4 **Min age:** 6 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis The ADD subjects all met minimal DSM-III criteria for ADD as determned by their treating physicians. Parent and/or teacher Conners' Rating Scales were available on 19 of the ADD children (16 having both); two psychiatrists independently reviewed the ADD children's charts Timing:	**Index test:** Neuropsychological,EF Variables in the multivariate linearequation were the Wisconsin Card Sorting Test Persevarative Errors and Failures to Maintain Set, Color Forms Time and Errors, and the Kaufman Assessment Battery for Children Number Recall and Gestalt Closure; stepwise discriminant function analysis Accuracy: 85 Rater agreement: Two psychiatrists independently reviewed the ADD children's charts and made ratings on 5-point scales for 1) how well each child's clinical presentation fit with DSM-III criteria; and 2) response to medication Kappa: 0.71 for the pooled DSM-III ratings and 0.75 for the pooled medication response ratings	N/A	N/A	N/A

Chen, 1994[190] Doyle, 2000[743] Case series N = 260 US Setting: Mixed	**Target:** Males, met diagnostic criteria for current ADHD with active symptoms for which they were receiving treatment; excluded if they had been adopted or if their nuclear family was not available for study; no major sensorimotor handicaps (paralysis, deafness, blindness), psychosis, autism; IQ>80 **Other:** Children without ADHD selected from active outpatients at pediatric medical clinics; models valdiated using siblings of ADHD probands and pediatric comparison probands **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 0% **Age mean:** **Min age:** 6 **Max age:** 18 **Ethnicity:** % White : 100 **Reference standard:** Clinical diagnosis Kiddie Schedule for Affective Disorders and Schizophrenia, Epidemiologic version (SADS-E), interview with mother and direct interview with children older than 12 Timing: Prior diagnosis	**Index test:** Parent rating CBCL-A (Child Behavior Checklist) attention problems scale, T-score cutoff 55; logistic regression, split-half cross validation sample using ADHD and pediatric comparison probands Sensitivity: 84 Specificity: 93	**Index test 2:** Parent rating CBCL-A (Child Behavior Checklist) attention problems scale, T score cutoff of 55;logistic regression, validation using brothers of ADHD and pediatric comparison probands Sensitivity: 61 Specificity: 94 AUC: 0.855 PPV: 65 NPV: 93	**Index test 3:** Parent rating CBCL-A (Child Behavior Checklist) attention problems scale,T score cutoff of 55; logistic regression, validation using sisters of ADHD and pediatric comparison probands Sensitivity: 67 Specificity: 94 AUC: 0.902 PPV: 50 NPV: 97	**Index text 4:** Neuropsychological,CPT,EF Neuropsychological tests administered to ADHD and pediatric comparison probands at 4-year follow-up visit: Wechsler Intelligence Scale for Children-Revised (<17 years old) or Wechsler Adult Intelligence Scale-Revised (>=17 years old) Freedom from Distract Sensitivity: 76 2 of 7 tests abnormal Specificity: 46 2 of 7 tests abnormal AUC: 0.69 0.70 corrected for IQ PPV: 63 2 of 7 tests abnormal NPV: 62 2 of 7 tests abnormal
Chen, 2019[187] Case series N = 108 China	**Target:** Participants with IQ>80, drug naive, right-handed, no lifetime history of head trauma with loss of consciousness, no history of neurological illness or other severe	**Index test:** EEG EEG 10 minute eyes closed resting-state EEG using relative spectral power, spectralpower ratio, complexity analyses, and	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Setting: Mixed	disease, and no history of psychiatric disorders including schizophrenia, affective disorder and pervasive developmental disorder; recruited from an outpatient clinic at the Peking University Institute of Mental Health **Other:** Age, gender, and handedness-matched typically develpoing children recruited from a local school **ADHD presentation:** inattentive : 52,combined : 48 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 18% **Age mean:** 10.44 (0.75) for ADHD group, 10.92 (0.69) for control group **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis based on CDIS structured and interviewer-administered scale based on DSM-IV criteria Timing: Prior diagnosis	bicoherence to extract featrues. Support vector machine (SVM) classifier using 14 features from various brain regions using different methods chosen out of all tested features. 10 fold cross validation. Accuracy: 85 Classifier model which selected from all tested features AUC: 0.9158 Classifier model which selected from all tested features			

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Chen, 2019[188] Case series N = 107 China Setting: Specialty care	**Target:** Children who are right-handed; no lifetime history of head trauma with loss of consciousness; no history of neurological illness or another severe disease; no history of psychiatric disorders; IQ higher than 80; no history of taking stimulants or other medication to treat inattention problems **Other:** Handedness and age matched typically developing children recruited from local schools **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 18% **Age mean:** 10.44 (0.75) for ADHD group, 10.92 (0.69) for control group **Min age: Max age:** **Ethnicity:** N/A : Assume Chinese ethnicity **Reference standard:** Clinical diagnosis Psychiatrist diagnosis using DSM-IV criteria Timing: Prior diagnosis	**Index test:** EEG EEG 10-minute resting state EEG. Convolutional neural network (CNN) classifier,10fold cross validation	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Chen, 2020[191] Wang, 2018[1155]; Wang, 2018[1156] Case series N = 86 China Setting: Other	**Target:** ADHD-200 dataset, Peking University subset 1 only **Other:** Healthy controls **ADHD presentation:** N/A : Dataset includes all subtypes **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 42% **Age mean:** N/A **Min age:** 8 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD-200 Dataset Diagnosis Timing: Prior diagnosis	**Index test:** Imaging,Imaging plus non-imaging fMRI resting-state functional connectivity, feature selection via support vector machine with recursive feature elimination, deep learning dual subspace classification algorithm (binary hypothesis testing), leave one out cross-validation Sensitivity: 100 Range 69%-95% [Subset Analysis] Specificity: 100 Range 82%-96% [Subset Analysis] Accuracy: 99.6 AUC: 0.996 Range 81%-92% [Subset Analysis]	**Index test 2:** Imaging,Imaging plus non-imanging MRI, raw features derived from the temporal variability between intrinsic connectivity networks as well as demographic and covariate variables, model based on the support vector machines, leave-one-out cross-validation and 10-folds cross-validations; best diagnostic model based on inter-intrinsic connectivity networks variability[1155] Sensitivity: 76 Specificity: 81 Accuracy: 79 AUC: 0.84	**Index test 3:** Imaging MRI, individual interregional morphological connectivity, support vector machine classification, leave one out cross validation[1156] Sensitivity: 75 Specificity: 74 Accuracy: 75	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Chen, 2021[189] Case series N = 70 Taiwan Setting: Specialty care	**Target:** Participants with no neurological disorders, chromosome or genetic disorders, autism spectrum disorder, or any other mental disorder **Other:** Typically developing children **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 21% **Age mean:** 5.68 (0.52) for ADHD group, 5.72 (0.46) for control group **Min age:** 5 **Max age:** 7 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis of participants with ADHD was provided or confirmed by the child and adolescent psychiatrists in a clinical setting. Timing: Concurrent	**Index test:** EEG Combination of Disruptive Behavior Disorder Rating Scale parent and teacher versions,1minute eyes open resting EEG, and 7.5 minute EEG recording during Conners Kiddie Continuous Performance Test, independent testing data (n=9) used for cross validation Sensitivity: 87 Specificity: 84 Accuracy: 86 AUC: 0.926 0.950 in independent cross validation test sample n=9 PPV: 87 NPV: 84	**Index test 2:** EEG EEG data, independent testing data (n=9) used for cross validation Sensitivity: 95 Specificity: 38 Accuracy: 69 AUC: 0.677 0.55 in independent cross validation test sample n=9 PPV: 64 NPV: 86	**Index test 3:** Combined rating Disruptive Behavior Disorder Rating Scale parent and teacher versions, independent testing data (n=9) used for cross validation Sensitivity: 66 Specificity: 84 Accuracy: 74 AUC: 0.812 0.75 in independent cross validation test sample n=9 PPV: 83 NPV: 68	**Index text 4:** CPT Conners Kiddie Continuous Performance Test, independent testing data (n=9) used for cross validation Sensitivity: 42 Specificity: 97 Accuracy: 67 AUC: 0.737 0.70 in independent cross validation test sample n=9 PPV: 94 NPV: 58

Chen, 2022[185] Case series N = 109 China Setting: School	**Target:** Children diagnosed with ADHD or subclinical ADHD **Other:** Recruited from 6 primary schools and 6 junior high schools **ADHD presentation:** N/A **Diagnosed by:** Researcher **Comorbidity:** N/A **Female:** 28% **Age mean:** 10.6 (1.9) for the ADHD group, 11.0 (1.9) for the subthreshold ADHD group, 11.6 (1.5) for the typically developing group **Min age:** 6 **Max age:** 13 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Chinese version of the Swanson Nolan and Pelham Rating Scale (SNAP-IV) parent rating and teacher rating, Conners Abbreviated Symptom Questionnaire parent rating and teacher rating, teacher interviews Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT Attention Network Test-Interaction and Backward-Making Majority Function Task, support vector machine classifier using the attentional effects of Alerting, Orienting, Conflict in Response Time, overall Response Time, and Cognitive Control Capacity (the relationship between response accuracy and information rate), 10-fold cross validation, binary classification ADHD versus typically developing peers Accuracy: 60 SD 2.6%	**Index test 2:** Neuropsychological,CPT Attention Network Test-Interaction, support vector machine classifier using the attentional effects of Alerting, Orienting, Conflict in Response Time, and overall Response Time, 10-fold cross validation, binary classification ADHD versus typically developing peers Accuracy: 64 SD 1.5%	**Index test 3:** Neuropsychological,CPT Attention Network Test-Interaction and Backward-Making Majority Function Task, support vector machine classifier using the attentional effects of Alerting, Orienting, Conflict in Response Time, overall Response Time, and Cognitive Control Capacity (the relationship between response accuracy and information rate), 10-fold cross validation, binary classification subclinical ADHD versus typically developing peers Accuracy: 65 SD 2.1%	**Index text 4:** Neuropsychological,CPT Attention Network Test-Interaction, support vector machine classifier using the attentional effects of Alerting, Orienting, Conflict in Response Time, and overall Response Time, 10-fold cross validation, binary classification subclinical ADHD versus typic Accuracy: 64 SD 2.0%
Chen, 2023[186] Case series N = 81 Taiwan	**Target:** Children with ADHD **Other:** Neurotypical developing children; no sample demographics or inclusion criteria reported	**Index test:** EEG EEG - 6 channel EEG; signals recorded during VR-based GO/NOGO task with introduced distractions;eXtreme Gradient	**Index test 2:** EEG EEG 6 channel EEG; signals recorded during VR-based GO/NOGO task with	**Index test 3:** EEG EEG 6 channel EEG; signals recorded during	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Setting: N/A	**ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** % N/A **Age mean:** N/A **Min age:** **Max age:** **Ethnicity:** N/A **Reference standard:** Other Method of ADHD diagnosis not reported Timing: Prior diagnosis	Boosting (XGB) classifier using behavioral task perormance, event-related evoked potentials (ERPs), and event-related spectral power (ERSP) from trials with and without distractions; 5-fold cross validation; ADHD versus neurotypical Sensitivity: 93 Specificity: 74 Accuracy: 85 AUC: 0.83 PPV: 85	introduced distractions;Decision Tree (DT) classifier using behavioral task perormance, event-related evoked potentials (ERPs), and event-related spectral power (ERSP) from trials without distractions; 5-fold cross validation; ADHD versus neurotypical Sensitivity: 90 Specificity: 66 Accuracy: 80 AUC: 0.78 PPV: 80	VR-based GO/NOGO task with introduced distractions;K-nearest neighbor (KNN) classifier using behavioral task perormance, event-related evoked potentials (ERPs), and event-related spectral power (ERSP) from trials with distractions; 5-fold cross validation; ADHD versus neurotypical Sensitivity: 82 Specificity: 71 Accuracy: 78 AUC: 0.77 PPV: 81	

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Chiarenza, 2018[192] Case series N = 50 Italy Setting: Specialty care	**Target:** Children diagnosed with ADHD combined subtype or ADHD combined subtype+ODD **Other:** No non-ADHD participants **ADHD presentation:** combined : 100 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 8% **Age mean:** 10.1 (3.1) for ADHD only group, 10.3 (2.2) for ADHD plus oppositional defiant disorder group **Min age:** 6 **Max age:** 15 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnoses were based on a DSM-V criteria Timing: Prior diagnosis	**Index test:** EEG EEG quantitative EEG, Quantitative EEG Tomographic Analysis, and the Junior TemperamentCharacter Inventory to classify ADHD only from ADHD+ODD AUC: 0.95 for the Junior Temperament Character Inventory Z-scores plus Z-spectra at the electrodes (quantitative EEG) and 0.91 for the Junior Temperament Character Inventory Z-scores plus Z-spectra at the sources (quantitative EEG tomographic analysis);	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Chow, 2019[197] Chow, 2019[717] Case series N = 60 Taiwan Setting: N/A	**Target:** Female children; not taking medications at time of testing; no history of epilepsy, mental retardation, drug abuse, head injury, or psychotic disorders; diagnosis meets DSM-V criteria **Other:** Age-matched controls **ADHD presentation:** inattentive : 100 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 100% **Age mean:** 7.8 (2.2) for ADHD group, 8.1 (2.0) for control group **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Clinical diagnosis from a pediatric neurologist or psychiatrist using DSM-V criteria Timing: Prior diagnosis	**Index test:** EEG EEG 20 minutes, eyes closed, Hjorth Mobility analysis of EEG, dataset randomly spiltinto a training set and a test set ina size ratio of 9:1 and repeated 20 times. Logisitic regression classifier with principle component analysis-based feature reduction, 10 fold cross validation. Sensitivity: 80 Specificity: 80 Accuracy: 79 AUC: 0.885	**Index test 2:** EEG EEG 20 minutes, eyes closed, Theta/Beta ratio (TBR) of the EEG band, dataset randomlyspilt into a training set and a test set ina size ratio of 9:1 and repeated 20 times. Logisitic regression classifier with principle component analysis-based feature reduction, 10 fold cross validation. Sensitivity: 46 Specificity: 74 Accuracy: 58 AUC: 0.633	**Index test 3:** EEG EEG 20 minutes, eyes closed, approximate entropy analysis of EEG,dataset randomly spiltinto a training set and a test set ina size ratio of 9:1 and repeated 20 times . Logisitic regression classifier with principle component analysis-based feature reduction, 10 fold cross validation.[717] Sensitivity: 85 Specificity: 81 Accuracy: 82 AUC: 0.862	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Chu, 2017[198] Case series N = 107 Taiwan Setting: Specialty care	**Target:** Children who have been diagnosed with ADHD based on clinical diagnosis according to DSM-IV **Other:** Healthy children without ADHD **ADHD presentation:** inattentive_other : n=32,hyperactive_other : n=4,combined_other : n=34 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % N/A **Age mean:** Age reported for each sub-type separately, Inattentive 9 (1.58) / Hyperactive 8.5 (1.91) / Combined 9.8 (1.52) **Min age:** 6 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed with ADHD by a medical professional using DSM-IV diagnostic standards Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT Diagnosis-supported attention deficit hyperactivity disorder (DS-ADHD) is a self-built diagnosis-supported ADHD screening system based on the Test of Variables of Attention (TOVA) Sensitivity: 85 Specificity: 63 Accuracy: 78 AUC: 0.867 (0.801, 0.933) PPV: 82 NPV: 67 Internal consistency: Cronbach's alpha ranged from 0.906 to 0.987 over 15 variables in the DS-ADHD. Variables include items such as response time, response time variability, omission errors, commission errors, and response sensitivity.	N/A	N/A	N/A

Cree, 2023[210] Danielson, 2021[731]; Wanga, 2022[1160] Case series N = 571 US Setting: Other	**Target:** Participants from South Carolina from 1 school district comprised of 20 schools **Other:** Children without ADHD from SC Re-PLAY sample **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 48% female in entire sample **Age mean:** 12.5 (0.3) **Min age:** 5 **Max age:** 17 **Ethnicity:** % White : 62 Other : 38% Other (includes non-Hispanic Black, Hispanic, non-Hispanic Asian, and other) **Reference standard:** Clinical diagnosis Children were considered to meet our ADHD case definition if they met both symptom and impairment criteria on the parent-reported Diagnostic Interview Schedule for Children—Version IV (DISC-IV) and had at least two or more teacher-reported ADHD symptoms on either the Behavior Assessment System for Children—Second Edition, Behavioral and Emotional Screening System (BASC-2- BESS) or the Strengths and Difficulties Questionnaire (SDQ); DISC-IV interviews were administered by trained interviewers supervised by a licensed psychologist or psychiatrist Timing: Concurrent	**Index test:** Other (e.g., ECG) : Reliability of parent report of diagnosis Parent-report of child ever receiving a diagnosis of ADHD Sensitivity: 67 (49, 82) Specificity: 80 (74, 85)	**Index test 2:** Other : Reliability of parent report of diagnosis Parent report of child currently having an ADHD diagnosis Sensitivity: 70 (54, 83) Specificity: 81 (75, 86)	N/A	N/A
Crippa, 2017[211] Case series N = 44 Italy Setting: Mixed	**Target:** Participants with IQ>80 with normal or corrected-to-normal vision and not taking any medication **Other:** Gender, age, and IQ matched typically developing children with no	**Index test:** Imaging,Imaging plus non-imaging Multi-domain profile of measures including near-infrared spectroscopy for functional measures, blood fatty acid profiles, and	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	Index Test 2	Index Test 3	Index Test 4
	DSM-4 diagnoses recruited by local pediatricians and from schools **ADHD presentation:** inattentive : 18.2,hyperactive : 36.4,combined : 45.5 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 0% **Age mean:** 11.5 (1.5) for ADHD group, 11.4 (1.9) for comparison group **Min age: Max age:** **Ethnicity:** % White : 100 **Reference standard:** Clinical diagnosis Diagnosis of ADHD based on DSM-IV TR Timing: Prior diagnosis	neuropsychological measures; feature extraction using principal components analysis, support vector machine classifier, nested 10-fold cross validation; model with best accuracy trained on neuropsychological, fatty acid profiles, and deoxygenated-hemoglobin features Sensitivity: 73 Model containing cognitive profile, fatty acid profile, and near-infrared spectroscopy deoxygenated-hemoglobin Specificity: 87 Model containing cognitive profile, fatty acid profile, and near-infrared spectroscopy deoxygenated-hemoglobin Accuracy: 81 Model containing cognitive profile, fatty acid profile, and near-infrared spectroscopy deoxygenated-hemoglobin AUC: 0.80 Model containing cognitive profile, fatty acid profile, and near-infrared spectroscopy deoxygenated-hemoglobin Rater agreement:			

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Culbertson, 1998[213] Case series N = 155 US Setting: Mixed	**Target:** Children drawn from consecutive referrals to a clinic specializing in the neuropsychological evaluation and treatment of ADHD; no history of mental retardation, severe psychiatric disturbance, or neurological injury/ disorder **Other:** Children nominated by teachers from a suburban, middle-class community who exhibited at least average academic performance in the classroom and no behavioral or work study problems **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 27% **Age mean:** **Min age:** 7 **Max age:** 12 **Ethnicity:** % White : 96 **Reference standard:** Clinical diagnosis Diagnosis using DSM-III-R criteria determined by structured parent interview, teacher and parent rating scales, and objective neuropsychological testing by a licensed psychologist Timing: Prior diagnosis	**Index test:** Neuropsychological,EF Tower of London - Drexel (total move and rule violation scores) Sensitivity: 64 Specificity: 80 Accuracy: 70 PPV: 85 Alpha: 30 ADHD participants (ages 7 to 10) were assessed on two occasions in a standardized manner with the temporal interval between assessment averaging 16.3 days (SD 8.9, range 7 to 41 days) Test-retest: 0.81 (p<0.05) for total test score, 0.79 (p<0.05) for total time violations, and 0.42 (p<0.005) for total rule violations	N/A	N/A	N/A

Das, 2021[214] Vimalajeewa, 2022[1143]; Rojas-Libano, 2019[1011]; Wainstein, 2017[1148] Case series N = 50 Multiple countries Setting: Mixed	**Target:** Participants diagnosed patients, discontinued stimulant medication 24 hours prior to testing **Other:** Healthy children; recruited from elementary schools in Chile **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 14% **Age mean:** 10.71 (0.54) for the ADHD group, 11.58 (0.50) for the control group **Min age:** 10 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis of ADHD and ADHD-C according to DSM-IV criteria by a neurologist Timing: Prior diagnosis	**Index test:** Other (e.g., ECG) : pupillometrics Pupillometrics (pupil-size dynamics) during visuospatialworking memory task, which consisted of multiple 8 s trials, during which pupil-sizes were measured; support vector machine classifier, nested 10-fold cross validation; non-medicated ADHD versus controls Sensitivity: 77 Support vector machine classifier Specificity: 75 Support vector machine classifier Accuracy: 76 Support vector machine classifier AUC: 0.856 Support vector machine classifier	**Index test 2:** Other : pupillometrics Pupillometrics (pupil-size dynamics). Subjects were required to complete a visuospatial working memory task, which consisted of multiple 8 s trials, during which pupil-sizes were measured; wavelet-based self-similarity behavior analysis method, support vector machine (SVM) classifier; for model fitting, 67% of the rows were randomly selected from each of the feature matrices for training; the remaining rows were used for testing, non-medicated ADHD versus controls[1143] Sensitivity: 97 Specificity: 72 Accuracy: 84	**Index test 3:** Other : pupillometrics Pupillometrics (pupil-size dynamics). Subjects were required to complete a visuospatial working memory task, which consisted of multiple 8 s trials, during which pupil-sizes were measured; association between max pupil diameter (z-score) and reaction time variability (s)	**Index text 4:** Other : pupillometrics Pupillometrics (pupil-size dynamics). Subjects were required to complete a visuospatial working memory task, which consisted of multiple 8 s trials, during which pupil-sizes were measured; association between max pupil diameter (z-score) and performance (Rater agreement: Max pupil diameter (z-score) and performance (fraction correct) Spearman correlations: All subjects (n=67) rho= 0.63, p<0.0001; ADHD off medication rho= 0.71, p<0.001); ADHD on medication rho= 0.47, p= 0.05; controls rho= 0.35, p= 0.10

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Deb, 2008[218] Case series N = 151 UK Setting: Specialty care	**Target:** Children who received clinical assessments for ADHD and intellectual disabilities in a specialist outpatient clinic **Other:** Children not diagnosed with ADHD at a specialist outpatient clinic for intellectual disibility and behavior problems **ADHD presentation:** inattentive : 24,hyperactive : 24,combined : 52 **Diagnosed by:** Specialist **Comorbidity:** Other : All participants had borderline IQ or intellectual disability **Female:** % 28% female in entire sample **Age mean:** **Min age:** 3 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Timing: Prior diagnosis	**Index test:** Parent rating CPRS-R (Conners' Parent Rating Scales-Revised), cut-off score of 50 Sensitivity: 83 Specificity: 89 AUC: 0.875 (0.776, 0.975) Rater agreement: Parent versus teacher total scores Kappa: ICC: 0.19 Alpha: 0.84	**Index test 2:** Teacher rating scale CTRS-R (Conners' Teacher Rating Scales-Revised), cut-off score of 48 Sensitivity: 56 Specificity: 83 AUC: 0.665 (0.478, 0.852) Alpha: 0.80	N/A	N/A

Deserno, 2022[223] Case series N = 434 US Setting: Other	**Target:** Part of a larger cohort of the Healthy Brain Network Biobank based on a community-referred recruitment model of children with developmental psychopathology; replication sample from the Oregon ADHD and Autism project **Other:** Children with autism spectrum disorder, neurotypical developing children **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 20% **Age mean:** 9.4 (1.7) for the ADHD group, 9.3 (1.6) for the ASD group, 9.4 (1.5) for the typically developing group; 10.11 (0.092) for replication sample, range 8-12 **Min age:** 7 **Max age:** 14 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Extensive clinicians-administered assessments including the Autism Diagnostic Observation Schedule, computerized Schedule for Affective Disorders and Schizophrenia-Children's Version (KSADS-COMP) parent interview and child interview Timing: Concurrent	**Index test:** Parent rating SWAN-H/I (Strengths and Weaknesses of ADHD symptoms and Normal-behaviors) ratings scale hyperactivity/impulsivity subscale and the Social Responsiveness Scale restricted interests and repetitive behaviors, social awareness, social cognition, social communication, social motivation, and innattention subscales; 3 category (ADHD vs ASD vs typically developing) random forest classification; replication sample Sensitivity: 69 For ADHD diagnostic group Specificity: 84 For ADHD diagnostic group Accuracy: 76	**Index test 2:** Parent rating SWAN-H/I (Strengths and Weaknesses of ADHD symptoms and Normal-behaviors) ratings scale hyperactivity/impulsivity subscale and the Social Responsiveness Scale restricted interests and repetitive behaviors, social awareness, social cognition, social communication, social motivation, and innattention subscales; 3 category (ADHD vs ASD vs typically developing) random forest classification; hold-out test set from 75% training/ 25% testing split Sensitivity: 67 For ADHD diagnostic group, recall = 79% Specificity: 84 For ADHD diagnostic group Accuracy: 72 (63,80) Rater agreement: Predicted diagnostic group versus actual diagnostic group 0.56	**Index test 3:** Parent rating SWAN-H/I (The Strengths and Weaknesses of ADHD symptoms and Normal-behaviors ratings scale) hyperactivity/impulsivity subscale and the Social Responsiveness Scale restricted interests and repetitive behaviors, social awareness, social cognition, social communication, social motivation, and innattention subscales; 3 category (ADHD vs ASD vs typically developing) random forest classification; hold-out test set from 75% training/ 25% testing split excluding the ADHD participants with comorbid ASD Sensitivity: 77	**Index text 4:** Sensitivity: Specificity: Accuracy: AUC: PPV: NPV: Rater agreement: Kappa: Internal consistency:

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
				For ADHD diagnostic group; recall = 79% Specificity: 74 For ADHD diagnostic group Accuracy: 71 (62, 79)	

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	Results: Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	Index Test 2	Index Test 3	Index Test 4
Doyle, 1997[230] Case series N = 156 US Setting: School	**Target:** Subset of children ascertained from a school-based early preventive intervention study of children at risk for conduct disorder; 1.75 standard deviations above the normative mean on the Hyperactivity Index of the Connors Teacher Rating Scale and the Connors Parent Rating Scale; diagnosed with ADHD only or ADHD + comorbid externalizing disorder **Other:** From same population and selection process as ADHD group, but did not meet criteria for a DSM-III-R diagnosis **ADHD presentation:** **Diagnosed by:** Researcher **Comorbidity:** **Female:** 19% **Age mean:** 9.0 (1.2) **Min age:** 6 **Max age:** 11 **Ethnicity:** % White : 95 **Reference standard:** Clinical diagnosis Diagnostic Interview for Children and Adolescents, Revised- Parent Version Timing: Prior diagnosis	**Index test:** Parent rating BASC-PRS (Behavior Assessment System for Children Parent Rating Scale), discriminantfunction analysis with a jackknife procedure, no diagnosis vs ADHD/ADHD+externalizing disorder Sensitivity: 88 Specificity: 37 AUC: 0.758 BASC-PRS total score Rater agreement: BASC-PRS clinical scales vs CBCL/4-18 clinical scales Pearson product-moment correlations: The most highly related scales were BASC-PRS Aggression versus CBCL/4-18 Aggression (r = 0.70), BASC-PRS Conduct Problems versus CBCL/4-18 Delinquency (r = 0.69), BASC Depression versus CBCL/4-18 Anxiety/Depression	**Index test 2:** Parent rating CBCL (Child Behavior Checklist 4-18); discriminant function analysis with a jackknifeprocedure, no diagnosis vs ADHD/ADHD+externalizing disorder Sensitivity: 80 Specificity: 44 AUC: 0.716 CBCL/4-18 total score	**Index test 3:** Parent rating BASC-PRS (Behavior Assessment System for Children Parent Rating Scale); discriminant function analysis with a jackknife procedure, no diagnosis vs ADHD only Sensitivity: 74 Specificity: 44	**Index text 4:** Parent rating BASC-PRS (Behavior Assessment System for Children Parent Rating Scale); discriminant function analysis with a jackknife procedure, no diagnosis vs ADHD+externalizing disorder Sensitivity: 92 Specificity: 68

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Doyle, 2007[231] Case series N = 251 US Setting: Other	**Target:** Probands and siblings diagnosed with ADHD **Other:** Probands and siblings participating in a longitudinal study of youth without ADHD **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 25% female in entire sample, all probands were males, sibling sets included both boys and girls **Age mean:** 14.6 (1.9) **Min age:** 12 **Max age:** 18 **Ethnicity:** Other : All probands were white, non-Hispanic **Reference standard:** Clinical diagnosis Schedule for Affective Disorders and Schizophrenia for School-Aged Children and Adolescents Epidemiologic Version (Kiddie SADS-E), independent interviews with the mother and direct interviews of children Timing: Concurrent	**Index test:** Teen/child self report ASEBA-YSR (Achenbach youth self-report) Accuracy: Total predictive value ranged from 85% to 90% over 8 subscales	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Duda, 2016[234] Case series N = 2925 US Setting: Other	**Target:** Siblings of the autism probands that reported a prior clinical diagnosisof ADHD; no documented diagnosis of autism **Other:** Children with autism and no comorbidity with ADHD **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** Autism : 95% **Female:** 37% **Age mean:** Median age range between the three different databases = 64.5-134.5 months **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Parent-reported clinical diagnosis Timing: Prior diagnosis	**Index test:** Parent rating SRS (Social Responsiveness Scale), Support Vector Classification, 10-fold cross validation, classification of ADHD vs ASD AUC: 0.965 5 of 65 features used	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Duda, 2017[233] Case series N = 422 US Setting: Mixed	**Target:** Children with only ADHD, diagnoses of ADHD were provided as parent report **Other:** Selected the subset of responses from parents of children with only ASD (n = 248) to serve as the survey sample, diagnoses of ASD were provided as parent report **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 34.5% **Age mean:** 10.4 (3.6) **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Other Survey sample: diagnoses of ASD or ADHD were provided as parent report. Archival data set: diagnoses of ASD were physician-confirmed and diagnoses of ADHD were reported as part of an extensive family medical history. Timing: Prior diagnosis	**Index test:** Parent rating SRS (Social Responsiveness Scale) subset of items, best AUC obtained withElastic Net and Linear discriminant analysis classifiers. Machine-learning pipeline consisted of three trials using subsamples of archival data, survey data, or a mixture of both; model used to discriminate between ADHD and ASD AUC: 0.89 ADHD versus ASD	N/A	N/A	N/A

DuPaul, 1992[237] Case series N = 68 US Setting: Specialty care	**Target:** Consecutive referrals to an outpatient psychiatry clinic specializing in the assessment of ADHD **Other:** **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 15% **Age mean:** 8.6 (1.6) **Min age:** 6 **Max age:** 11 **Ethnicity:** Other : The majority of children were Caucasian, with 10% of the sample either Hispanic or African-American **Reference standard:** Clinical diagnosis Diagnosis using DSM-III-R criteria including parent report of 8 or more symptoms of ADHD, onset of symptoms prior to age 7, and duration of symptoms greater than 6 months; Either a parent rating on the Hyperactivity factor of the Child Behavior Checklist or a teacher rating on the Child Attention Problems Scale greater than the 93rd percentile (i.e., T score equal to or greater than 65) for the child's sex and age Timing: Concurrent	**Index test:** Neuropsychological,CPT Gordon Vigilance Task, continuous performance test, number correct, cutoff abovethe 93rd percentile relative to age-based norms Rater agreement: CPT number correct versus criterion measures Agreement 22%, Disagreement 78%	**Index test 2:** Neuropsychological,CPT The Gordon Vigilance Task continuous performance test, number commission errors, cutoff above the 93rd percentile relative to age-based norms Rater agreement: CPT number commission errors versus criterion measures	**Index test 3:** Neuropsychological,CPT,EF Classification scheme defined as the child's performance being in the ADHD range on any of the three clinic test scores (CPT number correct, CPT number commission errors, matching familiar figures test median split) Rater agreement: CPT number correct or CPT commission errors or Matching Familiar Figures versus criterion measures Agreement 62%, Disagreement 38%	N/A
Ebesutani, 2010[241] Case series N = 476 US Setting: Specialty care	**Target:** Consecutively referred children and adolescents to two mental health clinics **Other:** Consecutively referred children and adolescents to two mental health clinics **ADHD presentation:** inattentive : 34,hyperactive : 2,combined : 45,N/A : ADHD-not otherwise specified 19% **Diagnosed by:** Specialist	**Index test:** Parent rating CBCL-AD/H (Child Behavior Checklist) attention deficit/hyperactivity problems scale DSM-oriented, ADHD vs No ADHD AUC: 0.75	**Index test 2:** Parent rating CBCL-A (Child Behavior Checklist) attention problems syndrome scale, ADHD vs No ADHD AUC: 0.76	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Comorbidity: N/A **Female:** % 32.8% female in entire sample **Age mean:** 11.4 (2.5) **Min age:** 6 **Max age:** 18 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Children's Interview for Psychiatric Syndromes, Parent Version (P-ChIPS) Timing: Concurrent				

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Edwards, 2015[242] Case series N = 95 US Setting: Specialty care	**Target:** Participants referred to a developmental center at a university medical center for evaluation of suspected ADHD; not on medication; diagnosed with ADHD **Other:** Consecutively referred to a developmental center at a university medical center for evaluation of suspected ADHD; not on medication; not diagnosed with ADHD **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 24% in entire sample **Age mean:** 8.7 (1.9) **Min age:** 6 **Max age:** 12 **Ethnicity:** % Hispanic or Latino : 2 % Black/African American : 18 % American Indian or Alaska Native : 1 % White : 79 **Reference standard:** Clinical diagnosis ADHD module from the parent version of the Computer-Diagnostic Interview Schedule for Children (C-DISC) and the parent and teacher versions of the Conners' ADHD/DSM-IV Scales (CADS) Timing: Concurrent	**Index test:** Parent rating CBCL-A (Child Behavior Checklist) attention problems scale; cutoff T-score 65 Sensitivity: 87 Specificity: 53 PPV: 64 NPV: 81 Rater agreement: Recalibrated efficiency (adjusted for base rates; 0= random test, 1.0= perfect test) Cohen's kappa 0.396 (95% CI 0.375, 0.424)	**Index test 2:** Teacher rating scale TRF-A (Teacher Report Form) Attention Problems Scale; cutoff T-score 65 Sensitivity: 78 Specificity: 76 PPV: 75 NPV: 79 Rater agreement: Cohen's kappa; recalibrated efficiency (adjusted for base rates; 0=random test, 1.0=perfect test) Kappa:0.537	**Index test 3:** Teacher rating scale TRF-A (Teacher Report Form) Attention Problems Scale; cutoff T-score 67 Sensitivity: 57 Specificity: 88 PPV: 81 NPV: 68 Rater agreement: Cohen's kappa; recalibrated efficiency (adjusted for base rates; 0= random test, 1.0= perfect test) 95%CI 0.427, 0.477 Kappa: 0.447 Internal consistency:	**Index text 4:** Parent rating CBCL-A (Child Behavior Checklist) Attention Problems Scale; cutoff T-score 67 Sensitivity: 78 Specificity: 63 PPV: 67 NPV: 76 Rater agreement: Cohen's kappa; recalibrated efficiency (adjusted for base rates; 0= random test, 1.0= perfect test) Kappa: 0.413 (95% CI: 0.393, 0.442) Internal consistency:

Eiraldi, 2000[244] Case series N = 242 US Setting: Specialty care	**Target:** Consecutive referrals to an ADHD evaluation and treatment program located in a university-affiliated pediatric hospital diagnosed with ADHD **Other:** Consecutive referrals to an ADHD evaluation and treatment program located in a university-affiliated pediatric hospital not diagnosed with ADHD **ADHD presentation:** inattentive : 24,hyperactive : 6,hyperactive_other : hyperactive presentation not included in analysis,combined : 48 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 21% female in entire sample **Age mean:** 8.7 (1.7) **Min age:** 6 **Max age:** 13 **Ethnicity:** % Hispanic or Latino : 3 % Black/African American : 21 % White : 76 **Reference standard:** Clinical diagnosis Diagnostic Interview for Children and Adolescents-Revised-Parent Version and Attention Problems subscale of the Teacher's Report Form Timing: Concurrent	**Index test:** Parent rating DSMD (Devereux Scales of Mental Disorders) attention subscale; children with anypresentation of ADHD versus controls, cutoff T>=65 Sensitivity: 77 Specificity: 78 PPV: 95 NPV: 39	**Index test 2:** Parent rating CBCL-A (Child Behavior Checklist) attention problems subscale; children with any presentationof ADHD versus controls, cutoff T>=70 Sensitivity: 51 Specificity: 83 PPV: 94 NPV: 24	N/A	N/A
Ekhlasi, 2022[245] Khare, 2023[881]; Talebi, 2022[1112] Case series N = 121 Iran Setting: Specialty care	**Target:** Children with ADHD symptoms; have taken Ritalin for about 6 months **Other:** Neurotypical developing children **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % N/A	**Index test:** EEG EEG recorded during a visual attention task; weighted directed graphs constructed using the Phase Transfer Entropy measure; Naive Bayes classifier, 10-fold cross validation; Feature matrix of all local graph measures (local efficiency, clustering coefficient, betweenness	**Index test 2:** EEG EEG recorded during a visual attention task; weighted directed graphs constructed using the Phase Transfer Entropy measure; Naive Bayes classifier, 10-fold cross validation; Feature matrix of all local graph	**Index test 3:** EEG EEG recorded during a visual attention task; nonlinear Causal Relationship Estimation by Artificial Neural Network	**Index text 4:** EEG EEG recorded during a visual attention task; combination of variational mode decomposition and Hilbert transform

	Age mean: 9.73 (1.76) **Min age:** 7 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed by an experienced psychiatrist Timing: Prior diagnosis	centrality, degree-in/out, strength-in/out) in theta band Accuracy: 91	measures (local efficiency, clustering coefficient, betweenness centrality, degree-in/out, strength-in/out) in delta band Accuracy: 90	(nCREANN) used to assess linear and nonlinear effective connectivity patterns of individuals based on their EEG signals; principal component analysis feature selection, artificial neural network (ANN) classifierusing all nCREANN measures (fusion of linear and nonlinear connectivity values), 10-fold cross validation, 90% training/10% testing split; ADHD versus neurotypically developing[1112] Sensitivity: Specificity: Accuracy: 99	(VMD-HT) feature extraction, explainable boosted machine (EBM) model classifier, 10-fold cross validation[881] Sensitivity: 100 Specificity: 100 Accuracy: 100 AUC: 1.00
Elkins, 2014[251] Case series N = 46 US Setting: Specialty care	**Target:** Children and adolescents with generalized anxiety disorder and diagnosed ADHD; those exhibiting symptoms of thought disorders, pervasive developmental disorders, organic brain syndromes, intellectual disabilities, or suicidal ideation were excluded **Other:** Children with generalized anxiety disorder and symptoms of inattention but no ADHD diagnosis	**Index test:** Parent rating CBCL-A (Child Behavior Checklist) attention problems scale Sensitivity: 74 All data abstracted is for cut-off score of 63, which is considered best by authors. Score of 57 has highest overall correct rate and sensitivity Specificity: 91.3 Accuracy: 82.6	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	ADHD presentation: N/A **Diagnosed by:** Specialist **Comorbidity:** Mood disorder **Female:** 54% **Age mean:** 12.03 (3.3) **Min age:** 7 **Max age:** 18 **Ethnicity:** % White : 80.4 **Reference standard:** Clinical diagnosis Diagnosed with ADHD per DSM-IV-R Timing: Prior diagnosis	Overall Correct Classification AUC: 0.84 SE 0.06 PPV: 89.5 NPV: 77.8			

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
El-Sayed, 1999[246] Case series N = 159 Sweden Setting: Mixed	**Target:** Participants with ADHD **Other:** Neurotypical children recruited from normal public schools from the same areas as the patients **ADHD presentation:** combined : 100 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 14% **Age mean:** 10.5 for ADHD group, 10.2 for neurotypical group **Min age:** 6 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Timing: Prior diagnosis	**Index test:** Neuropsychological,EF Gordon Diagnostic System Delay Task measuring impulse control, strategic planning, motivational effect, sense of time and rediness to respond generating an "Efficiency Ratio"score, cut-off <=0.78 Sensitivity: 59 Specificity: 81 AUC: 0.72 (0.64, 0.79)	**Index test 2:** Neuropsychological,CPT Gordon Diagnostic System Vigilance Task measuring the ability to sustain attention over a 9 minute period generating a "Correct Responses" score, cut-off <=38 Sensitivity: 49 Specificity: 87 Accuracy: AUC: 0.72 (0.64, 0.79)	**Index test 3:** Neuropsychological,CPT Gordon Diagnostic System Vigilance Task measuring the ability to sustain attention over a 9 minute period generating a "Errors of Commission" score, cut-off >7 Sensitivity: 51 Specificity: 85 Accuracy: AUC: 0.73 (0.65, 0.79)	N/A

Emser, 2018[253] Case series N = 60 Germany Setting: Mixed	**Target:** Participants with primary diagnosis of ADHD and IQ >=80; no other medical conditions such as hyperthyroidism, autism, epilepsy, brain disorders and any genetic or medical disorder associated with externalizing behavior; may have oppositional defiance disorder, conduct disorder, learning disorders, anxiety, or depression; medication stopped 2 days before testing; recruited through an ADHD outpatient clinic **Other:** Age and gender-matched children, no established or suspected ADHD diagnosis, or family history of ADHD, recruited through local schools **ADHD presentation:** inattentive : 27,hyperactive : 3,combined : 60,N/A : 10% subtype information not available **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 30% **Age mean:** 8.9 (1.4) for the ADHD group, 8.7 (1.2) for the control group **Min age:** 6.9 **Max age:** 11 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD diagnoses were based on a DSM-IV-oriented clinical interview Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT Linear support vector machine and feature selection using variables from the Conners-3 parent ratings, the Quantified Behavior Test for children, and the Test Battery of Attention for children. Leave-one-out cross validation Sensitivity: 83 Specificity: 90 Accuracy: 87 Internal consistency: Cronbach's alpha of 0.85 for the content scales and alpha = 0.79 for the symptom scales of the Conners 3 parent rating scale feeding into the model	**Index test 2:** Neuropsychological,CPT Linear support vector machine and feature selection using variables from the Quantified Behavior Test for children and the Test Battery of Attention for children only. Leave-one-out cross validation Sensitivity: 80 Specificity: 77 Accuracy: 78	N/A	N/A
Faraone, 2016[263] Case series N = 113 US Setting: Specialty care	**Target:** Participants diagnosed with ADHD; no history of psychosis or neurological disorder, low intellectual functioning, substance use disorders, conduct disorder, tic disorders, or physical impairments precluding game play; did not take stimulant medication on the testing days	**Index test:** Neuropsychological,CPT,EF Groundskeeper game designed to measure attention capabilities on a go/no go task, with the addition of visual, auditory, and visuo-spatial	**Index test 2:** Parent rating Conners subscales, parent-rated as a predictor of ADHD diagnoses AUC: 0.76	**Index test 3:** Neuropsychological,CPT CPT-II (Conners Continuous Performance Test II)	**Index text 4:** Neuropsychological,CPT,EF Combined the significant Groundskeeper factors with the Conners inattention

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	Results: Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	Index Test 2	Index Test 3	Index Test 4
	Other: Consecutive patients referred to a child psychiatrist not diagnosed with ADHD; may have major depressive disorder, dysthymia, generalized anxiety disorder, anxiety disorder not otherwise specified (NOS), social phobia, oppositional defiant disorder, panic **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 43% **Age mean:** groups differed significantly in age (12.3 vs. 13.6; p=0.01) **Min age:** 6 **Max age:** 17 **Ethnicity:** % White : 88,Other : in ADHD group, 82% in control group **Reference standard:** Clinical diagnosis Kiddie-Schedule of Affective Disorders and Schizophrenia- Present and Lifetime (K-SADS-PL), Version 19, a semistructured diagnostic interview by a psychiatric nurse and reviewed by two psychiatrists Timing: Concurrent	distractions at various frequencies Rater agreement: Kappa 0.15 for Groundskeeper versus Conners (z = 1.6, p = 0.06), 0.18 for Groundskeeper versus CPT (z = 1.9, p = 0.9), and 0.3 for Conners versus CPT (z = 3.2, p = 0.0007)			subscale and the CPT percent correct in the same model AUC: 0.87

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Ferrin, 2012[267] Case series N = 1,185 Australia Setting: Mixed	**Target:** Participants were stimulant medication naive at the time of their assessment and had only received school-based individual and/or group psychosocial treatments **Other:** Typically developing children and adolescents **ADHD presentation:** inattentive : 24.8,hyperactive : 7.2,combined : 67.9 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 22% **Age mean:** 131.44 months (38.93) for the ADHD group and 133.16 months (27.95) for the comparison group **Min age:** 6 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD status was categorically defined by the semistructured clinical interview of their parent's K–SADS–PL, and dimensionally by the Conners' Global Index (CGI) based on DSM–IV criteria Timing: Prior diagnosis	**Index test:** Neuropsychological,EF Scored Developmental Neurological Examination, total score of 13 or over Sensitivity: 67 Specificity: 89 AUC: 0.779 (0.742, 0.816) (95% CI 0.742–0.816) PPV: 98 NPV: 25 LR+: 6.16 LR-: 0.37	N/A	N/A	N/A

Forbes, 1998[276] Case series N = 146 US Setting: Specialty care	**Target:** Participants referred to a private practice of clinical child psychology to determine if they had an attention-deficit/hyperactivity disorder **Other:** Referred to a private practice of clinical child psychology to determine if they had an attention-deficit/hyperactivity disorder; received diagnoses other than ADHD including oppositional defiant disorder or conduct disorder, learning disabilities, adjust **ADHD presentation:** inattentive : 18,combined : 62 **Diagnosed by:** Researcher **Comorbidity:** N/A **Female:** 23% **Age mean:** **Min age:** 6 **Max age:** 12 **Ethnicity:** % White : 100 **Reference standard:** Clinical diagnosis Clinical assessment including parent and teacher behavioral ratings, parental reports of school problems, parental reported developmental and behavioral history, and behavioral observations during the interview ; all diagnoses were made by the author Timing: Concurrent	**Index test:** Neuropsychological,CPT TOVA (Test of Variables of Attention); cutoff any one measure exceeding 1.5 standard deviations from age and sex adjusted means; ADHD vs other diagnoses Sensitivity: 80 Specificity: 72	**Index test 2:** Neuropsychological,CPT The Test of Variables of Attention (TOVA); cutoff= two measures (excluding commission errors) exceeding 1.0 standard deviations from age and sex adjusted means; ADHD vs other diagnoses Sensitivity: 67 Specificity: 86	N/A	N/A
Francois-Sevigny, 2022[277] Case series N = 92 Canada Setting: Specialty care	**Target:** ADHD or ADHD+gifted; IQ>=130 on the Full-Scale Intelligence Quotient or the General Aptitude Index of the Wechsler Intelligence Scale for Children 5th edition to be included in the ADHD+gifted group; all drug naive; children with ASD or intellectual disability were excluded **Other:** Gifted children;IQ>=130 on the Full-Scale Intelligence Quotient or the General Aptitude Index of the	**Index test:** Combined rating Conners 3 content scales teacher and parent ratings; discriminant function analysis with 3 categories (ADHD+gifted vs ADHD vs gifted) Sensitivity: 72% of the ADHD+gifted children were correctly classified, 68% of the ADHD children were correctly classified	**Index test 2:** Combined rating Conners 3 symptom scales teacher and parent ratings; discriminant function analysis with 3 categories (ADHD+gifted vs ADHD vs gifted)	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Wechsler Intelligence Scale for Children 5th edition **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 29% **Age mean:** 9.85 (2.51) **Min age:** 6 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Semi-structured K-SADS-PL interview, Conners Continuous Performance Test, the Test of Everyday Attention for Children, the Delis-Kaplan Executive Function System (D-KEFS), the Tower of London test, the Behavior Assessment System for Children (BASC-3) Timing: Concurrent	Specificity: 100 Accuracy: 78	Sensitivity: 70% of the ADHD+gifted children were correctly classified, 66% of the ADHD children were correctly classified Specificity: 100 Accuracy: 76		

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Gao, 2020[282] Bethlehem, 2017[682]; Qureshi, 2016[991]; Qureshi, 2017[992]; Riaz, 2018[1003]; Miao, 2019[923]; Zou, 2017[1193]; Dey, 2014[735] Case series N = 83 US Setting: Other	**Target:** Children from ADHD-200 database, Kennedy Krieger Institute (KKI) **Other:** Typically developing children **ADHD presentation:** N/A : All subtypes included **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 45% **Age mean:** N/A **Min age:** 8 **Max age:** 13 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed with ADHD from the ADHD-200 datasets Timing: Prior diagnosis	**Index test:** Imaging,Imaging plus non-imaging fMRI and non-imaging data, combination of functional connectivity from resting state fMRI and phenotypic data (phenotypic-attribute attentional brain connectivity, age, and gender), support vector machine (SVM) classification; used ADHD-200 provided KKI test dataset for validation Sensitivity: 93 Specificity: 95 Accuracy: 95	**Index test 2:** Imaging,Imaging plus non-imanging fMRI and non-imaging data, functional connectivity calculation, feature selection, fusion of non-imaging data (age, gender, IQ), and classification, SVM classifier[1003] Sensitivity: 90 Specificity: 77 Accuracy: 87	**Index test 3:** Imaging fMRI, fractional amplitude of low-frequency fluctuation reflecting intensity of spontaneous neuronal activity combined with feature selection on fMRI[923]	**Index text 4:** Imaging fMRI and sMRI, deep learning-based classification method via 3-D convolutional neural networks applied to MRI, first extracting meaningful 3-D low-level features from functional MRI and structural MRI, investigating local spatial patterns of MRI features, Accuracy: 73

Garcia-Argibay, 2022[283] Case series N = 238696 Sweden Setting: Other	**Target:** For those with ADHD, all predictors selected from the registries were labeled as present if they occured either before or coincident with the diagnosis of ADHD, predictors related to the biological parents were also included **Other:** For those without ADHD, all predictors selected from the registries were labeled as present if they occured prior to age 18, predictors related to the biological parents were also included **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** % N/A **Age mean:** N/A **Min age: Max age:** 18 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Individuals with ADHD were identified based on either the presence of a diagnosis in the NPR (including inpatient and outpatient care services) from age 3 onwards using the International Classification of Diseases (ICD) version 9 code 314, ICD10-code F90 or a recorded prescription of any ADHD medications (Anatomical Therapeutic Chemical [ATC] codes N06BA04, N06BA01, N06BA02, N06BA09, and N06BA12) from the PDR Timing: Prior diagnosis	**Index test:** Other (e.g., ECG) : Registry data Data from multiple Swedish registries, the top 5 features contributing to classification were having a parent with criminal convictions, male sex, having a relative with ADHD, number of academic subjects failed, and speech/learning disabilities; deep neural network (DNN) classifier, 80%/20% training/testing split Sensitivity: 72 At the 0.45 probability threshold Specificity: 65 At the 0.45 probability threshold Accuracy: 69 AUC: 0.75 (0.74, 0.76)	N/A	N/A	N/A
Garcia-Sanchez, 1997[284] Case series	**Target:** Teenagers diagnosed with ADD with hyperactivity or ADD without	**Index test:** Neuropsychological,EF Neuropsychological tests developed for the assessment	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
N = 60 Spain Setting: School	hyperactivity by school psychologists using DSM-III criteria **Other:** Schoolmates of ADD group **ADHD presentation:** N/A : 64% ADD with hyperactivity, 36% ADD without hyperactivity **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 40% **Age mean:** 14.8 (0.5) for ADHD group, 14.9 (0.7) for control group **Min age:** 14 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis by school psychologists, family interview, Conners Teacher Rating Scale, Paced Auditory Addition Task, and Continuous Performance Test with and without auditory interference Timing: Prior diagnosis	of visuospatial skills and are sensitive tasks for right hemisphere functions; discriminant function analysis; final model included correct score from the WAIS Block-Design, correct score from the Benton's Line Orientation, and the correct score from the Raven's Progressive Matrices; 3 way classification (ADD with hyperactivity vs ADD without hyeractivity vs controls) Sensitivity: 53% for ADD with hyperactivity, 56% for ADD without hyperactivity Specificity: 74 Accuracy: 65			

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Gardner, 2007[285] Case series N = 269 US Setting: Primary Care	**Target:** Children and adolescents diagnosed with ADHD and psychosocial problems, particularly anxiety and depression **Other:** Children and adolescents not diagnosed with ADHD from same recruitment and selection process as ADHD participants **ADHD presentation:** N/A **Diagnosed by:** Researcher **Comorbidity:** N/A **Female:** % 53% female in entire sample **Age mean:** 8.1 (2.1) **Min age:** 8 **Max age:** 15 **Ethnicity:** % Black/African American : 6 % White : 90 Other : 4 **Reference standard:** Clinical diagnosis Schedule for affective Disorders and Schizophrenia for School-Age Children- Present and Lifetime version (K-SADS-PL) Timing: Concurrent	**Index test:** Parent rating PSC-17 (Pediatric Symptom Checklist 17-item) attention subscale, cut score >=7 Sensitivity: 58 Specificity: 91 AUC: 0.86 (0.78, 0.94) PPV: 25 5% prevalence NPV: 98 5% prevalence	**Index test 2:** Parent rating CBCL-A (Child Behavior Checklist) attention subscale Sensitivity: 68 Specificity: 90 Accuracy: AUC: 0.88 (0.80, 0.96) PPV: 26 5% prevalence NPV: 98 5% prevalence ICC: Internal consistency: Alpha: Test-retest: Temporal stability:	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Gargaro, 2014[287] Case series N = 49 Australia Setting: Other	**Target:** Children with ADHD or ADHD plus autism; excluded if they had previously experienced the following conditions: comorbid medical, hearing or visual, neurological, psychiatric or genetic disorders, other than the primary diagnoses of autism and/or ADHD **Other:** Children with autism alone (N = 12) or neurotypical (N = 12) **ADHD presentation:** combined : 100 **Diagnosed by:** Specialist **Comorbidity:** **Female:** 18.4% All 12 children with comorbid autism and ADHD were male **Age mean:** 11.2 (3.6) Autism 11.3 (3.6); ADHD 10.9 (3.2); comorbid autism and ADHD 11.1 (3.9); neurotypical 11.4 (3.6) **Min age:** 6 **Max age:** 18 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed with ADHD per DSM IV TR Timing: Prior diagnosis	**Index test:** Parent rating DBC-HI (Developmental Behaviour Checklist Hyperactivity Index), parent version questionnaire, cutoff point = 4 Sensitivity: 100 Sensitivity for differentiating ADHD + autism from autism alone = 83.3% for cut point at 7 Specificity: 92 Specificity for differentiating ADHD + autism from autism alone = 50.0% for cut point at 7 AUC: 0.997 0.98 to 1.10 AUC 0.722 (CI .507–.937) for discriminating autism + ADHD from autism alone Alpha: 0.931	**Index test 2:** Parent rating CPRS-R(S) (Conner's Parent Rating Scale-Revised Short Form) Sensitivity: 100 Sensitivity for differentiating autism + ADHD from autism alone = 75% for cut point score of 72 Specificity: 92 Specificity for differentiating autism + ADHD from autism alone = 67% for cut point score of 72 AUC: 0.994 0.975 to 1.00 AUC 0.782 (CI 0.596–0.979) for discriminating autism + ADHD from autism alone	N/A	N/A

Geurts, 2004[293] Case series N = 136 Netherlands Setting: Mixed	**Target:** Children with ADHD and children with ADHD+ODD/CD; required not to use any medication; IQ>=80; children with OCD, Tourette syndrome, and pervasive developmental disorders were excluded; medication discontinued at least 20 hours prior to testing **Other:** Neurotypical developing children from 4 regular schools and another research sample with the same recruitment methods, IQ>=80, no history of behavioral problems or a learning disability; Children with high functioning autism recruited from institutions sp **ADHD presentation:** inattentive : 30,hyperactive : 3,combined : 67 **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 0% **Age mean:** 9.3 (2.0) for ADHD group, 9.1 (1.7) for normal control group, and 9.4 (1.8) for high functioning autism group **Min age:** 6 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Child Communication Checklist parent and teacher, Disruptive Behavior Disorder rating scale parent and teacher, Diagnostic Interview Schedule for Children for DSM-IV parent version, and Revised Autism Diagnostic Interview Timing: Prior diagnosis	**Index test:** Neuropsychological,EF 3 group discriminant function analysis (ADHD vs high functioning autism vs neurotypical); z-scores of the following variables were included as predictors: Stop Signal Reaction Time, Self-Ordered Pointing task beta errors, Tower of London beta execution time, Wisconsin Card Sorting test percentage, perseverative responses, aggregated verbal fluency score, and aggregated non-exectutive function task score; leave-one-out cross-validation Sensitivity: 69 Accuracy: 61 56% using leave-one-out cross validation Rater agreement: In order to take into account chance agreement, the kappa coefficient was computed. A value of 1 for Kappa indicates perfect prediction, while a value of 0 indicates chance-level prediction Kappa: 0.40	**Index test 2:** Neuropsychological,EF 2 group discriminant function analysis (ADHD vs high functioning autism); z-scores of the following variables were included as predictors: Stop Signal Reaction Time, Self-Ordered Pointing task beta errors, Tower of London beta execution time, Wisconsin Card Sorting test percentage, perseverative responses, aggregated verbal fluency score, and aggregated non-exectutive function task score; leave-one-out cross-validation; 89 children were included in this analysis using 6 predictors, the ratio of the total sample size to the number of predictors is quite large and could lead to low reliability of the discriminant functions obtained Accuracy: 71 69% using leave-one-out cross validation Rater agreement: In order to take into account chance agreement, the kappa coefficient was computed. A value of 1 for Kappa indicates	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
			perfect prediction, while a value of 0 indicates chance-level prediction Kappa:0.38		

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Gibbons, 2020[297] Case series N = 801 US Setting: Specialty care	**Target:** English speaking children without autism spectrum, intellectual developmental, or a psychotic disorder that would limit their ability to provide accurate self-reports **Other:** Children without evidence of psychiatric disorder **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** Other : Study includes children with primary diagnosis of major depressive disorder, bipolar disorder with manic symptoms, anxiety, ODD, and CD **Female:** 32.2% **Age mean:** 11.1 (3.2) for ADHD group, 12.2 (3.1) for control group **Min age:** 7 **Max age:** 17 **Ethnicity:** % Hispanic or Latino : 5.4 % White : 61.2 **Reference standard:** Clinical diagnosis K-SADS-PL, Children's Global Assessment Scale (CGAS), review of medical record recruited from psychiatric institute and clinic, local clinics and providers Timing: Prior diagnosis	**Index test:** Combined rating K-CAT (Kiddie-Computerized Adaptive Test) using combined item response scale scores from parent and child; 3-fold cross validation Sensitivity: 75 with specificity fixed at 80 % Specificity: 80 fixed specificity Accuracy: 86 AUC: 0.86 (0.83, 0.89)	**Index test 2:** Parent rating K-CAT (Kiddie-Computerized Adaptive Test) using item response scale scores from parent, test administered using tablet computers; 3-fold cross validation AUC: 0.85 (0.81,0.88)	**Index test 3:** Teen/child self report K-CAT (Kiddie-Computerized adaptive test) using item response scale scores from child, test administered using tablet computers, items were tested for readability using the Flesch-Kincaid reading grade level; a research assistant offered to read the questions to the participant; 3-fold cross validation AUC: 0.71 (0.67,0.75)	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Gilbert, 2016[298] Clinical trial N = 70 China Setting: Mixed	**Target:** Participants with AD/HD combined type or AD/HD hyperactivity impulsive type, IQ>=80, no disorders of consciousness or head injuries, no comorbid mental disorders, asked to abstain from taking any stimulant medication for two weeks prior to testing **Other:** Healthy control children recruited from a local primary school, IQ>=80 **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 8.6% 91.4 **Age mean:** 9.3 mean age **Min age:** 7 **Max age:** 11 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed by clinician using DSM-IV criteria Timing: Prior diagnosis	**Index test:** Clinician tool,Activity Model with 5 variables: Full-Scale Response ControlQuotient from the Integrated Visual and Auditory Test, Full-Scale Response Attention Quotient, Kcal Wrist actigraph data, and Kcal Ankle actigraph data, and age group; movement counts from the wrist and ankle actigraphs were converted into kilocalories, i.e., units of energy expenditure; stepwise discriminant function analysis Sensitivity: 80 Specificity: 90 Accuracy: 82	**Index test 2:** Neuropsychological,CPT Continuous performance test quotient scores (Full-Scale Response Control Quotient from the Integrated Visual and Auditory Test, Full-Scale Response Attention Quotient) Sensitivity: 59 Specificity: 81 Accuracy: 70	**Index test 3:** Clinician tool,Activity Actigraph data (converted into kilocalories, i.e., units of energy expenditure) plus continuous performance test quotient scores (Full-Scale Response Control Quotient from the Integrated Visual and Auditory Test, Full-Scale Response Attention Quotient) Sensitivity: 83 Specificity: 91 Accuracy: 84	**Index text 4:** Clinician tool,Activity Actigraph data (converted into kilocalories, i.e., units of energy expenditure) continuous performance test scores (Full-Scale Response Control Quotient from the Integrated Visual and Auditory Test, Full-Scale Response Attention Quotient) plus age group Sensitivity: 80 Specificity: 90 Accuracy: 82

Goh, 2023[299] Goh, 2020[794]; Karalunas, 2017[874] Case series N = 399 US Setting: N/A	**Target:** Children meeting the diagnostic criteria for ADHD, without autism; drawn from the Oregon ADHD-1000 Cohort; IQ>=80; excluded children taking non-stimulant medications, children taking stimulant medications went through wash out period **Other:** Children who did not meet diagnostic criteria for ADHD; a few children without ADHD exhibited common comorbid conditions (e.g., mood, anxiety, ODD, CD, and Learning Disorders); drawn from the Oregon ADHD-1000 Cohort; IQ>=80 **ADHD presentation:** inattentive : 27,hyperactive : 3,combined : 70 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 30% **Age mean:** 9.6 (1.51) for the ADHD group, 9.0 (1.31) for the no ADHD group (mean ages at testing visit); Age range 7-13 years in Year 1 and 11-18 years in Year 6 **Min age:** 7 **Max age:** 18 **Ethnicity:** % White : 80 **Reference standard:** Clinical diagnosis Parent completed Conners' Rating Scales- 3rd edition, Strengths and Difficulties Questionnaire, ADHD Rating Scale, and Kiddie Schedule for Affective Disorders and Schizophrenia; children completed a brief unstructured clinical interview and a three-subtest short form of the WISC-IV and two subtests of the WIAT-II; all materials were scored and presented to a clinical diagnostic team comprised of a board-	**Index test:** Parent interview guide KSADS (Kiddie Schedule for Affective Disorders and Schizophrenia) parent report; 8 ADHD symptoms identified as "important" in predicting impairment outcomes included in model, random forest regression predicting ADHD diagnosis at baseline Sensitivity: 97 Specificity: 86 Accuracy: 92 PPV: 90 NPV: 96	**Index test 2:** Teacher rating scale ADHD-RS (ADHD Rating Scale) Teacher report; 8 ADHD symptoms identified as important in predicting impairment outcomes included in model, random forest regression predicting ADHD diagnosis at baseline Sensitivity: 92 Specificity: 88 Accuracy: 91 PPV: 91 NPV: 90	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	certified child psychiatrist and a licensed child neuropsychologist who were blind to one another' ratings Timing: Prior diagnosis				
Gomez, 2018[300] Cohort study N = 217 Australia Setting: Specialty care	**Target:** Patients referred to an outpatient psychiatric unit **Other:** None, test-retest study **ADHD presentation:** inattentive : 28.3,hyperactive : 6.7,combined : 65.0 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 22.5% **Age mean:** N/A **Min age:** 7 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis DSM-IV TR Timing: Prior diagnosis	**Index test:** Parent rating SWAN-M (Modified version of the Strengths and Weaknesses of ADHD-Symptoms and Normal Behavior) Scale, all maternal ratings, test-retest study of measurement invariance over a 12-month interval Internal consistency: Internal consistency coefficient alpha values were .89, .89. .92 for the IA and HI and combined (IA plus HI) scales, respectively, at Time 1; and 77, .80, .79, respectively, for Time 2 Alpha: 12 months apart Test-retest: Test-retest measurement invariance not reliability was tested	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Gomez, 2021[301] Case series N = 264 Australia Setting: Specialty care	**Target:** Children referred to a hospital outpatient psychiatric who were diagnosed with ADHD **Other:** Children referred to a hospital outpatient psychiatric unit who were not diagnosed with ADHD **ADHD presentation:** inattentive : 17,hyperactive : 12,combined : 71 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 26% **Age mean:** 9.21 (1.22) for ADHD group, 9.29 (1.18) for non-ADHD group **Min age:** 6 **Max age:** 11 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnoses of ADHD and ODD based on the ADISC-IV (Anxiety Disorders Interview Schedule for Children); a semistructured interview, based on the DSM-IV-TR diagnostic system Timing: Prior diagnosis	**Index test:** Parent rating Conners-3-P(S)+CBCL (Connors 3 Parent Short Form) and Child Behavior Checklist Sensitivity: 79 (73, 85) Specificity: 77 (63, 87) AUC: 0.85 (0.68, 0.85) PPV: 92 NPV: 50	**Index test 2:** Teacher rating scale TRF+Conners-3-T(S) Teacher's Report Form and Conners 3 Teacher Short Form, score of 17 used as cut-off Sensitivity: 72 (64, 79) Specificity: 75 (59, 97) Accuracy: AUC: 0.77 (0.79, 0.89) Child Behavior Checklist parent 0.86 (95% CI: 0.81, 0.90) PPV: 92 NPV: 41	**Index test 3:** Parent rating CBCL-Ag Child Behavior Checklist aggressive behavior scale Sensitivity: 60 (51.0, 68.5) Specificity: 75 (62.7, 85.5) PPV: 83.9 NPV: 46.9	**Index text 4:** Teacher rating scale TRF-Ag (Teacher's Report Form) aggressive behavior scale Sensitivity: 48 (39.5, 56.9) Specificity: 91 (80.4, 96.4) PPV: 91.5 NPV: 44.9

Grazioli, 2023[303] Case series N = 342 Italy Setting: Specialty care	**Target:** Children and adolescents referred for suspected ADHD who received a diagnosis of ADHD **Other:** Children and adolescents referred for suspected ADHD who did not receive a diagnosis of ADHD; 33% of the subjects received neither an ADHD diagnosis nor an ASD diagnosis, 8% of the subjects were diagnosed with ASD without ADHD **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 11% **Age mean:** 9 (2) **Min age:** 3 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Full neuropsychiatric evaluation in accordance with the DSM-5 criteria; clinicians perform clinical interviews, a neurologic examination, and a cognitive evaluation, Conners' Parent Rating Scale–Revised (CPRS-R), Child Behavior Checklist (CBCL), and Social Responsiveness Scale (SRS), Conners' Teacher Rating Scale–Revised (CTRS-R) Timing: Concurrent	**Index test:** Combined rating Conners' Parent Rating Scale–Revised (CPRS-R), Child Behavior Checklist (CBCL), and Conners' Teacher Rating Scale–Revised (CTRS-R); decision tree classifier, leave-one-out cross validation, ADHD versus non-ADHD Sensitivity: 92 Specificity: 50 Accuracy: 74 (69, 79) No information rate 59% (p<0.001) PPV: 72 NPV: 80	**Index test 2:** Combined rating Conners' Parent Rating Scale–Revised (CPRS-R), Child Behavior Checklist (CBCL), and Conners' Teacher Rating Scale–Revised (CTRS-R); support vector machine classifier, leave-one-out cross validation, ADHD versus non-ADHD Sensitivity: 81 Specificity: 66 Accuracy: 75 (70, 80) No information rate 59% (p<0.001) PPV: 77 NPV: 71	N/A	N/A
Grodzinsky, 1992[307] Grodzinsky, 1999[805] Case series N = 130 US Setting: Specialty care	**Target:** Consecutive referrals to an outpatient unit specializing in the treatment of hyperactivechildren diagnosed with ADHD; children with language-based learning disabilities or clinically significant conduct disorder were excluded; all male; Full Scale IQ between 85 and 125 **Other:** "Snowball" technique: Parents of ADHD boys referred peer(s) of their son's, parents of these children	**Index test:** Neuropsychological,EF Variables included commissions and omissions scores from the vigilance portion of the Gordon Diagnositc System and the Interference subtest of the Stroop test, stepwise discriminant function analysis Sensitivity: 82 Specificity: 80	**Index test 2:** Neuropsychological,CPT Continuous Performance Test (CPT); number correct; cutoff (1.5 SDs below the mean) <=34 for 6-8 years old and <=35 for for 9-11 years old; cutoff scores	**Index test 3:** Neuropsychological,EF Stroop Test; cutoff (1.5 SDs below the mean) <=44 for 6-8 years old and <= 41 for for 9-11 years old; cutoff scores	**Index text 4:** Neuropsychological,EF Controlled Oral Word Association FAS Test; cutoff (1.5 SDs below the mean) <=9 for 6-8 years old and <= 16 for

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	referred other children; also recruited through a local newspaper ad; all male; FSIQ between 85 and 125 **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 0% **Age mean:** **Min age:** 6 **Max age:** 11 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Medical history, parental interview, Children's Attention Profile; a teacher-completed inventory consisting of the 12 most discriminating geatures selected from the Inattention and Overactive subscales of the Child Behavior Cheklist-Teacher Form Timing: Prior diagnosis	Accuracy: 81	determined by utilizing data from the neurotypical children in the sample artificially restricting specificity to 93%[805] Sensitivity: 41 Specificity: Artificially restricted to 93% Accuracy: 67 PPV: 87 NPV: 61 Rater agreement: CPT number correct versus clinical diagnosis Kappa:34%	determined by utilizing data from the neurotypical children in the sample artificially restricting specificity to 93%[805] Sensitivity: 43 Specificity: Artificially restricted to 93% Accuracy: 68 PPV: 88 NPV: 62 Rater agreement: Stroop test versus clinical diagnosis Kappa: 36%	for 9-11 years old; cutoff scores determined by utilizing data from the neurotypical children in the sample artificially restricting specificity Sensitivity: 32 Artificially restricted to 93% Accuracy: 63 PPV: 88 NPV: 58 Rater agreement: FAS test versus clinical diagnosis Kappa: 26%

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Gungor, 2021[309] Case series N = 70 Turkey Setting: N/A	**Target:** Participants are drug-naive, without comorbid psychiatric disorders, genetic syndromes, metabolic disorders, neurological disease and obesity; IQ>80 **Other:** Age and sex-matched healthy children **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 42.85% **Age mean:** 8.83 (2.99) **Min age:** 6 **Max age:** 12 **Ethnicity:** Other **Reference standard:** Clinical diagnosis Clinical diagnosis using DSM-5 Timing: Prior diagnosis	**Index test:** Biomarker Serum erythropoietin levels Sensitivity: 100 Specificity: 97 AUC: 0.980	**Index test 2:** Biomarker Serum erythropoietin receptor levels Sensitivity: 100 Specificity: 100 AUC: 1.00	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Guttentag, 2022[311] Case series N = 176 US Setting: Specialty care	**Target:** Children with ADHD enrolled in a neuroimaging study; those with known genetic syndromes, medical illnesses requiring chronic treatment, use of antipsychotics withinthe past 6 months, and full-scale IQ below 70 were excluded **Other:** Children with Autism Spectrum Disorder; same exclusion criteria **ADHD presentation:** inattentive : 34.3,hyperactive : 9.8,combined : 51.0,combined_other : 5.9 **Diagnosed by:** Specialist **Comorbidity:** Autism : 56 patients w co-morbid ADHD + ASD **Female:** 18.2% **Age mean:** 8.2 (1.7) **Min age:** 6 **Max age:** 11 **Ethnicity:** % Hispanic or Latino : 24.4 % White : 60.8 Other : 23.9% other "minorities" **Reference standard:** Clinical diagnosis DSM V diagnosis of ADHD or ASD Timing: Prior diagnosis	**Index test:** Parent interview guide ASI (Autism Symptom Interview)–School-Age—verbal algorithm, based on questions from the Autism Diagnostic Interview – Revised , is a 20-minute telephone interview for parents of verbally fluent children Sensitivity: 0.73, CI 0.61–0.83 for ASD vs ADHD Specificity: 0.74, CI 0.64–0.82 for ASD vs ADHD AUC: 0.79 0.72–0.85	**Index test 2:** Parent rating SRS-2 (Social Responsiveness Scale – 2nd Edition), a caregiver questionnaire thatassesses social behaviors across several domains, including social awareness, social cognition, social communication, social motivation, and autistic mannerisms Sensitivity: 0.64, CI 0.52–0.74 for ASD vs ADHD Specificity: 0.78, CI 0.68–0.85 for ASD vs ADHD AUC: 0.78 0.74–0.85	**Index test 3:** Parent rating SCQ-L (Social Communication Questionnaire – Lifetime), caregiver questionnaire to diagnosis of individuals suspected of having ASD; questions cover social communication skills and behaviors Sensitivity: 0.41, CI 0.30–0.54 for ASD vs ADHD Specificity: 0.91, CI 0.83–0.96 for ASD vs ADHD AUC: 0.85 0.79–0.91	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Hager, 2021[312] Case series N = 130 Multiple countries Setting: Specialty care	**Target:** Participants without somatic conditions such as a diagnosed brain injury/neurological disorder and/or autism spectrum disorder, IQ>=70, not on ADHD medication when tested **Other:** Age and gender matched typically developing children, mostly drawn from Human Brain Indicies database **ADHD presentation:** inattentive : 21,combined : 79 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 39% **Age mean:** Mean (SD): ADHD 10.52 (1.2) and Typically developing children 10.58 (1.2) **Min age:** 9 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed at three different child psychiatry outpatient clinics in Norway in accordance with DSM 5 criteria. Some patients had participated in earlier studies applying DSM IV. Timing: Prior diagnosis	**Index test:** EEG Combination of EEG 3 min eyes-closed condition, 3 min eyes-opened, and 20 min during a cued go/no-gotask. Combined behavioral test scores from a cued visual go/no-go task and Event Related Potentials Accuracy: 98 AUC: Log10 Index AUC 0.977	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Hall, 2016[315] Pre-post study N = 80 UK Setting: Specialty care	**Target:** Participants diagnosed with or without QbTest **Other:** None; study examined time to diagnoses of ADHD with and without QbTest results **ADHD presentation:** N/A : All diagnoses made for Hyperkinetic disorder (F90), equivalent to "severe combined subtype" **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 20% female in the pre-QbTest group, 30% female in the QbTest group **Age mean:** 9.2 (2.3) for the QbTest group , 8.1 (2.4) for the pre-QbTest group **Min age:** 4 **Max age:** 14 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis completed using ICD-10 codes from patient records Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT QbTest is a neuropsychological test that measures the three main symptoms of ADHD, requires subjects to respond to stimulus while ignoring other stimuli Cost: 31	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Hall, 2020[314] Case series N = 250 UK Setting: Mixed	**Target:** Children referred for their first ADHD assessment to a child and adolescent mental health service or community pediatric clinic **Other:** Children not diagnosed with ADHD obtained from the "AQUA-Trial" RCT **ADHD presentation:** N/A **Diagnosed by:** Provider **Comorbidity:** N/A **Female:** % 21% in entire sample **Age mean:** 9.5(2.8) **Min age:** 6 **Max age:** 17 **Ethnicity:** % White : 89 % Multiracial : 6 Other : 5 **Reference standard:** Clinical diagnosis Clinician's diagnosis was made in accordance with DSM-IV/DSM-V criteria using a short clinical record pro forma after each consultation; Independent research diagnosis made with the Development and Well-Being Assessment (DAWBA) using DSM-V criteria Timing: Concurrent	**Index test:** Parent rating SNAP-IV parental rating; diagnostic accuracy of SNAP-IV compared to clinical diagnosis Sensitivity: 100 Specificity: 4 PPV: 82 NPV: 100	**Index test 2:** Teacher rating scale SNAP-IV teacher rating; diagnostic accuracy of SNAP-IV compared to clinical diagnosis Sensitivity: 97 Specificity: 26 PPV: 83 NPV: 67	**Index test 3:** Teacher rating scale SNAP-IV teacher rating; diagnostic accuracy of SNAP-IV compared to independent research diagnosis using the Development and Well-Being Assessment (DAWBA) Sensitivity: 91 Specificity: 31 PPV: 74 NPV: 60	**Index text 4:** Parent rating SNAP-IV parental rating; diagnostic accuracy of SNAP-IV compared to independent research diagnosis using the Development and Well-Being Assessment (DAWBA) Sensitivity: 87 Specificity: 57 PPV: 79 NPV: 70

Hamadache, 2021[316] Case series N = 118 Germany Setting: Mixed	**Target:** Recruited at the social-pediatric center of the university hospital in Aachen, most frequent comorbidities were motor disorder and premature birth, 27.8% of the children with ADHD had a comorbid specific language disorder, not on medication **Other:** The normally developing control group had been tested at their preschools within earlier research efforts, the specific language imparment group was recruited at the social-pediatric center of the university hospital in Aachen **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 19% **Age mean:** 5.53 (0.265) for the ADHD group, 5.45 (0.273) for the control group, 5.45 (0.050) for the specific language imparment group **Min age:** 5 **Max age:** 5 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis For the process of diagnosing ADHD at the SPZ Aachen, an anamnestic interview covering risk factors and symptom expression among other relevant information is conducted by a pediatrician. Rating scales are filled out by parents and preschool teachers, and an attentional as well as an IQ test (K-ABC-II) are administered. Psychologists observe children in active play with others. Diagnoses were issued by independent	**Index test:** Neuropsychological,CPT QbMini, continuous performance test assessing the symptomdomains inattention and impulsivity, and an infrared tracking system measuring the (hyper)activity level; ADHD vs normally developing controls Accuracy: 59 AUC: 0.816	**Index test 2:** Parent rating The Fremdbeurteilungsbogen für Vorschüler mit Aufmerksamkeits- und Hyperaktivitätsstörungen (FBB-ADHS-V) is a 42-item questionnaire for parents and preschool teachers used to assess typical ADHD symptoms in preschool age; It provides separate scales for inattention and hyperactivity/impulsivity; ADHD vs normally developing controls Accuracy: 77 AUC: 0.880 Rater agreement: QbMini vs FBB-ADHS-V The correlation of the QbMini's total performance score with the FBB-ADHS-V total score was moderate (r = .370)	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	pediatricians, psychologists, and speech pathologists Timing: Concurrent				
Hasaneen, 2017[319] Case series N = 35 Egypt Setting: Specialty care	**Target:** Participants with IQ>=80, no comorbid pyschiatric disorders **Other:** Age and sex matched healthy children recruited from ADHD patient's relatives **ADHD presentation:** inattentive : 41.2,combined : 58.8 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 29.4% **Age mean:** 8.38 (1.78) **Min age:** 6 **Max age:** 15 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis completed using examination with criteria of the DSM-IV, physical and neurological exams completed by trained pediatric neurologist Timing: Prior diagnosis	**Index test:** Imaging MRI, T2*-MRI used to assess brain iron content levels, and R2* value calculated (transverserelaxation rates-T2*, or its inverse R2*) Sensitivity: 71 Specificity: 94 Accuracy: 82.9 AUC: 0.863 PPV: 92 NPV: 77	N/A	N/A	N/A

Helgadottir, 2015[322] Case series N = 661 Iceland Setting: Mixed	**Target:** Participants diagnosed with ADHD and free of moderate or severe intellectual disability, comorbidities included **Other:** Typically developing children were reported to be free of any mental or developmental disorders by their parents and had a score of less than 1.5 SDs above the age-appropriate norm on the ADHD Rating Scale-IV recruited in three schools **ADHD presentation:** inattentive : 33,hyperactive : 2,combined : 65 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % Male:female ratio 3:1 ADHD group, 1:1 for control **Age mean:** 9.6 years for the ADHD group and 9.5 years for the control (typically developing) group **Min age:** 5.8 **Max age:** 14 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed according to DSM-IV using the K-SADS-PL semistructured interview, performed by experienced clinicians. Timing: Concurrent	**Index test:** EEG EEG 3 min with eyes closed at rest. EEG coherence measures and chronological age features,statistical pattern recognition (SPR) based on support vector machines, cross-validation and separate test group Accuracy: 76 Independent test cohort, 81% cross validation	N/A	N/A	N/A
Heller, 2013[323] Case series N = 52 US Setting: Specialty care	**Target:** Recruited from two outpatient clinics, diagnosed with ADHD, IQ>55, stimulant medications for ADHD were withheld on the day of testing **Other:** Age and sex-matched comparison subjects without ADHD recruited from two outpatient clinics, IQ>55 **ADHD presentation:** inattentive : 35,inattentive_other : 100% of the	**Index test:** Neuropsychological,CPT "Groundskeeper" video game using the Sifteo Cubes gaming platform; AdaBoost meta-algorithm, JRip rule-making algorithm, and J48 and RandomForest decision tree algorithms tested, binary classification=	**Index test 2:** Neuropsychological,CPT "Groundskeeper" video game using the Sifteo Cubes gaming platform; AdaBoost meta-algorithm, JRip rule-making algorithm, and J48 and RandomForest	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	ADHD participants had inattentive symptoms,combined : 65,combined_other : 65% of the ADHD participants had hyperactive symptoms in addition to inattentive symptoms **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 38% **Age mean:** 12.6 for the ADHD group, 14.7 for the no ADHD group **Min age:** 6 **Max age:** 17 **Ethnicity:** % Hispanic or Latino : 2 % Black/African American : 15 % White : 77 Other : 6% Other Race **Reference standard:** Clinical diagnosis Schedule for Affective Disorders and Schizophrenia for School-Age Children- Present and Lifetime version semistructured diagnostic interview, Conners' Brief Rating Scale- Parent version and Teacher version, previous Conner's CPT scores if available Timing: Concurrent	presence/absence of hyperactivity Sensitivity: 77 Specificity: 81 Accuracy: 75	decision tree algorithms tested, binary classification = binary classification= presence/absence of inattention Sensitivity: 59 Specificity: 83 Accuracy: 78		

Hinshaw, 2002[327] Case series N = 228 US Setting: Other	**Target:** Females recruited from multiple sources to attend one of three consecutive summer research programs; testing performed without stimulant medication (minimum 24 hour washout period); IQ>=70 **Other:** Recruited from multiple sources to attend one of three consecutive summer research programs; age and ethnicity-matched; all female; IQ>=70; girls with ODD or internalizing disorders not excluded from comparison group **ADHD presentation:** inattentive : 34,combined : 66 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 100% **Age mean:** **Min age:** 6 **Max age:** 12 **Ethnicity:** % Hispanic or Latino : 11 % Black/African American : 27 % Asian : 9 % White : 53 **Reference standard:** Clinical diagnosis Swanson, Nolan, and Pelham (SNAP) Parent and Teacher Scales, Child Behavior Checklist, Teacher Report Form, Diagnostic Interview Schedule for Children (DISC-IV) Timing: Prior diagnosis	**Index test:** Neuropsychological,EF Binary (ADHD vs comparison) discriminant function analysis; variables included in final model were Rey-Osterrieth Complex Figure Design errors, Porteus Maze test age, Cancel Underlining Test, Word Attack, Grooved Pegboard, Continuous Performance Test omissions, and Rapid Automatized Naming scores Sensitivity: 78 Specificity: 58 Accuracy: 78	**Index test 2:** Neuropsychological,EF Three category (ADHD combined vs ADHD inattentive vs comparison) discriminant function analysis Sensitivity: 63% for ADHD combined, 16% for ADHD inattentive Specificity: 73 Accuracy: 57	N/A	N/A
Hong, 2019[331] Case series N = 44 US Setting: Specialty care	**Target:** Children presenting to university affiliated outpatient clinics with early disruptive behavior problems diagnosed with ADHD and disruptive behavior disorder **Other:** Children presenting to university affiliated outpatient clinics with early disruptive behavior problems	**Index test:** Parent rating CBCL-AD/H (Child Behavior Checklist) attention-deficit/hyperactivity problems scale for ages 1.5 to 5 Sensitivity: 71 Specificity: 91 Accuracy: 80 AUC: 0.83 PPV: 88	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	not diagnosed with ADHD (diagnosed with disruptive behavior disorder only) **ADHD presentation:** hyperactive : 57.1,combined : 42.9 **Diagnosed by:** Specialist **Comorbidity:** ODD : 95.5% ODD, 25% CD **Female:** 20.5% **Age mean:** 4.61 (0.87) **Min age:** 3 **Max age:** 5 **Ethnicity:** % Hispanic or Latino : 29.4 % Black/African American : 4.5 % Asian : 2.3 % White : 56.8 % Multiracial : 4.5,Other : Defined by Other **Reference standard:** Clinical diagnosis Kiddie-Disruptive Behavior Disorders Schedule (K-DBDS) by supervised by a licensed clinical psychologist and diagnoses were confirmed through consensus Timing: Concurrent	NPV: 78			

Hudziak, 2004[336] Case series N = 370 US Setting: Mixed	**Target:** Probands with T-scores above 67 on the attention problems syndrome and/or the aggressive behavior syndrome scales of the Child Behavior Checklist, lives with at least one biological parent, has at least one sibling between ages 6 and 18, IQ>=70 **Other:** Probands with T-scores below 60 on both the attention problems syndrome and the aggressive behavior syndrome scales of the Child Behavior Checklist; randomly selected siblings of probands (one sibling from each family) used as cross validation sample **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 42% female in entire sample **Age mean:** **Min age:** 6 **Max age:** 18 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Vermont Structured Diagnostic inverview with mothers of the probands and siblings Timing: Prior diagnosis	**Index test:** Parent rating CBCL-A (Child Behavior Checklist) attention problems scale, T-score cutoff= 55, ROCanalysis using attention problems syndrome scale Sensitivity: 83 Sibling group Specificity: 88 Sibling group AUC: 0.841 for proband group, 0.904 for sibling group PPV: 80 Sibling group NPV: 90 Sibling group	N/A	N/A	N/A
Hult, 2018[24] Case series N = 182 Sweden Setting: Specialty care	**Target:** Children referred to specialty clinic with suspected ADHD, autism, or another neurodevelopmental disorder; IQ>70; unmedicated at time of assessment; comorbid ASD, tic disorders, developmental coordination disorder, borderline intellectual functioning, dyslexia, language disorder, and depression/anxiety disorder included	**Index test:** Neuropsychological,CPT QbTest Sensitivity: With cutoff set to 1.25 Q-score as recommended by the manufactor, sensitivity ranged from 47% to 67% Specificity: With cutoff set to 1.25 Q-score as recommended by the manufactor, specificity ranged from 72% to 84%	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Other: Children not diagnosed with ADHD referred to and selected from same specialty clinic as the ADHD group; 81% of these children diagnosed with ASD; tic disorders, developmental coordination disorder, borderline intellectual functioning, dyslexia, language **ADHD presentation:** inattentive : 24,hyperactive : 2,combined : 71,N/A : 3 ADHD-not otherwise specified **Diagnosed by:** Specialist **Comorbidity:** Autism : Non-ADHD clinical comparison (CC) group participants had ASD (81%) **Female:** 22% **Age mean:** 10.3 (1.7) ADHD group, 10.8 (1.8) comparison group **Min age:** **Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis of ADHD performed by a multi-professional team, based on DSM-IV behavioral criteria Timing: Concurrent	AUC: 0.62-0.76 over three test parameters with cutoff set at recommended 1.25 Q-Score PPV: 76%-86% NPV: 37%-50%			

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Ickowicz, 2006[338] Case series N = 620 Canada Setting: Specialty care	**Target:** Children referred to the outpatient psychiatry clinic of a pediatric hospital, IQ>=80, medication-free at time of evaluation **Other:** Normal control subjects recruited from advertisements placed in a hospital staff newsletter, IQ>=80 **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % Boy-to-girl ratio of 3.2:1 in clinic-referred cases **Age mean:** 8.67 (1.81) clinic-referred cases, 9.04 (1.63) control sample **Min age:** 6 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis 6-hour evaluation divided into two, 3-hour sessions, Teacher Telephone Interview, Conners' Rating Scales-Revised and Revised ontario Child Health Study Scales from parents and teachers Timing: Concurrent	**Index test:** Parent interview guide PICS (Parent Interview for Child Symptoms) Rater agreement: 48 randomly selected, videotaped interviews were rescored by an independent reviewer blinded to original ratings 0.93 for ADHD inattentive, 0.97 for ADHD hyperactive-impulsive Kappa: 0.73 ICC: 0.97	N/A	N/A	N/A

Jacobson, 2020[339] Case series N = 787 US Setting: Specialty care	**Target:** Youth referred for outpatient neuropsychological assessment in a large outpatient neuropsychology clinic **Other:** Non- ADHD clinical comparison group; part of same referral process as ADHD group **ADHD presentation:** inattentive : 50,hyperactive : 10,combined : 40 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 37.5% in entire sample **Age mean:** 11.29 (3.15), 8.71 (2.68), 9.65 (2.88) across groups **Min age:** 5 **Max age:** 18 **Ethnicity:** % Hispanic or Latino : 2.25 % Black/African American : 24.46 % Asian : 2.3 % White : 59.63 % Multiracial : 5.45 Other : 4.8% unknown **Reference standard:** Clinical diagnosis Categorized using modified Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5) ADHD symptom criteria, including caregiver-report symptom count on the ADHD Rating Scale-IV after neuropsychological assessment in a large outpatient neuropsychology clinic Timing: Concurrent	**Index test:** Parent rating BRIEF2 (Behavior Rating Inventory of Executive Function, second edition) global executive composite summary score Sensitivity: 38 Specificity: 96 Accuracy: 63 AUC: 0.806 PPV: 93 NPV: 54 Alpha: 0.965	N/A	N/A	N/A
Jahanshahloo, 2017[340] Castro-Cabrera, 2010[702]; Ghasemi, 2022[791] Case series N = 60	**Target:** Participant with nothing abnormal in their physical, normal hearing/vision and and IQ of 80 or higher, medication not taken for 24 hours before test; comorbid ODD, phobias, and learning problems accounted for	**Index test:** EEG EEG event-related Potential signals were recorded by three electrodes located in themidline of the head (Pz, Cz, and Fz) according to 10–20 international system in two modalities, auditory and visual, at sampling rate of 640 samples per second.	**Index test 2:** EEG EEG event-related potentials using 3 sets of features: morphological, wavelets, and nonlinear dynamics based, best combination of	**Index test 3:** EEG EEG event-related potential (ERP) signals were recorded according to the criteria ofthe Oddball	**Index text 4:** EEG EEG event-related potential (ERP) signals were recorded according to the criteria ofthe Oddball

Colombia Setting: School	**Other:** Control group. All participants recruited from educational institutions of the metropolitan area of Manizales. **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** % N/A **Age mean:** N/A **Min age:** 4 **Max age:** 15 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Medical diagnosis determined using neurophysiological examination based on the criteria in DSM-4. Timing: Prior diagnosis	Fra-wave characterization with v_SVM classifier, 10 fold cross validation. Accuracy: 99	features. Support vector machine (SVM) classification, leave one out cross validation[702] Sensitivity: 96 Specificity: 87 Accuracy: 91 AUC: 0.94	paradigm in two modes of auditory and visual stimulation; Deep learning classifier using the features Absolute Band Power that is normalized by maximum power (ABP-0), Absolute Band Power that is normalized by the average of powers across all frequencies (ABP-1) or Relative Band Power that is normalized by maximum of row ERP power(RBP-0) or Relative Band Power that is normalized by the average of row power (RBP-1); Delta band[791] Accuracy: 100 AUC: 0.9995	paradigm in two modes of auditory and visual stimulation; Deep learning classifier using the features Absolute Band Power that is normalized by maximum power (Accuracy: 100 AUC: 0.9995
Jarrett, 2018[342] Case series N = 388 US Setting: Specialty care	**Target:** Participants referred to an outpatient clinic diagnosed with ADHD; stimulant medication instructed not to take medication on day of assessment, nonstimulant medication not asked to stop medication for assessment	**Index test:** Parent rating CBCL-A (Child Behavior Checklist) attention problems AUC: 0.66 (0.59, 0.72) Alpha: 0.76	**Index test 2:** Teacher rating scale TRF-A (Teacher Report Form) Attention Problems AUC: 0.65 (0.60, 0.71)	**Index test 3:** CPT Conners CPT Hit Reaction Time Standard Error LR+:Diagnostic likelihood ratio	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Other: Children referred from community pediatricians, schools, and mental health professionals presenting at an outpatient clinic for a psychoeducational assessment not diagnosed with ADHD **ADHD presentation:** inattentive : 29,hyperactive : 3,combined : 68 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 32% **Age mean:** 10.21 (2.73) **Min age:** 5 **Max age:** 17 **Ethnicity:** % Hispanic or Latino : 1.5 % Black/African American : 4 % White : 93 Other : 1.5% Race other **Reference standard:** Clinical diagnosis Participants were diagnosed with ADHD using the Diagnostic Interview Schedule for Children–IV–Parent Version (DISC-IV-P) with agreement between two investigators. Timing: Concurrent		LR+: Diagnostic likelihood ratio of 1.55 for individuals in the highest risk group (scores >=66.28) Alpha: 0.95	of 1.87 for individuals with high scores (>=74.5)	

Jensen-Doss, 2013[344] Case series N = 82 US Setting: Specialty care	**Target:** Children presenting for treatment at county community mental health clinics inTexas **Other:** Children presenting for treatment at county community mental health clinics inTexas; recruitment took place through the mental health authority's Eligibility Center (EC), a clinic where all new clients are screened for service eligibility **ADHD presentation:** inattentive : 4,combined : 74,N/A : ADHD-not otherwise specified 22% **Diagnosed by:** Other (specify) **Comorbidity:** N/A **Female:** % 24% in entire sample **Age mean:** 9.89 (2.82) **Min age:** 6 **Max age:** 16 **Ethnicity:** % Hispanic or Latino : 52 % Black/African American : 39 % White : 4 % Multiracial : 5 **Reference standard:** Clinical diagnosis 15 clinicians conducted the initial eligibility evaluations for the clients; four were licensed mental health professionals, five were interns, and six were qualified mental health professionals; the diagnoses were obtained from clinic records; data were not available on the diagnostic methods used by the EC staff, EC staff informally reported that, without funding for additional assessment tools, most clinicians used unstructured interviews with parents and children, guided by clinical judgment, to determine diagnoses Timing: Concurrent	**Index test:** Parent rating CBCL-A (Child Behavior Checklist) attention deficit/ hyperactivity problems subscale AUC: 0.55 (0.43, 0.68) Rater agreement: Percent disagreement= 45.1 Kappa between Child Behavior Checklist score versus clinical chart diagnosis was 0.10	N/A	N/A	N/A

Jimenez-Figueroa, 2017[346] Case series N = 152 Colombia Setting: School	**Target:** Spanish-speaking participants with IQ >=70; no clinical history of any major neurologic disease and/or developmental disorders or psychotic disorders; the ADHD checklist questionnaire was applied to all students (n = 845) from 1st to 6th grades attending a medium socio-economic stratum public school in Barranquilla, Colombia; participants with a T score >=60 in the ADHD checklist were selected as probable ADHD probands **Other:** Children with T scores <=55 on the ADHD checklist questionnaire **ADHD presentation:** inattentive : 30,combined : 70 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 29% **Age mean:** 7.75 (1.46) for the ADHD group, 8.84 (1.54) for the control group **Min age:** 6 **Max age:** 11 **Ethnicity:** Other : Community has predominantly mix ethnicity (racial intermix between white European [Andalusian-Spanish], black African, Syrian-Lebanese [Arabian], Jewish, and Amerindian people) **Reference standard:** Clinical diagnosis The Spanish version of the DSM-IV Mini International Neuropsychiatry Interview was administered to the parents of this sample by trained neuropsychologist as the gold standard diagnostic tool Timing: Concurrent	**Index test:** Neuropsychological,CPT,EF Go/No-Go task using a multi-operational apparatus for reaction times (MOART); 4 variables: prepotent response reaction time, prepotent response reaction time variablility, prepotent response inhibition reaction time, prepotent response inhibition reaction time variability; discriminant function analysis Sensitivity: 68 (60, 80) Specificity: 84 (74, 93) Accuracy: 73 (66, 80) AUC: 0.73 (0.66, 0.79) PPV: 90 NPV: 55 LR+: 4.16 LR-: 0.38	N/A	N/A	N/A

Johansson, 2021[347] Case series N = 340 Sweden Setting: Other	**Target:** Participants diagnosed with ADHD recruited from The Child and Adolescent Twin Study in Sweden (CATSS), which consists of twins born from 1992 and onward recruited from the Swedish twin registry. From CATSS, same-sex twins born from 1993 to 1995 were invited to participate in The Developmental Outcomes in a Genetic Twin Study in Sweden (DOGSS) if at least one of the twins in a pair had screened positive in the Autism-Tics, ADHD, and Other Comorbidities (A-TAC) inventory for ASD, ADHD, tic disorder (TD), language disorder (LD), developmental coordination disorder (DCD), or behavioral disorders with known neurodevelopmental comorbidities, such as obsessive compulsive disorder (OCD), oppositional defiant disorder (ODD), conduct disorder (CD), or eating disorder (ED) **Other:** Twin of ADHD particpant and randomly selected controls recruited from The Child and Adolescent Twin Study in Sweden (CATSS), which consists of twins born from 1992 and onward recruited from the Swedish twin registry **ADHD presentation:** inattentive : 25,hyperactive : 2,combined : 73 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 29% **Age mean:** All participants were age 15 **Min age:** 15 **Max age:** 15 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis	**Index test:** Neuropsychological,CPT The QbTest is a further development of the CPT by adding simultaneous measurements of motor activity, and it aims to measure the three core symptoms of ADHD: hyperactivity, inattention, and impulsivity Sensitivity: 67 Specificity: 58 AUC: 0.58 PPV: 36 NPV: 83	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	Results: Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	Index Test 2	Index Test 3	Index Test 4
	Trained psychologists, blind to all previous information and to the results of the examination of the co-twin, performed separate clinical interviews with each teenager and one or both parents. For the diagnostic assessment, the psychologists used the diagnostic interview Schedule for Affective Disorders and Schizophrenia in School-Age Children (K-SADS), and the global functioning level measured with Children's Global Assessment Scale (C-GAS) was determined. The diagnoses were later verified by a clinical doctor specialized in child and adolescent psychiatry, who was “blind” to the presumptive status according to the A-TAC interview. Questionnaires regarding psychosocial information such as school performance, peer problems, internalizing problems, antisocial behavior, misuse of alcohol and illicit drugs were administered to the participants. The participants and their parents also completed the Strengths and Difficulties Questionnaire. Timing: Prior diagnosis				

Johnstone, 2021[351] Case series N = 214 China Setting: Specialty care	**Target:** Participants with first-presentation, drug-naïve, full-scale IQ scores >80; no (a) diagnosis or history of head trauma with loss of consciousness, (b) history of neurological illness or other severe disease, and (c) diagnosis of schizophrenia, affective disorders, anxiety, tic disorders, pervasive developmental disorders, or mental retardation **Other:** Typically-developing children **ADHD presentation:** inattentive : 100 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 19% **Age mean:** 8.85 for the ADHD group, 8.92 for the control group **Min age:** 7 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis DSM-V diagnosis, using the Schedule for Affective Disorders and Schizophrenia for School-Age Children Present and Lifetime Version (K-SADS-PL) by a child and adolescent psychiatrist Timing: Concurrent	**Index test:** EEG Combination of NCAT (Neurocognitive assessment tool) combined model; 8 variables used for classification:EEG (EO TBR): 1 from SNAP-IV (DSM Inattentive), 2 from the BPNS-Parent (Relatedness at Home, Autonomy at School), 3 from the EF tasks (WM Search RT, TS Simple Switch RT, TS Flexible Switch RT), 1 from the CSBQ (Cognitive Self-Regulation); stepwise discriminant function analysis, leave-one-out cross validation Sensitivity: 85 Specificity: 92 Accuracy: 91	**Index test 2:** Other : parent rating but not English	**Index test 3:** Neuropsychological,EF NCAT (Neurocognitive assessment tool) core model; 8 variables used for classification: one from the BPNS-Child (Competence At School), three from the BPNS-Parent (Autonomy At Home, Relatedness at Home, Autonomy At School), two from the EF tasks (WM Search RT, TS Flexible Switch RT), and two from the CSBQ (Prosocial, Behavioural Self-Regulation); stepwise discriminant function analysis, leave-one-out cross validation Sensitivity: 79 Specificity: 90 Accuracy: 88	**Index text 4:** EEG EEG 4 variables used for classification: EO Alpha Power, FO Alpha Power, ThetaActivation, and EO TBR; stepwise discriminant function analysis, leave-one-out cross validation Sensitivity: 62 Specificity: 83 Accuracy: 81
Juneja, 2019[352] Case series N = 100	**Target:** Children presenting with features suggestive of ADHD at a pediatric outpatient department;	**Index test:** Neuropsychological,EF Children’s Color Trails Test part	**Index test 2:** Neuropsychological,EF	N/A	N/A

India Setting: Specialty care	IQ>=70; no neurological disorders likely to affect upper limb motor performance or compliance with directions for the test, had not received any treatment for behavioral problems/ADHD **Other:** Age and sex-matched controls enrolled from a pediatric outpatient department **ADHD presentation:** inattentive : 20,hyperactive : 2,combined : 78 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 0% **Age mean:** Median (IQR) of whole sample (n=100): 9 (8,12) years **Min age:** 8 **Max age:** 15 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD was diagnosed by a developmental pediatrician using the DSM-V criteria, after interviewing the child and the parents. CPRS and CTRS were administered, and scores on various sub-scales were obtained Timing: Prior diagnosis	1, a page with circled numbers 1-15 placed randomly on a paper (even numbers printed in yellow circles and odd in pink circles, the child has to rapidly connect numbers in sequence using a pencil; the test takes 15-20 minutes for administration, examiner records the time taken to complete each trail and errors committed, to arrive at the score of each part; score <=32 Sensitivity: 74 (60, 85) Specificity: 74 (60, 85) Accuracy: AUC: 0.800 (0.71, 0.87) Rater agreement: Children Collor Trails Test 1 versus Parent and Teacher Conners Rating Scale Scores Parent subscales (all correlations p<0.001): Inattention r= -0.498, Hyperactivity r= -0.556, Learning problems r= -0.383, Executive functioning r= -0.535, Aggression r= -0.448, Peer relationship r= -0.458. Teacher subscales (all correlations p<0.001)	Children's Color Trails Test part 2, numbers from 2–15 are presented twice, as both pink and yellow circles, the child has to rapidly connect the numbered circles in sequence, alternating between pink and yellow circles; the test takes 15-20 minutes for administration, examiner records the time taken to complete each trail and errors committed, to arrive at the score of each part; score <=40 Sensitivity: 84 (71, 93) Specificity: 72 (58, 84) AUC: 0.854 (0.77, 0.92) Rater agreement: Children Collor Trails Test 2 versus Parent and Teacher Conners Rating Scale Scores Parent subscales (all correlations p<0.001): Inattention r= -0.524, Hyperactivity r= -0.596, Learning problems r= -0.579, Executive functioning r= -0.534, Aggression r= -0.487, Peer relationship r= -0.581. Teacher subscales (all correlations p<0.001):		
Kam, 2010[355] Case series N = 142	**Target:** Recruited from a regular elementary school, diagnosed with ADHD	**Index test:** Clinician tool,Activity Monitoring children's school activities using a 3-axial actigraph placed on	**Index test 2:** Clinician tool,Activity Monitoring children's school activities using	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Korea Setting: School	**Other:** Recruited from a regular elementary school, 5 children diagnosed with psychiatric problems other than ADHD **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 20% **Age mean:** 7.44 (0.62) **Min age:** 7 **Max age:** 9 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Children who scored high on the questionnaires were clinically examined by child psychiatrists, who then confirmed ADHD; Questionnaires using the K-CBCL (Korean Child Behavior Checklist) and K-ARS (Korean ADHD Rating Scale-IV) were administered to the subject children's parents and homeroom teachers; interviews included K-SADS-PL-K (Kiddie Schedule for Affective Disorder and Schizophrenia-Present and Lifetime Version-Korean Version) based on the DSM-IV and mentality test Timing: Concurrent	the non-dominant wrist for 1-3 days, for 3 hours per day; mean, variance, and ratios of low-level (0.5-1.0G) and high-level (1.6-3.2G) activity were extracted as activity features; decision-tree models were constructed using the C5.0 algorithm from whole hours (class + playtime), 10-fold cross-validation Sensitivity: 100 Specificity: 99 Accuracy: 99 AUC: 0.9996 PPV: 91 7% prevalence NPV: 100 LR+: 132 LR-: 0	a 3-axial actigraph placed on the non-dominant wrist for 1-3 days, for 3 hours per day; mean, variance, and ratios of low-level (0.5-1.0G) and high-level (1.6-3.2G) activity were extracted as activity features; decision-tree models were constructed using the C5.0 algorithm from hours during classes, 10-fold cross-validation Sensitivity: 100 Specificity: 99 Accuracy: 99 AUC: 0.9985 PPV: 83 7% prevalence NPV: 100 LR+: 66		

Karabiber Cura, 2023[356] Case series N = 33 Turkey Setting: Specialty care	**Target:** Inclusion criteria not reported **Other:** Age-matched healthy children **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 53% **Age mean:** 12 for the ADHD group, 13 for the control group **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Other Unknown, clinical diagnostic process for ADHD patients not reported Timing: Prior diagnosis	**Index test:** EEG EEG eyes-closed resting state EEG signals analyzed using the intrinsic time-scale decomposition(ITD): different combinations of the modes, known as Proper Rotation Components (PRCs), produced by ITD, are used to extract a variety of connectivity-based features (magnitude square coherence, cross power spectral density, correlation coefficient, covariance, cohentropy coefficient, correntropy coefficient); combination of PRC1, PRC2, and PRC3, transversal plane, Bagged Tree classifier Sensitivity: 99 Specificity: 99 Accuracy: 99 10-fold cross-validation 99%, Leave-one-subject-out validation 97% PPV: 99	**Index test 2:** EEG EEG eyes-closed resting state EEG signals analyzed using the intrinsic time-scale decomposition(ITD): different combinations of the modes, known as Proper Rotation Components (PRCs), produced by ITD, are used to extract a variety of connectivity-based features (magnitude square coherence, cross power spectral density, correlation coefficient, covariance, cohentropy coefficient, correntropy coefficient); combination of PRC1, PRC2, and PRC3, longitudinal plane, Bagged Tree classifier Sensitivity: 99 Specificity: 99 Accuracy: 99 10-fold cross-validation 99%, Leave-one-subject-out validation 96% PPV: 99	**Index test 3:** EEG EEG eyes-closed resting state EEG signals analyzed using the intrinsic time-scale decomposition(ITD): different combinations of the modes, known as Proper Rotation Components (PRCs), produced by ITD, are used to extract a variety of connectivity-based features (magnitude square coherence, cross power spectral density, correlation coefficient, covariance, cohentropy coefficient, correntropy coefficient); combination of PRC1, PRC2, and PRC3, transversal plane, Support Vector Machine classifier Sensitivity: 99 Specificity: 99 Accuracy: 99	**Index text 4:** EEG EEG eyes-closed resting state EEG signals analyzed using the intrinsic time-scale decomposition(ITD): different combinations of the modes, known as Proper Rotation Components (PRCs), produced by ITD, are used to extract a variety of connectivity-based fea Sensitivity: 96 Specificity: 99 Accuracy: 98 10-fold cross-validation 98%, Leave-one-subject-out validation 97% PPV: 99

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
				10-fold cross-validation 99%, Leave-one-subject-out validation 98% PPV: 99	

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Karr, 2021[359] Kibby, 2015[884]; Kibby, 2014[885] Case series N = 223 Canada Setting: Other	**Target:** Participants diagnosed with ADHD or ADHD with comorbid reading disorder and IQ>=80 **Other:** Children with no diagnosis and children with reading disorder or other diagnoses **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 43% female in entire sample **Age mean:** 9.49 (1.35) **Min age:** 8 **Max age:** 12 **Ethnicity:** % Hispanic or Latino : 3 % Black/African American : 5 % White : 86 Other : 6 other ethnicities including multiracial **Reference standard:** Clinical diagnosis Clinical neuropsychologist conducted assessment according to DSM-IV criteria through a three-part process including a parent interview, a diagnostic questionnaire, and the BASC-2 to assess symptom severity for ADHD and other disorders Timing: Prior diagnosis	**Index test:** Teacher rating scale BASC-2-EF (Behavior Assessment System for Children, Second Edition, Executive Function screener) teacher rating scale global sum score, cutoff score= 51; analysis of ADHD (without comorbidity) vs children with no diagnosis Sensitivity: 79 Specificity: 71 AUC: 0.831 (0.761, 0.901) Alpha: 0.95	**Index test 2:** Parent rating BASC-2-EF (Behavior Assessment System for Children, Second Edition, Executive Function screener) parent rating scale global sum score, cutoff score= 32; analysis of ADHD (without comorbidity) vs children with no diagnosis Sensitivity: 91 Specificity: 84 AUC: 0.919 (0.858, 0.979) Alpha: 0.91	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Kennerley, 2018[362] Case series N = 55 New Zealand Setting: Specialty care	**Target:** Children who were on medication: Ritalin, Rubifen, Concerta, Methamphetamine **Other:** None **ADHD presentation:** inattentive : 43,hyperactive : 11,combined : 39,N/A : 7% ADHD-not otherwise specified **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 20% **Age mean:** 104.33 months (23.67 months) **Min age:** 6 **Max age:** 12 **Ethnicity:** % Asian : 1.8,Other : Chinese % White : 83.6,Other : 78.2% New Zealand European, 3.6% British, and 1.8% Australian % Multiracial : 7.3,Other : New Zealand European/ Maori Other : 5.5% Maori **Reference standard:** Clinical diagnosis Kiddie Schedule for Affective Disorders and Schizophrenia Timing: Prior diagnosis	**Index test:** Teacher rating scale ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale–4th edition) teacher rating Rater agreement: Teachers versus parents Significant positive correlation between the total number of symptoms endorsed by parents and teachers ($r = 0.251$, $p < 0.05$). Kappa: 0.292	**Index test 2:** Parent rating ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale–4th edition) parent rating	**Index test 3:** Clinician tool,Observation BOSS (Behavioral Observation of Students in Schools) Clinician versus parent and clinician versus teacher	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Kim, 2015[366] Case series N = 97 Korea Setting: Specialty care	**Target:** Hyperactive children attending camp; IQ>70; no brain damage, a neurologicaldisorder, a genetic disorder, substance dependence, epilepsy or any other mental disorder; not receiving drug treatment **Other:** Children who exhibited no abnormalities based on the DISC-IV criteria and who had no personal history of any psychological disorder or accompanying disease **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 13% **Age mean:** 10.16 (1.90) for ADHD group, and 9.62 (1.72) for control group **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD diagnosis was based on a Korean version of the Diagnostic Interview Schedule for Children Version IV (DISC-IV), and was confirmed by multiple child and adolescent psychiatrists Timing: Prior diagnosis	**Index test:** EEG EEG theta-phase gamma-amplitude coupling Accuracy: 72	N/A	N/A	N/A

Kim, 2015[365] Case series N = 157 Korea Setting: Other	**Target:** Children with ADHD except for those with ADHD not otherwise specified, IQ>70; no brain damage, neurological disorders, genetic disorders, substance dependence, epilepsy or any other mental disorder reported during a personal history and anamnesis; not on mediation **Other:** Children with no Korean version of the Diagnostic Interview Schedule for Children diagnosis and no personal history of psychological disorder or accompanying disease **ADHD presentation:** inattentive : 42,hyperactive : 24,combined : 34,N/A : Children diagnosed with ADHD-not otherwise specified were excluded from the study **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 19% **Age mean:** 9.25 (1.63) for the ADHD group, 9.56 (1.98) for the control group **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD diagnosis was based on a Korean version of the Diagnostic Interview Schedule for Children Version IV (DISC- IV), and diagnoses were confirmed by more than one child and adolescent psychiatrists Timing: Prior diagnosis	**Index test:** EEG EEG quantitative electroencephalography Accuracy: 61% for the delta power and 56% for the theta wave	**Index test 2:** CPT Integrated Visual and Auditory Continuous Performance Test Accuracy: 82% for commission error, and 79% for omission error	N/A	N/A
Koh, 2021[369] Case series N = 123 Singapore Setting: Specialty care	**Target:** Children and adolescent participants consenting to EEG and ECG procedures **Other:** Children with conduct disorder without ADHD **ADHD presentation:** N/A	**Index test:** Other (e.g., ECG) : ECG data transformed via Mathlab function Continuous 12-channel ECG signals recorded 3 minutes from each during complete relaxation with eyes open using the BIOPAC	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Diagnosed by: Provider **Comorbidity:** ODD **Female:** 11.4% **Min age:** 7 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis DSM-IV-TR Timing: Prior diagnosis	ECG100C electrocardiogram amplifier interfaced to proprietary MP150 data acquisition and AcqKnowledge analysis software; each recording was divided into 20-second segments comprising 5000 data points each; eight entropy features (approximate, sample, fuzzy, Tsallis, permutation, Kolmogorov Sinai, modified multiscale and higher-order spectra) were extracted from the modes of the transformed ECG signal data; "Bagged Tree," the most successful classification method is reported here Sensitivity: 88 Specificity: 86 Accuracy: 87.2			

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Koh, 2022[370] Raine, 2019[993]; Tor, 2021[1119] Case series N = 123 Singapore Setting: Specialty care	**Target:** Participants with ADHD only, or with ADHD + conduct disorder **Other:** Conduct disorder only (16 participants) **ADHD presentation:** N/A **Diagnosed by:** Provider **Comorbidity:** ODD **Female:** 11.2% **Age mean:** N/A **Min age:** 7 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Primary diagnosis made by child's attending physician Timing: Prior diagnosis	**Index test:** Other (e.g., ECG) : ECG Continuous 12-channel electrocardiography (ECG) signals recorded over 3 min during complete relaxation with eyes open, bagged tree three class classification (ADHD vs ADHD+CD vs CD only), 10-fold cross validation Sensitivity: 88 Specificity: 86 Accuracy: 88	**Index test 2:** Other : ECG Continuous 12-channel electrocardiography (ECG) signals recorded over 3 min during complete relaxation with eyes open, K-nearest neighbor three class classification (ADHD vs ADHD+CD vs CD only), 10-fold cross validation Sensitivity: 83 Specificity: 85 Accuracy: 84	**Index test 3:** EEG EEG (electroencephalogram) during resting-state, eyes open for 3 minutes, K-nearestneighbor three class classification (ADHD vs ADHD+CD vs CD only), 10-fold cross validation[1119] Sensitivity: 97 Specificity: 100 Accuracy: 98	**Index text 4:** EEG EEG (electroencephalogram) during resting-state, eyes open for 3 minutes, baggedtree three class classification (ADHD vs ADHD+CD vs CD only), 10-fold cross validation[1119] Sensitivity: 94 Specificity: 100 Accuracy: 96

Krieger, 2021[379] Case series N = 260 Spain Setting: Specialty care	**Target:** Participant with no history of tics; neurological disorders, or sensory impairments (seizures or brain injury); mental health conditions including autism spectrum disorder, motor or communication disorders and Tourette's syndrome, IQ > 85; psychostimulant medication withheld for 24 hours prior to each testing session **Other:** Typically developing children **ADHD presentation:** inattentive : 50.7,combined : 49.3 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 26.09% **Age mean:** ADHD-Combined 12.91 (12.04), ADHD-Inattentive 11.26 (2.34), Typically developing 11.70 (2.35) **Min age:** 8 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Participants required to meet established criteria in DSM-5, confirmed by two psychologist and a psychiatrist who specialize in child and adolescents Timing: Prior diagnosis	**Index test:** Neuropsychological,EF For 8-12 year olds: working memory and processing speed assessed with Wechsler Intelligence Scale for Children (WISC-IV) and attention with the d2 attention test; stepwise discriminant analysis Sensitivity: 76 Specificity: 93	**Index test 2:** Neuropsychological,EF For 13-16 year olds: working memory and processing speed assessed with Wechsler Intelligence Scale for Children (WISC-IV) and attention with the d2 attention test; discriminant function analysis; stepwise discriminant analysis Sensitivity: 79 Specificity: 78	N/A	N/A
Kurokami, 2022[382] Case series N = 276 Japan Setting: Mixed	**Target:** Children diagnosed with ADHD at a specialized outpatient department for children with neurodevelopmental disorders and specific learning disorders; IQ>80; not on medication at the time of examination **Other:** Children enrolled in regular classes at a public elementary school; IQ>80; data on non-ADHD participants	**Index test:** Neuropsychological,CPT MOGRAZ, a visual continuous performance test developed in Japan; multiple logistic regression analysis was performed using the results of MOGRAZ, age, and sex as parameters, ADHD-inattentive versus non-ADHD	**Index test 2:** Neuropsychological,CPT MOGRAZ, a visual continuous performance test developed in Japan; multiple logistic regression analysis was performed using the results of	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	extracted from a study of visual sustained attention in normal children and children with ADHD **ADHD presentation:** inattentive : 61,combined : 39 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 18% **Age mean:** **Min age:** 6 **Max age:** 12 **Ethnicity:** % Asian : 100,Other : Japanese **Reference standard:** Clinical diagnosis Diagnosed by a doctor with a pediatric specialist qualification Timing:	AUC: 0.884 (0.837, 0.932)	MOGRAZ, age, and sex as parameters, ADHD-combined versus non-ADHD AUC: 0.914 (0.869, 0.959)		

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Lau, 2018[385] Case series N = 3,464 Canada Setting: Specialty care	**Target:** Clinically referred children/youth across 39 mental health agencies in Ontario, Canada between 2012 and 2016 **Other:** Data were collected from clinically referred children/youth across 39 mental health agencies in Ontario, Canada between 2012 and 2016 **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 40% female in entire sample **Age mean:** 11.85 (3.58) **Min age:** 4 **Max age:** 18 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Provisional diagnoses were obtained from the clinical record or completed by the psychiatrist, attending physician, or qualified psychologist at the time of assessment Timing: Concurrent	**Index test:** Clinician tool InterRAI Child and Youth Mental Health Hyperactive/Distraction Scale (HDS), a semi-structured clinician assessment tool; analysis done on subsample that had undergone a diagnostic assessment Sensitivity: Using a combination of Youden's index and Pythagorean's method, optimal sensitivity ranged from 77.6 to 81.8% at a score of 7 Specificity: Using a combination of Youden's index and Pythagorean's method, optimal specificity ranged from 60.7 to 65.1% at a score of 7 AUC: 0.79 (0.770, 0.803) Standardized Cronbach's Alpha (using polychoric correlations) Alpha: 0.86	N/A	N/A	N/A

Lee, 2022[388] Lee, 2022[899] Case series N = 596 Korea Setting: Mixed	**Target:** Elementary school students from first to sixth grade living in Seoul, South Korea diagnosed as ADHD or at risk to develop ADHD **Other:** Elementary school students from first to sixth grade living in Seoul, South Korea not diagnosed with ADHD **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % N/A **Age mean:** **Min age:** 8 **Max age:** 13 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Four psychiatrists divided the children into three categories on the basis of the RGB image analysis results and the child behavior checklist (CBCL) and Korean ADHD Diagnostic Scale (K-ADHDS) results: ADHD, ADHD-RISK, or normal Timing: Concurrent	**Index test:** Clinician tool,Activity Skeleton data collected using the Azure Kinect comprised the subject's joint movements; skeleton data and RGB images aquired while children were performing a specific task, 6 standby skeleton data points and 5 game data points used as input data; deep learning long short-term memory algorithm using a bidirectional layer and a weighted cross-entropy loss function, 3-category classification ADHD vs ADHD-risk versus normal, leave-one-person-out cross-validation Sensitivity: 98 ADHD-risk 93% Specificity: 100 Accuracy: 98 PPV: 92 ADHD-Risk 100% NPV: 97	**Index test 2:** Clinician tool,Activity Skeleton data collected using the Azure Kinect comprised the subject's joint movements; skeleton data and RGB images were aquired while the children were performing a specific task, a total of six standby skeleton data points and a total of five game data points were used as input data; bidirectional long short-term memory (LSTM)-based deep learning with channel attention model, importance of each stage verified by passing the feature for each stage through the channel attention layer, 3-category classification ADHD versus ADHD-risk versus normal, leave-one-person-out cross-validation[899] Sensitivity: 100 ADHD-risk 94% Specificity: 100 Accuracy: 98 PPV: 93 ADHD-risk 100% NPV: 98	N/A	N/A
Lefler, 2012[389] Case series N = 58	**Target:** Participants were recruited either through their participation in a previous research project, word of	**Index test:** Clinician tool Primary Care Mental Health Screener (PCMHS) for children; cutoff 17 points (81st percentile)	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
US Setting: Other	mouth, or flyers advertising the study; IQ>=70 **Other:** Same recruitement as ADHD group **ADHD presentation:** N/A **Diagnosed by:** Researcher **Comorbidity:** N/A **Female:** % 47% female in entire sample **Age mean:** 5.82 (1.71) **Min age:** 3 **Max age:** 8 **Ethnicity:** % Hispanic or Latino : 3 % Black/African American : 2 % Asian : 3 % White : 92 **Reference standard:** Clinical diagnosis Wechsler Preschool and Primary Scale of Intelligence–Third Edition, Wechsler Abbreviated Scale of Intelligence, Wechsler Individual Achievement Test–Second Edition, Gray Oral Reading Test–Fourth Edition, Computerized Diagnostic Interview Schedule for Children–IV (C–DISC–IV), Child Symptom Inventory–Fourth Edition (CSI–4), Behavior Assessment System for Children–Second Edition (BASC–2)	AUC: 0.98 Rater agreement: Primary Care Mental Health Screener (PCMHS) versus Computerized Diagnostic Interview Schedule for Children–IV (C-DISC-IV), Child Symptom Inventory–Fourth Edition (CSI–4), or Behavior Assessment System for Children–Second Edition (BASC–2) PCMHS inattention subscale vs C-DISC-IV r=0.76, CSI-4 r=0.84, BASC-2 r=0.70 (p<0.001 for all); PCMHS hyperactivity subscale vs C-DISC-IV r=0.82, CSI-4 r=0.89, BASC-2 r=0.85 (p<0.001 for all)			

Lesica, 2023[390] Case series N = 524 US Setting: Other	**Target:** Recruitment of participants was conducted online via the CloudResearch MechanicalTurk Toolkit; mothers with a child who has been previously diagnosed with ADHD who were instructed to complete the PRASIS questionnaire, endorsing behaviors displayed by their child **Other:** Recruitment of participants was conducted online via the CloudResearch Mechanical Turk (MTurk) Toolkit; The control group in this study was composed of mothers of children who do not have ADHD who were instructed to complete the PRASIS questionnaire hones **ADHD presentation:** N/A **Diagnosed by:** Other (specify) Multiple sources including pediatrician, psychiatrist, psychologist, school psychologist, and therapist, counselor, or social worker **Comorbidity:** N/A **Female:** % 42.9% female in entire study 1 sample, 43.8% female in entire study 2 sample, 42.5% female in entire study 3 sample **Age mean:** 7.6 (2.7) for study 1 participants, 7.3 (2.6) for study 2 participants, 8 (2.3) for study 3 participants **Min age:** 4 **Max age:** 12 **Ethnicity:** Other : 13.6% in study 1, 13.8% in study 2, 10.2% in study 3 Other : 14.3% in study 1, 11.3% in study 2, 18.0% in study 3 Other : 4.5% in study 1, 0.5% in study 2, 2.4% in study 3 Other : 3.9% in study 1, 7.4% in study 2, 7.8% in study 3	**Index test:** Parent rating PRASIS-I-19 (parent-reported ADHD symptom infrequency scale); ADHD total scale19 items (9 hyperactivity/Impulsivity, 10 attention), infrequency scale 19 items; cutoff >=15 (>= cutoff score indicates that the patient is flagged for symptom exaggeration); discrimination of ADHD simulators from controls and ADHD participants Sensitivity: 62 Specificity: 91 PPV: 64 Base rate of 28% simulators; 19% PPV at 5% base rate NPV: 85 Base rate of 28% simulators; 98% NPV at 5% base rate Rater agreement: PRASIS ADHD subscale scores versus ADHD Rating Scale-5 scores Pearson's correlations: PRASIS ADHD Total scores and ADHD Rating Scale-5 Total scores, r(152) = 0.81, p < 0.001, PRASIS ADHD Inattention scores and ADHD Rating Scale-5 Inattention scores, r(152) = 0.76, p < 0.001, PRASIS ADHD Hyperactivity/Impulsivity Internal consistency: PRASIS infrequency scale alpha= 0.84, PRASIS ADHD total scale alpha= 0.93	**Index test 2:** Parent rating PRASIS-I-30 (parent-reported ADHD symptom infrequency scale); ADHD total scale 19 items (9 hyperactivity/Impulsivity, 10 attention), infrequency scale 30 items; cutoff >= 21 (>= cutoff score indicates that the patient is flagged for symptom exaggeration); discrimination of ADHD simulators from controls and ADHD participants Sensitivity: 70 Specificity: 90 Accuracy: AUC: PPV: 73 Base rate of 28% simulators; 26% PPV at 5% base rate NPV: 88 Base rate of 28% simulators; 98% NPV at 5% base rate LR+: LR-: Rater agreement: PRASIS ADHD subscale scores versus ADHD Rating Scale-5 scores Pearson's correlations: PRASIS ADHD Total scores and ADHD Rating Scale-5 Total scores, r(201) = 0.88,	**Index test 3:** Parent rating PRASIS-I-16 (parent-reported ADHD symptom infrequency scale); ADHD total scale 19 items (9 hyperactivity/Impulsivity, 10 attention), infrequency scale 16 items; cutoff >=12 (>= cutoff score indicates that the patient is flagged for symptom exaggeration); discrimination of ADHD simulators from controls and ADHD participants Sensitivity: 74 Specificity: 88 Accuracy: AUC: PPV: 70 Base rate of 28% simulators; 24% PPV at 5% base rate NPV: 89 Rater agreement: PRASIS ADHD subscale scores versus ADHD Rating Scale-5 scores	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Other : 72.7% in study 1, 79.3% in study 2, 77.8% in study 3 Other : Prefer not to say/other: 0.6% in study 1, 1.5% in study 2, 1.2% in study 3 **Reference standard:** Clinical diagnosis Mothers were asked to provide details related to the diagnosis, including when the ADHD evaluation occurred, what type of professional completed the assessment, whether the assessment included an interview, a symptom questionnaire, and/or cognitive testing, and whether medication was prescribed; ADHD rating scale-5 home version completed by mothers Timing: Prior diagnosis		p < 0.001, PRASIS ADHD Inattention scores and ADHD Rating Scale-5 Inattention scores, r(201) = 0.86, p < 0.001, PRASIS ADHD Hyperactivity/Impulsivity Internal consistency: PRASIS infrequency scale alpha= 0.90, PRASIS ADHD total scale alpha= 0.93	Kappa: Internal consistency: PRASIS infrequency scale alpha= 0.87, PRASIS ADHD total scale alpha= 0.94	

Levy, 2017[391] Case series N = 139 US Setting: Specialty care	**Target:** Participants from a comprehensive psychologicaltesting clinic for cognitive and/or personality assessment **Other:** Children without ADHD, part of same referral and selection process as ADHD group, diagnosed with other disorders such as ODD, CD, anxiety disorder, or depressive disorder **ADHD presentation:** inattentive : 54,combined : 46 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 41% female in entire validation sample **Age mean:** 10.7(3.1) **Min age:** 6 **Max age:** 17 **Ethnicity:** % Black/African American : 7 % Native Hawaiian or Pacific Islander : 1 % White : 91 % Multiracial : 1 **Reference standard:** Clinical diagnosis Symptom Inventories-4 scores for parent and teacher; Psychiatrist conducted evaluation; patients in the testing clinic are routinely administered behavior checklists and measures of executive functioning. Clinically assigned diagnoses and reasons for referral (as coded by the clinician responsible for the testing) were abstracted from test reports in the charts Timing: Prior diagnosis	**Index test:** Parent rating CHAOS (Conduct-Hyperactive-Attention Problem- Oppositional Symptom) scale parent, subscales include attention problems, hyperactivity-impulsivity, oppositional behavior, and conduct problems Rater agreement: Mother versus father rating Pearson correlations: Ranged from 0.58 to 0.63 over three subscales, the fourth subscale, conduct problems , interrater agreement was not statistically signficant Pearson correlations: the magnitude of the correlations, although statistically significant, was small in most cases Parent report Attention Problems subscale; Stroop Color and Word Test -0.22, Counting Interference Test -0.19, Conners' CPT 0.22, Kaufman Internal consistency: Cronbach's alpha ranged from 0.80 to 0.91 over four subscales Test-retest between 1 and 829 days Test-retest: Ranged from 0.74 to 0.87 over four subscales	**Index test 2:** Teacher rating scale CHAOS (Conduct-Hyperactive-Attention Problem- Oppositional Symptom) scale teacher, subscales include attention problems, hyperactivity-impulsivity, oppositional behavior, and conduct problems Rater agreement: Teacher versus parent rating Correlations for the teacher-report CHAOS scores and the cognitive test scores (Stroop Color and Word Test, Counting Interference Test, Conners' CPT, and Kaufman Brief Intelligence Test) were generally not significant Internal consistency: Cronbach's alpha ranged from 0.64 to 0.91 over four subscales	N/A	N/A
Li, 2005[395] Case series N = 113 China	**Target:** Outpatient children in Psychology Hyperactivity Department of the Central Hospital of Anshan City diagnosed with ADHD; excluding those with nervous system organic disease,	**Index test:** EEG EEG theta 4-8 Hz / beta 13-32 Hz Sensitivity: 84 Specificity: 83	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Setting: Specialty care	pervasive developmental disorder, mental retardation, epilepsy, psychotic disorder, acoustical and visual abnormalities **Other:** Outpatient children in Psychology Hyperactivity Department of the Central Hospital of Anshan City not diagnosed with ADHD **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 22.1% **Age mean:** 10 (3) **Min age:** 6 **Max age:** 14 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed with ADHD according to DSM-IV criteria Timing: Prior diagnosis				

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Li, 2016[393] Yale University, 2012[1182] Case series N = 60 China Setting: Other	**Target:** Participant with any presentation of ADHD or who were considered to be subthreshold for ADHD, free of any other co-morbid psychiatric condition, medication naive or had discontinued medication 6 months prior to study **Other:** Age and gender-matched typically developing children **ADHD presentation:** inattentive : 17,hyperactive : 13,combined : 63,combined_other : 3.5% subthreshold combined type, and 3.5% subthreshold inattentive type **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 7% **Age mean:** 8.95 (1.88) **Min age:** 6 **Max age:** 12 **Ethnicity:** % Asian : 100,Other : All participants were of Han ancestry **Reference standard:** Clinical diagnosis Diagnosis based on DSM-5 criteria for ADHD Timing: Prior diagnosis	**Index test:** Neuropsychological Movement intensity measures included a composite measure of total movement intensity and a movement intensity distribution measure, infrared motion tracking system to monitor and record movement intensity during a modified Go/No-Go Task Sensitivity: 97 Specificity: 83 AUC: 0.904	**Index test 2:** Neuropsychological,CPT,EF Movement intensity distribution measure across 15 frequency bands; infrared motion tracking system to monitor and record movement intensity during a modified Go/No-Go Task Sensitivity: Reaction time variability Specificity: Reaction time variability AUC: Between 0.867 and 0.932 for the 15 frequency band measures	**Index test 3:** Activity,Neuropsychological Performance measures on the Go/No-Go task, 6 measures omission errors, commission errors, accuracy, multiple response errors, reaction time, and reaction time variability Between 0.69 and 0.93 across Go/No-Go task measures	**Index text 4:** Neuropsychological Go/No-Go task accuracy AUC: 0.844

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Li, 2018[394] Case series N = 141 China Setting: Mixed	**Target:** Participants with IQ>=80, free of other neurological disease or serious head injuries, normal or corrected vision **Other:** Typically developing children **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 56% **Age mean:** 8.7 **Min age:** 7 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis of ADHD based on DSM of Mental Disorders Timing: Prior diagnosis	**Index test:** EEG EEG signals collected during a Simon-spatial Stroop task. Multiple event-related potential (ERP) feature channels combining time domain and frequency domain features. Support vector machine (SVM) classifier. Accuracy: 97 Stroop Incongruent experiment pattern on feature channel in inferior parietal cortex using multiple features to train the support vector machine classifier.	**Index test 2:** EEG EEG signals collected during a Simon-spatial Stroop task. Multiple event-related potential (ERP) feature channels combining time domain and frequency domain features. K- nearest neighbor (KNN) classifier.	**Index test 3:** EEG EEG signals collected during a Simon-spatial Stroop task. Multiple event-related potential (ERP) feature channels combining time domain and frequency domain features. BP neural network classifier.	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Liechti, 2013[397] Case series N = 62 Switzerland Setting: Mixed	**Target:** Participants with IQ >=80; medication free or suspended treatment at least 48 hours before testing **Other:** Typically developing children matched on age, gender, and IQ **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 37.5% **Age mean:** 11.1 (2.1) for ADHD group, 11.2 (2.1) for control group **Min age:** 8 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD combined subtype (DSM-IV) were diagnosed using the clinical diagnostic interview PACS (parental account of children's symptoms) plus Conners' teacher rating scale—revised Timing: Prior diagnosis	**Index test:** EEG EEG topographic 48-channel resting electroencephalogram Sensitivity: 72 Stepwise selection of all resting EEG and event related potential variables Specificity: 73 Stepwise selection of all resting EEG and event related potential variables Accuracy: 73 Stepwise selection of all resting EEG and event related potential variables	N/A	N/A	N/A

Lin, 2022[402] Case series N = 567 Taiwan Setting: Specialty care	**Target:** Clinical records for January 2011– September 2020 were collected from local general hospitals in northern Taiwan; received an ADHD-Inattentive or ADHD-Combined diagnosis; No (i) neurological diseases, including disorders of the brain and central nervous system (e.g., epilepsy); (ii) intellectual disabilities (for patients who had taken an intelligence test); (iii) other serious psychological disorders, such as schizophrenia, bipolar disorder, and major depressive disorder; and (iv) physiological diseases potentially affecting attention and activity level **Other:** The control group comprised patients who had received attention and activity level assessments in a hospital and for whom psychological assessment and psychiatric evaluation indicated no ADHD-I or ADHD-C **ADHD presentation:** inattentive : 29,combined : 71 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 19% **Age mean:** **Min age:** 6 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Patients were first evaluated by psychiatrists from the Child and Adolescent Psychiatry Division to determine whether they had ADHD-I or ADHD-C, as defined by the DSM-V. Timing: Prior diagnosis	**Index test:** Neuropsychological Combination of demographic information, SNAP-IV scale results by parents and teachers, and CPT-2 results; artificial neural network, k-fold cross-validation, 70% training/15% verification/15% testing split; ADHD-inattentive versus ADHD-combined versus absence of ADHD; test set Sensitivity: Test set: ADHD-Inattentive 67%, ADHD-Combined 85%; Training set ADHD-Inattentive 82%, ADHD-Combined 91% Specificity: 65 Training set: 77% Accuracy: 77 87% in the training set	**Index test 2:** Neuropsychological Combination of demographic information, SNAP-IV scale results by parents and teachers, CPT-2 results, and intelligence data; artificial neural network, k-fold cross-validation, 70% training/15% verification/15% testing split; ADHD-inattentive versus ADHD-combined versus absence of ADHD; test set Sensitivity: Test set: ADHD-Inattentive 64%, ADHD-Combined 85%; Training set ADHD-Inattentive 87%, ADHD-Combined 93% Specificity: 67 Training set: 80% Accuracy: 75 89% in the training set	N/A	N/A
Lin, 2023[400] Zhou, 2021[1188]; Bernanke,	**Target:** U.S. population-based cohort from longitudinal Adolescent Brain and	**Index test:** Imaging Multimodal MRI, neuroimaging features selected from MRI data (resting-	**Index test 2:** Imaging,Imaging plus non-imanging	**Index test 3:** Imaging sMRI and fMRI, and	**Index text 4:** Clinician tool,Activity

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
2022[681]; Kim, 2023[887] Case series N = 7,805 US Setting: Other	Cognitive Development study 3.0 release **Other:** U.S. population-based cohort from longitudinal Adolescent Brain and Cognitive Development (ABCD) study 3.0 release **ADHD presentation:** N/A **Diagnosed by:** Researcher **Comorbidity:** N/A **Female:** 36% **Age mean:** 9.9 (0.6) **Min age:** 8 **Max age:** 11 **Ethnicity:** % Hispanic or Latino : 20 % Black/African American : 14 % Asian : 2 % White : 55 % Multiracial : 8,Other : Mixed/Others Other : Undetermined <1% **Reference standard:** Clinical diagnosis Parent Diagnostic Interview scales for the Kiddie-Schedule for affective Disorders and Schizophrenia (K-SADS) from the ABCD database Timing: Prior diagnosis	state fMRI, structural MRI, and diffusion MRI); RIDGE regularized logistic regression feature selection, extreme gradient boosting classifier; 4:1 training/ testing split with 5 repeats of 10-fold cross validation; validation test set Sensitivity: 57 Specificity: 65 AUC: 0.576 (0.546, 0.610)	Multimodal MRI plus clinical features (age, sex, race, highest parental education, and handedness), neuroimaging features selected from multimodal MRI data (resting-state fMRI, structural MRI, and diffusion MRI); hierarchical clustering feature selection, support vector machine with radial kernel classifier; 4:1 training/ testing split with 5 repeats of 10-fold cross validation; validation test set Sensitivity: 60 Specificity: 56 AUC: 0.613 (0.580, 0.645)	Diffusion Tensor Images data integration, Boruta based feature selection, multiple kernel learning, and support vector machine classifier, 10-fold cross validation and repeated nested 5-fold cross validation; ABCD database participants (116 ADHD, 116 controls)[1188] Sensitivity: 61 Specificity: 68 Accuracy: 64 AUC: 0.698	Fitbit, 21 days of wearable data (Fitbit Wearable Wrist Tracker); hyperensemble smote undersampled random forest (hyperSMURF) algorithm with best performing light gradient-boosting machine (LightGBM) classifier includes sex, age, height, weight, heart rat Sensitivity: 76 Specificity: 72 Accuracy: AUC: 0.798 PPV: 16 NPV: 98

Lin, 2023[401] Case series N = 122 Taiwan Setting: Mixed	**Target:** Children with ADHD recruited from several local ADHD hospitals; regular medication users were asked to stop taking their medications throughout testing days; IQ>80 **Other:** Gender and grade-matched typically developing (TD) children recruited from local primary schools **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 26% **Age mean:** 11.21 for ADHD group, 11.03 for typically developing group **Min age:** 10 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Clinical diagnoses of this study were made based on a comprehensive psychological evaluation by a licensed Ph.D. psychologist and a senior pediatric neurologist with 20 years of experience in ADHD. The diagnosis procedure was conducted through a four-part process, including diagnostic interviews with children, a review of medical and school records, a diagnostic questionnaire inquiring about the presence of ADHD using the DSM-5 criteria, and psychological testing using the Wechsler Intelligence Scale for Children. Participants' parents completed the Conners 3 - Parent Assessment Report. Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT Visual search tasks with structured and unstructured (associated with high-level spatial uncertainty) layouts; randomized, two-period crossover design; accuracy and speed combined into a quality of search score (Q score) AUC: 0.956	N/A	N/A	N/A
Lindhiem, 2022[403] Case series N = 30	**Target:** Participants not on medication during the testing period	**Index test:** Clinician tool,Activity LemurDx app prototype on Apple smarwatch tracking motion, heart rate, and	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
US Setting: N/A	**Other:** Recruited via a web-based research registry through the University of Pittsburgh's Clinical and Translational Science Institute program **ADHD presentation:** N/A : ADHD-combined and hyperactive subtypes only **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 40% **Age mean:** 9.6 (1.6) for the ADHD group, 10.1 (1.8) for the control group **Min age:** 6 **Max age:** 11 **Ethnicity:** % Black/African American : 7 % White : 83 % Multiracial : 3 Other : 7% race not reported **Reference standard:** Clinical diagnosis ADHD module of the Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime Version (K-SADS-PL) and the hyperactivity items of the Vanderbilt Assessment Scale-Parent report (VAS-P) Timing: Prior diagnosis	locationof participants paired with acitivity labels in 30 minute increments reported by the parents; random forest classifier, leave-one-participant-out cross validation Sensitivity: 93 Specificity: 86 Accuracy: 89 PPV: 87 NPV: 92			

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Liu, 2022[404] Case series N = 60 China Setting: Specialty care	**Target:** Exclusion criteria for ADHD group were other neurological or psychotic disorders, traumatic brain injury, and undergoing any types of treatment before the test; IQ>85, right-handed, and their eyesight or corrective vision was normal **Other:** Age-matched and no other physical or mental illness; IQ>85, right-handed, and their eyesight or corrective vision was normal **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 20% **Age mean:** 8.93 (2.22) for the ADHD group, 9.93 (2.46) for the control group **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD group was screened by DSM-V criteria for inattentive, hyperactivity or combined ADHD type at Tianjin Anding Hospital Timing: Prior diagnosis	**Index test:** EEG EEG Cross-frequency phase-amplitude coupling (PAC) applied to resting-state EEG datasets; PAC intensity and graph theory properties of low-frequency coupling with high-gamma frequency AUC: 0.990	**Index test 2:** EEG EEG cross-frequency phase-amplitude coupling (PAC) applied to resting-state EEG datasets; PAC intensity and graph theory properties of low-frequency coupling with low-gamma frequency AUC: 0.727	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Longridge, 2019[405] Case series N = 288 UK Setting: Specialty care	**Target:** Children attending two child and adolescent mental health services **Other:** Children with no diagnosis of ADHD per Development and Well-Being Assessment, part of the same referral process as ADHD group **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 13.8% **Age mean:** 7.4 (1.6) for ADHD group, 8.0 (1.7) for comparison group **Min age:** 5 **Max age:** 11 **Ethnicity:** % White : 69 Other : 31% Black and Minority ethnicity **Reference standard:** Clinical diagnosis Clinicians completed a brief questionnaire in 6 month intervals assessing multiple clinical conditions including ADHD Timing: Later diagnosis	**Index test:** Combined rating Development and Well-Being Assessment (DAWBA) with parents and teacher ratings, a smodular standardised diagnostic assessment with structured questions that are based directly on DSM-IV (APA 2000) and ICD-10 (WHO 2009) diagnostic criteria; If a respondent reports any difficulty in any one module, semistructured questions are used to expand on the details of these reported difficulties; a computerised algorithm generates provisional diagnoses Rater agreement: DAWBA provisional diagnosis versus clinician diagnosis during the study period Kappa was 0.40 for those with a definite or possible diagnosis at any time point Kappa: 0.30	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Luo, 2022[408] Case series N = 161 China Setting: Specialty care	**Target:** Participants enrolled from Peking University Sixth Hospital in Beijing; IQ>80 **Other:** Age and sex-matched controls recruited from communitites in Beijing **ADHD presentation:** inattentive : 51,combined : 49 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 20% **Age mean:** 12.0 (1.71) for the ADHD group, 11.6 (1.81) for the control group **Min age:** 8 **Max age:** 15 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed by a qualified psychiatris using the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) Timing: Prior diagnosis	**Index test:** EEG EEG resting-state eye-closed EEG; microstate features (temporal microstate dynamics)anddelta and TBR power components entered into the algorithm, support vector machine with recursive feature elimination (SVM-RFE), 5-fold cross-validation Sensitivity: 67 Specificity: 76 Accuracy: 73	N/A	N/A	N/A

Luo, 2022[407] Case series N = 110 China Setting: Specialty care	**Target:** Outpatients of Beijing Anding Hospital, IQ>=70, no previous use of medication for ADHD; no comorbidity with various developmental disorders such as mental retardation and autism spectrum disorder or comorbid severe psychiatric disorders such as schizophrenia and bipolar disorder **Other:** The control group recruited children with normal development and excluded other disorders and also included children with symptoms of ADHD scored by the SNAP-IV but did not meet the diagnosis of ADHD under the gold standard **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 15% **Age mean:** 8.8 (1.76) for the ADHD group, 8.95 (1.50) for the control group **Min age:** 6 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Detailed clinic interview between the two senior specialists and the subject's family, as well as from clinical observations of the subject, combined with certain physical examinations to rule out other causes of the symptoms Timing: Prior diagnosis	**Index test:** Clinician tool,Activity Self-developed Wearable Diagnostic Assessment System (WeDA) based on the DSV-5;the user wears 6 motion sensors on their head, hands, feet and waist and complete 10 tasks by interacting with a touch screen or 3D printed device within a set time frame; performance is scored based on the completion of the tasks (including accuracy, error rate, time consumption and other information), on the user's body posture (obtained through the wearable device), and on the user's body movements observed via the six motion sensors; Information was integrated and Random forest and Bayesian network were employed to build diagnosis models Sensitivity: 98 (89, 100) Specificity: 95 (84, 99) Accuracy: 96 AUC: 0.964 PPV: 98 (89, 100) NPV: 95 (84, 99) LR+: 52 (7.45, 362.98) LR-: 0.06 (0.02, 0.17)	N/A	N/A	N/A
Marcano, 2018[412] Case series N = 7 US Setting: Other	**Target:** Children diagnosed with ADHD and on medication **Other:** Children part of an ongoing longitudinal study focused on frontal lobe development from infancy through childhood without a diagnosis of ADHD **ADHD presentation:** N/A	**Index test:** EEG EEG data collected during the child version of the Attention Network Task; classification using a Universal Background Model, sample split with 4 participants for training (2 ADHD, 2 control)	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Diagnosed by: Unclear/NR **Comorbidity:** N/A **Female:** 0% **Age mean:** N/A **Min age:** 6 **Max age:** 6 **Ethnicity:** N/A **Reference standard:** Other Diagnosis of ADHD was obtained via maternal report Timing: Prior diagnosis	and 3 for validation (2 ADHD, 1 control)			

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Markovska-Simoska, 2017[413] Case series N = 60 Macedonia Setting: Specialty care	**Target:** Male, right handed participants with no serious medical or neurological problems like seizures, or recent head trauma<6 months; not taking psychostimulants **Other:** Age-matched children selected from the Human Brain Index (HBI) database **ADHD presentation:** N/A : No subtypes in the article **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 0% **Age mean:** 9 (2.44) for ADHD group, 10.46 (2.27) for control group **Min age:** 6 **Max age:** 14 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Children diagnosed by neuropsychologist, pediatrician and clinical psychologist plus Conners Rating Scale for teachers and parents Timing: Prior diagnosis	**Index test:** EEG EEG 5 minute eyes open resting state, absolute theta Cz Sensitivity: 100 Specificity: 71	**Index test 2:** EEG EEG 5 minute eyes open resting state, theta/beta ratio Cz Sensitivity: 59 Specificity: 92 AUC: 0.810	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Martín-Brufau, 2017[415] Case series N = 50 Spain Setting: Specialty care	**Target:** Children with typical ADHD symptomatology **Other:** EEG records from sex-matched typically developing children **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** % Reports subjects matched by sex, no other information **Age mean:** N/A **Min age:** 6 **Max age:** 15 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed with ADHD Timing: Prior diagnosis	**Index test:** EEG EEG eyes-closed resting EEG. Direct analysis of EEG specific montages performed by untrainedindividuals in EEG interpretation. AUC: 0.868 Acheived by 55.5% of the untrained individuals (p<0.01). AUC = 0.726 (p>0.05) for the remaining 44.5%.	**Index test 2:** EEG EEG eyes-closed resting EEG analyzed by the Theta/ Beta Ratio method after decompositionwith the Fast Fourier Transformation AUC: 0.929	**Index test 3:** EEG EEG eyes-closed resting EEG analyzed with the Delta + Theta / Alpha index obtained byvisual position decomposition-Verley method. AUC: 0.917	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Martin-Martinez, 2012[416] Case series N = 63 Spain Setting: Mixed	**Target:** Children with combined type ADHD and no type of sleep disorder such as restless legs syndrome or periodic limb movement **Other:** Children without ADHD from public hospitals and health centers **ADHD presentation:** combined : 100 **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** % N/A **Age mean:** N/A **Min age:** 6 **Max age:** 6 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed as having the combined kind of ADHD according to the DSM-IV criteria. Timing: Prior diagnosis	**Index test:** Clinician tool,Activity Nonlinear signal processing of 24 h-long actigraphic registries Sensitivity: 97 By means of multidimensional classifiers driven by combined features from different time intervals Specificity: 84 By means of multidimensional classifiers driven by combined features from different time intervals Accuracy: 90 By means of multidimensional classifiers driven by combined features from different time intervals AUC: 0.9496 By means of multidimensional classifiers driven by combined features from different time intervals	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Matier-Sharma, 1995[417] Case series N = 129 US Setting: Specialty care	**Target:** Consecutive unmedicated referrals to the child psychiatry outpatient clinic of an urban medical center diagnosed with ADHD **Other:** Consecutive unmedicated referrals to the child psychiatry outpatient clinic of an urban medical center not diagnosed with ADHD; Neurotypical developing boys recruited from a neighborhood school **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 22% in entire sample **Age mean:** **Min age:** 6.5 **Max age:** 13 **Ethnicity:** Other : Primarily African-American or Hispanic **Reference standard:** Clinical diagnosis Child Behavior Checklist, Conners Teacher's Questionnaire, clinical interviews with parent and child, clinician rating scale that consisted of DSM-III-R items Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT CPT modelled after the A-X task; discriminant function analysis including the variables CPT-dyscontrol and CPT-inattention; ADHD versus neurotypical controls Sensitivity: 63 Specificity: 94 Accuracy: 72	**Index test 2:** Activity,Neuropsychological,CPT CPT modelled after the A-X task and actigraph measures taken during CPT task; discriminant function analysis including the variables activity level, CPT-inattention, and CPT-impulsivity; ADHD versus non-ADHD Sensitivity: 68 Specificity: 66 Accuracy: 66	**Index test 3:** Activity,Neuropsychological Actigraph measures taken during CPT task; ADHD versus neurotypical controls Sensitivity: 25 Specificity: 94 PPV: 91 NPV: 36	**Index text 4:** Activity Actigraph measures taken during CPT task; ADHD versus non-ADHD Sensitivity: 25 Specificity: 95 Accuracy: PPV: 77 NPV: 63

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Maya-Piedrahita, 2022[420] Case series N = 63 Colombia Setting: N/A	**Target:** Diagnosed with ADHD by child psychiatrists **Other:** Children without the presence of ADHD symptoms, neurodevelopmental alterations, learning disorders, or psychiatric pathologies **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % Boys-to-girls ratio of 2.4 : 1 **Age mean:** 9.4 (1.9) **Min age:** 6 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Child psychiatrists performed ADHD diagnosis according to established DSM-IV-R criteria and Conners rating scale; the Behavior Assessment System for Children (BASC) scale was also applied Timing: Prior diagnosis	**Index test:** EEG EEG recorded EEG under the Reward Stop Signal Task, EEG signals characterized from hiddenMarkov models (HMM), classifying subjects based on similarity measures for probability functions, and spatially interpreting the results using graphic embeddings of stochastic dynamic models; the methodology learns a single HMM for EEG signal from each patient; the Probability Product Kernel, specifically developed for assessing the similarity between HMMs, fed a support vector machine that classifies subjects according to their stochastic dynamics; beta band under the Increasing Condition (IC) rewards; ADHD versus neurotypically developing; 80/20 split used for validation Accuracy: 97	N/A	N/A	N/A

Mayes, 2002[421] Dickerson Mayes, 2001[737] Case series N = 230 US Setting: Specialty care	**Target:** Participants referred to a diagnostic clinic at a university-affiliated hospital for learning, attention, or behavior problems diagnosed with ADHD; IQ>=80; not on stimulant medication on the day of testing (no washout period) **Other:** Referred to a diagnostic clinic at a university-affiliated hospital for learning, attention, or behavior problems not diagnosed with ADHD; IQ>=80; diagnosed with other disorders such as oppositional defiant disorder, depression, anxiety, adjustment disord **ADHD presentation:** combined : 100 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 18% **Age mean:** 9.3 (2.5) for the ADHD group, 11.6 (2.9) for the non-ADHD group **Min age:** 6 **Max age:** 16 **Ethnicity:** % White : 96 **Reference standard:** Clinical diagnosis Children were evaluated by a licensed psychologist and by a child psychiatrist or developmental pediatrician; diagnoses were based on information obtained from the parent and teacher ratings on the Pediatric Behavior Scale, parental interview, clinical observations of the child, and review of records. Timing: Concurrent	**Index test:** Neuropsychological,EF Gordon Diagnostic System scores; cutpoint= IQ minus the GDS Composite score >= 13 Sensitivity: 92 Specificity: 70 Accuracy: 88 PPV: 92 NPV: 70	**Index test 2:** Neuropsychological,EF WISC-III scores; cutpoint= IQ minus Freedom from Distractibility >0 Sensitivity: 79 Specificity: 52 Accuracy: 74 PPV: 89 NPV: 38	**Index test 3:** Neuropsychological,EF Gordon Diagnostic System and WISC-III scores; cutpoint= IQ minus GDS Composite >=13 or IQ minus Freedom from Distractibility >=11 Sensitivity: 97 Specificity: 65 Accuracy: 91 PPV: 92 NPV: 86 Rater agreement: U~D iagnostic agreement benveen the Gordon Diagnostic System and Freedom from Distractibility 70.0% agreement overall, 75.5% in the ADHD group, and 47.8% in the non-ADHD group	**Index text 4:** Neuropsychological,CPT Gordon Diagnostic System scores; cutpoint= IQ minus the GDS Composite score >= 13[737] Sensitivity: 90 Specificity: 70 Accuracy: 86 PPV: 91 NPV: 67
Mayes, 2004[422] Dickerson Mayes, 1998[736] Case series	**Target:** Participant referred for learning, attention, and/or behavior problems, IQ>=80, off medication for testing, and no head injury with loss of consciousness	**Index test:** Neuropsychological,EF 12 Wechsler Intelligence Scale for Children- Third Edition (WISC-III) subtests comprising the four	**Index test 2:** Neuropsychological,EF Wechsler Intelligence Scale for Children-Third Edition (WISC-	**Index test 3:** Neuropsychological,EF Wechsler Intelligence	N/A

N = 809 US Setting: Specialty care	**Other:** Children with autism, brain injury, or mood and behavior disorders with or without learning disorders **ADHD presentation:** inattentive : 21,combined : 79 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 26% female in entire sample **Age mean:** 9 (3) **Min age:** 6 **Max age:** 16 **Ethnicity:** % White : 92 Other : 8% were Black, Hispanic, or Asian **Reference standard:** Clinical diagnosis DSM-IV diagnoses agreed upon by both a child psychologist and child psychiatrist Timing: Prior diagnosis	Indexes, Verbal Comprehension, Perceptual Organization, Freedom from Distractibility, and Processing Speed and the Wechsler Individual Achievement Test (WIAT) Basic Reading Compreshension, Numberical Operations, and Written Expression subtests; classification using the Low Coding or Freedom from Distractibility Index (FDI) without Low Comprehension Profile, ADHD group combined with learning disability group for the predictive validity analysis Sensitivity: 59 Specificity: 77 PPV: 93 NPV: 27	III) factor scores; (Freedom from Distractibility index + Processing Speed index) < (Verbal Comprehension index + Perceptual Organization index); 87 ADHD vs 32 clinical controls[736] Sensitivity: 87 Specificity: 47 Accuracy: 77 This percentage is not meaningfully different from the base rate of 73.1% of the sample with ADHD	Scale for Children- Third Edition (WISC-III) factor scores; (Freedom from Distractibility index + Processing Speed index) < (Verbal Comprehension index + Perceptual Organization index); replication sample 52 ADHD vs 23 clinical controls[736] Sensitivity: 77 Specificity: 61 Accuracy: AUC: PPV: 82 NPV: 54 LR+: Rater agreement: Kappa: Internal consistency:	
Mayfield, 2018[423] Case series N = 337 US Setting: Other	**Target:** Children with no co-morbid intellectual disability, pervasive developmental disorder, or history of neurological disorder **Other:** None; study comparing mother and father ratings **ADHD presentation:** inattentive : 62.9,combined : 37.1 **Diagnosed by:** Unclear/NR	**Index test:** Parent rating DSM-ADHD-SRS (symptom rating scale) total score mother rating Rater agreement: DSM-ADHD-SRS (symptom rating scale) mother-rating versus father-rating Mother and father ratings (ICC) correlated .51 for inattention,	**Index test 2:** Parent rating DSM-ADHD-SRS (symptom rating scale) total score father rating Alpha: 0.91	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Comorbidity: N/A **Female:** 27.9% **Age mean:** 10.3 (2.83) **Min age:** 6 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis DSM-IV diagnosis of ADHD Timing: Concurrent	.56 for hyperactivity, and .58 for impulsivity. Alpha: 0.90			

McCarthy, 2016[424] Case series N = 1622 US Setting: Specialty care	**Target:** Youth who entered outpatient treatment and who had ADHD as their DSM-IV Axis I primary or secondary diagnosis **Other:** Patients who had at least one psychiatric DSM-IV diagnosis at the time of their intake interview, but whose diagnosis/diagnoses did not include ADHD **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 33.6% **Age mean:** 10.51 (3.75) for ADHD group, 11.46 (4.10) for non-ADHD group **Min age:** 3 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD as primary or secondary DSM-IV Axis I diagnosis. Clinician-completed Brief Psychiatric Rating Scale for Children (BPRS-C) and Children's Global Assessment Scale (CGAS), consists of 21 distinct symptoms, each rated for severity on a 7-point Likert-type scale based on the clinician's interview with the child and parent. Timing: Concurrent	**Index test:** Parent rating PSC (Pediatric Symptom Checklist) Attention Subscale parent-completed measureof childand adolescent psychosocial functioning Sensitivity: 55 Specificity: 81 Alpha: 0.90 Temporal stability: BPRS-C-PE and PSC-AS correlated 0.56 at intake and 0.53 at a 3-month follow up appointment.	N/A	N/A	N/A
McIntosh, 1995[427] Case series N = 265 US Setting: School	**Target:** Participants with no other medical problems, not adopted **Other:** Randomly selected neurotypical children who were in regular education classrooms and were not receiving remedial or special education services **ADHD presentation:** N/A **Diagnosed by:** Specialist	**Index test:** Parent rating MPS (Maternal Perinatal Scale), questions and a condition checklist Sensitivity: 61 Specificity: 73 Accuracy: 67 PPV: 69 NPV: 66	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Comorbidity: N/A **Female:** 15% **Age mean:** 9.6 (1.6) for the ADHD group, 10.4 (1.7) for the undifferentiated ADD group, 9.5 (1.8) for the neurotypical group **Min age:** 6 **Max age:** 13 **Ethnicity:** % Black/African American : 1 % White : 94 Other : 5% Other **Reference standard:** Clinical diagnosis Diagnosed by physicians and licensed psychologists and verified by the investigators through school health and testing records Timing: Prior diagnosis				

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Merzon, 2022[429] Case series N = 73 Finland Setting: N/A	**Target:** Participants not taken medication within 24 hours prior to assessment **Other:** Typically developing children, matched on age and gender **ADHD presentation:** N/A **Diagnosed by:** Provider **Comorbidity:** N/A **Female:** 22% **Age mean:** 10.4 (1.0) for the ADHD group, 10.8 (1.2) for the typically developing group **Min age:** 9 **Max age:** 13 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD diagnosis made by a licensed medical doctor and verified via the National Medical Database Timing: Prior diagnosis	**Index test:** Other (e.g., ECG) : Eye movement Eye movement data collected during Executive Performance in Everyday Living (EPELI) VR task; includes 13 task scenarios where the participants perform everyday chores in a virtual environment; support vector machine classifier using the eye movement features Fixation Duration, Saccade Duration, and Saccade Amplitude; 10-fold cross validation Sensitivity: 84 Specificity: 78 AUC: 0.91	N/A	N/A	N/A

Mikolas, 2022[434] Case series N = 299 Germany Setting: Specialty care	**Target:** Individuals who were referred to a secondary care outpatients unit with a suspected ADHD diagnosis, or in whom an ADHD diagnosis was the suspected diagnosis after the initial consultation **Other:** Patients who did not fulfill diagnostic criteria for ADHD **ADHD presentation:** N/A : 64% predominantly hyperactive-impulsive type, 27.5% predominantly inattentive type, 8.5% comorbidwith conduct disorder **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 14% **Age mean:** 10.0 (2.4) for the ADHD group, 10.5 (2.5) for the non-ADHD group **Min age: Max age:** 18 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis The standardized diagnostic process included several consultations with the child and caregivers together and individually. Parents and (nursery) school teachers completed general and ADHD-specific rating scales. Further, general intelligence and attention were assessed via standardized testing batteries. In addition, somatic conditions which may contribute to any existing attention problems were excluded (e.g., laboratory measures, ophthalmological and ENT evaluations, EEG).The final diagnostic decision was given strictly based on ICD-10 clinical criteria assessed by a senior specialist in child	**Index test:** Clinician tool 30 featues extracted from medical record data, linear support vector machine classifier, 10-fold cross-validation. Features include: age and gender; symptom ratings from Conners-3 parent/teacher ratings and a computed a set of 'consistency indices' describing the consistency between parent and teacher ADHD specific Conners-3 ratings; neuropsychological measures from 3 TAP subtests (GoNogo, Divided Attention, and Alertness) and the Wechsler Intelligence Scale for Children IV or V Sensitivity: 67 Specificity: 65 Accuracy: 66 AUC: 0.66	**Index test 2:** Clinician tool 19 most predictive features selected from the original 30 using sequential floating forward selection, linear support vector machine classifier, 10-fold cross-validation Accuracy: 68	**Index test 3:** Clinician tool Secondary classification without demographic features: linear support vector machine classifier, 10-fold cross-validation, non-demographic features only Sensitivity: 65 Specificity: 65 Accuracy: 65 AUC: 0.663	**Index text 4:** Clinician tool Secondary classification without missing data: 19 features selected from the original 30 using sequential floating forward selection, linear support vector machine classifier, 10-fold cross-validation, performed only on subjects without any missing data Sensitivity: 63 Specificity: 74 Accuracy: 69 AUC: 0.696

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	and adolescent psychiatry or psychology. Timing: Later diagnosis				

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Mitchell, 1990[436] Case series N = 204 US Setting: School	**Target:** Participants in special education placement or regular class with resource specialist, no coexisting major medical problems or centrally active medications other than stimulants, IQ >=80, asked to omit medication for 2 to 3 days prior to testing **Other:** Selected from two elementary schools **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 19% **Age mean:** 10.2 (1.77) for the hyperactive group, 9.08 (2.14) for the control group **Min age:** 5 **Max age:** 13 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis by psychologist or physician of hyperactivity and/or attention deficit disorder, revview of school files including all psychometric testing, Conners Abbreviated Teacher Questionnaire, the Matching Familiar Figures Test Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT Four tasks designed for use on the Apple IIe microcomputer described to subjects as a game on which they could earn points, similar to video game; summary score representing the number of measures on which the child scored above the 95th percentile with a cutoff point of 4 of 21 measures Sensitivity: 60 Specificity: 95 Allowed false positive rate of 5% Rater agreement: Agreement was defined as the proportion of subjects with abnormal scores on the Matching Familiar Figures Test who were also abnormal using the video game summary score Agreement = 75%	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Miyahara, 2014[437] Case series N = 169 New Zealand Setting: Mixed	**Target:** Clinical sample who were professionally diagnosed by mental health professionals **Other:** Community sample recruited from city-sponsored pre-kindergarten programs **ADHD presentation:** inattentive : 10,hyperactive : 41,combined : 42,N/A : ADHD-NOS 7% **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 26% **Age mean:** **Min age:** 3 **Max age:** 4 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Parent and teacher ratings on the Attention Deficit Hyperactivity Disorder-Rating Scale-Fourth Edition (ADHD-RS-IV) Home Version and School Version; clinical sample who were professionally diagnosed by mental health professionals (e.g, pediatricians, neurologists, school psychologists) Timing: Prior diagnosis	**Index test:** Clinician tool,Activity Actigraph measures recorded during psychometric assessment (2 hours) at the waist on day 2 Accuracy: 70	**Index test 2:** Clinician tool,Activity Actigraph measures recorded during psychometric assessment (2 hours) at the waist on day 2 and the ankle on day 1 Accuracy: 68	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Moghaddari, 2020[438] National Brain Mapping Lab, 2019[949]; Mohammadi, 2016[932]; Allahverdy, 2016[663]; Sho'ouri, 2022[1060] Case series N = 61 Iran Setting: Other	**Target:** Children with ADHD; taking ritalin for up to 6 months **Other:** Healthy children **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 29% **Age mean:** 9.64 (1.73) for ADHD group, 9.85 (1.77) for control group **Min age:** 7 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Child and adolescent psychiatrist determined diagnosis - using criteria from DSM-IV Timing: Prior diagnosis	**Index test:** EEG EEG recording was performed according to the international 10–20 standard using 19 channels with reference electrodes located on earlobes while participants were doing a continuous mental task for four minutes at 512Hz. Frequency band separation making RGB images with three channels, deep learning convolution neural networks (CNN) classifier, 5 fold cross validation, subject-based test sample. Accuracy: 98	**Index test 2:** EEG EEG non linear functions were extracted from EEG, and the data was selected as inputsto the multi-layer perceptron neural network using double input symmetrical relevance and the minimum redundancy maximum relevance to select best features for distinguishing ADHD from healthy subjects. 70% of sample used for training/10% for validation/20% for testing[932]	**Index test 3:** EEG EEG data, multilayer perceptron neural network as a classifier with one hidden layer by 5 neurons, the output function of the neural network was sigmoidal function, features extracted from the frontal region of scalp EEG[663] Accuracy: 97	**Index text 4:** Other : EOG signals Electrooculogram signals; approximate entropy and Petrosian's fractal dimension features, support vector machine classification, 10-fold cross validation structure, only 10 samples from the control group were used to train the SVM and 117 samples were use Sensitivity: 85 Specificity: 79 Accuracy: 85 AUC: 0.82 SVM with radial basis function kernel

Moura, 2017[446] Case series N = 116 Portugal Setting: Specialty care	**Target:** Children with ADHD only and with ADHD+developmental dyslexia; IQ ≥ 85; native speakers of European Portuguese; absence of a visual, hearing, or motor handicap; never diagnosed with a language impairment, emotional disturbance, developmental dyscalculia, disruptive, impulse-control, and conduct disorders, neurological impairment or other psychiatric disorder **Other:** Typically developing children; children with developmental dyslexia only not included in abstracted outcomes **ADHD presentation:** N/A **Diagnosed by:** Provider **Comorbidity:** N/A **Female:** 75% ADHD+DD group 77.8% female **Age mean:** 8.79 (0.73) **Min age:** 8 **Max age:** 10 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis of ADHD only was confirmed by a comprehensive clinical diagnostic assessment made by two qualified neurodevelopmental pediatricians. The assessments were based on a clinical evaluation during an interview session using the DSM–4th edition (American Psychiatric Association, 2000) criteria, both parent and teacher ratings of at least 1.5 standard deviations (T ≥ 65) above the mean on the ADHD Index of the Conners Rating Scale–Revised Timing: Prior diagnosis	**Index test:** Neuropsychological,EF Shifting - Trail-B subtest from the Coimbra Neuropsychological Assessment Battery was administered to examine participants' shifting ability; the Trail–B subtest requires the child to draw a line connecting 25 circles containing numbers or letters randomly distributed on a sheet of paper, alternating between numbers and letters (1, A, 2, B, etc.); ADHD only vs typically devloping children Sensitivity: 56 Specificity: 79 AUC: 0.727	**Index test 2:** Neuropsychological,EF Visuospatial short-term memory - corsi blocks: The Corsi Blocks and the Rey Complex Figure subtests from the BANC were administered to measure visuospatial short-term memory. ADHD only vs typically devloping children Sensitivity: 63 Specificity: 62 AUC: 0.744	**Index test 3:** Neuropsychological,EF Naming speed - RAN: The Naming Speed subtest from the BANC comprises two tasks. In the RAN task, the child was asked to name 50 visual stimuli (numbers 2, 4, 6, 7, and 9) as quickly as possible, which were randomly displayed on a card in a 10 × 5 matrix. For both tasks, the raw scores were converted to age-scaled scores. ADHD only vs typically devloping children Sensitivity: 75 Specificity: 88 AUC: 0.844	**Index text 4:** Neuropsychological,EF Naming speed - RAS: The Naming Speed subtest from the BANC comprises two tasks. In the Rapid Alternating Stimulus (RAS) task, the child was asked to name 50 visual stimuli (circle, rectangle, square, and triangle, which were colored yellow, red, black, an Sensitivity: 75 Specificity: 88 AUC: 0.825

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Moura, 2019[445] Case series N = 179 Portugal Setting: Primary Care	**Target:** Native speakers of European Portuguese, with no neurological impairment, no visual, motor, or hearing impairments, no language impairment, no oppositional defiant disorder or conduct disorders; children on psychostimulants did not receive medication during the week of evaluation **Other:** Age and gender matched children **ADHD presentation:** inattentive : 36.7,hyperactive : 36.7,combined : 26.5 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 23.5% **Age mean:** 8.55 (1.92) **Min age:** 6 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed using the DSM-5, ADHD confirmed by psychologist Timing: Prior diagnosis	**Index test:** Neuropsychological,EF WISC-III (Wechsler Intelligence Scale for Children) Freedom from DistractibilityIndex, 4 lowest subtests Sensitivity: 28 Specificity: 95 PPV: 87 NPV: 52	**Index test 2:** Neuropsychological,EF Wechsler Intelligence Scale for Children (WISC-III) Freedom from Distractibility Index composite score, optimal cut-off score <=17 Sensitivity: 49 Specificity: 91 AUC: 0.781 (0.713, 0.839)	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Mouti, 2019[447] Case series N = 162 Australia Setting: Mixed	**Target:** Children with dual diagnoses of ADHD and autism spectrum disorder, IQ above 70 **Other:** Children with autism spectrum disorder severity levels 1 and/or 2 and typically developing children **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** Autism : 29 with dual diagnosis **Female:** 10.8% **Age mean:** 11.27 (3.28) **Min age:** 6 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD group provided documentation of their diagnosis that included evidence of pediatric/psychiatric assessment using DSM criteria Timing: Prior diagnosis	**Index test:** Parent rating SCQ (Social Communication Questionnaire) Lifetime version, total score cutoff of 13 todifferentiate between autism spectrum disorder and ADHD Sensitivity: 96% autism spectrum disorder vs ADHD groups Specificity: 87% autism spectrum disorder vs ADHD groups AUC: AUC 0.96 (0.91, 1.0) autism spectrum disorder vs ADHD groups Alpha: 0.93	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Mulhern, 1994[448] Post-only N = 245 US Setting: N/A	**Target:** Children consecutively referred to a university hospital-based pediatric practice between 1981 and 1992 for school related learning and/or behavior problems diagnosed with ADHD **Other:** Children consecutively referred to a university hospital-based pediatric practice between 1981 and 1992 for school related learning and/or behavior problems not diagnosed with ADHD **ADHD presentation:** N/A **Diagnosed by:** Provider **Comorbidity:** Other : Significant school-related problems were diagnosed in 92% of subjects **Female:** 19% **Age mean:** 8.1 **Min age:** 4 **Max age:** 15 **Ethnicity:** % White : 92 **Reference standard:** Clinical diagnosis Clinical diagnosis from a Pediatrician, using DSM-III-R Criteria Timing: Concurrent	**Index test:** Parent rating Parental-concern concerns from parents reported on questionnaire for one or more major symptoms of ADHD Sensitivity: 87 Specificity: 41 PPV: 47 NPV: 84	N/A	N/A	N/A

Muthuraman, 2019[449] Case series N = 22 Germany Setting: N/A	**Target:** Male participants with ADHD without conduct disorders or tic disorders, right handed, with normal or corrected-to-normal vision; no other neuropsychiatric as well as no documented comorbidities; sufficient compliance of child and family; normal school achievement; IQ>85; no MEG exclusion criteria; medication was stopped at least 48 h before recordings **Other:** Male age-matched non-ADHD controls **ADHD presentation:** N/A : All ADHD children met the criteria for combined type or hyperactive-impulsive type **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 0% **Age mean:** 13.1 (1.8) and 13.2 (1.5) **Min age:** 10 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis The diagnosis of ADHD was supported by the parents' version of a German adaptive Diagnostic Checklist for ADHD (FBB-ADHD)31,32 and by the psychiatric interview 'Kinder-DIPS' Timing: Prior diagnosis	**Index test:** EEG EEG multimodal electroencephalography: eyes closed, resting state. 56 channelswereselected from 61 equidistantly placed scalp Ag–AgCl electrodes using a standard cap sampled with 1200 Hz. Support vector machine (SVM) classifier using renormalized partial directed coherence, temporal partial directed coherence, source power, and source coherence parameters and all 5 frequency bands (delta, theta, alpha, beta, and gamma). 10-fold cross validation. Accuracy: 98	**Index test 2:** EEG EEG multimodal magnetoencephalogra phy (MEG): Eyes closed, resting state recordings wereperformed using a whole-head system at a sampling rate of 1200Hz in a synthetic third-order gradiometer configuration. Support vector machine (SVM) classifier using renormalized partial directed coherence, temporal partial directed coherence, source power, and source coherence parameters and all five frequency bands (delta, theta, alpha, beta, and gamma). 10-fold cross validation. Accuracy: 97	N/A	N/A
Mwamba, 2019[450] Case series N = 30 South Africa Setting: Specialty care	**Target:** Participants with no known history of severe mental illness **Other:** Controls, non-ADHD youth **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 54% **Age mean:** 10	**Index test:** Neuropsychological,CPT PANDAS (Paediatric Attention-Deficit/Hyperactivity DisorderApplication Software):Tablet-based game, Support vector machine (SVM) classifier; 75/25 train/test split Sensitivity: 75 Specificity: 100	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Min age: 5 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Other Subjects had been consulted by a specialist at a private paediatric practice at the Cape Gate Medi-Clinic. Timing: Prior diagnosis	Accuracy: 86 PPV: 100 NPV: 75			

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Newman, 2017[462] Case series N = 152 US Setting: N/A	**Target:** Participants with ADHD and no diagnosis of brain injury or seizure disorder and/or treated pharmacologically for psychiatric conditions other than ADHD **Other:** Age, gender, and race-matched children not diagnosed with ADHD **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 31.6% **Age mean:** 8.68 (1.84) **Min age:** 6 **Max age:** 12 **Ethnicity:** % Black/African American : 51.3 % White : 48.7 **Reference standard:** Clinical diagnosis ADHD diagnosis from a pediatric neurologist, psychiatrist, and/or psychologist using DSM-IV-TR criteria Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT,EF PADDS (Pediatric Attention Disorders Diagnostic Screener) includes 4 components:A Computer Administered/Scored Diagnostic Interview, the Swanson, Nolan, and Pelham-IV (SNAP-IV) questionnaire (parent and/or teacher), the Target Tests of Executive Functioning (3 computer-based tasks), and a Nomographic Evidence-Based Report Analysis that combines the incremental validation of information from parent and teacher ratings with results from the three executive functioning tests to determine the likelihood of an ADHD diagnosis Sensitivity: 88 Specificity: 84 Accuracy: 86 PPV: 85 NPV: 88	N/A	N/A	N/A

Nolan,1999[463] Case series N = 222 US Setting: Specialty care	**Target:** Consecutive referrals to a child psychiatry outpatient clinic; children and adolescents who received a diagnosis of ADHD and who exhibited some symptoms of ADHD, but the clinician was uncertain if all of the DSM-IV diagnostic criteria were met were included in the sample **Other:** **ADHD presentation:** inattentive : 48,hyperactive : 10,combined : 42 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 23% **Age mean:** **Min age:** 3 **Max age:** 18 **Ethnicity:** % Hispanic or Latino : 6 % Black/African American : 10 % White : 82 Other : 2% Other race **Reference standard:** Clinical diagnosis Interviews with the care provider and child patient, informal observations of parent-child interaction, observations of the child in clinic-based simulated classrooms and in public school settings, review of school history, school reports, and psychoeducational and special education evaluations, developmental, medical, and family histories, and scores from a number of parent- and teacher-completed behavior rating scales including the Child Behavior Checklist, the Teacher's Report Form, and the IOWA Conners Teacher's Rating Scale Timing: Concurrent	**Index test:** Parent rating SI-P (Symptom Inventory Parent) rating Rater agreement: Parent versus Teacher Kappa: Inattentive category 0.68, Hyperactive-impulsive category 0.42, Combined category 0.56	**Index test 2:** Teacher rating scale SI-T (Symptom Inventories Teacher) rating	N/A	N/A
Ogrim, 2012[465] Case series	**Target:** Participant with IQ>=70 **Other:** Normal gender and age-matched controls with no psychiatric	**Index test:** EEG EEG quantitative EEG Accuracy:	**Index test 2:** CPT,EF Go/NoGo task recording omission	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
N = 101 Norway Setting: Mixed	diagnosis, developmental disorders, learning disability, or brain injury **ADHD presentation:** inattentive : 32,combined : 68 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 32% **Age mean:** 11 (3) **Min age:** 7 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnoses were according to DSM IV-TR and accepted clinical guidelines. A senior neuropsychologist, pediatrician, and a clinical psychologist were responsible for diagnostic conclusions Timing: Prior diagnosis	63% for theta, 58% for theta/beta ratio	and commission errors, reaction time, and variability of response Accuracy: 85 For omission errors		

O'Neill, 2021[464] Case series N = 70 US Setting: Specialty care	**Target:** Children with IQ of at least 70 and off-medication at least 24 h prior to testing, including children with ADHD plus prenatal alcohol exposure and familial ADHD without prenatal alcohol exposure; children in the ADHD without prenatal alcohol exposure group had to have one or more first-degree relatives with diagnosed ADHD **Other:** Typically developing controls; compared to the two ADHD groups separately **ADHD presentation:** N/A : Met DSM-V criteria for ADHD, any subtype **Diagnosed by:** Researcher **Comorbidity:** Other : ADHD+prenatal alcohol exposure **Female:** 33% **Age mean:** 9.7 (1.6) , 10.7 (0.9), 11.3 (1.6) across subgroups **Min age:** 8 **Max age:** 13 **Ethnicity:** % Hispanic or Latino : 18.6 % Black/African American : 5.7 % Asian : 5.7 % White : 44.3 % Multiracial : 20 **Reference standard:** Clinical diagnosis Clinician-administered Schedule for Affective Disorders and Schizophrenia for School-Aged Children Parent Version Timing: Prior diagnosis	**Index test:** Parent rating BRIEF2+Conners-3 (Behavioral Regulation Index of the Behavior Rating Inventory of Executive Function) Parent Rating Scale Inattention and Hyperactivity/Impulsivity scores) to discriminate between children with ADHD+Prenatal alcohol exposure and typically developing children AUC: 0.90 All 3 scale measures alone AUC >0.90, p<0.0005	**Index test 2:** Parent rating BRIEF2+Conners-3 (Behavior Rating Inventory of Executive Function) Conners 3 Parent Rating Scale Inattention (CIn) and Hyperactivity/Impulsivity (CHp)scores and Behavioral Regulation Index (BRI) to discriminate between children with ADHD+familial history of ADHD(no prenatal alcohol exposure) and typically developing children AUC: 0.95 All 3 scale measures alone AUC >0.95, p<0.0005	**Index test 3:** Imaging MRS+DTI Magnetic resonance spectroscopy and diffusion tensor imaging to discriminate between children with ADHD+Prenatal alcohol exposure and typically developing children AUC: 0.68	**Index text 4:** Imaging MRS+DTI Magnetic resonance spectroscopy and diffusion tensor imaging to discriminate between children with ADHD+familial history of ADHD (no prenatal alcohol exposure) and typically developing children AUC: 0.70
Oztekin, 2021[467] Case series N = 162 US Setting: Mixed	**Target:** Participant with IQ>=70, no confirmed history of Autism Spectrum Disorder **Other:** Typically developing children **ADHD presentation:** N/A **Diagnosed by:** Specialist	**Index test:** Combined rating Emergent Metacognition Index t-score from the Behavior Rating Inventory of Executive Function (Preschool or Child version) parent and teacher ratings combined; support	**Index test 2:** Neuropsychological,EF Executive function tasks: Flanker task, the Dimensional Change Card Sorting task, and the Head-Toes-Knees-	**Index test 3:** Imaging sMRI scans assessing neural measures of cortical	**Index text 4:** Imaging,Imaging plus non-imaging Full model includes demographics, parent/teacher

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Comorbidity: N/A **Female:** 26% **Age mean:** mean 5.55 **Min age:** 4 **Max age:** 7 **Ethnicity:** % Hispanic or Latino : 82.6 **Reference standard:** Clinical diagnosis Computerized-Diagnostic Interview Schedule for Children and Disruptive Behavior Disorders Rating Scale, Impairment Rating Scale Timing: Prior diagnosis	vector machine classifier, 5-fold cross validation Sensitivity: 74 Accuracy: 93 AUC: 0.982 PPV: 94 Internal consistency: Cronbach's alpha 0.976 for teacher ratings and 0.970 for parent ratings on the Preschool version; 0.724 for teacher ratings and 0.978 for parent ratings on the Child version.	Shoulders task; support vector machine classifier, 5-fold cross validation Sensitivity: 64 Specificity: Accuracy: 67 AUC: 0.738 PPV: 71	thickness in target regions that support executive function; support vector machine classifier, 5-fold cross validation Sensitivity: 65 Accuracy: 61 AUC: 0.624 PPV: 64	ratings, cognitive measures of executive function, and cortical thickness in the left anterior cingulate, the left intraparietal transverse parietal sulci and the left superior frontal gyrus from sMRI; supp

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Oztoprak, 2017[468] Case series N = 108 Turkey Setting: N/A	**Target:** Males, unmedicated, not using drug therapy, all without comorbidities, and without uncorrected visual or hearing defects. IQ range 90-129 **Other:** Male age-matched healthy controls **ADHD presentation:** combined : 100 **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 0% **Age mean:** N/A **Min age:** 6 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD-C subtype was diagnosed using the DSM-IV Timing: Prior diagnosis	**Index test:** EEG EEG event-related potentials extracted from EEG recordings during performanceof Stroop task. Electrodes located according to the 10–10 system (reference: combined mastoids). Feature extraction using the Time-Frequency Hermite Atomizer technique, and classification by support vector machine with recursive feature elimination (SVM RFE). 5-fold cross validation. Accuracy: 100 Test dataset, N=10. Training dataset: 99.5% with the use of 5 features.	N/A	N/A	N/A

Park, 2019[469] Case series N = 114 Korea Setting: Specialty care	**Target:** Participants with IQ>=70, not on ADHD medication within the past 3 months, no past or current history of schizophrenia, organic mental disorder, or pervasive developmental disorder, or presence of seizure or other neurologic disorders, recruited from outpatient pediatric psychiatry clinic **Other:** Children with a negative ADHD diagnosis, IQ>=70. May have comorbid disorders such as tics, and depressive or anxiety disorder, but no past or current history of schizophrenia, organic mental disorder, or pervasive developmental disorder, or presence of se **ADHD presentation:** inattentive : 45.6,hyperactive : 5.1,combined : 36.6,N/A : 12.7% ADHD- not otherwise specified **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 25.3% **Age mean:** 7.6 (1.5) for ADHD group, 8.6 (2.1) for control group **Min age:** 6 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed as ADHD using DSM-IV-TR and Kiddie- Schedule for Affective Disorders and Schizophrenia– Present and Lifetime version (K-SADS-PL) Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT Advanced Test of Attention Sensitivity: 85 Specificity: 46 Accuracy: 72.8 AUC: 0.653 PPV: 78 NPV: 57 Temporal stability: Test-retest no ICC greater than 0.5 was found in ADHD retest participants	N/A	N/A	N/A
Parker, 2016[18] McGonnell, 2009[916]; Davidson, 2016[732]	**Target:** Children of an ADHD clinic which is restricted to children who have no previous diagnosis of ADHD, are psychotropic medication-naïve, and have not received a	**Index test:** Combined rating Teacher telephone interview and parent interview for child symptoms combined	**Index test 2:** Combined rating CTRS+CPRS (Conners Teacher Rating Scale and	**Index test 3:** Parent rating BRIEF (Behavior Rating Inventory	**Index text 4:** Parent rating,Teacher rating scale,Neuropsy

Case series N = 279 Canada Setting: Specialty care	psychoeducational assessment within the past 2 years **Other:** Children referred to the ADHD clinic who were not diagnosed with ADHD; 66% of these children were diagnosed with another mental disorder or a learning disability, the remaining children were not diagnosed with ADHD, a learning disability, or any other men **ADHD presentation:** inattentive : 26.0,hyperactive : 6.8,combined : 66.4,N/A : 0.7 ADHD-not otherwise specified **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 30.8% **Age mean:** 8.49 (1.70) **Min age:** 5.95 **Max age:** 12.67 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Semistructured diagnostic interview based on DSM-IV criteria for use with parents, the child also received a standard psychoeducational assessment battery; ADHD Clinic team made possible diagnoses based on the results of the above measurements Timing: Concurrent	Sensitivity: 92 Specificity: 71	Conners Parent Rating Scale) combined Sensitivity: 84 Specificity: 36	of Executive Functioning) parent rating; discriminant function analysis, classification depended mostly on the Working Memory subscale (0.90), followed by the Plan/Organizze subscale (0.74), the Inhibit subscale (0.69) and the Shift subscale (0.51)[732] Sensitivity: 100 Specificity: 90 Accuracy: 95	chological,EF BRIEF-P+BRIEF-T+DKEFS (Behavior Rating Inventory of Executive Functioning) teacher rating, BRIEF parent rating, and the Delis-Kaplan Executive Functiong System performance-based tasks (color-word interference, trail making, and tower test); discriminant f Sensitivity: 100 Specificity: 90 Accuracy: 95
Peijnenborgh, 2016[470] Case series N = 136 Netherlands Setting: Mixed	**Target:** Patients of the outpatient clinic Center for Neurological Learning Disabilities, without comorbid DSM-V diagnosis, without medication for attentional problems and hyperactive behavior **Other:** Typically developing children **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A	**Index test:** Neuropsychological,CPT,EF A computer-based game developed to assess specific cognitive functions (eg, attention, planning, and working memory), time perception, and reward mechanisms in young school-aged children Sensitivity: 89 Specificity: 69	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Female: 25% **Age mean:** 6.90 (0.74) **Min age:** 6 **Max age:** 8 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis of ADHD according to DSM-V Timing: Prior diagnosis	Accuracy: 78 (76/97) of the children were correctly classified as being in the ADHD group or in the control group			

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Pereda, 2018[473] Gonzalez, 2013[795] Case series N = 33 Spain Setting: Specialty care	**Target:** Males with combined type ADHD **Other:** Male children of hospital staff **ADHD presentation:** combined : 100 **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 0% **Age mean:** 8(0.3) for ADHD group, 8.1 (0.48) for control group **Min age:** 6 **Max age:** 10 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis DSM-IV criteria of ADHD combined type or ICD-10 criteria of Hyperkinetic Disorder Timing: Prior diagnosis	**Index test:** EEG EEG 1.5 hour eyes open and eyes closed resting-state EEG recordings at 256 Hz, international10/20 extended system, 8 channles. Functional connectivity pattern using phase locking value (PLV) phase synchronisation from dataset including the 5 most stationary segments, population-based Scatter Search algorithm, and K2 and Hill Climbing search strategies in Bayesian Network Classifier. Cross validation. Sensitivity: 95 Specificity: 93 Accuracy: 94	N/A	N/A	N/A

Perugini, 2000[475] Case series N = 41 US Setting: Other	**Target:** Boys previously diagnosed with ADHD; IQ>=80; meet DSM-IV criteria for ADHD Combined Type or Hyperactive/Impulsive Type based on the Diagnostic Interview Schedule for Children-IV, have a T-score greater than or equal to 65 on the Behavior Assessment System for Children-Parent Rating Scale Hyperactivity Subscale (mothers' ratings), have no history of treatment with stimulant drugs or, if such a history, agree to be removed from medication for 24 hours prior to evaluation in the study **Other:** Boys in a community control group; participated in earlier studies conducted at the University of Connecticut and were recruited by phone; IQ>=80; Participants in the control group had no history of mental health services for behavioral or emotional probl **ADHD presentation:** N/A : Combined and Hyperactive subtypes only, did not include inattentive subtype **Diagnosed by:** Researcher **Comorbidity:** N/A **Female:** 0% **Age mean:** 9.7 in the ADHD group, 9.2 in the control group **Min age:** 6 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Peabody Picture Vocabulary Test – Revised (PPVT-R), the Diagnostic Interview Schedule for Children – IV (DISC-IV) and the Behavioral Assessment System for Children – Parent Report Scale (BASC-PRS)	**Index test:** Neuropsychological,CPT,EF 7-test battery: K-ABC Hand Movements, Stroop Color-Word Association Test, Controlled Oral Word Association Test (FAS), Trail Making Test part B, the Arithmetic and Digit Span Subtests of the WISC-III, and Conners CPT Overall Index; at least 2 impaired scores out of 7 Sensitivity: 62 Specificity: 91 Accuracy: 77 PPV: 87 NPV: 71	**Index test 2:** Neuropsychological,CPT,EF 3-test battery: Trail Making Test part B, Digit Span Subtest of the WISC-III, and Conners CPT Overall Index; at least 1 impaired score out of 3 Sensitivity: 76 Specificity: 59 Accuracy: 67 PPV: 64 NPV: 72 Rater agreement: Kappa: Internal consistency: Alpha: Test-retest: Temporal stability:	**Index test 3:** Neuropsychological,CPT Conners CPT Overall Index; cut-off score >9 Sensitivity: 67 Specificity: 73 Accuracy: 70 PPV: 70 NPV: 70	**Index text 4:** Neuropsychological,EF Trail Making Test part B; cut-off score 1.5 SD below the mean of the control group Sensitivity: 29 Specificity: 91 Accuracy: 60 AUC: PPV: 75 NPV: 57

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Timing: Prior diagnosis				

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Pineda, 2011[477] Case series N = 288 Colombia Setting: Specialty care	**Target:** Children with ADHD; required to have Paisa descent for more than two generations and more than two members affected with ADHD; pedigrees with bilineal transmission of ADHD were excluded; IQ>=81 **Other:** Children without ADHD selected from Paisa families inhabiting the Medellin metropolitan area of the State of Antioquia, Columbia; required to have Paisa descent for more than two generations and more than two members affected with ADHD; pedigrees with bil **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 23% **Age mean:** 9.63 (2.74) for ADHD group, 11.47 (3.03) for the non-ADHD group **Min age:** 6 **Max age:** 16 **Ethnicity:** Other : 100% Paisa **Reference standard:** Clinical diagnosis The diagnostic interview for children and adolescents-revised-parent version (DICA-IV-P) Timing: Prior diagnosis	**Index test:** Neuropsychological,EF Generalized linear model with a binomial link including sex, the Wechsler intelligence scale for children-revised block design, the A cancelation and vigilance test correct response, the Rey-Osterrieth complex figure test copy time, copy, and memory time, the semantic Verbal fluency test, and the Token test Sensitivity: 81 at 0.2759 cutoff Specificity: 81 at 0.2759 cutoff AUC: 0.862	N/A	N/A	N/A

Power, 1998[479] Case series N = 92 US Setting: Specialty care	**Target:** Consecutive referrals to the ADHD Evaluation and Treatment Program; IQ>=80; children were excluded if they were on psychotropic medication for ADHD or related disorders within 6 months of the time of evaluation **Other:** Children not diagnosed with ADHD from same referral process as ADHD group **ADHD presentation:** inattentive : 53,hyperactive : 3,combined : 44 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 26% in entire sample **Age mean:** 9.0 (2.2) **Min age:** 6 **Max age:** 14 **Ethnicity:** % Hispanic or Latino : 3 % Black/African American : 22 % White : 75 **Reference standard:** Clinical diagnosis Diagnostic Interview for Children and Adolescents-Revised (DICA-R), Child Behavior Checklist (CBCL), Child Attention Profile (CAP) Timing: Concurrent	**Index test:** Teacher rating scale ADHD-RS-IV-I (ADHD Rating Scale-IV) inattention scale- Teacher ratings; logistic regression; ADHD-inattentive vs clinical controls Sensitivity: 74 AUC: 0.80 Rater agreement: ADHD Rating Scale-IV teacher ratings of Inattention and diagnostic status r= 0.38	**Index test 2:** Teacher rating scale ADHD-RS-IV-I (Rating Scale-IV) inattention scale- Teacher ratings; logistic regression; ADHD-combined vs clinical controls Sensitivity: 80 AUC: 0.84 Rater agreement: ADHD Rating Scale-IV teacher ratings of Inattention and diagnostic status r= 0.44	**Index test 3:** Combined rating ADHD-RS-IV-I (Rating Scale-IV Inattention Scale) Teacher ratings and parent ratings combined; logistic regression; ADHD-inattentive vs clinical controls Sensitivity: 72 AUC: 0.84 Rater agreement: ADHD Rating Scale-IV ratings of Inattention and diagnostic status	**Index text 4:** Combined rating ADHD-RS-IV-H/I (ADHD Rating Scale-IV) Hyperactivity/Impulsivity Scale Teacher ratings and parent ratings combined; logistic regression; ADHD-combined vs clinical controls Sensitivity: 75 AUC: 0.81 Rater agreement: ADHD Rating Scale-IV ratings of Hyperactivity/Impulsivity and diagnostic status Model with both teacher and parent rating entered jointly; teacher ratings r= 0.32, parent ratings r= 0.22
Preston, 2005[482] Case series N = 167 US Setting: N/A	**Target:** Children at high risk for ADHD and meet one or more of the following inclusion criteria: previous record of diagnosis or treatment for ADHD, suspicion of having ADHD via verbal report by parent or teacher, or reported parental concern about behavior problems based on parent scores of	**Index test:** Neuropsychological,CPT TOVA (Test of Variables of Attention); classification criterion is defined as a score of 1.5 standard deviations below the normative mean on omission errors, response time, or response time variability	**Index test 2:** Neuropsychological,CPT TOVA (Test of Variables of Attention); classification criterion is defined as a score of 1.0 standard deviations below the	**Index test 3:** Parent rating SNAP-IV (Swanson–Nolan–and-Pelham–IV) parent ratings Sensitivity: 55 Specificity: 66	**Index text 4:** Teacher rating scale SNAP-IV (Swanson–Nolan–and-Pelham–IV) teacher ratings Sensitivity: 40 Specificity: 71

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	the Swanson, Nolan and Pelham Questionnaire-IV **Other:** Children with subclinical levels of attention/behavioral problems recruited through epidemiological sampling to ensure a representative sample of children at high risk for ADHD; did not meet criteria for any DSM-IV behavioral diagnostic group **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 60% Selected using a gender stratified random design that oversampled girls by a marginof 2:1 **Age mean:** 9.10 for the ADHD group, 9.07 for the subclinical control group **Min age:** 6 **Max age:** 14 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis The diagnostic interview schedule for children, fourth version (DISC-IV) Timing: Prior diagnosis	Sensitivity: 37 Specificity: 61	normative mean on two or more of omission, commission, response time, and response time variability Sensitivity: 30 Specificity: 70		

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Qin , 2018[486] Case series N = 275 China Setting: Mixed	**Target:** Participants with IQ>=85; no intellectual disability, learning disorder, tic disorders and autism spectrum disorder, and no history of treatment for ADHD using medications **Other:** Healthy children **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 17% **Age mean:** 9.1 (2.1) for ADHD group, 9.3 (1.5) for control group **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Clinical diagnosis made by psychiatrists using DSM-IV criteria Timing: Prior diagnosis	**Index test:** Neuropsychological,EF DN:CAS (Das-Naglieri Cognitive Assessment System), test of cognitive abilitiesbased on four cognitive processes based on Planning, Attention, Simultaneous, and successive Theory (PASS). Two different sets of tests were carried out according to various age groups (5–7 year-olds and 8–17 year-olds). Classification performance of Planning subscale when the cut-off point was set at 25-points Sensitivity: 73 Specificity: 79 AUC: 0.808 (0.756, 0.853)	**Index test 2:** Neuropsychological,EF The Das-Naglieri Cognitive Assessment System (DN: CAS). Test of cognitive abilities based on four cognitive processes based on Planning, Attention, Simultaneous, and successive Theory (PASS). Two different sets of tests were carried out according to various age groups (5–7 year-olds and 8–17 year-olds). Classification performance of Attention subscale when the cut-off point was set at 29-points. Sensitivity: 79 Specificity: 58 AUC: 0.730 (0.673, 0.782)	N/A	N/A

Quintana, 2007[487] Case series N = 26 US Setting: Specialty care	**Target:** Children who presented to a child psychiatric clinic because a parent and/or school official suspected they might have ADHD who were diagnosed with ADHD with or without associated disorders or co-morbidities; not on medication at time of study or in the prior 6 months **Other:** Children who presented to a child psychiatric clinic because a parent and/or school official suspected they might have ADHD who were not diagnosed with ADHD; diagnosed with other disorder or no diagnosis **ADHD presentation:** inattentive : 63,hyperactive : 6,combined : 31 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 12.5% **Age mean:** **Min age:** 6 **Max age:** 16 **Ethnicity:** % Black/African American : 15.4 % Asian : 3.8 % White : 76.9 Other : 3.8% Middle Eastern **Reference standard:** Clinical diagnosis Psychiatric evaluation; Schedule for Affetive Disorders and Schizophrenia-Lifetime Version and Supplement for Behavioral Disorders, Clinical Global Assessment Scale and clinical Global Impression-Severity subscale Timing: Concurrent	**Index test:** Parent rating ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale, Version-IV) Sensitivity: 81 Specificity: 22 Accuracy: 60 PPV: 65	**Index test 2:** EEG EEG eyes closed and eyes open resting state, frontal beta power with 2 SD cutoff, theta/beta ratio with 1.5 SD cutoff; performed blinded to psychiatric evaluation and rating scale results Sensitivity: 94 Specificity: 100 Accuracy: 96	N/A	N/A
Raiker, 2017[491] Case series N = 620 US Setting: Specialty care	**Target:** Participants with from urban, community mental health center with clinical or self-reported ADHD **Other:** Children and adolescents recruited using a prospective, consecutive case series design from all intakes at an urban, community	**Index test:** Teacher rating scale ASEBA (Achenbach System of Empirically Based Assessment) Teacher Report Form AUC:	**Index test 2:** Parent rating ASEBA (Child Behavior Checklist Achenbach System of Empirically Based Assessment)	**Index test 3:** Teen/child self report ASEBA (Youth Self-Report Achenbach System of	N/A

	mental health center not diagnosed with ADHD **ADHD presentation:** inattentive_other : Age 5 to 11: 9%. Age 12 to 18: 10%,hyperactive_other : Age 5 to 11: 4%. Age 12 to 18: 4,combined_other : Age 5 to 11: 53%. Age 12 to 18: 25%,N/A : ADHD not otherwise specified Age 5 to 11: 7%. Age 12 to 18: 13%. **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % Age 5 to 11 32% female, age 12 to 18 46% female **Age mean:** Age 5 to 11: 7.63 (1.65), age 12 to 18: 13.43 (1.85) **Min age:** 5 **Max age:** 18 **Ethnicity:** % Hispanic or Latino : Age 5 to 11: 3%. Age 12 to 18: 0%. % Black/African American : Age 5 to 11: 87%. Age 12 to 18: 89%. % White : Age 5 to 11: 6%. Age 12 to 18: 6. Other : Ethnicity Other age 5 to 11: 4%. Age 12 to 18: 4%. **Reference standard:** Clinical diagnosis Diagnoses of ADHD were made in accordance with DSM-IV-TR Timing: Prior diagnosis	Age 5 to 11: AUC 0.62 (0.55-0.70), age 12 to 18: AUC 0.56 (0.50-0.62)	AUC: Age 5 to 11: AUC 0.72 (0.65-0.80), age 12 to 18: AUC 0.0.73 (0.67-0.78)	Empirically Based Assessment) AUC: 0.56 (0.49, 0.62)	
Reddy, 2021[493] Case series N = 52 US Setting: Specialty care	**Target:** Participants recruited through a University-based Child and Adolescent ADHD research clinic **Other:** Children with no psychiatric diagnoses and not receiving any special educational services selected from the standardization sample of the Woodcock Johnson III Tests of Cognitive Abilities matched on five	**Index test:** Neuropsychological,EF Woodcock Johnson III Tests of Cognitive Abilities (WJ III COG) includes 20 tests that fall into Verbal Ability, Thinking Ability, and Cognitive Efficiency that generate a General Intellectual Ability Score (GIA) for Standard and Extended batteries; 4	**Index test 2:** Neuropsychological,EF Nine Woodcock Johnson III Tests of Cognitive Abilities (WJ III COG): Auditory Attention, Auditory Working Memory, Concept Formation, Decision Speed,	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	demographic variables (age, gender, race, mother's **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 15% **Age mean:** **Min age:** 5 **Max age:** 10 **Ethnicity:** % Hispanic or Latino : 6 % Black/African American : 8 % White : 86 **Reference standard:** Clinical diagnosis Primary diagnosis of ADHD by a pediatric neurologist, psychiatrist, and/or psychologist, The Structured Diagnostic Interview for Parents Timing: Prior diagnosis	clinical clusters devired from two or more individual tests were used in the study: Working Memory, Broad Attention, Cognitive Fluency, and Executive Processes; cut-score of 85 Sensitivity: 69 Specificity: 62 Accuracy: 65 AUC: 0.65 PPV: 64 NPV: 67	Numbers Reversed, Pair Cancellation, Planning, Retrieval Fluency, and Rapid Picture Naming; cut-score of 85 Sensitivity: 85 Specificity: 77 Accuracy: 81 AUC: 0.80 PPV: 79 NPV: 83		

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Rezaeezadeh, 2020[494] Khoshnoud, 2018[883] Case series N = 24 Iran Setting: Specialty care	**Target:** Patients of Atieh Comprehensive Centre for Psychology and Nerve Disorders, right-handed **Other:** Age-matched right-handed neurotypical children **ADHD presentation:** N/A : included hyperactive-impulsive, inattentive, and combined subtypes **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** % N/A **Age mean:** NA **Min age:** 7 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed with ADHD AT Atieh Comprehensive Centre for Psychology and Nerve Disorders, Tehran, Iran Timing: Prior diagnosis	**Index test:** EEG EEG resting state eyes closed EEG, classification by Radial Basis Function supportvectormachine based on a combination of non-linear univariate features, 75/25 training/testing split rearranged randomly 20 times for validation Accuracy: 100	**Index test 2:** EEG EEG resting state eyes closed EEG, classification by probabilistic neural network (PNN)based on brain regions using multivariate features, 75/25 training/testing split rearranged randomly 20 times for validation Accuracy: 91	**Index test 3:** EEG EEG eyes-closed resting EEG (19 channels) analysed using nonlinear analysis metrics.Three measures of nonlinear dynamics: the largest Lyapunov exponent, approximate entropy, and the height and width of the multifractal singularity spectrum of the EEG time series. Classification using support vector machine (SVM) classifier, 4 fold cross validation[883] Accuracy: 83	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Riaz, 2020[495] Riaz, 2018[1004]; Itani, 2019[852]; Sun, 2020[1090]; Itani, 2018[851] Case series N = 222 US Setting: Other	**Target:** Children from New York University medical center dataset (NYU) from ADHD-200 dataset **Other:** Healthy children **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 35% **Age mean:** N/A **Min age:** 7 **Max age:** 18 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD-200 dataset Timing: Prior diagnosis	**Index test:** Imaging fMRI, end-to-end deep learning model using pre-processed fMRI time-series signals; ADHD-200 provided NYU test set for validation Sensitivity: 66 Specificity: 92 Accuracy: 73	**Index test 2:** Imaging,Imaging plus non-imanging fMRI, decision tree machine learning predictive models based on phenotypic characteristics and resting-state functional magnetic resonance Images, validated using test set[852] Sensitivity: 79 Specificity: 58 Accuracy: 73	**Index test 3:** Imaging MRI, whole-brain resting-state functional connectivity patterns, support vector machine (SVM) classification, leave one out cross validation[1090] Sensitivity: 82 Specificity: 88 Accuracy: 85	**Index text 4:** Imaging,Imaging plus non-imaging Computer-aided diagnosis using MRI data, multi-level decision tree[851] Accuracy: 68

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Rielly, 1999[496] Case series N = 99 Canada Setting: Specialty care	**Target:** Children with a preschool history of language disorders; IQ>=70 **Other:** School-aged boys with a history of suspected language disorders; IQ>=70 **ADHD presentation:** N/A **Diagnosed by:** Researcher **Comorbidity:** N/A **Female:** 0% **Age mean:** 8.2 (0.43) **Min age:** 7 **Max age:** 9 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Assessment in diagnostic clinic for children with a preschool history of language disorders Timing: Concurrent	**Index test:** Neuropsychological,CPT GDS (Gordon Diagnostic System), portable, single-component, microcomputer-based device that can be used to administer 11 measures of sustained attention and impulsivity; any 7 out of 11 scores abnormal at 25th percentile cutoff Sensitivity: 68 Specificity: 54 PPV: 33 NPV: 83	**Index test 2:** Neuropsychological,C PT GDS (Gordon Diagnostic System), portable, single-component, microcomputer- based device that can be used to administer 11 measures of sustained attention and impulsivity; any 4 out of 11 scores abnormal at 5th percentile cutoff Sensitivity: 60 Specificity: 49 PPV: 28 NPV: 78	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Rishel, 2005[498] Case series N = 236 US Setting: Specialty care	**Target:** Children and adolescents with attention deficit disorder treated at community mental health clinic **Other:** "Non psychotic" children treated at community mental health clinic **ADHD presentation:** N/A **Diagnosed by:** Provider **Comorbidity:** N/A **Female:** 43% **Age mean:** 11.3 (3.4) **Min age:** 6 **Max age:** 17 **Ethnicity:** % Black/African American : 11.8,Other : Mother's race % White : 86,Other : Mother's race **Reference standard:** Clinical diagnosis DSM IV per Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) Timing: Concurrent	**Index test:** Parent rating CBCL (Child Behavior Checklist), parent rating Sensitivity: 72.0% differentiating "ADD" from non-ADD children in mental health clinic Specificity: 80.9% differentiating "ADD" from non-ADD children in mental health clinic Accuracy: 77.8% overall correct AUC: 0.83 PPV: 66.7% differentiating "ADD" from non-ADD children in mental health clinic NPV: 84.4% differentiating "ADD" from non-ADD children in mental health clinic	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Robles, 2021[499] Case series N = 52 Mexico Setting: Specialty care	**Target:** Participants without the presence of communication difficulties, cognitive dysfunctions, and disabilities; seeking mental health services at two specialized psychiatric care facilities **Other:** Children seeking mental health services at two specialized psychiatric care facilities in Mexico City not diagnosed with ADHD **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 37% **Age mean:** 11.9 (3.2) **Min age:** 6 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Two psychiatrists independently established diagnosis, blind to each others evaluation Timing: Concurrent	**Index test:** Clinician tool Evaluation of interrater reliability of ICD11 diagnostic guidelines for mental and behavioral disorders in children and adolescents to assess clinical utility. Each participant was interviewed by a pair of psychiatrists (interviewer and observer), who independently codified established diagnoses and evaluated the clinical utility of the guidelines. Rater agreement: 2 clinicians, one conducted the interview, the other was observer Kappa: 0.46	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Rodríguez, 2018[500] Case series N = 338 Spain Setting: Mixed	**Target:** Participants with IQ 70-130, no comorbid disorders, stopped medication 72 hours before testing **Other:** Children without ADHD or other psychiatric diagnosis; IQ>=70 **ADHD presentation:** inattentive : 32,hyperactive : 15,combined : 23 **Diagnosed by:** Researcher **Comorbidity:** N/A **Female:** % 29% in entire sample **Age mean:** 10.84 (3.01) **Min age:** 6 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD group was composed of children with a diagnostic report (by a Clinical Center) specifying the type of ADHD presentation. Using this information, the researchers confirmed the diagnosis and its presentation using the symptomatology described in DSM-5 and scoring the subject on the scale Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT Aula Nesplora Virtual Reality Continuous Performance Test; discrimination between ADHD-IH vs ADHD-I vs ADHD-C vs controls Accuracy: 57 Discrimination between ADHD-IH vs ADHD-I vs ADHD-C vs controls Alpha: 0.72	**Index test 2:** Neuropsychological,CPT Test of Variables of Attention (TOVA); discrimination between ADHD-IH vs ADHD-I vs ADHD-C vs controls Accuracy: 34 Discrimination between ADHD-IH vs ADHD-I vs ADHD-C vs controls	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Roessner, 2007[501] Case series N = 66 Germany Setting: Specialty care	**Target:** Children and adolescents in Germany who were patients of specialty clinics **Other:** Healthy controls **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** % N/A **Age mean:** 12.1 (3.2) **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis All children were referred and fulfilled DSMIV-TR criteria for ADHD. Timing: Prior diagnosis	**Index test:** Biomarker Urine tetrahydroisoquinolines levels, salsolinol (free) Sensitivity: 56 Specificity: 95	**Index test 2:** Biomarker Urine tetrahydroisoquinolines levels, N-methyl-Salsolinol (free) Sensitivity: 93 Specificity: 94	**Index test 3:** Biomarker Urine tetrahydroisoquinolines urine levels, Norsalsolinol (free) Sensitivity: 88 Specificity: 80	**Index text 4:** Biomarker Urine tetrahydroisoquinolines levels, N-methyl-Norsalsolinol (free) Sensitivity: 69 Specificity: 94

Rogers, 2022[502] Case series N = 253 US Setting: Specialty care	**Target:** Youth evaluated in a private practice setting; comorbidities include reading disorder, mathematics disorder, written expression disorder, oppositional defiant disorder, developmental coordination disorder, anxiety disorder, mood disorder, and adjustment disorder **Other:** **ADHD presentation:** inattentive : 64,combined : 36 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 30% **Age mean:** 10.4 (2.9) **Min age:** 6 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Parents completed the Behavior Assessment System for Children, Second Edition (BASC-2) and DSM-IV ADHD Symptom Rating Scale (SRS) as part of a comprehensive evaluation to establish ADHD diagnoses; ADHD diagnoses were established by a pediatric neuropsychologist according to DSM-IV diagnostic criteria, based on a comprehensive assessment of general intelligence, attentional difficulties, academic achievement, executive functioning, and behavior, supplemented with parent interviews, teacher ratings, and academic and medical records; ADHD diagnoses were not blind to SRS results Timing: Concurrent	**Index test:** Parent rating ADHD-SRS-Im (ADHD Symptom Rating Scale, an 18-item scale modified from the ADHD RatingScale-IV and evaluates symptoms that compose the inattention, hyperactivity, and impulsivity domains; only mothers' ratings were considered because these were most consistently available in the data; ADHD-combined versus ADHD-inattentive; SRS Impulsivity scale cut-score 0.67 Sensitivity: 81 Specificity: 69 AUC: 0.82 (0.77, 0.87) PPV: 59 NPV: 13 LR+: 2.61 LR-: 0.28 Rater agreement: SRS impulsivity scale versus BASC attention problems scale or BASC hyperactivity scale (Convergent Validity) Pearson's correlations: SRS impulsivity vs BASC attention problems r=0.24 (p<0.01), SRS impulsivity vs BASC hyperactivity r=0.63 (p<0.01)	**Index test 2:** Parent rating ADHD-SRS-H (ADHD Symptom Rating Scale), 18-item scale modified from the ADHD Rating Scale-IV and evaluates symptoms that compose the inattention, hyperactivity, and impulsivity domains; only mothers' ratings were considered because these were most consistently available in the data; ADHD-combined versus ADHD-inattentive; SRS Hyperactivity scale cut-score 0.67 Sensitivity: 78 Specificity: 69 AUC: 0.80 (0.74, 0.86) PPV: 58 NPV: 15 LR+: 2.52 LR-: 0.32 Rater agreement: SRS hyperactivity scale versus BASC attention problems scale or BASC hyperactivity scale (Convergent Validity) Pearson's correlations: SRS hyperactivity vs BASC attention problems r=0.30 (p<0.01), SRS hyperactivity vs BASC	**Index test 3:** ADHD-SRS-In (ADHD Symptom Rating Scale), 18-item scale modified from the ADHD Rating Scale-IV and evaluates symptoms that compose the inattention, hyperactivity, and impulsivity domains; only mothers' ratings were considered because these were most consistently available in the data; ADHD-combined vs ADHD-inattentive; SRS Inattention scale Rater agreement: SRS inattention scale versus BASC attention problems scale or BASC hyperactivity scale (Convergent Validity)	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
			hyperactivity r=0.68 (p<0.01)		

Rucklidge, 2002[506] Case series N = 98 Canada Setting: Specialty care	**Target:** Participants previously assessed and new referrals; IQ>=80 **Other:** Adolescents with reading disabilities recruited through advertisements looking for volunteers for research; Adolescents in the control group were recruited through Hospital staff and community resources; IQ>=80 **ADHD presentation:** inattentive : 100 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 48% female in the ADHD inattentive group, 25% female in the ADHD inattentive + reading disability group **Age mean:** **Min age:** 13 **Max age:** 16 **Ethnicity:** **Reference standard:** Clinical diagnosis Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL), Wide-Range Achievement Test (WRAT3) and Woodcock Reading Mastery Test-Revised (WRMT-R); confirmed diagnosis of ADHD in childhood based on a standard clinical diagnostic protocol and standardized parent and teacher behavior rating scales Timing: Prior diagnosis	**Index test:** Teen/child self report Brown-ADD-Scale for Adolescents; cutoff >=55; participant groups collapsed into ADHD vs non-ADHD Sensitivity: 53 Specificity: 98 Accuracy: 78 Rater agreement: Brown ADD total scales (teen) vs Symptoms of ADHD inattentive from the K-SADS (parent) Pearson correlation 0.747	**Index test 2:** Teen/child self report Brown-ADD-Scale+CWASR Brown Attention Deficit Disorder Scales for Adolescents and the Conners-Wells Adolescent Self-report Scale; discriminant function analysis, function included Brown subscale of Attention, Brown subscale of Effort, and Family Problems subscale of the Conners-Wells; participant groups collapsed into ADHD vs non-ADHD Sensitivity: 78 Specificity: 94 Accuracy: 87 Rater agreement: Brown ADD total scales versus Adolescent Conners ADHD scale Pearson correlation 0.809	N/A	N/A
Satin, 1985[514] Case series N = 92 US Setting: Specialty care	**Target:** Subjects diagnosed with ADHD **Other:** Subjects came from a telephone-augmented mail survey of human service needs in eastern Long Island, N.Y., not diagnosed with ADHD **ADHD presentation:** N/A **Diagnosed by:** Specialist	**Index test:** Parent rating ARS (Conners' Abbreviated Rating Scale) total score, cutoff >=0.7 Sensitivity: 92 Specificity: 72 PPV: 51 Rater agreement:	**Index test 2:** Parent rating ARS (Conners' Abbreviated Rating Scale) 5 item subset that are identicalto items in the Teacher Rating Scale, cutoff >=0.7	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Comorbidity: N/A **Female:** 0% **Age mean:** **Min age:** 6 **Max age:** 9 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Tested for intelligence (Peabody Picture Vocabulary Test), perceptual motor performance (Developmental Test of Visual Motor Integration), and reading and mathematics achievement (Peabody Individual Achievement Test); each boy was given a conventional unstructured mental status examination by a child psychiatrist. Parents completed the Werry-Weiss-Peters Activity Scale and interviewed by a psychiatrist Timing: Later diagnosis	Conners' Abbreviated Rating Scale versus clinical diagnosis kappa 0.50	Sensitivity: 91 Specificity: 73 PPV: 51 Rater agreement: Conners' Abbreviated Rating Scale 5 item subset versus clinical diagnosis kappa 0.51		

Schatz, 2001[515] Case series N = 48 US Setting: Mixed	**Target:** Attentional symptoms must be primary to a learning disability if present, individuals with a pervasive neurological condition such as autism or comorbid psychiatric disorders were excluded **Other:** Children with normal neurodevelopmental histories and at an appropriate grade level for their chronological age; recruited from general pediatric clinics, advertisements in parent magazines and at local fairs, radio advertisements, and through contacts wi **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % N/A **Age mean:** 11.1 (3.6) for ADHD group, 9.8 (2.7) for control group **Min age:** 5 **Max age:** 17 **Ethnicity:** Other : Predominantly white **Reference standard:** Clinical diagnosis Medical history, neurological exam, parent and teacher historical reports, and psychological testing Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT TOVA (Test of Variables of Attention), cutoff at least one T score >=65 Sensitivity: 86 Specificity: 70	**Index test 2:** Parent rating CPRS-HI (Conners Parent Rating Scale), Hyperactivity Index, cutoff T score >=65 (1.5 SD above the mean) Sensitivity: 79 Specificity: 100	N/A	N/A
Scheeringa, 2020[516] Case series N = 58 US Setting: Specialty care	**Target:** Children consecutively recruited from one private outpatient child and adolescent psychiatry clinic that specialized in very young children without primary diagnosis of Autism Spectrum Disorder **Other:** Same recruitement process as ADHD group **ADHD presentation:** N/A **Diagnosed by:** Researcher	**Index test:** Parent rating DIPA (Diagnostic Infant and Preschool Assessment) rating scale version Rater agreement: ADHD DIPA-L versus ADHD-SNAP Pearson correlation first interview r=0.80 (p<0.0001), second interview r=0.94 (p<0.0001)	**Index test 2:** Parent rating DIPA-L (Diagnostic Infant and Preschool Assessment revised to include Likert ratings) Alpha: The Diagnostic Infant and Preschool Assessment including Likertratings (DIPA-L)	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Comorbidity: N/A **Female:** 25% **Age mean:** 4.67 (1.15) **Min age:** 2 **Max age:** 6 **Ethnicity:** % Hispanic or Latino : 8 % Asian : 1 % White : 87 % Multiracial : 4 **Reference standard:** Clinical diagnosis Swanson, Nolan, and Pelham scale (SNAP) parent rating Timing: Concurrent	Alpha: 0.92 The Diagnostic Infant and Preschool Assessment including Likertratings (DIPA-L) first interview versus second interview. Interval between interviews based on scheduling availability. Test-retest: ICC 0.91 (p<0.0001)	first interview versus second interview. Interval between interviews <=30 days ICC 0.91 (p<0.0001) Test-retest: ICC 0.91 (p<0.0001) Temporal stability: Kappa 0.84		

Schirmer, 2021[518] Case series N = 100 US Setting: Other	**Target:** Children with primary diagnosis of autism spectrum disorder who met diagnostic criteria for ADHD and children with ADHD; IQ at or above the normal range **Other:** Age and full-scale IQ matched neurotypical controls with no immediate family members diagnosed with ADHD or autism spectrum disorder **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** Other : 25 children with primary diagnosis of Autism spectrum disorder who met diagnostic criteria for ADHD in test set,N/A **Female:** 28% **Age mean:** 10.4 (1.3) **Min age:** 8 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnostic Interview for Children and Adolescents (DICA-IV), Fourth Edition or the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) for School-Aged Children-Present and Lifetime Version, in addition Conners' Parent or Teacher Rating Scales-Revised Long Version, Conners-3, ADHD Rating Scale- IV, Home or School Versions. Timing: Prior diagnosis	**Index test:** Imaging fMRI, resting state, support vector machines, linear regression (l1 or l2 regularization), random forest, k-nearest neighbor, and naive Bayes classifiers Sensitivity: 95 75% in test set. False negative rate ranged from 0.05 to 0.3, false discovery rate ranged from 0.16 to 0.33 Specificity: 55 25% in test set Accuracy: 75 50% in test set AUC: 0.73 0.48 in test set PPV: 68 50% in test set NPV: 92 50% in test set Rater agreement: Matthews correlation coefficient 0.55 in validation set	**Index test 2:** Imaging fMRI, resting state, tangent Pearson connectivity, SVM trained regularized by the statistical independence between the classifier decision scores and 3 types of demographic information: gender, age, and handedness score Sensitivity: 75 50% in test set Specificity: 70 50% in test set Accuracy: 73 53% in test set AUC: 0.85 0.54 in test set PPV: 71 52% in test set NPV: 74 52% in test set Matthews correlation coefficient 0.45 in validation set	**Index test 3:** Imaging fMRI, resting state, mean and standard deviation, Pearson correlation, tangent, covariance, and tangent Pearson Sensitivity: 80 50% in test set Specificity: 85 60% in test set Accuracy: 83 55% in test set AUC: 0.89 0.47 in test set PPV: 84 56% in test set NPV: 81	**Index text 4:** Imaging fMRI, resting state, long short-term memory network was used, AAL ROIs were first selected based on consistent connectivity differences between ADHD and controls in bootstrapped samples, time-series from these ROIs were input to an LSTM, with the demograp Sensitivity: 70 70% in test set Specificity: 65 65% in test set Accuracy: 68 68% in test set AUC: 0.72 0.66 in the test set PPV: 67 67% in test set NPV: 68 70% in test set Rater agreement: Matthews correlation coefficient 0.35 in the validation set Kappa:

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
					Internal consistency:

Schneider, 2020[519] Case series N = 84 US Setting: Mixed	**Target:** Participants presenting with ADHD symptoms for at least 6 months and cross-situational impairment; IQ>=80; free of intellectual disability or autism spectrum disorder, visual impairment, treatment with psychotropic medications other than for ADHD, history of DSM-IV or DSM-V Axis I diagnosis other than oppositional defiant disorder or adjustment disorder, neurological disorder, documented hearing loss >= 25 decibels loss in either ear, reported history of physical sexual, or emotional abuse, and history of a developmental language disorder **Other:** Typically developing children **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 40.8% **Age mean:** ADHD group: 5.0 (0.6), comparison group: 4.9 (0.5) **Min age:** 4 **Max age:** 5 **Ethnicity:** % Black/African American : 5 % Asian : 3 % White : 90 % Multiracial : 1 Other : Other 1% **Reference standard:** Clinical diagnosis Adapted from the NIH Preschoolers with Attention-Deficit/ Hyperactivity Disorder Treatment Study, Diagnostic Interview Schedule for Children-Young Child used for 4-year-olds and Diagnostic Interview for Children and Adolescents, Fourth Edition used for 5-year-olds Timing: Prior diagnosis	**Index test:** Teacher rating scale BRIEF (Behavior Rating Inventory of Executive Function)- Preschool Version (same form for teachers and parents) Rater agreement: Teacher versus parent Using standardized score totals, analysis of group-by-rater interaction effects revealed significant interactions for two scales: Working Memory, and Plan/Organize. Of note, the effect size for group differences (ADHD vs. TD) for these two scales was ess Within the ADHD group, there were significant associations between parent and teacher ratings on four of the five scales (correlations ranging from 0.30 to 0.34), with only the Shift scale showing non-significant inter-rater association (r = −.01).	**Index test 2:** Parent rating BRIEF (Behavior Rating Inventory of Executive Function)- Preschool Version (same form for teachers and parents)	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Serrallach, 2016[524] Case series N = 147 Germany Setting: Specialty care	**Target:** Children and adolescents with ADHD and ADD **Other:** Age matched healthy children, children with dyslexia **ADHD presentation:** inattentive : 49,inattentive_other : F 98.8 (ADD) ICD-10 classification,combined : 51,combined_other : F 90.0/F90.1 (ADHD) ICD-10 classification **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 22% **Age mean:** 10.8 (1.9) for ADHD group, 11.0 (2.6) for ADD group, 10.7 (1.8) for dyslexic group, and 11.0 (1.3) for control group **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis DSM IV (ICD-10), re- validated with informal interviews by specialist and "Parent assessment sheet for hyperactivity disorder, which is part of 'Diagnostic System for Psychiatric Disorders in Children and Adolescents' (DISYPS-K) Timing: Prior diagnosis	**Index test:** Imaging MRI, T1-weighted sMRI to investigate the anatomy of the auditory cortex; Neuromag-122 whole-head MEG system to measure the response of the auditory cortex to acoustic stimuli, audiometric and psychoacoustic tests stimuli were presented binaurally with a Hammerfall DSP Multiface System and closed dynamic headphones; pooled disorder group (dyslexia, ADHD, and ADD) vs control group Accuracy: 84.4% pooled disorder group vs controls	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	Results: Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	Index Test 2	Index Test 3	Index Test 4
Shemmassian, 2016[527] Shemmassian, 2012[1040] Case series N = 195 US Setting: Other	**Target:** Youths with elevated levels of attention and hyperactivity problems; with or without psychotropic medications; IQ>=70 **Other:** Neurotypical children without ADHDrecruited from local elementary schools and pediatric offices using fliers containing ‘‘neutral’’ language (i.e., did not refer to ADHD-related problems) ; youth who met criteria for any disorder other than ADHD (e.g., an **ADHD presentation:** inattentive : 42,hyperactive : 12,combined : 46 **Diagnosed by:** Researcher **Comorbidity:** N/A **Female:** 30% **Age mean:** 7.4 (1.1) **Min age:** 6 **Max age:** 10 **Ethnicity:** % Hispanic or Latino : 10 % Black/African American : 7 % White : 53 % Multiracial : 22 Other : 4 **Reference standard:** Clinical diagnosis Any subtype of ADHD according to DISC-IV Timing: Concurrent	**Index test:** Teacher rating scale DBD (Disruptive Behavior Disorder) ratings scale, teacher rating Sensitivity: 2-year predictive sensitivity 48 Specificity: 2-year predictive specificity 70 PPV: 2 year predictive PPV 65 NPV: 2 year predictive NPV 54	**Index test 2:** Parent rating DBD (Disruptive Behavior Disorder) ratings scale, parent rating Sensitivity: 2 year predictive sensitivity 73 Specificity: 2 year predictive specificity 93 Accuracy: AUC: PPV: 2 year predictive PPV 93 NPV: 2 year predictive NVP 75 Internal consistency: Parent-rated inattention Cronbach's alpha 0.94, Parent rated hyperactivity/impulsivity Cronbach's alpha 0.91	**Index test 3:** Combined rating OR rule, i.e., teacher or parent rating indicates ADHD (Teacher Disruptive Behavior Disorder (DBD) Ratings Scale or Parent Disruptive Behavior Disorder (DBD) Ratings Scale) Sensitivity: 2 year predictive snsitivity 88 Specificity: 2 year predictive sensitivity 63 PPV: 2 year predictive PPV 73	**Index text 4:** Combined rating AND rule, i.e., teacher and parent rating indicates ADHD (Teacher Disruptive Behavior Disorder (DBD) Ratings Scale or Parent Disruptive Behavior Disorder (DBD) Ratings Scale) Sensitivity: 2 year predictive sensitivity 25 Specificity: 2 year predictive specificity 98 PPV: 2 year predictive PPV 93 NPV: 2 year predictive NPV 53

Shemmassian, 2017[528] Case series N = 151 US Setting: Mixed	**Target:** Children with IQ>=70, free from a previous pervasive developmental, seizure, or neurological disorder, or any medical condition that prevented full participation in the study; recruited from local elementary schools, pediatric offices, and clinical service providers **Other:** Youth who met criteria for any disorder other than ADHD, as well as those with a sub-clinical ADHD included in comparison group; IQ>=70, free from a previous pervasive developmental, seizure, or neurological disorder, or any medical condition that prevent **ADHD presentation:** inattentive : 43,hyperactive : 12,combined : 45 **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 29% **Age mean:** 7.4 (1.2) **Min age:** 5 **Max age:** 10 **Ethnicity:** % Hispanic or Latino : 9 % Black/African American : 10 % Asian : 4 % White : 54 % Multiracial : 21,Other : Biracial Other : 2% race category other **Reference standard:** Clinical diagnosis Diagnostic Interview Schedule for Children, 4th edition Timing: Prior diagnosis	**Index test:** Teacher rating scale DBD (Disruptive Behavior Disorder) rating scale, teacher rating. Total predictive value calculated for each level of each teacher-rated ADHD symptom against ADHD versus non-ADHD status derived from the DISC-IV. "Observed" classification algorithm: >=6 of 9 inattention and/or hyperactivity/impulsivity symptoms Sensitivity: 82 Specificity: 55 PPV: 67 NPV: 73 Internal consistency: Cronbach's alpha 0.94 for both teacher-rated inattention and hyperactivity symptom counts on the Disruptive Behavior Disorder Rating Scale	**Index test 2:** Parent rating DBD (Disruptive Behavior Disorder) rating scale, parent rating. total predictive value calculated for each level of each parent-rated ADHD symptom against ADHD versus non-ADHD status derived from the DISC-IV; observed classification algorithm: >=6 of 9 inattention and/or hyperactivity/impulsivity symptoms Sensitivity: 88 Specificity: 80 PPV: 82 NPV: 87 Internal consistency: Cronbach's alpha 0.94 for parent-rated inattention symptoms and 0.91 for parent-rated hyperactivity symptoms on the Disruptive Behavior Disorder Rating Scale	N/A	N/A
Silverstein, 2016[536] Cohort study N = 156 US	**Target:** Children enrolled from a pediatric primary care clinic of an urban safety-net hospital or an urban, federally qualified community health center	**Index test:** Other (e.g., ECG) : clinical data Best performing model contained parent Vanderbilt scale plus child age, history of grade retention, presence of child anxiety or	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Setting: Mixed	**Other:** Children from same enrollment process not diagnosed with ADHD **ADHD presentation:** N/A **Diagnosed by:** Other (specify) Child psychiatrist, developmental behavioral pediatrician **Comorbidity:** N/A **Female:** 31% **Age mean:** 8.7 (2.1) **Min age:** 6 **Max age:** 12 **Ethnicity:** % Hispanic or Latino : 27 % Black/African American : 60 % Asian : 1 % White : 16 Other : 22% Other **Reference standard:** Clinical diagnosis ADHD assessment complied with DSM-IV guidelines Timing: Concurrent	depression, presence of clinically significant oppositional defiant symptoms, and history of parental substance abuse Accuracy: 84 (52, 99)			

Simões, 2021[537] Case series N = 160 Brazil Setting: School	**Target:** Participants who are drug naïve, no comorbidities, normal or corrected-to-normal vision; excluded students with developmental delays, poor academic performance, epilepsy, previous history of traumatic brain injury, psychosis, mood disorders, or learning disabilities **Other:** Healthy control children **ADHD presentation:** N/A : Teachers instructed to select students with "attention problems" **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** % N/A **Age mean:** 9.3 (1.40) for ADHD group, 9.2(1.41) for healthy control group **Min age:** 5 **Max age:** 18 **Ethnicity:** Other : Sample is all Brazilian **Reference standard:** Clinical diagnosis The Brazilian Teacher Rating Form (BTRF), psychosocial interview with parents and students, health records available in the schools. A student was included in the ADHD group if there were not any discrepancies among the rating scale, the qualitative observations by the teachers, the oral information from parents, and the clinical interview. Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT Continuous Auditory Attention Test (CAAT); Parameters measured include omission errors (OEs), commission errors (CEs), reaction time (RT), and variability of reaction time (VRT). Coefficient of variation was also calculated (CofV = VRT / RT). Sensitivity: 73 Specificity: 63 Accuracy: 70	**Index test 2:** Neuropsychological,CPT Continuous Visual Attention Test (CVAT); Parameters measured include omission errors (OEs), commission errors (CEs), reaction time (RT), and variability of reaction time (VRT). Coefficient of variation was also calculated (CofV = VRT / RT). Sensitivity: 70 Specificity: 56 Accuracy: 66	**Index test 3:** Neuropsychological,CPT Discriminant function analysis of both the CAAT and the CVAT; auditory omission errors was the most reliable variable for discriminating between groups, followed by visual commission errors, auditory commission errors, and auditory coefficient of variation Accuracy: 76	N/A
Skogli, 2013[541] Case series N = 130 Norway Setting: Specialty care	**Target:** Consecutive referrals from 7 outpatient Child and Adolescent Mental Health Centers for assessment of ADHD, IQ>= 70, not on medication **Other:** Recruited from local schools; IQ>=70 **ADHD presentation:** N/A	**Index test:** Neuropsychological,EF Random Forest classification using EF tests assessing working memory, inhibition, cognitive flexibility, planning, and verbal fluency; 75/25 testing/validation split	**Index test 2:** Neuropsychological,EF Random Forest classification using EF tests assessing working memory, inhibition, cognitive flexibility, planning,	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Diagnosed by: Specialist **Comorbidity:** N/A **Female:** 46% **Age mean:** 11.2 for ADHD boys, 11.9 for ADHD girls, 11.4 for control boys, 11.9 for control girls **Min age:** 8 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Kiddie-Schedule for Affective Disorders and Schizophrenia semi-structured clnical interviews conducted separately for children/adolescents and parents, ADHD Rating Scale IV, and teacher reports Timing: Concurrent	performed 5,000 times on different random splits; ADHD boys versus control boys Accuracy: 73 SD 7.8 Rater agreement: Observed classification results versus expected classification results kappa SD 0.152 Kappa: 0.466	and verbal fluency; 75/25 testing/validation split performed 5,000 times on different random splits; ADHD girls versus control girls Accuracy: 79 SD 7.8 Rater agreement: Observed classification results versus expected classification results Kappa:0.507 (SD 0.175)		

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Slaby, 2022[542] Case series N = 27,270 US Setting: Other	**Target:** Participants with both ADHD and one or more psychiatric disorders **Other:** Controls lacked psychiatric and other neurological disorders; learning disabilities and mild/moderate intellectual disability were not excluded. **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** Other : 54% of ADHD participants had psychiatric comorbidities **Female:** % 49% female in entire sample **Age mean:** 11(6) **Min age:** **Max age:** **Ethnicity:** % Black/African American : 44 % White : 52 Other : 4% Other **Reference standard:** Other Chart abstractions and behavioral surveys added evidence in support of the psychiatric diagnoses, conducted an independent electronic medical record review for random cases that were pulled out by the algorithms to confirm they were “true” cases Timing: Prior diagnosis	**Index test:** Clinician tool Multi-source/multi-approach electronic health record rule-based phenotype algorithm with natural language processing text mining developed to discriminate cases with ADHD in isolation from cases with ADHD with comorbidities PPV: 95	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Slobodin, 2020[543] Berger, 2020[680] Case series N = 458 Israel Setting: Mixed	**Target:** Clinic-referred children recruited from out-patient pediatric clinics of a Neuro-Cognitive Centre, based in a tertiary care university hospital, drug naive, no intellectual disability, no chronic use of medications, and no primary psychiatric diagnosis **Other:** Typically developed children recruited from regular primary schools **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 33% **Age mean:** 8.68 (1.77) **Min age:** 6 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis based on DSM-V criteria for ADHD Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT Neuro-Tech Solutions Limited MOXO-CPT which includes visual and auditory stimuli serving as measurable distractors. Analyzed using random forest technique. Machine learning model included four continuous performance test indices (attention, timeliness, hyperactivity, and impulsiveness) and four control variables (age, gender, day of the week, and time of day). 60/40 training/testing split used for validation. Sensitivity: 89 (83, 95) Specificity: 84 (76, 92) Accuracy: 87 (81, 93)	N/A	N/A	N/A

Smith, 2000[547] Case series N = 131 US Setting: Specialty care	**Target:** Children and adolescents residing in a psychiatric facility with either a primary or secondary diagnosis of ADHD and children diagnosed with ADHD from prior study; children diagnosed with both ADHD and conduct disorder were excluded **Other:** Clinical data collected from two sources: 1) archival data from children and adolescents residing in a psychiatric facility, patients who had either a primary or secondary diagnosis of conduct disorder were eligible for inclusion in the present study; 2) **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 12% **Age mean:** **Min age:** 5 **Max age:** 18 **Ethnicity:** % Black/African American : 15,Other : ADHD group % White : 82,Other : ADHD group Other : 3% Other race in ADHD group **Reference standard:** Clinical diagnosis Interviewed and evaluated on admission by a multidisciplinary treatment team including a board-certified psychiatrist, a social worker, a registered psychiatric nurse, and the licensed clinical staff supervisor Timing:	**Index test:** Parent rating DSMD (Devereux Scales of Mental Disorders), ADHD versus conduct disorder, cutoff>=8 ADHD items Sensitivity: 63 Specificity: 70 Accuracy: 66 PPV: 65 NPV: 68 Rater agreement: ADHD versus conduct disorder, cutoff >=8 ADHD items agreement 0.32	**Index test 2:** Parent rating DSMD (Devereux Scales of Mental Disorders); ADHD versus non-clinical comparison group, cutoff >=7 ADHD items Sensitivity: 69 Specificity: 88 Accuracy: 81 PPV: 73 NPV: 85 Rater agreement: ADHD versus non-clinical comparison group, cutoff >=7 ADHD items	N/A	N/A
Smith, 2003[546] Case series N = 150 Australia Setting: Mixed	**Target:** Children and adolescents referred to a private ADHD clinic, comorbidities excluded, all drug naive prior to testing **Other:** Children and adolescents recruited from the local community and	**Index test:** EEG EEG event-related potential data collected using EEG while participants completed twoblocks of an auditory odd-ball task; discriminant function analysis using 7 variables; leave-one-out	**Index test 2:** EEG EEG event-related potential data collected using EEG while participants completed twoblocks of an auditory odd-ball task;	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	reported by their parents to be free of psychiatric and neurological disorders **ADHD presentation:** inattentive : 50,combined : 50 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % Male:female ratio 4:1 **Age mean:** **Min age:** 8 **Max age:** 18 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis made by an experienced psychologist using DSM-IV criteria and confirmed by an independent pediatrician who was blind to the participant's status; Connoers' Parent and Teacher Rating Scales, the Child Behavior Checklist, and a developmental interview of parent(s) Timing: Prior diagnosis	cross-validation; children 8-12 years old Sensitivity: 71 Specificity: 77 Accuracy: 73	discriminant function analysis using 4 variables; leave-one-out cross-validation; adolescents 13-18 years old Sensitivity: 57 Specificity: 63 Accuracy: 59		

Snyder, 2008[548] Case series N = 159 US Setting: Specialty care	**Target:** Participants diagnosed with ADHD; no patients stabilized by multiple medications and individuals on non-stimulants directed toward conditions other than ADHD **Other:** Children diagnosed with disorders other than ADHD or no diagnosis **ADHD presentation:** inattentive : 43,hyperactive : 5,combined : 52 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 36% in entire sample **Age mean:** 10.5 (3.4) **Min age:** 6 **Max age:** 18 **Ethnicity:** % Hispanic or Latino : 3 % Black/African American : 37 % Asian : 1 % White : 59 **Reference standard:** Clinical diagnosis Performed by clinicians assisted with a semi-structured clinical interview (Kiddie Schedule of Affective Disorders and Schizophrenia -Present and Lifetime Version) including the supplements for behavioral disorders, affective disorders, and anxiety disorders; Clinical Global Assessment Scale and Clinical Global Impression-Severity subscale Timing: Concurrent	**Index test:** EEG EEG eyes-open and eyes-closed resting state EEG (N= 159); theta/beta ratio, comparedto normative database values with ADHD predicted at a standard deviation cutoff of 1.5 Sensitivity: 87 Specificity: 94 Accuracy: 89 PPV: 95 NPV: 82	**Index test 2:** Combined rating ADHD Rating Scales-IV (N=101) Sensitivity: 55 Specificity: 43 Accuracy: 50 PPV: 63 NPV: 36 Rater agreement: Parent versus teacher ratings	**Index test 3:** Combined rating Conners Rating Scales-Revised (N=103) Sensitivity: 72 Specificity: 19 Accuracy: 53 PPV: 62 NPV: 27 Rater agreement: Parent versus teacher ratings 64% agreement Kappa: Internal consistency:	N/A
Snyder, 2015[27] Case series N = 275 US Setting: Mixed	**Target:** Children and adolescents diagnosed with ADHD; willing to stop medication; IQ>=70; no history of seizure disorder, EEG abnormalities, or anticonvulsant use for seizure control; metal plate or device in the head; suicidal ideation or gesture and/or homicidal ideation or gesture; and known serious medical problems	**Index test:** EEG Combination of theta/beta ratio from EEG with a clinician's regular ADHD evaluation, 10 minute eyes open resting-state EEG, clinical evaluation included: physical examinations, clinician interviews, with initial impressions and reference to	**Index test 2:** Clinician tool Clinician ADHD evaluation on physical examinations, clinician interviews, with initial impressions and reference to DSM-IV-TR criteria, Kiddie-	N/A	N/A

	Other: Children and adolescents consecutively presenting with attentional and behavior concerns to 13 geographically distinct clinics who were not diagnosed with ADHD by reference standard **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 36% **Age mean:** 10.1 (2.9) **Min age:** 6 **Max age:** 17.99 **Ethnicity:** % Hispanic or Latino : 4 % Black/African American : 17 % American Indian or Alaska Native : 2 % Asian : 1 % White : 73 N/A : 4 **Reference standard:** Clinical diagnosis Multidisciplinary team consensus diagnosis comprised a clinical psychologist, a neurodevelopmental pediatrician, and a child/adolescent psychiatrist using DSM- IV-TR criteria and AACAP practice parameters Timing: Prior diagnosis	DSM-IV-TR criteria, Kiddie-Schedule of Affective Disorders and Schizophrenia–Present and Lifetime Version (K-SADSPL) and Supplements with interviewer notes, Children's Global Assessment Scale, Clinical Global Impression-Severity subscale, ADHD-IV Rating Scales completed by investigator with parent informant and 1–2 teachers, Wechsler Abbreviated Scale for Intelligence-long version, (8) Wide Range Achievement Test-4, Questionnaires on socioeconomic status, education and family histories, and any further testing if deemed necessary by the clinician on a patient-by-patient basis; clinician's diagnostic conclusions were summarized as "positive," "negative," or "uncertain" for ADHD; EEG categories were "low," "moderate," or "high" Sensitivity: 82 (74, 87) Specificity: 94 (89, 97) Accuracy: 88 (84, 91) PPV: 92 (86, 96) NPV: 85 (79, 90) Alpha: Theta/Beta ratio repeated measures collected on two different visits; ICC model chosen was two-way, random, single-measure, consistency Temporal stability: ICC 0.83	Schedule of Affective Disorders and Schizophrenia–Present and Lifetime Version (K-SADSPL) and Supplements with interviewer notes, Children's Global Assessment Scale, Clinical Global Impression-Severity subscale, ADHD-IV Rating Scales completed by investigator with parent informant and 1–2 teachers, Wechsler Abbreviated Scale for Intelligence-long version, (8) Wide Range Achievement Test-4, Questionnaires on socioeconomic status, education and family histories, and any further testing if deemed necessary by the clinician on a patient-by-patient basis; clinician's diagnostic conclusions were summarized as "positive," "negative," or "uncertain" for ADHD Sensitivity: 89 (83, 93) Specificity: 36 (29, 44) Accuracy: 61 (55, 67) PPV: 56 (49, 62) NPV: 79 (67, 87)		

Soliva, 2010[549] Tremols, 2008[1121] Case series N = 78 Spain Setting: Specialty care	**Target:** Participants taking methylphenidate with IQ>=80; no severe psychiatric illness including anxiety, mood disorders, developmental disorder, or dissociative disorder; no brain damage, neurological illness, head trauma, deafness, blindness, severe language delay, cerebral palsy, seizures, or autism **Other:** Handedness and IQ matched controls **ADHD presentation:** inattentive : 18,hyperactive : 20,combined : 62 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 10% **Age mean:** 10.90 (2.83) for the ADHD group, 11.46 (2.86) for the control group **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed by a team consisting of a psychologist and a psychiatrist. Scoring was based on parent and teacher rating scales as well as a semi-structured clinical interview. Timing: Prior diagnosis	**Index test:** Imaging Morphometric MRI using a novel semi-automated caudate segmentation procedure to obtain volumetric caudate nucleus data; analyzed right caudate nucleus body volume/ total bilateral caudate volume and right caudate nucleus body volume/ bilateral caudate body volume ratios; training and test set Sensitivity: 42 (20, 66) For optimal cut-off value <=0.4818 of the right caudate nucleus body volume/ bilateral caudate body volume ratio in the test group Specificity: 95 (74, 99) For optimal cut-off value <=0.4818 of the right caudate nucleus body volume/ bilateral caudate body volume ratio in the test group AUC: 0.84 (0.69, 0.94) For optimal cut-off value <=0.4818 of the right caudate nucleus body volume/ bilateral caudate body volume ratio in the test group PPV: 89 (53, 98) For optimal cut-off value <=0.4818 of the right caudate nucleus body volume/ bilateral caudate body volume ratio in the test group NPV: 62 (52, 71) For optimal cut-off value <=0.4818 of the right caudate nucleus body volume/ bilateral caudate body volume ratio in the test group	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	Results: Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	Index Test 2	Index Test 3	Index Test 4
		Rater agreement: Inter-rater reliability of the caudate segmentation procedure 0.87 for the caudate head and 0.89 for the caudate body at the beginning of the study using 10 randomly selected subjects (5 ADHD and 5 controls)			
Spencer, 2018[553] Case series N = 41 US Setting: Specialty care	**Target:** Children from an urban pediatric practice and diagnosed with ADHD **Other:** Age and gender-matched children recruited during a well-child visit at an urban pediatric practice not diagnosed with ADHD **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 49% female in entire sample **Age mean:** 7.9 (1.4) **Min age:** 6 **Max age:** 10 **Ethnicity:** % Hispanic or Latino : 85 **Reference standard:** Clinical diagnosis MINI-KID (Miniature International Neuropsychiatric Interview) for Children Timing: Later diagnosis	**Index test:** Parent rating PSC-AS (Pediatric Symptom Checklist Attention Scale), cutoff score 4 Sensitivity: 82 Specificity: 50 AUC: 0.728 PPV: 64 NPV: 73	**Index test 2:** Parent rating CBCL-A (Child Behavior Checklist) attention problems subscale cutoff score 56 Sensitivity: 80 Specificity: 81 Accuracy: AUC: 0.837 PPV: 80 NPV: 81	N/A	N/A

Sprafkin, 2002[559] Case series N = 224 US Setting: Specialty care	**Target:** Participants diagnosed with ADHD **Other:** Consecutive referrals to a child psychiatric outpatient clinic in a research-oriented university hospital not diagnosed with ADHD **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 23% female in entire sample **Age mean:** 4.55 (0.77) **Min age:** 3 **Max age:** 6 **Ethnicity:** % Hispanic or Latino : 6 % Black/African American : 6 % Asian : 1 % White : 87 **Reference standard:** Clinical diagnosis Clinical diagnoses were made by staff child and adolescent psychiatrists in a research-oriented teaching hospital setting based on interviews with the children and their caregivers; informal observation of parent–child interaction; school reports, psychoeducational and special education evaluations; a questionnaire of developmental, school, medical, and family histories; school observations (for many children); and scores from several parent- and teacher-completed behavior ratings scales including the Child Behavior Checklist (CBCL), Teacher's Report Form (TRF), Inattention/Overactivity With Aggression (IOWA) Conners Teacher's Rating Scale, and ECI-4. Timing: Concurrent	**Index test:** Parent rating RCI-4 (Early Childhood Inventory-4) parent rating Sensitivity: 66 Specificity: 57 PPV: 50 NPV: 71 Rater agreement: Pearson correlations between parent and teacher ratings; ADHD-inattentive (r = 0.40, p < 0.001), ADHD-Hyperactive/Impulsive (r = 0.42, p < 0.001), ADHD-Combined (r = 0.40, p < 0.001) Kappa: Early Childhood Inventory-4 (ECI-4) Screening Cutoff Scores versus Data-Based Psychiatric Diagnoses 0.21 Internal consistency: ADHD-inattentive alpha= 0.91, ADHD-hyperactive/impulsive alpha= 0.90	**Index test 2:** Teacher rating scale ECI-4 (Early Childhood Inventory-4) teacher rating Sensitivity: 68 Specificity: 69 Accuracy: 69 PPV: 62 NPV: 75 Rater agreement: Early Childhood Inventory-4 (ECI-4) Screening Cutoff Scores versus Data-Based Psychiatric Diagnoses Kappa:0.37 Internal consistency: >0.84 for the disruptive behavior disorders	**Index test 3:** Combined rating ECI-4 (Early Childhood Inventory-4) parent and teacher rating Sensitivity: 90 Specificity: 41 Accuracy: 62 PPV: 53 NPV: 85 Rater agreement: Early Childhood Inventory-4 (ECI-4) Screening Cutoff Scores versus Data-Based Psychiatric Diagnoses Kappa: 0.54	**Index text 4:** Combined rating ECI-4 (Early Childhood Inventory-4) parent and teacher rating where children who received a diagnosis of pervasive developmental disorder (PDD) and who met ECI-4 screening cutoff for the PDD symptom category were not considered false positives Sensitivity: 88 Specificity: 68 Accuracy: 77 PPV: 67 NPV: 89 Rater agreement: Early Childhood Inventory-4 (ECI-4) Screening Cutoff Scores versus Data-Based Psychiatric Diagnoses Kappa: 0.54

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	Results: Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	Index Test 2	Index Test 3	Index Test 4
Sprafkin, 2007[558] Case series N = 207 US Setting: Specialty care	**Target:** Consecutive referrals to a university hospital child psychiatry outpatient service diagnosed with ADHD **Other:** Consecutive referrals to a university hospital child psychiatry outpatient service not diagnosed with ADHD; other diagnoses include ODD/CD, anxiety disorder, pervasive developmental disorder, depressive disorder, and adjustment disorder **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 25% female in entire sample **Age mean:** **Min age:** 5 **Max age:** 17 **Ethnicity:** % Hispanic or Latino : 4 % Black/African American : 7 % White : 88 Other : 1% Other **Reference standard:** Clinical diagnosis Timing: Concurrent	**Index test:** Parent rating ADHD-SC4-P (ADHD Symptom Checklist-4 Parent), randomized-order Sensitivity: 58 Specificity: 60 PPV: 68 NPV: 49 Internal consistency: Coefficient alpha 0.92 for inattentive scale, 0.87 for hyperactive/impulsive scale	**Index test 2:** Parent rating ADHD-SC4-P (ADHD Symptom Checklist-4 Parent), standard diagnostic-cluster version Sensitivity: 61 Specificity: 59 PPV: 67 NPV: 53 Internal consistency: Coefficient alpha 0.95 for inattentive scale, 0.95 for hyperactive/impulsive scale	**Index test 3:** Teacher rating scale ADHD-SC4-T (ADHD Symptom Checklist-4 Teacher), randomized-order Sensitivity: 66 Specificity: 57 PPV: 75 NPV: 57 Internal consistency: Coefficient alpha 0.89 for inattentive scale, 0.88 for hyperactive/impulsive scale	**Index text 4:** Teacher rating scale ADHD-SC4-T (ADHD Symptom Checklist-4 Teacher), standard diagnostic-cluster version Sensitivity: 70 Specificity: 59 PPV: 67 NPV: 62 Internal consistency: Coefficient alpha 0.95 for inattentive scale, 0.95 for hyperactive/impulsive scale

Stepanova, 2021[563] Case series N = 44 US Setting: School	**Target:** Participants recruited from community advertisements and physician referrals, not currently taking psychostimulants, without bipolar disorder **Other:** Children with psychiatric conditions other than ADHD and bipolar disorder, as well as healthy individuals **ADHD presentation:** inattentive : 33,combined : 67 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 33% **Age mean:** 12.23 (3.87) **Min age:** 6 **Max age:** 17 **Ethnicity:** % Hispanic or Latino : 11,Other : reported separately as ethnicity % Black/African American : 59 % Asian : 2 % White : 21 Other : 18 **Reference standard:** Clinical diagnosis Completed Mini-International Neuropsychiatric Interview 7 and was evaluated by a board certified psychiatrist; ADHD Rating Scale–IV to assess symptom severity Timing: Prior diagnosis	**Index test:** Biomarker Blood sample analyzed for membrane potential ratio, ADHD cutoff score provided by the MPR™ test developersof >0.75 is considered positive for ADHD Sensitivity: 79 Specificity: 25 Accuracy: 55	N/A	N/A	N/A
Stevanovic, 2023[564] Case series N = 1274 Sweden Setting: Specialty care	**Target:** Retrospective chart review research for which data were extracted from available medical records of children and adolescents who had undergone assessments with the QbTest at the department of child and adolescent psychiatry in one of few general hospitals located in western Sweden during the period of January 1, 2004, to December 31, 2017; diagnosed with ADHD only or co-	**Index test:** Neuropsychological,CPT QbTest (for ages 6-12) combining a computerized CPT and a motion tracking system; QbActivity parameter (data measured by the motion-capturing device only from the second half of the test) Sensitivity: 22 Specificity: 96	**Index test 2:** Neuropsychological,CPT QbTest (for ages 6-12) combining a computerized CPT and a motion tracking system; QbInattention parameter (CPT omission errors, reaction time, and	**Index test 3:** Neuropsychological,CPT QbTest (for ages 6-12) combining a computerized CPT and a motion tracking system; Qb Impulsivity	**Index text 4:** Neuropsychological,CPT QbTest Plus (for ages >=13) combining a computerized CPT and a motion tracking system; QbActivity

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	occurrence with other mental, behavioral, or neurodevelopmental disorders **Other:** Children with diagnoses other than ADHD or no specific clinical diagnoses **ADHD presentation:** inattentive : 25,combined : 70,N/A : 5% ADHD other/unspecified presentation **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 40.1% female in entire sample **Age mean:** 13.5 (3.2) **Min age:** 6 **Max age:** 18 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis All children referred to the clinic with a suspected neurodevelopmental or psychiatric disorder underwent a diagnostic process according to the clinic´s standard diagnostic procedure Timing: Concurrent	Accuracy: AUC: 0.59 (0.54, 0.64) PPV: 95 NPV: 24	reaction time variation variables have the most significant weight) Sensitivity: 50 Specificity: 79 Accuracy: AUC: 0.64 (0.59, 0.69) PPV: 90 NPV: 28	parameter (CPT commission errors, normalized commission errors, and anticipatory response variables have the most significant weight) Sensitivity: 26 Specificity: 93 AUC: 0.59 (0.54, 0.64) PPV: 94 NPV: 24	parameter (data measured by the motion-capturing device only from the second half of the test) Sensitivity: 40 Specificity: 84 AUC: 0.62 (0.57, 0.66) PPV: 86 NPV: 35

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Straub, 2021[566] Case series N = 350 US Setting: Other	**Target:** Children from hospitals who met a clinical definition for specific neurodevelopmental disorders including ADHD with 2 or more medical encounters to qualify with a diagnostic code using ICD-9 and -10 **Other:** Study also included children with other disorders, but they were not compared to ADHD group; study objective to validate healthcare claim-based algorithms using medical records as the reference **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % N/A **Age mean:** N/A **Min age:** 1 **Max age:** 14 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Study used medical records as the fold standard, data comes from ICD-9 codes- used to develop algorithms based on ICD-9, and translated to ICD-10 to make data applicable to more current years Timing: Prior diagnosis	**Index test:** Clinician tool Claim-based algorithms for neurodevelopmental disorders including ADHD PPV: 88 (76, 95)	N/A	N/A	N/A

Sullivan, 2007[570] Case series N = 92 US Setting: Other	**Target:** Subset of participants diagnosed with ADHD in a Memory, Attention, and Planning Study; IQ>=80 **Other:** Subset of participants not diagnosed with ADHD in a Memory, Attention, and Planning Study recruited with announcements distributed to local physicians, schools, bulletin boards, a counseling center, and the newspaper; IQ>=80; participants either had no cl **ADHD presentation:** inattentive : 34,combined : 66 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 15% **Age mean:** 11.32 (1.99) **Min age:** 9 **Max age:** 15 **Ethnicity:** % Hispanic or Latino : 8 % Black/African American : 11 % Asian : 1 % White : 80 **Reference standard:** Clinical diagnosis Comprehensive psychological evaluation that included measures of cognitive ability, achievement, language, memory, executive function, attention, behavior, and emotional functioning Timing: Prior diagnosis	**Index test:** Combined rating BRIEF (Behavior Rating Inventory of Executive Function) parent and teacher forms Rater agreement: Behavior Rating Inventory of Executive Function (BRIEF) parent versus teacher ratings Parent ratings on the BRIEF scales were significantly correlated with teacher ratings on the same scales (all <=0.05), range 0.31 to 0.59 (median 0.48) over 11 subscales ICC: 0.48	**Index test 2:** Combined rating CPRS+CTRS (Conners' Parent Rating Scale- Short Form and Conners' Teacher Rating Scale- Short Form) Rater agreement: Parent ratings on the Conners' scales were significantly correlated with teacher ratings on the same scales, Range 0.51 to 0.58 (median 0.54) over 4 subscales ICC: 0.54	N/A	N/A
Sun, 2018[571] Case series N = 170 China Setting: Mixed	**Target:** Participants with newly diagnosed and never-treated ADHD from the Department of Psychiatry, West China Hospital, Sichuan University; IQ>=90, right-handed, no Axis I psychiatric comorbid disorders; no current or past treatment with psychotropic medication; no substance abuse; no physical illness that might	**Index test:** Imaging sMRI and diffusion-tensor MRI, anatomic and diffusion-tensor magnetic resonance imaging, cerebral radiomic features based random forest models, repeated 10-fold cross validation Sensitivity: 70 Specificity: 77 Accuracy: 74	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	affect brain anatomy and function; and contraindications to MR imaging **Other:** Age and sex matched healthy children recruited from local schools with an advertisement **ADHD presentation:** inattentive : 48,combined : 52 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 14% **Age mean:** 10.83 (2.30) ADHD group, 11.21 (2.51) control group **Min age:** 7 **Max age:** 15 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis of ADHD by two clinical psychiatrists using the Chinese version of the Structured Clinical Interview for Diagnotic and Statistical Manual 4 Text Revision Axis I Disorders, or SCID Timing: Prior diagnosis	Rater agreement: 100 runs of 10-fold cross-validation (1000 training-testing cycles) 100 runs of 10-fold cross-validation (1000 training-testing cycles) 0.47			

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Tallberg, 2019[576] Case series N = 80 Sweden Setting: Specialty care	**Target:** Clinical retrospective data from ADHD assessments from Child and Adolescent Psychiatry clinical records; children who screened positive for ADHD were referred for further assessments **Other:** Children without ADHD **ADHD presentation:** inattentive : 28,hyperactive : 2,combined : 70 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 29% **Age mean:** 12.5 1st-3rd quartiles (9.6-14.4) **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Psychiatric evaluation Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT Conners' CPT II AUC: 0.73 p<0.001	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Tang, 2022[581] Bellec, 2017[679]; ADHD-200 Consortium, 2011[655]; ADHD-200 Consortium, 2012[725]; ADHD-200 Consortium, 2012[656]; Chen, 2022[706] Case series N = 194 China Setting: Other	**Target:** Children with ADHD, Peking University (PU) dataset from ADHD-200 **Other:** Healthy control children from ADHD-200 PU dataset **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 27% **Age mean:** N/A **Min age:** 8 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD-200 Consortium identified children with ADHD Timing: Prior diagnosis	**Index test:** Imaging fMRI, brain functional connectivities, deep-learning classification architecture based on a binary hypothesis testing framework and a modified auto-encoding network, leave one out cross validation Sensitivity: 99 Specificity: 100 Accuracy: 99.6 AUC: 0.997	N/A	N/A	N/A

Tang, 2023[580] Case series N = 167 China Setting: Specialty care	**Target:** Right-handed, meeting the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria for ADHD, no functional neurological disorders, no concomitant disorders of other organs, no other disorders that may affect brain function and structure, no history of previous medication, and no abnormalities on routine brain MRI; all ADHD children included in the study were diagnosed for the first time, and no psychotropic drugs were used before MRI examination **Other:** Age and sex-matched healthy children; right-handed, no functional neurological disorders, no concomitant diseases of other organs, no other diseases that may affect brain function and structure, and no abnormalities in routine brain MRI examinations, and **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 47% **Age mean:** 8.57 (2.38) for the ADHD group, 8.67 (2.56) for the healthy children **Min age:** 5 **Max age:** 13 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis All ADHD children were diagnosed by senior doctors in the Department of Psychology, Children's Hospital of Chongqing Medical University; the ADHD children included in the study met the DSM-V criteria for ADHD Timing:	**Index test:** Imaging MRI 3-dimensional pseudocontinuous arterial spin labeling perfusion imaging; cerebral (frontal love region) blood flow perfusion values obtained by software post-processing AUC: 0.901	**Index test 2:** Imaging MRI three-dimensional pseudocontinuous arterial spin labeling (3D-pcASL) perfusion imaging; cerebral blood flow (CBF) perfusion values were obtained by software post-processing; CBF in caudate nucleus region AUC: 0.841	N/A	N/A

Ter-Minassian, 2022[582] Case series N = 56,258 UK Setting: Specialty care	**Target:** Children diagnosed with ADHD with linked education and health data residing in South London from 2007 to 2013; enrolled in mainstream state educational services, and who had education and attainment characteristics as captured at the Early Years Foundation Stage Profile and at Key Stage 1; excluded pupils who were diagnosed with ADHD prior to their Key Stage 1 assessment **Other:** Children not diagnosed with ADHD from same population cohort as ADHD participants; purely clinical cohort containing only the children who were present in the CRIS dataset containing samples of children who presented with ADHD and non-ADHD diagnoses **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 49% female in entire population cohort; 32% female in entire clinical cohort **Age mean:** **Min age:** 6 **Max age:** 7 **Ethnicity:** % Black/African American : 41,Other : 35% in clinical cohort % Asian : 9,Other : 3% in clinical cohort % White : 32,Other : 41% in clinical cohort % Multiracial : 13,Other : 16% in clinical cohort Other : 5% in both population and clinical cohorts **Reference standard:** Clinical diagnosis Existing data linkage between the National Pupil Database (NPD) and	**Index test:** Other (e.g., ECG) : Linked education and health data Linked education and health data; dataset was randomly divided into a training set (n=42 192; 75.0%), validation set (n=7033; 12.5%) and test set (n=7033; 12.5%) with a similar proportion of ADHD cases (~1%) in each set; feature set includes race/ethnicity, Key Stage 1 writing score and attendance, Early Years Foundation Stage Profile personal, social and emotional development, attendance, problem-solving, reasoning and numeracy, gender, no special education need, and english as first language; population cohort, logistic regression classifier Sensitivity: 84 (82, 85) 83% in test set; 81% in reweighted fair dataset resulting from the bias reduction algorithm ('privileged' group being both white and speaking English as first language) AUC: 0.862 (0.840, 0.874) 0.900 in test set; 0.880 in reweighted fair dataset resulting from the bias reduction algorithm ('privileged' group being both white and speaking English as first language)	**Index test 2:** Other : Linked education and health data Linked education and health data; dataset was randomly divided into a training set (n=42 192; 75.0%), validation set (n=7033; 12.5%) and test set (n=7033; 12.5%) with a similar proportion of ADHD cases (~1%) in each set; feature set includes race/ethnicity, Key Stage 1 writing score and attendance, Early Years Foundation Stage Profile personal, social and emotional development, attendance, problem-solving, reasoning and numeracy, gender, no special education need, and english as first language; population cohort, random forest classifier Sensitivity: 82 (80, 83) 80% in test set; 80% in reweighted fair dataset resulting from the bias reduction algorithm ('privileged' group being both white and speaking English as first language) AUC: 0.857 (0.842, 0.869) 0.860 in test set, 0.858 in reweighted fair dataset	**Index test 3:** Other : Linked education and health data Linked education and health data; feature set includes race/ethnicity, Key Stage 1 writing score and attendance, Early Years Foundation Stage Profile personal, social and emotional development, attendance, problem-solving, reasoning and numeracy, gender, no special education need, and english as first language; clinical cohort, logistic regression classifier Sensitivity: 66 (65, 67) 65% in test set Specificity: Accuracy: AUC: 0.718 (0.701, 0.735) 0.694 in test set	**Index text 4:** Other : Linked education and health data Linked education and health data; feature set includes race/ethnicity, Key Stage 1 writing score and attendance, Early Years Foundation Stage Profile personal, social and emotional development, attendance, problem-solving, reasoning and numeracy, gender, Sensitivity: 64 (61, 67) 65% in test set AUC: 0.699 (0.682, 0.71 0.689 in test set

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	South London and Maudsley National Health Service Foundation Trust Child and Adolescent Mental Health Services (SLaM CAMHS); SLaM is one of Europe's largest providers of mental healthcare and the monopoly provider of local CAMHS services, including ADHD diagnostic services; Anonymised individual-level clinical data for these services are accessible for research via the Clinical Record Interactive Search (CRIS); Individual-level diagnosis of ADHD was measured from both structured and unstructured diagnosis fields in CRIS Timing: Concurrent		resulting from the bias reduction algorithm ('privileged' group being both white and speaking English as first language)		

Tian, 2022[583] Case series N = 139 China Setting: Mixed	**Target:** Outpatients with ADHD were recruited from Beijing Children's Hospital; IQ>80 **Other:** Age and gender-matched healthy children voluntarily recruited through school; examined by trained pediatricians, all routine urine tests and biochemical tests, were in the normal range; children with all types of genetic diseases and clinical laboratory v **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 13% **Age mean:** 7.9 (2.0) for the ADHD group, 8.7 (1.8) for the ADHD+tic disorders group, 7.8 (1.8) for the healthy control group **Min age:** 1 **Max age:** 18 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis A senior child psychiatrist interviewed the participants according to the DSM-5 criteria, Conners' parent rating scales were completed by each patient's parents, a continuous performance test (CPT) was administered to all the patients by a technician to obtain behavioral measures of attention, patients with ADHD with comorbid tic disorders were examined by the Yale Global Tic Severity Scale (YGTSS) Timing: Concurrent	**Index test:** Biomarker Urine metabolite panel consisting of FAPy-adenine, N-acetylaspartylglutamic acid, and dopamine 4-sulphate; unsupervised principal component analysis (PCA) and supervised orthogonal partial least squares method discriminant analysis (OPLS-DA); ADHD with and without tic disorders versus normal controls Sensitivity: 94 Training set Specificity: 83 Training set AUC: 0.923 Training set; Test set AUC 0.877	**Index test 2:** Biomarker Urine metabolite panel consisting of FAPy-adenine, 3-methylazelaic acid, and phenylacetylglutamine; unsupervised principal component analysis (PCA) and supervised orthogonal partial least squares method discriminant analysis (OPLS-DA); ADHD without tic disorders vs normal controls Sensitivity: Above 80% for training set Specificity: Above 80% for training set AUC: 0.918 Training set; Test set AUC 0.96	**Index test 3:** Biomarker Urine metabolite panel consisting of FAPy-adenine, N-acetylaspartylglutamic acid, dopamine 4-sulphate, aminocaproic acid and asparaginyl-Leucine; unsupervised principal component analysis (PCA) and supervised orthogonal partial least squares method discriminant analysis (OPLS-DA); ADHD with tic disorders versus normal controls Sensitivity: 83 Training set Specificity: 91 Training set AUC: 0.918 For both training and test sets	N/A
Tillman, 2005[584] Case series N = 264 US	**Target:** Consecutive new case ascertainment from outpatient child psychiatric and pediatric sites; IQ>=70; no current or past mania, hypomania, or major depressive disorder	**Index test:** Parent rating Conners' Abbreviated Parent Questionnaire; diagnostic performance outcomes calculated by using data for all 10 items from the ADHD	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Setting: Specialty care	**Other:** Identified through a random survey that matched the comparison participants to participants with a prepubertal and early adolescent bipolar disorder phenotype by age, gender, socioeconomic status, ethnicity, and zip code; participants with bipolar disorde **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % Both males and females included in study **Age mean:** **Min age:** 7 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Current DSM-IV ADHD with a Children's Global Assessment Scale score <=60, The Washington University in St Louis Kiddie Schedule for Affective Disorders and Schizophrenia semistructured interview (parents and children) Timing: Prior diagnosis	subjects and the healthy comparison subjects Sensitivity: 99 Specificity: 95			

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Tripp, 2006[587] Case series N = 184 New Zealand Setting: Specialty care	**Target:** Children diagnosed with ADHD at specialized clinic **Other:** Children referred to the ADHD Research Clinic at the University of Otago for assessment that did not meet ADHD diagnosis criteria. **ADHD presentation:** inattentive : 17.6,hyperactive : 4.6,combined : 77.8 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 23.4% **Age mean:** 7.9 (1.6) **Min age:** 5 **Max age:** 12 **Ethnicity:** % Native Hawaiian or Pacific Islander : 12.0 % White : 76.1 N/A : 8.7,Other : Other 3.2 **Reference standard:** Clinical diagnosis DSM IV by clinical psychologist experienced in ADHD assessment Timing: Concurrent	**Index test:** Parent rating CBCL (Child Behavior Checklist), parent rating Sensitivity: 77 Specificity: 33 Accuracy: 59	**Index test 2:** Teacher rating scale TRF (Teacher Report Form) Sensitivity: 79 Specificity: 64 Accuracy: 73	**Index test 3:** Teacher rating scale CTRS (Conners Teacher Rating Scale) Sensitivity: 81 Specificity: 69 Accuracy: 76.4 :	**Index text 4:** Parent rating CPRS (Conners Parent Rating Scale) Sensitivity: 79 Specificity: 32 Accuracy: 59.7

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Uyulan, 2023[591] Case series N = 39 Turkey Setting: N/A	**Target:** Children with ADHD **Other:** Children without a neuropsychiatric condition **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 32% **Age mean:** 10.25 (1.94) for the ADHD group, 10.15 (2.13) for the control group **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis The children were screened using appropriate scales as well as clinical interviews for establishing the diagnosis, Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL) and Turkish versions of the short-form Conners' teacher and parent rating scales Timing: Prior diagnosis	**Index test:** Imaging fMRI during which participants completed a spatial attention paradigm; blood-oxygenation-level-dependent (BOLD) signal analysis; ResNet-50 type pre-trained 2D-convolutional neural network classifier; 10-fold cross validation Sensitivity: 93 Specificity: 95 Accuracy: 93 AUC: 0.94	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Vahid, 2019[592] Wang, 2022[1149] Case series N = 144 Germany Setting: Specialty care	**Target:** Participant diagnosed as ADD (ICD-10 F9838) or ADHD (ICD-10 F90.0 or F90.1) without other severe or acute psychiatric comorbidities **Other:** Healthy control children **ADHD presentation:** inattentive : 52,inattentive_other : Referred to as ADD in study,combined : 48,combined_other : Referred to as ADHD in study **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 22% **Age mean:** 10.9 (2.4) for ADD group, 10.6 (1.9) for ADHD-combined group, 11.3 (2.2) for control group **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Standard clinical guidelines by child/adolescent psychiatrists using family, school interviews and IQ, attention testing, and questionnaires Timing: Prior diagnosis	**Index test:** EEG EEG Event-related EEG recording during an interval-timing task, deep learning (EEGNet)classifer,leave one out subject (LOOS) cross validation, 2 category classification ADHD inattentive type versus healthy control Sensitivity: 89 Specificity: 84 Accuracy: 83 2 class classification	**Index test 2:** EEG EEG event-related EEG recording during an interval-timing task, deep learning (EEGNet)classifer, leave one out subject (LOOS) cross validation, 2 category classification ADHD combined type versus healthy control Sensitivity: 83 Specificity: 82 Accuracy: 80 2 class classification	**Index test 3:** EEG EEG event-related EEG recording during an interval-timing task, deep learning (EEGNet)classifer, leave one out subject (LOOS) cross validation, 3 category classification ADHD inattentive type versusADHD combined type versus healthy control Accuracy: 69 3 class classification	**Index text 4:** EEG EEG event-related EEG collected in a time estimation task; the ERP data input to theneural network model was only preprocessed such as denoising and was still a time-domain waveform without calculating any features; convolution neural network (CNN) and lo Sensitivity: 98 Specificity: 99 Accuracy: 98 AUC: 0.9964

Varela Casal, 2019[599] Case series N = 92 Spain Setting: Mixed	**Target:** Participants with ADHD, not on medication; free of a history of head injury with loss of consciousness or other neurological illness, mental retardation or other significant disorders like a pervasive developmental disorder and visual or auditory problems; recruited through the Child and Adolescent Health Mental Center from the Hospital Mataró of the Consorci Sanitari del Maresme **Other:** Non-ADHD clinical controls referred to the hospital for attentional and/ or conduct problems, healthy children showing no attention or conduct problems recruited from a public school **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % N/A **Age mean:** 10.67 (2.64) **Min age:** 7 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis All the clinical diagnoses of ADHD were made by clinical psychiatrists using the DSM- IV-TR criteria Timing: Prior diagnosis	**Index test:** Other (e.g., ECG) : Eye vergence BGaze system to test eye vergence ADHD versus healthy controls. Two-layer classification model: First layer= Radial Basis Function support vector machine (RBF-SVM) , second layer = two k-nearest-neighbor models. 30-fold stratified cross-validation routine over the S1 subsample, which, at each iteration, was further split into an 80-20 train-test random resampling. Then, the resulting model was tested on the S2 subsample, which so far had been unseen by it. Accuracy: 96 AUC: 0.99	**Index test 2:** Other : Eye vergence BGaze system to test eye vergence ADHD versus clinical controls. Two-layer classification model: First layer= Radial Basis Function support vector machine (RBF-SVM) , second layer = two k-nearest-neighbor models. 30-fold stratified cross-validation routine over the S1 subsample, which, at each iteration, was further split into an 80-20 train-test random resampling. Then, the resulting model was tested on the S2 subsample, which so far had been unseen by it. Accuracy: 86 AUC: 0.90	N/A	N/A
Vogt, 2011[600] Case series N = 108 UK Setting: Specialty care	**Target:** Individuals with a referral for ADHD made to a local generic child and adolescent mental health services clinic over 2 years **Other:** Individuals from same referral group not diagnosed with ADHD **ADHD presentation:** N/A : QbTest group: 16% combined, 14%	**Index test:** Combined rating SDQ (Strengths and Difficulties Questionnaire) parent and teacher ratings compared to clinical diagnosis for QbTest group Rater agreement: Mixed SDQ rating (disagreement between parent and teacher ratings) versus clinician's diagnosis	**Index test 2:** Combined rating SDQ (Strengths and Difficulties Questionnaire) parent and teacher ratings compared to clinical diagnosis for control group Alpha:	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	inattentive; control group 11% inattentive **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 16% female in the QbTest group **Age mean:** 10.5 for the QbTest group, 9 for the control group **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Clinical interview by the child and adolescent psychiatrists at the clinic, a medical examination and the administration of rating scales by parents and teachers Timing: Concurrent	Among those with a positive/negative SDQ in both the control and QbTest groups the majority of parents' SDQs (10/13, 77%) agreed with the clinician's diagnosis of ADHD, whereas the majority of teacher's SDQs (13/18, 72%) agreed with the clinician's reject Follow-up over 1 year of the participants referred for an attention-deficit hyperactivity disorder (ADHD) assessment with a diagnosis rejected at the initial assessment Test-retest: n=19; lost to follow-up n=1, reassessed and diagnosed with ADHD at 1-year follow-up n=0	Follow-up over 1 year of the participants referred for an attention-deficit hyperactivity disorder (ADHD) assessment with a diagnosis rejected at the initial assessment n=19; lost to follow-up n=3, reassessed and diagnosed with ADHD at 1-year follow-up n=7; The majority of the revised assessments were for girls (n = 4) Test-retest: n=19; lost to follow-up n=3, reassessed and diagnosed with ADHD at 1-year follow-up n=7; The majority of the revised assessments were for girls (n = 4)		

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Wang, 2018[603] Case series N = 40 Taiwan Setting: Specialty care	**Target:** Participants who are medication naive; no major physical illnesses or a history of comorbid major neuropsychiatric diseases **Other:** Children without any known major physical illnesses or any of the aforementioned major neuropsychiatric diseases within the same catchment area **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 30% In the test group **Age mean:** 8.7 (2.2) for the ADHD test group, 9.2 (2.5) for the control test group **Min age:** 6 **Max age:** 16 **Ethnicity:** % Asian : 100,Other : Han Chinese **Reference standard:** Clinical diagnosis Diagnosed with ADHD based off DSM-IV- TR criteria and the Chinese version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children, epidemiologic version (K-SADS-E) Timing: Prior diagnosis	**Index test:** Biomarker miRNA panel using 13 miRNA candidate biomarkers, SVM classifier Sensitivity: 90 For test group Specificity: 80 For test group Accuracy: 85 For test group AUC: 0.91 Test set	N/A	N/A	N/A

Wassenberg, 2004[605] Case series N = 72 US Setting: Primary Care	**Target:** Children diagnosed with ADHD; study design consisted of a consecutive series ofsubjects who survived a severe traumatic brain injury compared with an individually matched comparison group of subjects who sustained a mild traumatic brain injury, and a second matched control group of subjects who sustained an orthopaedic injury with no evidence of traumatic brain injury **Other:** Children not diagnosed with ADHD; study design consisted of a consecutive series of subjects who survived a severe traumatic brain injury compared with an individually matched comparison group of subjects who sustained a mild traumatic brain injury, and a **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 25% in entire sample **Age mean:** Mean age at injury 8.76 (3.13), mean age at assessment 10.93 (3.41) **Min age:** 5 **Max age:** 14 **Ethnicity:** % White : 97 **Reference standard:** Clinical diagnosis Kiddie Schedule for Affective Disorders and Schizophrenia for Shool-Age Children-Epidemiology Verion supplemented by a posttraumatic stress disorder module Timing: Concurrent	**Index test:** Parent rating CBCL-A (Child Behavior Checklist) attention problems subscale, cutoff t>=60, ADHD vs no ADHD Sensitivity: 84 Specificity: 84 Accuracy: 84	**Index test 2:** Parent rating CBCL-SP (Child Behavior Checklist) social problems subscale, cutoff t>=60 scores, ADHD vs no ADHD Sensitivity: 74 Specificity: 86 Accuracy: 83	N/A	N/A
Webster, 2000[607] Case series N = 132 US	**Target:** Children referred for psychoeducational evaluations who had been previously identified by at least two professionals as having	**Index test:** Neuropsychological,EF Learning Efficiency Test -II Accuracy: 84	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Setting: Specialty care	ADHD only, ADHD+learning disability, or ADHD-predominantly inactive type **Other:** Children referred for other reasons such as underachievement, family problems, or emotional concerns **ADHD presentation:** inattentive : 25,combined : 46,N/A : ADHD+ Learning Disability 29% **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 21.21% **Age mean:** 12.57 (3.10) **Min age:** 8 **Max age:** 16 **Ethnicity:** % Hispanic or Latino : 1 % Black/African American : 34 % White : 65 **Reference standard:** Clinical diagnosis ADHD group had been previously diagnosed by at least 2 professionals as having the disorder Timing: Prior diagnosis				

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Westerberg, 2004[614] Case series N = 80 Sweden Setting: Specialty care	**Target:** Children taking stimulant medication refrained for 24 hours before testing, no major neurological or psychiatric co-diagnoses, IQ>80 **Other:** Age-matched neurotypical children **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 0% **Age mean:** 11.4 (2.2) for ADHD group, 11.4(2.0) for control group **Min age:** 8 **Max age:** 15 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed by experienced physicians specialised in pediatric neurology or child-psychiatry Timing: Prior diagnosis	**Index test:** Neuropsychological,EF Choice reaction time and visuo-spatial working memory tests Sensitivity: 74 Specificity: 94 PPV: 19 NPV: 99	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Weyandt, 1994[615] Case series N = 115 US Setting: School	**Target:** Children diagnosed with ADHD enrolled in a regular education classroom and not receiving special education services with average to above-average intelligence as assessed by the Raven's Coloured Progressive Matrices **Other:** Children with developmental language disorder and neurotypical children; both groups had average to above-average intelligence as assessed by the Raven's Coloured Progressive Matrices and enrollment in a regular classroom **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 0% **Age mean:** **Min age:** 6 **Max age:** 12 **Ethnicity:** % White : 100 **Reference standard:** Clinical diagnosis Diagnosed by a pediatrician or psychologist using DSM criteria, Revised Conners Teacher Rating Scale and Parent Rating Scale, ADHD Rating scale Timing:	**Index test:** Neuropsychological,EF Executive function tasks: Visual search, verbal fluency, the Wisconsin CardSorting Test, Matching Familiar Figures Test, Tower of Hanoi, and mazes; Two nonexecutive function tasks: Peabody Picture Vocabulary Test-Revised and the Boston Naming test; discriminant function analysis Sensitivity: 67 Percent of ADHD group correctly classified Specificity: 78 Percent of neurotypical developing group correctly classified	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Williams, 2010[21] Case series N = 350 Australia Setting: N/A	**Target:** IQ >= 80; no personal or family history of Axis I psychiatric disorder other than oppositional defiant disorder, learning disorder, conduct disorder, depression, and anxiety; free of a physical brain injury, neurologic disorder, genetic disorder, other serious medical conditions, drugs, and alcohol **Other:** Age, sex, school grade, and IQ matched healthy control subjects **ADHD presentation:** inattentive : 38,hyperactive : 3,combined : 59 **Diagnosed by:** Provider **Comorbidity:** N/A **Female:** 23% **Age mean:** 12.29 (3.08) for ADHD group, 12.24 (3.10) for control group **Min age:** 6 **Max age:** 18 **Ethnicity:** % Asian : 37 % White : 63 **Reference standard:** Clinical diagnosis Clinical interview using DSM-IV criteria by referring pediatrician, and Conner's Parent Rating Scales: Revised-Long Version Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT,EF Cognitive and brain-function assessments using proprietary testing software "IntegNeuro" and "LabNeuro;" combination of sustained attention, impulsivity, intrusions, inhibition, and response variablility; severity threshold for determining impairment <= 1.0 SD below the mean Sensitivity: 88 Specificity: 91 PPV: 96 NPV: 88	**Index test 2:** Neuropsychological,CPT,EF Cognitive and brain-function assessments using proprietary testing software "IntegNeuro" and "LabNeuro;" combination of sustained attention, impulsivity, intrusions, inhibition, and response variablility; severity threshold for determining impairment <= 2.0 SD below the mean Sensitivity: 84 Specificity: 94 PPV: 88 NPV: 95	N/A	N/A

Wodka, 2008[625] Case series N = 123 US Setting: Specialty care	**Target:** Participant with IQ>=80; no history of speech/language disorder or a reading disability; no evidence of visual or hearing impairment, or history of other neurological or psychiatric disorder; children with DSM-IV diagnoses other than oppositional defiant disorder or specific phobias were excluded; participants taking stimulant mediation were asked to withhold medication the day of testing and the day prior **Other:** Participants recruited through the local school district and flyers posted in the community; attempted matching between groups of age, FSIQ, sex, and race **ADHD presentation:** inattentive : 35,hyperactive : 4,combined : 61 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 41% **Age mean:** 11.8 (2.2) for ADHD group, 11.0 (1.9) for control group **Min age:** 8 **Max age:** 16 **Ethnicity:** % Hispanic or Latino : 2 % Black/African American : 12 % Asian : 2 % White : 79 Other : 5% Other race **Reference standard:** Clinical diagnosis Structured parent interview that utilized DSM-IV criteria (Diagnostic Interview for Children and Adolescents, Fourth Edition (DICA-IV), Conners' Parent Rating Scale-Revised, Long Form Timing: Concurrent	**Index test:** Neuropsychological,EF Four subtests from the Delis-Kaplan Executive Function System (D-KEFS): Trail Making, Verbal Fluency, Color-Word Interference, and Tower tests	N/A	N/A	N/A

Wood, 2009[627] Case series N = 453 UK Setting: Mixed	**Target:** Children of European ancestry recruited from the London subsample of the International Multicentre ADHD Genetics project; entry criteria for probands were a clinical diagnosis of DSM-IV combined subtype ADHD and having one or more full siblings available for ascertainment of clinical information and DNA collection; IQ>=70, no autism, epilepsy, brain disorders, or any genetic or medical disorder associated with externalizing behaviors that may mimic ADHD; a minimum of 48-hour medication-free period before testing was required **Other:** Siblings of ADHD probands; IQ>=70 and control siblings from primary and secondary schools in London chosen to be, as far as possible, age- and sex- matched to the proband and their siblings **ADHD presentation:** combined : 100 **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 10% **Age mean:** 11.90 (2.74) for ADHD probands, 11.51 (2.85) for siblings of ADHD probands, 12.20 (2.28) for control siblings **Min age:** 6 **Max age:** 18 **Ethnicity:** % White : 100,Other : European ancestry **Reference standard:** Clinical diagnosis The Parental Account of Childhood Symptoms (PACS) interview was conducted with the parents of probands with a clinical diagnosis of ADHD as well as siblings who were thought on the basis of parents'	**Index test:** Clinician tool,Activity Motion sensor data from actigraphs collected during a cognitive testing session; mean intensity of movements from the waist and leg AUC: 0.79 (0.73, 0.86) Rater agreement: Phenotypic and sibling correlations (+95% Confidence Intervals) for mean intensity of movements from the waist and leg with ADHD status from a constrained, phenotypic model, plus familial correlations from a multivariate familial model Phenotypic correlations with ADHD status: 0.48 (0.37, 0.58); Cross sibling correlations with ADHD status: 0.18 (0.06, 0.30); Familial correlations with ADHD status: 0.90 (0.47, 1.00)	**Index test 2:** Activity,Neuropsychological Motion sensor data from actigraphs collected during a cognitive testing session; mean number of movements from the waist and leg AUC: 0.75 (0.68, 0.83) Rater agreement: Phenotypic and sibling correlations (+95% Confidence Intervals) for mean number of movements from the waist and leg with ADHD status from a constrained, phenotypic model, plus familial correlations from a multivariate familial model Phenotypic correlations with ADHD status: 0.31 (0.18, 0.43); Cross sibling correlations with ADHD status: 0.04 (-0.09, 0.17); Familial correlations with ADHD status: 0.27 (-0.08, 0.98)	**Index test 3:** Activity Motion sensor data from actigraphs collected during a cognitive testing session; mean intraindividual variability in intensity of movements from the waist and leg AUC: 0.75 (0.68, 0.83) Rater agreement: Phenotypic and sibling correlations (+95% Confidence Intervals) for mean intraindividual variability in intensity of movements from the waist and leg with ADHD status from a constrained, phenotypic model, plus familial correlations from a multivariate fam	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	descriptions of behavior to have ADHD; com bined with parent- and teacher-rated Conners DSM-IV ADHD subscale to determine diagnosis Timing: Concurrent				
Yao, 2018[630] Case series N = 62 China Setting: Mixed	**Target:** Male drug-naive, right handed children, full-scale IQ score>80, attend Peking University Sixth Hospital psychiatrist clinics **Other:** Age-matched healthy controls from local primary schools **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 0% **Age mean:** 9.79 (1.86) for ADHD group, 10.29 (1.67) for control group **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD participants from child and adolescent psychiatric clinics of Peking University Sixth Hospital Timing: Concurrent	**Index test:** Imaging fMRI, functional connectivity pattern derived from resting-state fMRI; novel feature selection method based on relative importance and ensemble learning (FS_RIEL), 5-fold cross validation; the most frequently selected functional connectivity patterns were mainly involved in frontoparietal network, default network, salience network, basal ganglia network and cerebellum network Sensitivity: 95 Specificity: 76 Accuracy: 86	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Yasumura, 2020[631] Yasumura, 2014[1184] Case series N = 99 Japan Setting: Mixed	**Target:** Participants with no severe comorbidities; IQ >=80 **Other:** Typically developing children without ADHD **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 15.0% **Age mean:** Test set: 10.27 (2.2) for ADHD group, 10.16 (1.55) for control group **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Japanese version of the 26-item Swanson, Nolan and Pelham–IV plus neurologist evaluation Timing: Prior diagnosis	**Index test:** Imaging,Imaging plus non-imaging NIRS (near-infrared spectroscopy) to quantify change in prefrontal cortex oxygenated hemoglobin during reverse Stroop task; classification using support vector machine; items for machine learning were based on past research: age group (<10 years, 10-12 years, >=13 years), task results (number of responses and reaction time on the noninterference condition; number of responses, reaction time, number of errors, and interference ratio on the interference condition) and NIRS data Sensitivity: 89 Specificity: 84 Accuracy: 86 AUC: 0.898 LR+: 5.47 LR-: 0.13	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Yeh, 2020[632] Case series N = 68 China Setting: Specialty care	**Target:** Children with good vision, without intellectual or neurological disabilities who have never been on ADHD treatment; no epilepsy, learning disabilities, severe cognitive impairment or other major illnesses **Other:** Control group of children without ADHD **ADHD presentation:** N/A **Diagnosed by:** Provider **Comorbidity:** N/A **Female:** % 38% female in entire sample **Age mean:** 8.58 (1.48) **Min age:** 6 **Max age:** 12 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Swanson, Nolan, and Pelham, version IV (SNAP-IV) and Conners' parent symptom questionnaire used in clinician diagnosis Timing: Prior diagnosis	**Index test:** Neuropsychological,CPT Virtual Reality classroom: cognitive tasks, continuous performance tests,and audio tests were embedded into the virtual environment. Captured task performance and neuro-behavior data. Analyzed with extreme gradient boosing (XGB) machine learning classifier. 5-fold cross validation with 5 repeats Accuracy: 82	**Index test 2:** Neuropsychological,CPT Virtual Reality (VR) classroom: VR cognitive tasks, continuous performance tests, and audio tests were embedded into the virtual environment. Captured task performance and neuro-behavior data. Analyzed with support vector machine (SVM) classifier. 5-fold cross validation with 5 repeats Accuracy: 83	**Index test 3:** Neuropsychological,CPT Virtual Reality (VR) classroom: VR cognitive tasks, continuous performance tests, and audio tests were embedded into the virtual environment. Captured task performance and neuro-behavior data. Analyzed with logistic regression. 5-fold cross validation with 5 repeats Accuracy: 72	N/A

Yoo, 2020[633] Seoul National University Childrens Hospital, 2015[1033] Case series N = 130 Korea Setting: Other	**Target:** Participants with IQ>=70, no hereditary genetic disorders, current/past history of brain trauma, organic brain disorders, seizure or any neurological disorders, autism spectrum disorder, communication disorder or learning disorder, schizophrenia or any other childhood-onset psychotic disorder, major depressive disorder or bipolar disorder, Tourette's syndrome or chronic motor/vocal tic disorder, obsessive-compulsive disorder, and no history of methylphenidate treatment for >1 year or having taken methylphenidate in the previous 4 weeks **Other:** Age and IQ-matched typically developing children **ADHD presentation:** inattentive : 46.8,inattentive_other : 27.8% in test group,hyperactive : 6.4,hyperactive_other : 22.2% in test group,combined : 29.8,combined_other : 27.8% in test group,N/A : 17% not otherwise specified **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 25% **Age mean:** Test set: 9.44 (2.41) for ADHD group, 10.06 (2.69) for control group. Training set: 10.06 (2.24) for ADHD group, 10.00 (2.60) for control group. **Min age:** 6 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis DSM-IV criteria confirmed with the Korean Kiddie Schedule for Affective	**Index test:** Imaging,Imaging plus non-imaging sMRI, fMRI, and diffusion-tensor MRI, age, sex, and IQ; best accuracy model: machine learning algorithms with multi-measures, multi-modal neuroimaging data (sMRI, resting-state fMRI, diffusion tensor imaging); selected variables all tensors + CT/CTV + SA/MC + Volume [CT cortical thickness; CTV cortical thickness variability; SA surface area; MC mean curvature]; multiple linear SVM recursive feature elimination for feature selection, random forest classifier, leave one out cross validation; age, sex and IQ were also entered as predictors for random forest regression; results from independent test dataset Accuracy: 78 AUC: 0.70	**Index test 2:** Imaging,Imaging plus non-imanging sMRI, fMRI, and diffusion-tensor MRI, age, sex, and IQ; lesser feature with equivalent performance model: machine learning algorithms on multi-measures, multi-modal neuroimaging data (structural MRI, Resting-state fMRI, diffusion tensor imaging); selected variables CT/CTV + Volume [CT cortical thickness; CTV cortical thickness variability]; multiple linear SVM recursive feature elimination for feature selection, random forest classifier, leave one out cross validation; age, sex and IQ also entered as predictors for random forest regression; results from independent test dataset Accuracy: 69 AUC: 0.65	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Disorders and Schizophrenia – Present and Lifetime version Timing: Prior diagnosis				
Zadehbagheri, 2019[635] Case series N = 120 Iran Setting: Specialty care	**Target:** Children with no other psychiatric disorders, a history of severe head injury, neurodevelopmental disorders, dysaudia, vision disorder, epilepsy or cardiovascular disorders and IQ>85; none received drug treatment for ADHD **Other:** Age and sex-matched controls **ADHD presentation:** inattentive : 10,hyperactive : 5,combined : 85 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 31.67% **Age mean:** 9.97 (1.44) **Min age: Max age:** **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosed with ADHD based on DSM-IV with structured interview Timing: Concurrent	**Index test:** Biomarker miRNA hsa-miR101-3p Sensitivity: 82 Specificity: 95 AUC: 0.959	**Index test 2:** Biomarker miRNA hsa-miR-106b-5p Sensitivity: 86 Specificity: 82 AUC: 0.942	**Index test 3:** Biomarker miRNA hsa-miR-138-5p Sensitivity: 82 Specificity: 79 AUC: 0.856	**Index text 4:** Biomarker mIRNA combined biomarkers hsa-miR101-3p, hsa-miR-106b-5p, hsa-miR-138-5p, hsa-miR-130a-3p,hsa-miR-195-5p Sensitivity: 68 Specificity: 71 AUC: 0.68

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Zelko, 1991[638] Case series N = 89 US Setting: Mixed	**Target:** Boys with ADHD drawn from pediatric neurology and child guidance clinics **Other:** Two groups: a) subjects with psyc diagnoses such as adjustment disorder, depression, anxiety disorder, conduct disorder, etc. b) normal subjects drawn from regular educational settings. **ADHD presentation:** N/A : 27 ADD with hyperactivity, 3 ADD without hyperactivity **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 0% **Age mean:** 9.71 (1.1) **Ethnicity:** % Hispanic or Latino : 3.4 % Black/African American : 6.7 % White : 84.3 Other : 5.6% other **Reference standard:** Clinical diagnosis Diagnosis by pediatric neurologist, child psychiatrist or psychologist. Verified by author interview of child and parents based on DSM III> Timing: Prior diagnosis	**Index test:** Parent rating ARS (Conners Abbreviated Rating Scale) parent	**Index test 2:** Parent rating CBCL (Child Behavior CheckList) parent	**Index test 3:** Parent rating SCRS (Self Control Rating Scale) parent	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Zelnik, 2012[639] Case series N = 230 Israel Setting: Specialty care	**Target:** Participants with no major psychiatric conditions, mental retardation, autistic spectrum disorder, and epilepsy and treated with psychotropic drugs **Other:** Children referred to ADHD clinic not diagnosed with ADHD **ADHD presentation:** inattentive : 39,hyperactive : 15,combined : 46 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 29% in entire sample **Age mean:** 10.0 (2.7) **Min age:** 6 **Max age:** 17 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Clinical Diagnosis using DSM-IV diagnostic criteria, family interviews about the behavioral and neurodevelopmental history of the child, neurological evaluation, observation at the physician's office, and employment of the Conners' Rating Scales (Teacher, Parent) Timing: Concurrent	**Index test:** Neuropsychological,CPT Test of Variables of Attention Sensitivity: 91 Specificity: 22 Rater agreement: Test of Variables of Attention versus reference standard Kappa: 0.152	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Zhou, 2018[642] Case series N = 339 US Setting: Specialty care	**Target:** Children diagnosed with ADHD diagnosed in multiple clinics across the United States by the practicing clinicians **Other:** A population proportion stratified random sample of the US child and adolescent population collected for the BASC-3 standardization matched on age, education level, gender, and ethnicity **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 27% **Age mean:** 11.85 (3.43) **Min age:** 6 **Max age:** 18 **Ethnicity:** % Hispanic or Latino : 13 % Black/African American : 8 % Asian : 3 % White : 71 Other : Other 5% **Reference standard:** Clinical diagnosis Diagnosed by practicing clinicians using DSM criteria Timing: Prior diagnosis	**Index test:** Teacher rating scale BASC-3 (Behavior Assessment System for Children-Third Edition) teacher rating scale; cutoff point posterior probability of 0.80 or higher Sensitivity: 70 Specificity: 73 PPV: 22 10% prevalence NPV: 96 10% prevalence	**Index test 2:** Parent rating BASC-3 (Behavior Assessment System for Children-Third Edition) parent ratingscale; cutoff point posterior probability of 0.80 or higher Sensitivity: 94 Specificity: 51 PPV: 17 10% prevalence NPV: 99 10% prevalence	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
Zhou, 2022[641] Case series N = 10 China Setting: N/A	**Target:** Newly diagnosed children with ADHD in a children's hospital **Other:** **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** % N/A **Age mean:** **Min age:** 6 **Max age:** 16 **Ethnicity:** % Asian : 100 **Reference standard:** Clinical diagnosis Diagnosed by professional at a children's hospital Timing: Prior diagnosis	**Index test:** EEG EEG fully connected neural network model; CADWELL video EEG monitoring system used forat least 24 hours; the McCulloch–Pitts neuron model abstracts the data into a mathematical model Accuracy: 92.7	**Index test 2:** EEG EEG convolutional neural network model; CADWELL video EEG monitoring system used forat least 24 hours; convolutional network can reduce a lot of parametersthan the fully connected network, reducing the complexity of the network model and accelerating the training speed of the model; the main structure of a convolutional neuralnetwork is a convolutional layer and a pooling layer Accuracy: 97.7	N/A	N/A

Zhu, 2022[644] Case series N = 742 China Setting: Specialty care	**Target:** ADHD subjects were newly diagnosed without any treatment; IQ>85 **Other:** 430 healthy children who came to the Health Care Department for routine physical examination were randomly selected as controls matched to ADHD subjects by age, gender, height, and weight; no clinical symptoms or abnormal examination records (physical exa **ADHD presentation:** inattentive : 39,hyperactive : 15,combined : 46 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 15% **Age mean:** 8.16 (1.81) for ADHD group, 8.04 (1.71) for healthy control group, 7.97 (1.64) for pneumonia group, 8.60 (2.07) for vitamin D deficiency group **Ethnicity:** N/A **Reference standard:** Clinical diagnosis Diagnosis of ADHD was routinely made independently by 2 senior pediatricians with ADHD expertise and met the criteria proposed by DSM-V with a structured interview; the Conners' Parent Symptom Questionnaire (PSQ) was used as a screening diagnostic instrument Timing: Concurrent	**Index test:** Biomarker miRNA panel with 5miRNAs (miR-4516, miR-6090, miR-4763-3p, miR-4281, and miR-4466); regressionanalysis; validation group Sensitivity: 83 Specificity: 86 AUC: 0.927 (0.901, 0.966)	N/A	N/A	N/A
Zulueta, 2019[647] Case series N = 407 Spain Setting: Mixed	**Target:** Children with normal IQ >80 **Other:** Typically developing children **ADHD presentation:** inattentive : 49.30,combined : 50.70 **Diagnosed by:** Specialist **Comorbidity:** N/A	**Index test:** Neuropsychological,CPT AULA virtual reality based neuropsychological continuous performance test Sensitivity: 68 Specificity: 75	N/A	N/A	N/A

Study: Author, Year; Multiple Publications; Study Design; Study Size; Location	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity; Reference Standard	**Results:** Index Test; Diagnostic Accuracy; Rater Agreement; Other Outcomes	**Index Test 2**	**Index Test 3**	**Index Test 4**
	Female: 26.76% **Age mean:** ADHD Combined Subtype (Mean 9.78, SD 2.66) ADHD Inattentive Subtype (Mean 10.62, SD 2.79) **Min age:** 6 **Max age:** 16 **Ethnicity:** N/A **Reference standard:** Clinical diagnosis ADHD diagnosis by clinical diagnostic team considering data from parents' and teacher's rating and clinical interviews with children and their parents Timing: Concurrent				

Notes: ADHD = attention deficit hyperactivity disorder; N/A = not available

Table C.2. KQ2 evidence table

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
CAM	Aviv, 2021[128] ID: ID NA RCT Single center N = 123 Israel Setting: Community	**Target:** Children with ADHD currently taking stimulant medication; those with co-occurring psychological disorders excluded **Other:** Parents reported some outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV-TR by pediatric neurologist **Comorbidity:** N/A **Female:** 27.7 % **Age mean:** 8.97 (1.68) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** Other : 100% Israeli	**Intervention:** Horseback riding sessions plus medication (not further specified), 30-min therapeutic sessions, after completing each activity with the horse, the instructors and the children analyzed the children's and the horse's behaviors to strengthen the riders' monitoring abilities by teaching them to observe and analyze their actions using the horse's reactions as a feedback and to correct their behaviors accordingly, for 20 weeks **Control:** Wait list Wait list plus medication (not further specified) **Comparator:** NA **Follow-up:** 8 months	Conners' Parent Rating Scales, Revised (CPRS-R) emotional regulation scale Lower scores in the intervention group. Behavior Rating Inventory of Executive Functions (BRIEF): Behavioral Regulation Index score - Intervention 54.02 (9.46) Control 63.85 (9.94); Meta-cognition score - Intervention 86.03 (15.63); Control 99.57 (11.65). Lower is better., statistical significance not reported.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
CAM	Binesh, 2020[150] Research Institute for Islamic and Complementary Medicine, 2019[998] ID: IRCT20090527001957N9 RCT Single center N = 50 Iran Setting: N/A	**Target:** Children with ADHD according to DSM-5 criteria, Child Severity Inventory-4 score, clinical judgment of a psychiatrist, and a family physician; Child Severity Inventory-4 questionnaire scores for the attention deficit section >6 and the hyperactivity section >5 **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-V **Comorbidity:** N/A **Female:** 18.2 % **Age mean:** 9.8 (2) **Minimum age:** 6 **Maximum age:** 14 **Ethnicity:** N/A	**Intervention:** Auricular therapy was performed at six ear acupoints, stimulated bilaterally for20 sec at each point, each participant evaluated and received stimulation for 15 min, each point labeled with small sections of adhesive tape that contained a small granule (Vaccaria seeds), participants' supervisors were asked to apply medium pressure once a day for 1 min on each of the seeds after stimulation, repeated once a week for 6 weeks **Control:** Attention-matched control Nonacupuncture points were not electrically stimulated and only the seedless adhesive tapes were attached, adhesive replacement was performed once a week for 6 weeks **Comparator:** NA **Follow-up:** 2.5 months	Hyperactivity Scores, Comprehensive Behavior Rating Scale, Parent's version Hyperactivity impulsiveness, and anger improvement improvement, investigator evaluation Patients exhibited significantly greater improvement after receiving auricular therapy than did children in the sham control group ($p < .05$).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
CAM	Frei, 2001[279] ID: NA Clinical trial Single center N = 115 Switzerland Setting: Specialty care	**Target:** Participants with ADHD with a Clinical Global Impressions of 14 or higher **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 20 % **Age mean:** mean age 8.3 **Minimum age:** 3 **Maximum age:** 17 **Ethnicity:** N/A	**Intervention:** Homeopathic liquid LM-potencies (LM-3 to LM-30) every day or every second day, used for 4 weeks, moving on to the next higher level (eg LM-6) after a treatment free interval of several days to one week, total duration of 3 months **Control:** NA **Comparator:** MedicationMethylphenidate for patients who did not reach sufficient clinical improvement, or whose behavior remained unacceptable despite a certain response to homeopathy after reevaluation, optimal dosage was adjusted over 3 months **Follow-up:** 3 months	CGI (Clinical Global Impression) scale During homeopathic treatment the mean CGI rating fell to 9.27 corresponding to an amelioration of 55%, and with MPD to 10.96, corresponding to an amelioration of 48%.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
CAM	Frei, 2005[278] ID: NA Crossover trial Single center N = 83 Switzerland Setting: Specialty care	**Target:** Children with ADHD with neuropsychological correlates, the necessity for treatment, and absence of any chronic physical, neurological or psychiatric disorders **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV by neuropsychologist **Comorbidity:** N/A **Female:** 12.8 % **Age mean:** Arm A: 10 (range 7–15); Arm B: 10 (range 7–15) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** N/A	**Intervention:** Verum homeopathic treatment daily for 6 weeks **Control:** Placebo Placebo **Comparator:** NA **Follow-up:** 5.5 months	Conners' Global Index (CGI) Intervention group had significantly more improvement than control group (p=0.0479).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
CAM	Hong, 2016[332] Trial registration, 2010[719] ID: KCT0000019 RCT Single center N = 93 Korea Setting: Specialty care	**Target:** Participants with an ADHD diagnosis (of any subtype) receiving any intervention (pharmacological, psychosocialtherapy, educational, occupational therapies etc.) without change in ADHD treatments/ symptoms for last 2 weeks or no current treatment; no diagnosis of mental retardation or pervasive developmental disorders, past history of epilepsy or other neurotic disorder, pregnancy, change in medications during the course of the study **Other:** Parent reported some outcomes **ADHD presentation:** N/A : Mean Hyperactivity/Impulsivity score = 11.0 in each group. **Diagnosis:** Confirmation by specialist DSM IV criteria **Comorbidity:** N/A **Female:** 18.7 % **Age mean:** 11.0 (2.8) **Minimum age:** 7 **Maximum age:** 18 **Ethnicity:** % Asian : 100	**Intervention:** Acupuncture treatment for twenty minutes, twice per week for six weeks **Control:** Wait list Wait list **Comparator:** NA **Follow-up:** 1.5 months	Child Behavior Checklist (CBCL), change from baseline No significant difference between groups (p = 0.393). ADHD-RS change Change in score did not differ significantly between groups (p = 0.561). 3 headaches in acupuncture group, none in control group; no other adverse events reported.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
CAM	Zhuo, 2022[646] ID: NCT03917953 RCT Single center N = 78 China Setting: Specialty care	**Target:** Children with ADHD; those with other mental or neurodevelopmental disorders, use of ADHD medication, or prior acupuncture were excluded **Other:** Parents and teachers provided one outcome each **ADHD presentation:** inattentive : 46.2,hyperactive : 0,combined : 53.8 **Diagnosis:** Confirmation by specialist DSM V by two experienced child psychiatrists **Comorbidity:** N/A **Female:** 17.9 % **Age mean:** 8.3 (1.33) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Asian : 100	**Intervention:** Transcutaneous electrical acupoint stimulation, acupuncture points selected according to theory that Yin-Yang disharmony is implicated in the development of ADHD, acupoints were located on the midsagittal line at the intersection of a line connecting the ear apices as well as two acupoints are located on the dorsum and medial side of the foot, 8 sessions, 20 min per session, 2-3 day interval between each pair of sessions per week for 4 weeks **Control:** Attention-matched control Sham transcutaneous electrical acupoint stimulation, group stimulated at the same acupuncture points as those used in intervention group, 8 sessions, 20 min per session, 2-3 day interval between each pair of sessions per week **Comparator:** NA **Follow-up:** 1 month	Conners Parent Rating Scale, Revised CGI-I improved CGI-I: Significantly greater % of intervention group improved (p 0.005), improvement in CPRS-R and CTRS-R (teacher rating) not significantly differently between groups. Improvement in accuracy for go/no-go trials, a computerized task that measures inhibition control, was larger for intervention group (p 0.049). Any adverse event 2 members of intervention group and 1 in control group reported an adverse events, none were serious.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Cognitive training	Azami, 2023[129] ID: NCT02780102 RCT Single center N = 48 Iran Setting: Specialty care	**Target:** Male children with ADHD; those with comorbid psychiatric disorders, epileptic seizures in the last 2 years, motor disability, and other medical conditions were excluded **Other:** Parents reported symptom outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist psychiatrist clinical interview, rating scales, parental clinical interview **Comorbidity:** N/A **Female:** 0 % **Age mean:** Intervention 10.37 (0.88), sham 10.37 (1.15), medication 10.12 (1.02) **Minimum age:** 9 **Maximum age:** 12 **Ethnicity:** N/A,Other : Persian	**Intervention:** Cognitive motor rehabilitation, computerassisted, 20 group sessions (3 per week, 5 participants); 1-hour sessions of 5 min of warm-up, 5 min of cool-down, and 50 min of performing progressive associative tasks, for 7 weeks **Control:** Attention-matched control Sham cognitive motor rehabilitation, 20 group sessions (3 one-hour sessions per week) **Comparator:** MedicationMethylphenidate 2–3 tablets of 10 mg (immediate release) per day; medication stopped 24 hour before follow-up assessment **Follow-up:** 3 months	SNAP IV, parent report, ADHD-C score Cognitive motor training group improved significantly more than sham or medication group (p<0.05) on all SNAP IV scales. RASS (symptoms during academic assignments) negative scores Significant effect of the interventions compared to sham training (p0.003). Cognitive motor rehabilitation outperformed methylphenidate on dictation (p < 0.01) .

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Cognitive training	Benzing, 2019[139] Universität Bern, 2016[1125] ID: KEK 393/15, DRKS00010171 RCT Single center N = 51 Switzerland Setting: Other	**Target:** Children diagnosed with ADHD based upon the ICD-10; no neurological disorder, Tourette syndrome, or an epileptic disorder **Other:** **ADHD presentation:** N/A : Scores entered above reflect dimensional ADHD-RS symptoms, not ADHD subtypes **Diagnosis:** Confirmation by specialist ICD-10 **Comorbidity:** N/A **Female:** 17.6 % **Age mean:** 10.63 (1.32) **Minimum age:** **Maximum age:** **Ethnicity:**	**Intervention:** Kinect exergaming training for Xbox, 3 times a week for at least 30 minutes for 8 weeks **Control:** Wait list Waitlist control, no intervention **Comparator:** NA **Follow-up:** 2 months	Conners-3 Scale, German version, Global Index Score, parents Significant effects favoring the intervention were detected on the total global index score (p=0.022). ADHD symptoms (DSM-IV-TR scales) No significant group effects (p > .05). For the Motor ability - German Motor test the intervention group showed a significantly better total performance than the control group (p=0.008).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Cognitive training	Bigorra, 2016[148] Bigorra, 2016[687] ID: ISRCTN00767728 RCT Single center N = 66 Spain Setting: Specialty care	**Target:** Children with ADHD, comorbidity with other disruptive behavior disorders accepted, diagnoses were confirmed using the semi-structured Kiddie-Schedule for Affective Disorders and Schizophrenia, Present and Lifetime Version interview; T scores on the Conners ADHD index for parents and teachers >70 at the time of diagnosis; no previous psychological or pharmacological treatment for ADHD **Other:** **ADHD presentation:** combined : 100 **Diagnosis:** Confirmation by specialist DSM-IV-TR by clinician **Comorbidity:** N/A **Female:** 55 % **Age mean:** 8.92 (1.75) **Minimum age:** 7 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 95.4	**Intervention:** Cogmed Working Memory Training adaptive training, visual-spatial, auditory,and location memory and tracking of moving visual objects as working memory tasks, each training session included 90 trials and had a duration of 30–45 min, participants attended a total of 25 sessions 5 sessions per week, for 5 weeks **Control:** Placebo Control group (non-adaptive training) engaged in the MegaMemo, which consists of the same working memory tasks but without the adjustment for difficulty, i.e. they performed simpler tasks **Comparator:** NA **Follow-up:** 6 months	Behaviour Symptoms Index (mean parent, teacher) On adjusted multiple linear regression analysis, there were no significant improvements in the outcome measures. ADHD Composite Index (Conners, SDQ) A significant improvement was noted for the intervention group compared to the control group (p 0.01). Weiss Functional Impairment Rating Scale (WFIRS-P)- Parent Significant improvements for the intervention group compared to the control group were registered on the school learning behavior subscale (p 0.02) but not on any other subscale. With respect to executive functions scales (BRIEF), the the experimental group improved significantly more than the control group (p 0.01). No statistically significant differences between the groups for Theory of Mind composite score were recorded at any point in time (p 0.57).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Cognitive training	Bikic, 2018[56] Region Syddanmark, 2012[996] ID: NCT01752530 RCT Multicenter N = 78 Denmark Setting: Mixed	**Target:** Children fulfilling DSM-IV criteria for ADHD; no diagnosis of comorbid conduct disorder, autism spectrum disorders, depression or schizophrenia; no medical history of head injury or a verified neurological disorder; IQ>80; no motor or perceptual handicaps which would interfere with computer use; no medical condition requiring primary treatment; and no informed consent from custody **Other:** Parents **ADHD presentation:** inattentive : 42.6,hyperactive : 5.7,combined : 50 **Diagnosis:** Confirmation by specialist interviewed by one of three trained psychologists, to confrm the ADHD diagnosis, using the ADHD section of the Kiddie-Schedule for Afective Disorders and Schizophrenia (K-SADS) **Comorbidity:** N/A **Female:** 16 % **Age mean:** 9.95 (1.7) **Minimum age:** 6 **Maximum age:** 13 **Ethnicity:** N/A	**Intervention:** Computer program ACTIVATE 6 times a week plus ADHD treatment as usual, for 8 weeks **Control:** Other Treatment as usual alone, which consisted of diagnostic and cognitive assessment, psycho-education, pedagogical counseling, and questionnaires for parents and teachers, home and school visits and, for some children, medical treatment **Comparator:** NA **Follow-up:** 5.8 months	ADHD-RS-IV (ADHD-Rating Scale-IV), parent rating There was no significant effect for training (p-0.69). Weiss functional impairment rating scale-parent report form (WFIRS-P) There were no significant differences between the intervention and the control group (p=0.54). No significant effect of training on sustained attention, parent-rated-BRIEF, or teacher-rated-BRIEF.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Cognitive training	Bul, 2016[166] Bul, 2018[698] ID: ISRCTN62056259 RCT Multicenter N = 170 Multiple countries Setting: Mixed	**Target:** Children stable on pharmacological and/or psychological treatment for ADHD 8 weeks before baseline **Other:** **ADHD presentation:** inattentive : 22.4,hyperactive : 3.5,combined : 74.1 **Diagnosis:** Confirmation by specialist DSM-IV-TR by psychologist **Comorbidity:** N/A **Female:** 19.4 % **Age mean:** 9.85 (1.26) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Game intervention plus treatment as usual, maximum of 65 minutes approximately 3 times per week for 10 weeks **Control:** TAU Treatment as usual for the first 10 weeks and the crossed over to the serious game intervention in addition to treatment as usual for the subsequent 10 weeks **Comparator:** NA **Follow-up:** 5 months	Behavior Rating Inventory of Executive Function (BRIEF, subscale Plan/Organized) showed significantly greater improvements (p=0.004). 10 adverse events that could be related to the intervention, all were mild or moderate severity, including pain in the fingers, irritability, and headache, one participant did not want to paly the game anymore because he could not concentrate during his s

Cognitive training	Denton, 2020[221] University of Texas, 2010[1117]; Dvorsky, 2021[750] ID: NCT01133847 RCT Multicenter N = 222 US Setting: School	**Target:** Patients with ADHD and a standard score ≤ 25th percentile on either the Woodcock-Johnson III Letter-Word Identification or Word Attack subtests or the Basic Reading Skills composite **Other:** Parents received training and provided some outcomes **ADHD presentation:** inattentive : 46.1,combined : 53.9 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** Learning disability **Female:** 39.0 % **Age mean:** 8.8 (1.3) **Minimum age:** 5 **Maximum age:** 7 **Ethnicity:** % Black/African American : 72.1 % White : 19.6 % Multiracial : 6.4	**Intervention:** Reading intervention plus medication plus parent training; the reading interventionwas provided individually or in groups of two students in 45- minute lessons, 4 days per week; medication treatment in children typically began with a low dose of extended-release methylphenidate, which was titrated up in weekly visits to a dosage at which the child had a satisfactory response with limited side effects for a total of 12 weeks; the behavioral parent training consisted of 9 group sessions over 10 weeks, topics included psychoeducation about ADHD and evidence-based strategies for behavior management, a possible total of 64 lessons over 16 weeks **Control:** Other Parent training plus medication only; treatment typically began with a low dose of extended-release methylphenidate, which was titrated up in weekly visits to a dosage at which the child had a satisfactory response with limited side effects; the behaviora **Comparator:** NA **Follow-up:** 4 months	Inattention, SNAP (Swanson, Nolan, and Pelham Checklist for DSM-IV), parent rating Combined intervention group improved more than group receiving reading instruction alone. Same for SNAP Parent Rating of Hyperactivity-Impulsivity, SNAP- Teacher Rating of Inattention, and SNAP- Teacher Rating of Hyperactivity-Impulsivity. Test of Word Reading Efficiency (TOWRE) Phonemic Decoding Efficiency: combined intervention (p 0.03) and reading group alone (p 0.007) had significantly higher posttest means than medication and parent treatment alone. Improvement in WIAT-3 Reading Comprehension means was superior for medication plus parent training group compared to both groups receiving a reading intervention (p 0.008).
Cognitive training	Dentz, 2020[222] Université du Québec a Montréal, 2017[1126] ID: NCT03335748 RCT Single center N = 52	**Target:** Youths diagnosed with ADHD combined type with comorbid learning disability, oppositional defiance disorder, or Tourette syndrome, and under stable pharmacological treatment for ADHD for at least the past 2 months **Other:** Parents provided outcomes **ADHD presentation:** combined : 100	**Intervention:** Cogmed program plus ADHD medication, cognitive training software targeting verbal and visuospatial components of working memory, each training session 30-45 min, at least 5 sessions per week for 5 weeks	Conners, parent report, attention score No significant between group difference in parent rated attention or hyperactivity scores. WIAT Reading

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
	Canada Setting: Other	**Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** Other : either learning disabled, ODD, or Tourette's **Female:** 13 % **Age mean:** Intervention: 10.44 (1.18), control: 9.60 (2.08) **Minimum age:** 7 **Maximum age:** 13 **Ethnicity:** % White : 86.5	**Control:** Attention-matched control Comparison version of the Cogmed program with a low and invariable level of difficulty, which was expected to dampen the program's effects plus ADHD medication **Comparator:** NA **Follow-up:** 2.5 months	No significant difference between groups in WAIT reading or math scores. No significant difference between groups in behavior rating inventory of executive function (BRIEF) score, continuous performance test (CPT) which measures attentional functions and inhibition., or working memory.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Cognitive training	Dong, 2022[227] ID: ID NA RCT Multicenter N = 850 China Setting: Other	**Target:** Kindergarteners with ADHD, with sibling in Grade 7 or 8 **Other:** Parents or siblings participated **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Diagnosed by licensed clinical psychologists per DSM **Comorbidity:** N/A **Female:** 50.3 % **Age mean:** 5.35 (0.20) **Minimum age:** **Maximum age:** **Ethnicity:** % Asian : 100	**Intervention:** Dialogic reading with parent 25 minutes twice per week; a shared bookreading approach where parent engages in dialog with the child through interactive question and answer communication while reading picture books together, for 12 weeks **Control:** Attention-matched control Reading books with parent 25 minutes twice per week for 12 weeks, but without dialogic reading **Comparator:** Cognitive trainingDialogic reading with older sibling 25 minutes twice per week for 12 weeks; a shared book reading approach where parent engages in dialog with the child through interactive question and answer communication while reading picture books together **Follow-up:** 3 months	Group interaction effects on recep-tive vocabulary, expressive vocabulary, character reading, morpho-logical awareness, phonological awareness, listening comprehension, and reading interest were significant ($p < .001$) in favor of the dialog reading groups over the control reading group; sibling dialog reading was significantly superior to parent dialog reading regarding expressive vocabulary, character reading , morphological awareness, phono-logical awareness, and reading interest ($p < .001$ for all) but inferior regarding improvement in listening comprehension ($p < .001$).

Cognitive training	Dovis, 2015[229] Dovis, 2015[742] ID: NTR2728 RCT Multicenter N = 89 Netherlands Setting: Specialty care	**Target:** Participants with DSM-IV-TR diagnosis of ADHD combined type diagnosed by a child psychologist or child psychiatrist, score on Disruptive Behavioral Disorder Rating Scale (Dutch translation) in 9th to 100th percentile for both parent and teacher version ADHD scale, met criteria for ADHD combined type on ADHD section of Diagnostic Interview Schedule for Children, parent version; IQ score greater than or equal to 80 on Dutch Wechsler Intelligence Scale for Children-III; no conduct disorder, autism spectrum disorder, neurological disorder, sensory or motor impairment reported by parents, medications other than methylphenidate or dextroamphetamine **Other:** Parents & teachers provided some outcomes **ADHD presentation:** combined : 100 **Diagnosis:** Confirmation by specialist DSM IV TR **Comorbidity:** N/A **Female:** 20 % **Age mean:** Full-active intervention 10.6 (1.4), partially-active intervention 10.3 (1.3), control (sham) group 10.5 (SD 1.3) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Executive functioning training on computer ("Braingame Brian"), total of 25 training sessions, each session taking between 35-50 minutes, all tasks were in training mode and level is adjusted to child's level of performance for 5 weeks **Control:** Attention-matched control Braingame Brain in sham condition: working memory, inhibition, and cognitive-flexibility tasks were presented in the same way as training mode except the stop-trials and switch-trials were replaced by go-trials and non-switch trials and difficulty level w **Comparator:** Cognitive trainingPartially-active condition in which the working memory tasks were in sham mode which did not adjust difficultly to performance while the inhibition and cognitive-flexibility tasks were in training mode **Follow-up:** 4.25 months	Disruptive Behavior Disorder Rating Scale (DBDRS), Inattention scale, parent report No effect of treatment group on parent or teacher Disruptive Behavior Disorder Rating Scale (DBDRS) No signifcant difference of treatment outcome on any executive function measures
Cognitive training	Egeland, 2013[243] Hovik, 2013[840] ID: ISRCTN19133620 RCT Single center N = 75 Norway	**Target:** Children in treatment for ADHD, IQ>=70; no comorbid diagnosis of Pervasive Developmental Disorders, Tourette's Disorder, evidence of psychosis or Bipolar Disorder and Conduct Disorder **Other:** **ADHD presentation:** N/A	**Intervention:** Working Memory training (RoboMemo) performed on a daily basis at school, sessionslast for 30–45 minutes, for 5–7 weeks **Control:** Wait list Offered the possibility to train after the completion of the study	ADHD-RS-IV (ADHD-Rating Scale IV), parent There was no significant difference between groups. Strengths & Difficulties Questionnaire (SDQ), parent There was no significant difference between groups.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
	Setting: School	**Diagnosis:** Confirmation by specialist F-90 ICD-10 Hyperkinetic Disorder (equivalent to DSM-IV) **Comorbidity:** N/A **Female:** 24 % **Age mean:** 10.4 (0.7) **Minimum age:** 10 **Maximum age:** 12 **Ethnicity:** N/A	**Comparator:** NA **Follow-up:** 8 months	Training group had significant gains in working memory performance measures.
Cognitive training	Estrada-Plana, 2019[258] ID: NA RCT Single center N = 29 Spain Setting: Other	**Target:** Children with ADHD; without having any other mental disorders; IQ>80 **Other:** **ADHD presentation:** inattentive : 23.1,hyperactive : 76.9 **Diagnosis:** Confirmation by specialist Psychiatrists or Clinical Psychologists **Comorbidity:** N/A **Female:** 46.2 % **Age mean:** 9.46 (1.20) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 97 Other : Does not specify the other 3%	**Intervention:** Cognitive training based on board games, closed groups of 6-8 participants, 60 minutes each, 1 game per week, for 5 weeks **Control:** Wait list Wait-list control group **Comparator:** NA **Follow-up:** 1 month	Conners CPRS-48 Conduct Problems Subscale There was no significant difference between groups for Conners CPRS-48. Hyperactivity Index, Conners CPRS-48 (CPRS-48) Strengths and Difficulties Questionnaire (SDQ) Intervention participants showed lower conduct problems in the SDQ subscale compared to control group participants (p<0.001). Number of participants with adverse events No patients with adverse events. No adverse effects were found during the intervention.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Cognitive training	Hahn-Markowitz, 2020[313] Hahn-Markowitz, 2017[814]; Hadassah Medical Organization, 2013[811] ID: NCT01792921 Crossover trial Multicenter N = 107 Israel Setting: Mixed	**Target:** Children with ADHD **Other:** Parents and teachers provided some outcomes **ADHD presentation:** inattentive : 48.6,hyperactive : 4.7,combined : 46.7 **Diagnosis:** Confirmation by specialist DSM-IV, assessed by a certified pediatric neurologist/psychiatrist, including a semi-structured interview with the child and parents, medical/neurological/psychiatric examination, and completion of a ADHD diagnostic questionnaire **Comorbidity:** N/A **Female:** 38 % **Age mean:** 8.5 (0.85) **Minimum age:** 7 **Maximum age:** 10 **Ethnicity:** N/A	**Intervention:** Cog-Fun: integrative intervention using effortful executive strategies and supplemented by environmental adaptations, weekly 1-hr sessions with child and parent over 12 weeks **Control:** Wait list Wait list which crossed over to intervention after first group finished. **Comparator:** NA **Follow-up:** 3 months	CPRS-R (Conners' Parent Rating Scales–Revised), global index total Greater improvement in intervention group compared to control group (p <.01) . BRIEF Global Executive Composite, completed by parents: intervention group superior (p < .01). No significant group difference s in changes in BRIEF Global Executive Composite completed by teachers (p = .73) No adverse events or side effects occurred among participants in either group.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Cognitive training	Kim, 2022[367] ID: ID NA RCT Single center N = 30 Korea Setting: Specialty care	**Target:** Children with ADHD; those with symptoms other than ADHD symptoms and those with medical conditions that affect use of intervention were excluded **Other:** Parents reported some outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM V by psychiatrist via K-SADS-PL **Comorbidity:** N/A **Female:** 23.3 % **Age mean:** 9.1 (1,77) **Minimum age:** 6 **Maximum age:** 13 **Ethnicity:** % Asian : 100	**Intervention:** Attention and working memory improvement training program, AI-based (NeuroWorld DTx), game-based cognitive therapy software, plus conventional medication (not described) for 4 weeks **Control:** Other Conventional medication (not described) **Comparator:** NA **Follow-up:** 1 month	Child Behavior CheckList (CBCL), Total Behavior Problems No difference between groups (p 0.349) K-ARS (Korean ADHD RS) No difference in improvement between groups (p 0.795). Likelihood of re-participation 80% of participants would participate again in the intervention.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Cognitive training	Kofler, 2020[368] ID: NA RCT Single center N = 54 US Setting: Other	**Target:** Children with ADHD and clinical/borderline elevations on at least 1 parent and one teacher ADHD rating scale, or previous psychoeducational evaluation documenting cross-informant symptoms; pretreatment working memory test scores not in the average range or higher **Other:** **ADHD presentation:** inattentive : 27.7,hyperactive : 3.7,combined : 68.5 **Diagnosis:** Confirmation by specialist DSM-5 by clinical psychologist based on K-SADSK-SADS **Comorbidity:** N/A **Female:** 22 % **Age mean:** 10.41 (1.46) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 11 % Black/African American : 9 % White : 74 % Multiracial : 6	**Intervention:** Inhibitory control training, web-based, weekly in-office sessions with the child (1 hour), combined with parent-supervised in-home training (15-min/day, 2–3 days/week), for 10 weeks **Control:** NA **Comparator:** Cognitive trainingWeb-based central executive training (CET) targeting central executive working memory deficits; identical to ICT in terms of website address, name, art, animations, storylines, layouts, interfaces, and use of adaptive training algorithms to maximize inte **Follow-up:** 2.5 months	ADHD-RS-5, parent and teacher reports Both interventions were equivalent for parent-reported Hyperactivity/Impulsivity (p = 0.89) and Attention Problems (p = 0.47); executive function training was superior for teacher-reported ADHD-RS-5 Attention Problems (p = 0.01). Parent satisfaction ICT and CET did not differ in parent-reported post-treatment satisfaction (p=.22) Central executive training was superior for improving phonological (p < .001) and visuospatial (p = 0.01) working memory and go/no-go (inhibitory control) (p = 0.0.1), but not stop-signal inhibition (p = 0.08).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Cognitive training	Kollins, 2020[372] Akili Interactive Labs, Inc., 2016[658] ID: NCT02674633 RCT Multicenter N = 348 US Setting: Other	**Target:** Children with ADHD according to DSM-5; IQ>=80; no significant comorbid psychiatric diagnoses and no use of ADHD medications that could not be discontinued **Other:** Parents **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Participants diagnosis of ADHD according to DSM-5 criteria was confirmed. **Comorbidity:** N/A **Female:** 28.7 % **Age mean:** Intervention 9.7 (1.3), control 9.6 (1.3) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Digital therapeutic AKL-T01 delivered through a video game-like interface via at-home play for 25 min per day, 5 days per week for 4 weeks **Control:** Attention-matched control Control was designed to match AKL-T01 on expectancy, engagement, and time on task in the form of a challenging and engaging digital word game, targeting cognitive domains not targeted by the AKL-T01 intervention and not primarily associated with ADHD; th **Comparator:** NA **Follow-up:** 1 month	CGI (Clinical Global Impressions) scoring 2 or more No difference in improvement between groups. ADHD-RS-IV, number with at least 30% improvement No difference in improvement between groups (p = 0.23). Impairment Rating Scale improved by 1 point Marginal effect on impairment (p 0.049). No significant difference in improvement between groups in working memory (p 0.62) or inhibit (p 0.75) scales. Participants experiencing intervention emergent adverse events The rate was 7% in the intervention compared to 2% in the control group. There were no serious intervention-related adverse events or discontinuations due to adverse events in either group.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Cognitive training	Nejati, 2021[456] Nejati, 2020[955] ID: NA RCT Single center N = 30 Iran Setting: Specialty care	**Target:** Children with ADHD and no psychiatric comorbidities **Other:** **ADHD presentation:** inattentive : 16.7,hyperactive : 23.3,combined : 60.0 **Diagnosis:** Confirmation by specialist Diagnosis by psychiatrist via DSM-V **Comorbidity:** N/A **Female:** 47 % **Age mean:** 10.74 (1.81) **Minimum age:** 8 **Maximum age:** 14 **Ethnicity:** N/A,Other : Presumably 100% Persian	**Intervention:** Cognitive training with paper and pencil tasks, twelve to fifteen sessions of intervention,each session took about 40− 50 minutes, 3 per week for 4–5 weeks **Control:** No intervention No intervention. **Comparator:** NA **Follow-up:** 1.25 months	ADHD score, SNAP IV There was no significant difference. No effect of group on Persian Attention Registration Test, total time (p = .744) or .Stroop Test, Selective Attention Index (p =.285) or Trail Making Test.
Cognitive training	Nejati, 2022[457] ID: ID NA RCT Multicenter N = 35 Iran Setting: School	**Target:** Children with ADHD **Other:** Blinded parents completed outcome instruments **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM V **Comorbidity:** N/A **Female:** 13.3 % **Age mean:** 6.23 (0.32) **Minimum age:** 6 **Maximum age:** 7 **Ethnicity:** N/A	**Intervention:** Attentive Rehabilitation of Inhibition and Selective Attention program, 6 progressive computerized tasks targeting 3 types of inhibitory control, 10-12 sessions, each 30-45 minutes, for 4-5 weeks **Control:** Attention-matched control Story telling group with opportunity for intervention after study ended **Comparator:** NA **Follow-up:** 1.5 months	Child Behavior Checklist total Significant (p 0.001) intervention effect compared to control. SNAP-IV ADHD scale Significant (p 0.001) intervention effect compared to control. Flanker test (assessing selective attention) scores favor intervention (p = .05) .Go/No-go task (measuring prepotent inhibition) scores favor intervention (p = .001).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Cognitive training	Raghuveer, 2020[489] ID: NA RCT Multicenter N = 70 India Setting: School	**Target:** Children with ADHD who were not on medication; children with learning disabilities, autism spectrum disorders, musculoskeletal impairments, developmental delay, visual or audio impairments were excluded **Other:** Therapists or parents **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV criteria per clinician interview **Comorbidity:** N/A **Female:** % N/A **Age mean:** 4.5 (1.06) **Minimum age:** 3 **Maximum age:** 6 **Ethnicity:** N/A	**Intervention:** Structured games which utilize visual-spatial sketch pad and phonological loop, 4 sessions per week for 5 weeks **Control:** NA **Comparator:** Parent trainingTraining of one or both parents on behavioral controls strategies including praising, organizing the child's possessions (toys, clothing, etc.) and keep a routine schedule. One session of training was providing. Parents received a list of do's and don'ts **Follow-up:** 1.25 months	Intervention group performed significantly better (p <0.05) on the Sequin Form Board Test Time.

Cognitive training	Tamm, 2013[578] ID: ID NA RCT Single center N = 105 US Setting: Specialty care	**Target:** Children with ADHD; exclusion criteria included IQ <85, history of head injury, history of prenatal drug exposure, diagnosis of other neurological conditions, and participating in other non-pharmacological interventions for ADHD **Other:** Parents and teachers provided some outcomes **ADHD presentation:** inattentive : 39,hyperactive,combined : 59,N/A : 2 **Diagnosis:** Confirmation by specialist DSM IV based on interviews **Comorbidity:** N/A **Female:** 32.4 % **Age mean:** 9.3 (1.35) **Minimum age:** 7 **Maximum age:** 15 **Ethnicity:** % Hispanic or Latino : 11.4 % Black/African American : 4.8 % Asian : 4.8 % White : 70.5 % Multiracial : 8.6	**Intervention:** Attention training, bi-weekly sessions of Pay Attention!; materials are designed to train sustained, selective, alternating, and divided attention using visual and auditory stimuli, for 8 weeks **Control:** Wait list Wait list **Comparator:** NA **Follow-up:** 3 months	Behavioral Assessment System for Children, Second Edition (BASC-II), parent rating, Behavioral Symptoms Index No significant differences between groups in BASC II parent or teacher rating scales (externalizing, behavioral symptoms, hyperactivity, attention problems) except for parent reported attention problems where intervention was superior at follow up (p 0.01 CGI (Clinician Global Impairment rating) severity Clinician ratings indicated lower severity and greater improvement for the intervention than the waitlist control group. Swanson, Nolan, and Pelham (SNAP-IV) inattention scale, parent report Intervention group improved more on parent-rated SNAP IV Inattention (p<0.001) and Hyperactivity/Impulsivity (p 0.007) scores. Similar results for clinician rated SNAP IV scores; no difference in teacher rated SNAP IV scores. Behavior Rating Inventory of Executive Function (BRIEF): No significant difference in any teacher-rated scale. Intervention group improved more in all but one parent rated scale (emotional regulation).
Cognitive training	van der Donk, 2015[595] van der Donk, 2020[1138] ID: NA RCT Single center N = 105 Netherlands	**Target:** Children with ADHD, some with comorbid learning disabilities and/or oppositional defiant disorder **Other:** **ADHD presentation:** inattentive : 25.0,combined : 64.0,N/A : not specified-11% **Diagnosis:** Confirmation by specialist	**Intervention:** Working memory and compensatory training (Paying Attention in Class), participants trained individually outside the classroom, 5 times a week, 45 min a day for 5 weeks **Control:** NA **Comparator:** Cognitive trainingCogmed Working Memory	CBCL (Child Behavior Checklist), parent report There were no significant differences between groups for either subscale (attention problems, p=0.593, externalizing problems, p=0.243). No significant differences between groups at follow-up for BRIEF, Behavioral Regulation Index, parent

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
	Setting: School	Parents were also asked to send a copy of the diagnostic psychiatric report of their child to establish the subtype of ADHD and rule out other potential psychiatric problems **Comorbidity:** N/A **Female:** 28.0 % **Age mean:** 9.9 (1.3) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** N/A	Training is a computerized training program consisting of a variety of game format tasks. 5 weeks, five times a week, about 45 min a day **Follow-up:** 6 months	report (p 0.46), BRIEF (Behavioral Regulation Index, teacher report; p 0.217) and Learning efficiency quotient, word reading fluency score.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Cognitive training	Wennberg, 2018[613] ID: NA RCT Multicenter N = 46 Sweden Setting: N/A	**Target:** Children and adolescents with ADHD and parent-reported difficulties with daily time management, despite medication for ADHD; no autism spectrum disorder; no IQ<70 **Other:** Parents of children with ADHD **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist ADHD diagnosis was determined in accordance with DSM-IV criteria by an experienced clinician **Comorbidity:** N/A **Female:** 26 % **Age mean:** Intervention group mean age (11.7) and SD (1.83). Control group mean age (11.1) and SD (1.71). **Minimum age:** 9 **Maximum age:** 15 **Ethnicity:** N/A	**Intervention:** Training in time-processing ability, compensation and remediation plus ADHD medication: compensation were 1.5-hour sessions with 3-4 sessionsin the study period, remediation training sessions 3 times per week with 20 minutes per day assigned outside of sessions, for of 12 weeks **Control:** TAU Standard methods of care alone including ADHD medication **Comparator:** NA **Follow-up:** 8 months	The Kit for assessing time-processing ability (KaTid) assesses time perception, time orientation and time management. The intervention group improved more on total score (p = 0.019), time perception score (p = 0.046), time orientation (p = 0.010), but not time management (p = 0.764).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Cognitive training	Wu, 2023[628] ID: ID NA Clinical trial Single center N = 127 China Setting: Specialty care	**Target:** Children with ADHD; those with serious medical conditions, neuropsychiatric diseases, or on any ADHD medication excluded **Other:** Parents reported outcomes **ADHD presentation:** inattentive_other : Mean ADHD-RS inattention score: intervention 17.3 (4.50), comparator 18.2 (3.79),hyperactive_other : Mean ADHD-RS hyperactivity score: intervention 13.9 (5.30), comparator 13.8 (6.09) **Diagnosis:** Confirmation by specialist DSM IV by child psychiatrists, via K-SADS-PL **Comorbidity:** N/A **Female:** 15 % **Age mean:** 8.35 (1.26) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Asian : 100	**Intervention:** Cognitive training, ADHD-specific executive function training, computer-based batteryof several digital cognitive trainings designed to improve impaired executive functions; training tasks were adapted from N-back task, visual-spatial memory task, Schulte Grid, Go/No-go task, and mental calculation; difficulty is automatically adjusted to match participants' progressive skills; participants were required to complete 48 training sessions within 2 months **Control:** NA **Comparator:** Cognitive trainingCognitive training, general executive function training, a multiple component training targeting cognitive functions which are not closely associated with ADHD, such as processing speed, reasoning, and planning; participants were required to complete 48 t **Follow-up:** 2 months	ADHD-RS total, parent report No significant difference in improvement No significant difference in improvement on Behavior Rating Inventory of Executive Function (BRIEF)—Parent scores or Cambridge Neuropsychological Test Automated Battery (CANTAB) scores

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Combined pharmacological + behavioral	Abikoff, 2004[107] Hechtman, 2004[826]; Klein, 2004[888] ID: N/A RCT Multicenter N = 103 Multiple countries Setting: Mixed	**Target:** Children with ADHD free of conduct and learning disorders, who responded to short-term methylphenidate who had a current or had a previous positive response to methylphenidate **Other:** Parents **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-III-R criteria by child psychologists **Comorbidity:** N/A **Female:** 7 % **Age mean:** 8.2 (0.8) **Minimum age:** 7 **Maximum age:** 9 **Ethnicity:** % Hispanic or Latino : 2 % Black/African American : 13 % White : 84	**Intervention:** Multimodal treatment plus methylphenidate, intensive multimodal psychosocial treatment, methylphenidate maximum dose design up to maximum 50mg/day divided 3 times per day, multimodal treatment modules manual-based delivered once weekly during the first year (requiring 2 clinic visits per week) and once monthly during the second year (requiring 2 clinic visits per month), for 2 years **Control:** Other Methylphenidate alone, no other intervention (except for crisis sessions when required); after the child was stabilized on medication, children and parents were seen once per month by a child psychiatrist; the dose was maintained, precluding side effects **Comparator:** Medication + behavioralAttention control psychological treatment plus methylphenadate **Follow-up:** 24 months	Observation with Classroom Observation Code during academic classes Classroom behaviors yielded no significant group or interaction effects. C-GAS (Children's Global Assessment Scale) There was no significant difference between groups. Mean number of ADHD symptoms at school ADHD diagnosis Significant improvements occurred across all treatments. Social functioning No advantage was found on any measure of social functioning for the combination treatment over methylphenidate alone or methylphenidate plus attention control; significant improvement occurred across all treatments and continued over 2 years. Combination treatment did not facilitate methylphenidate discontinuation.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Combined pharmacological + behavioral	Coelho, 2017[201] ID: NA Crossover trial Unclear/Not reported N = 67 Brazil Setting: Specialty care	**Target:** Participants with ADHD as a primary disorder and no signs of neurodevelopmental delay, epilepsy, genetic syndromes, HIV, hydrocephalus, brain damage, and not currently taking other medications **Other:** **ADHD presentation:** inattentive : 47,combined : 54 **Diagnosis:** Confirmation by specialist DSM-4, clinicians who specializes in diagnosing children and adolescents with neurodevelopmental disorders **Comorbidity:** N/A **Female:** 25 % **Age mean:** 10.2 (2.0) **Minimum age:** 7 **Maximum age:** 14 **Ethnicity:** % White : 100	**Intervention:** CBT plus medication, group cognitive-behavioral therapy prolonged-release methylphenidate20mg, group cognitive-behavioral therapy attended by parents and children, 40 min family sessions, 80 min children sessions; intervention for 20 weeks **Control:** Other Prolonged-release methylphenidate 20 mg for 20 weeks alone **Comparator:** NA **Follow-up:** 5 months	CBCL (Child Behavior Checklist), total problems Cognitive and behavioral outcome measures showed no differences between treatment groups. On social skills, multimodal showed more improvement in frequency indicators on empathy, assertiveness, and self-control subscales and in the difficulty on assertiveness and self-control subscales

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Combined pharmacological + behavioral	David, 2021[216] Babes-Bolyai University, 2018[670] ID: ISRCTN92640175 RCT Single center N = 59 Romania Setting: Specialty care	**Target:** Children diagnosed with ADHD by a child psychiatrist and/or certified psychologist, IQ score of at least 80 on Colored Raven Matrices, and no previous treatment for ADHD received **Other:** **ADHD presentation:** inattentive : 22.0,hyperactive : 15.3,combined : 62.7 **Diagnosis:** Confirmation by specialist Structured Clinical Interview for DSMIV Childhood Diagnoses (KID-SCID) by clinician **Comorbidity:** N/A **Female:** 20.3 % **Age mean:** 8.46 (1.57) **Minimum age:** 6 **Maximum age:** 11 **Ethnicity:**	**Intervention:** CBT and rational emotive behavior therapy plus pharmacological non-stimulant treatment, cognitive-behavioral psychological treatment, 0.8 mg/kg/day and 1.2 mg/kg/day of atomoxetine; weekly psychotherapy session with parents alone (30 min) and with child alone (30 min), for 16 weeks **Control:** Other Pharmacotherapy non-stimulant treatment atomoxetine alone, once daily in the morning, began treatment at 0.5 mg/kg/day with weekly increases to a dose of 0.8 mg/kg/day and 1.2 mg/kg/day, unless side effects were reported by patients (maximum increase 1.8 **Comparator:** NA **Follow-up:** 4 months	ADHD-RS-IV (ADHD-rating scale IV-Home Version Romanian) Clinician rated ADHD diagnosis at posttreatment Combined treatment seems to be superior to the medication alone on parent ratings on ADHD symptoms (p=0.01) but no significant differences between groups regarding ADHD diagnosis at posttreatment were found (p=0.329). No significant differences were found on internalizing problems reported by teachers (effect size−0.32, CI −0.33, 0.97). Appetite decrease Rates were similar. None of the participants reported severe side effects and none discontinued for adverse events. None of the patients reported suicidal ideation. Some participants reported mild side-effects.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Combined pharmacological + behavioral	FIU, 2015[275] ID: NCT02502799 RCT Unclear/Not reported N = 158 US Setting: Specialty care	**Target:** Adolescents with ADHD at elevated risk for substance use disorder; those with substance use disorder or on any psychiatric medications were excluded **Other:** None **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM V **Comorbidity:** Other : high risk for SUD **Female:** 25.9 % **Age mean:** 13.94 (1.38) **Minimum age:** 12 **Maximum age:** 16 **Ethnicity:** % Hispanic or Latino % Black/African American : 8.9 % American Indian or Alaska Native % Asian : 0.6 % Native Hawaiian or Pacific Islander : 0 % White : 78.5 % Multiracial : 9.5	**Intervention:** Brief early intervention plus parent training and adolescent cognitive behavioral therapy plus methylphenidate; designed to strengthen problem-solving, resisting peer pressure, and coping with emotions, 5 individual sessions received by adolescents; parents joined portions of 3 sessions, then participated in behavioral parent training and adolescents participated in cognitive behavioral therapy to reduce substance use **Control:** No intervention Monitoring only, no further intervention **Comparator:** NA **Follow-up:** 6 months	Disruptive Behavior, Deviant Behavior Scale, youth self-report Higher score in the intervention group, significance unclear. Functional Impairment self report Higher score in the intervention group, significance unclear. Adverse events Hospitalizations unrelated to the intervention. No all cause mortality across groups.

Combined pharmacological + behavioral	Jensen, 2007[343] No author, 2011[669]; Abikoff, 2001[649]; Acosta, 2016[651]; Arnold, 1997[664]; Arnold, 1997[665]; Arnold, 2004[666]; Arnold, 2003[667]; Babinski, 2019[671]; Brinkman, 2018[695]; Carey, 2000[700]; Conners, 2001[724] ID: NCT00000388 (MTA) RCT Multicenter N = 579 US Setting: N/A	**Target:** Children with ADHD combined type **Other:** **ADHD presentation:** combined : 87.5,N/A : comm control 79.5 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** **Female:** 21 % **Age mean:** 11.8 (0.95) **Minimum age:** 11 **Maximum age:** 13 **Ethnicity:** % Hispanic or Latino : 36 % Black/African American : 20.2 % White : 61.7 Other : 10.7%	**Intervention:** Multimodal Treatment Study of Children With ADHD (MTA), intensive multicomponent behavior therapy consisting of medication management and behavior modification, for 14 months, afterwards the families were free to choose their own treatment **Control:** TAU Usual community care **Comparator:** NA **Follow-up:** 36 months	Oppositional defiant disorder symptoms, SNAP parent and teacher average rating Ratings were similar across groups. SWAN Both groups improved from baseline. CIS (Columbia Impairment Scale) No significant moderator effects of comorbidity were found in the treatment comorbidity group interactions (p 0.21). Wechsler Individual Achievement Test (WIAT) Both groups improved from baseline. None of the treatment groups differed significantly on the social skills rating system (SSRS). After 14 months, children treated with methylphenidate had gained less height and less weight (-1.23 cm per year and -2.48 kg per year) than untreated children[669]; Followup into young adulthood (25 yo) within naturalistic subgroups of ADHD cases, ext Children with ADHD and manic symptoms respond robustly to methylphenidate during the first month of treatment and are not more likely to have an adverse response to methylphenidate.[785]
Combined pharmacological +	Karakaya, 2019[357] ID: NA RCT Single center N = 41 Turkey Setting: Specialty care	**Target:** Adolescents receiving treatment ADHD, on medication, residing in the city center **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist diagnosed prior to study; were already receiving medication tx through clinic **Comorbidity:** N/A	**Intervention:** Solution-focused approach comprised of 6 sessions, each 45-60 minutes, individually and face-to-face, in addition to ADHD medication treatment with psychostimulants and clinic follow-up, 1 session per week for 6 weeks **Control:** Other	General Self-Efficacy Scale (GSE) evaluates the extent to which individuals perceive themselves as adequate in coping with difficulties. Intervention group score was higher at follow up (p<0.001).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
		Female: 19.5 % **Age mean:** 13.2 (1.25) **Minimum age:** 12 **Maximum age:** 18 **Ethnicity:** N/A	No intervention, but ADHD medication treatment with psychostimulants as usual **Comparator:** NA **Follow-up:** 3 months	

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Combined pharmacological + behavioral	Perez-Alvarez, 2009[474] ID: NA RCT Single center N = 96 Spain Setting: Specialty care	**Target:** Children and adolescents with Swanson, Nolan, and Pelham Questionnaire-IV teacher rating scores of at least 2.5 and parent ratings of at least 1.8, planning dysfunction according to planning, attention, successive and simultaneous scales; no medical and psychiatric comorbidities **Other:** Parents and teachers provided some outcome data **ADHD presentation:** inattentive : 79,hyperactive : 0,combined : 21 **Diagnosis:** Confirmation by specialist ADHD diagnostic interview schedule for children module was completed face-to-face with the child ' s principal caregiver by trained research interviewers. **Comorbidity:** N/A **Female:** 20 % **Age mean:** ADHD-Combined 9 (2), ADHD-Inattentive 12 (3) **Minimum age:** 7 **Maximum age:** 15 **Ethnicity:** N/A	**Intervention:** Humanistic intervention plus methylphenidate; extended release methylphenidate hydrochlorideadministered at an optimal dose plus humanistic psychological intervention conducted as 24 sessions, 1 every 15 days, for 12 months **Control:** Other Extended release methylphenidate hydrochloride alone **Comparator:** NA **Follow-up:** 12 months	Swanson, Nolan, and Pelham scale 18 (SNAP-IV-18), number in remission (score <= 1.0) Combined intervention scored better than humanistic intervention alone and slightly better than medication alone. PASS (planning, attention, successive, and simultaneous processes) cognitive assessment: only significant difference at follow-up was for planning scale; intervention group improved more (p <.05).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Combined pharmacological + behavioral	Riggs, 2011[497] University of Cinncinnati, 2006[1129] ID: NCT00264797 RCT Multicenter N = 303 US Setting: Specialty care	**Target:** Adolescents meeting DSM-IV criteria for current ADHD and at least one non-tobacco substance user disorder; no current or past psychotic disorder, bipolar disorder, suicide risk, opiate dependence, methamphetamine abuse or dependence, cardiac illness or serious medical illness, pregnancy, past month use of psychotropic medications or participation in other substance or mental health treatment **Other:** **ADHD presentation:** inattentive : 28.1,hyperactive : 2.6,combined : 68.6 **Diagnosis:** Confirmation by specialist DSM-IV per Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiologic Version (K-SADS-E) **Comorbidity:** Other : SUD **Female:** 21.1 % **Age mean:** 16.5 (1.3) **Minimum age:** 13 **Maximum age:** 18 **Ethnicity:** % Hispanic or Latino : 15.2 % Black/African American : 23.2 % White : 61.7	**Intervention:** CBT plus OROS, cognitive behavioral therapy, osmotic-release methylphenidate 72mg once daily and manual-standardized, individual CBT using motivational enhancement approaches, for 16 weeks **Control:** Other Cognitive behavioral therapy plus matching placebo, manual-standardized, individual CBT using motivational enhancement approaches **Comparator:** NA **Follow-up:** 4 months	Treatment responders based on CGI-I (score of 1 or 2) Rates of treatment response were not significantly different (P=0.418) between treatment (23.4%) and control (19.1%). ADHD-RS There were no group differences on reduction in ADHD-RS scores. Substance use in the past 28 days: there was no between-group difference (p 0.321). Adolescents treated with OROS-MPH + CBT had significantly more negative urine drug screens compared to participants treated with placebo + CBT (p 0.05). Treatment-emergent study-related adverse events Participants treated with OROS-MPH reported more treatment-emergent study-related AEs than control group (p=0.02). No statistically significant differences between groups on self-reported medication abuse (taking more medication than prescribed, 4.8% vs 2.8%, p>0.05) or diversion (selling medication to others, 2.1% vs 1.4%, p>0.05; letting others take your medication,

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Combined pharmacological + behavioral	Sprich, 2016[560] Massachusetts General Hospital, 2009[911] ID: NCT01019252 Crossover trial Single center N = 46 US Setting: Specialty care	**Target:** Adolescents with ADHD and no change in dose for at least 2 months of medication without severe comorbid disorders, active suicidality, conduct disorder, active substance abuse or dependence, organic mental disorder, mental retardation, pervasive developmental disorder, or prior CBT for ADHD **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Kiddie-Schedule for Affective Disorders and Schizophrenia-Epidemiologic Version No **Comorbidity:** N/A **Female:** 21.7 % **Age mean:** Intervention 15.17 (1.01), control 15.09 (1.11) **Minimum age:** 14 **Maximum age:** 18 **Ethnicity:** % Black/African American : 2.17 % Asian : 0 % Native Hawaiian or Pacific Islander : 2.17 % White : 93.5	**Intervention:** CBT plus medication, 7 modules of cognitive behavioral therapy over 12 sessions; 10 were one-on-one, two also included parent; all patients were also on an FDA-approved medication; average duration of 17 weeks **Control:** Wait list Wait list received no psychosocial treatment for 4 months but continued to receive FDA-approved medication **Comparator:** NA **Follow-up:** 4 months	CGI (Clinical Global Impression) score Favored intervention ($p < .01$). ADHD-RS (ADHD Rating Score) total, parent report Both parent reported ($p < .01$) and patient reported ADHD RS ($p < .01$) favored intervention group. No study related serious adverse events.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Combined pharmacological + behavioral	Tutty, 2003[589] ID: ID NA RCT Single center N = 100 US Setting: Specialty care	**Target:** Children newly diagnosed with ADHD initiating stimulant treatment in primary care; those with conduct disorders, oppositional defiant disorder, Tourette syndrome, affective disorders, active alcohol or other substance abuse during the previous 90 days, or a chronic medical illness were excluded **Other:** Parents received education and provided some outcomes **ADHD presentation:** inattentive : 41,combined : 59 **Diagnosis:** Confirmation by specialist DSM-IV by staff pediatrician **Comorbidity:** N/A **Female:** 25 % **Age mean:** 9.2 (1.25) **Minimum age:** 5 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 1 % Black/African American : 6 % Asian : 6 % White : 87	**Intervention:** Behavioral and social skills class plus stimulant medication, class for children and their parents, 1 session per week for 8 weeks **Control:** TAU All children were on stimulant medication as selected by their healthcare provider **Comparator:** NA **Follow-up:** 6 months	ADHD RS, parent report Intervention group improved more (p 0.00). No significant between-group differences in psychostimulant use (52.94% vs 39.02%; p 0.184).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Combined pharmacological + behavioral	van der Oord, 2007[597] ID: ID NA RCT Multicenter N = 50 Netherlands Setting: Specialty care	**Target:** Children with ADHD with no prior use of methylphenidate **Other:** Parents & teachers received training and provided outcomes **ADHD presentation:** inattentive : 32,hyperactive : 6,combined : 62 **Diagnosis:** Confirmation by specialist DSM IV per Diagnostic Interview Schedule for children (DISC-IV) **Comorbidity:** N/A **Female:** 10 % **Age mean:** 9.9 (1.2) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** % Black/African American : 2 % White : 89 % Multiracial : 9	**Intervention:** Multimodal child and parent behavioral therapy and teacher behavioral training plus methylphenidate, therapy integrated family-based and school-based interventions with cognitive behavior therapy for the child; parent intervention was weekly sessions of 90 min group training based on Barkley's training for defiant children; teacher training was a 2-hour workshop where psycho-education on ADHD, structuring the classroom environment, implementing contingency management in the classroom, and a daily report card system, for 10 weeks **Control:** Other Methylphenidate only for 10 weeks **Comparator:** NA **Follow-up:** 2.5 months	Disruptive Behavior Disorder Rating Scale, ADHD symptom scale, parent report Groups did not differ in improvement on parent or teacher report. Groups did not differ in improvement in parent or teacher reported social skills (SSRS) or child reported anxiety (State Trait Anxiety Inventory for Children).

FDA-approved pharmacological	Abikoff, 2007[109] Greenhill, 2006[800]; Ghuman, 2007[793]; Swanson, 2006[1105]; Wigal, 2006[1175]; Kollins, 2006[889] ID: ID NA RCT Multicenter N = 114 US Setting: School	**Target:** Children with ADHD and an impairment scale score of less than or equal to 55 on the Children Global Assessment Scale who had not responded to 10 weeks of parent training; no prior use of stimulants for > 5 weeks, major psychological or medical co-morbidities **Other:** Parents and teachers **ADHD presentation:** inattentive : 0,hyperactive : 29.51,combined : 70.49 **Diagnosis:** Confirmation by specialist DSM-IV, psychiatrists interview **Comorbidity:** N/A **Female:** 19.67 % **Age mean:** 4.39 (0.72) **Minimum age:** 3 **Maximum age:** 5.5 **Ethnicity:** % Hispanic or Latino : 19.67 % Black/African American : 19.67 % White : 59.02	**Intervention:** Methylphenidate (immediate-release), 1.25, 2.5, 5, or 7.5 mg 3 times per day for 4 weeks **Control:** Placebo Placebo treatment, 3 times per day for 4 weeks **Comparator:** NA **Follow-up:** 1 month	CGI-S (Clinical Global Impression-Severity) Proportion of excellent responders Scale scores were significantly better for children in the treatment group compared to the placebo group (p < 0.0001) but only 21% on best-dose MPH and 13% on placebo achieved MTA-defined categorical criterion for remission set for school-age children wit SWAN (Strengths and Weaknesses of ADHD-Symptoms and Normal Behaviors), parent There was no significant difference between treatment group and placebo group for parent or teacher report Social Skills Rating System (Parent) (SSRS-P), measures social function Treatment effect not statistically significant. There was no significant difference in parental stress across the treatment and placebo groups. Growth rates During methylphenidate treatment, annual growth rates for completers were 20.3% less than expected for height and 55.2% less for weight There were eight serious adverse events, but only one, a possible seizure, was thought to be related to medication. There were no episodes of mania, hypomania, depression, or suicidality
FDA-approved	Abikoff, 2009[108] NA ID: ID NA Crossover trial Single center	**Target:** Medication naive children with ADHD who had problems with organization, time management, and planning **Other:** Parents and teachers provided outcome data	**Intervention:** Methylphenidate OROS (osmotic-release oral system), 48.3 mg (range 18-54 mg) daily for 2 weeks, 4 weeks total **Control:** Placebo	SNAP IV (Swanson, Nolan, and Pelham, Version IV) total score, parent rating Mean SNAP IV parent rating , total score, and mean SNAP IV teacher rating, total score, were significantly

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
	N = 19 US Setting: Specialty care	**ADHD presentation:** inattentive : 58,hyperactive : 0,combined : 42 **Diagnosis:** Confirmation by specialist DSM IV criteria based on Diagnostic Interview Schedule for Children IV (DISC-IV)-Parent version **Comorbidity:** Other : impaired organizational skills per Children's Organizational Skills Scale **Female:** 21 % **Age mean:** 10.05 (1.62) **Minimum age:** 8 **Maximum age:** 13 **Ethnicity:** N/A	Placebo **Comparator:** NA **Follow-up:** 2 months	lower in intervention group at follow-up (p < .005 for both outcomes). Lower is better. Mean Children's Organizational Skills Scale (COSS) total score, teacher rating, was significantly higher at follow-up for the intervention group (p < .01). Mean Children's Organizational Skills Scale (COSS) total score, parent rating, was also significantly higher at follow-up for the intervention group (p < .05). Higher is better.

FDA-approved pharmacological	Allen, 2005[118] ID: NA RCT Multicenter N = 148 US Setting: Mixed	**Target:** Children with ADHD according to DSM-IV and concurrent Tourette syndrome or chronic motor tic disorder, scores on the Attention Deficit/Hyperactivity Disorder Rating Scale-IV-Parent Version: Investigator Administered and Scored at least 1.5 standard deviations above the age and sex norm, have scores of at least 5 on the Yale Global Tic Severity Scale; no Children's Yale–Brown Obsessive Compulsive Scale total score larger or equal to 15, have a Children's Depression Rating Scale–Revised total score of larger than 40, history of bipolar disorder or psychosis, seizure disorder, or current use of any psychotropic medication other than study drug **Other:** **ADHD presentation:** inattentive : 35.8,hyperactive : 3.4,combined : 60.8 **Diagnosis:** Confirmation by specialist Schedule for Affective Disorders and Schizophrenia for School-age Children–Present and Lifetime Version16 (K-SADSPL) **Comorbidity:** Tic disorder **Female:** 11.5 % **Age mean:** 11.2 (2.5) **Minimum age:** 7 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 6.1 % Black/African American : 4.7 % Asian : 0.7 % White : 87.8 Other : Other: 4/148 (2.7%)	**Intervention:** Atomoxetine 0.5 to 1.5 mg/kg/day administered daily as a divided dose in the morning and late afternoon for approximately 18 weeks **Control:** Placebo Matching placebo 2 times a day for 18 weeks **Comparator:** NA **Follow-up:** 5 months	ADHD-RS Total Significant treatment effects were obtained on all ADHD measures. Reduction in Yale Global Tic Severity Scale total score between placebo and atomoxetine is not statistically significant (p = 0.063). Decreased appetite Decrease appetite was reported in 15.9% of intervention and 2.8% of placebo participants. Discontinuations due to an adverse were 2 in the atomoxetine group (headache, vomiting) and 1 in the placebo group (upper abdominal pain); none was evaluated as serious.
FDA-approved	Ashkenasi, 2011[127] ID: N/A RCT Single center	**Target:** Children who met the DSM IV Edition criteria for attention deficit hyperactivity disorder (any subtype) and who demonstrated difficulty sleeping; no previous intolerance, adverse response,	**Intervention:** Methylphenidate transdermal patch sequence of 9 hours, 10 hours, 11 hours, and 12hours patch wear times maintained Monday through	Connor's Global Impression-Parent There was no significant difference between groups (p=0.114).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
	N = 26 US Setting: Other	or allergy to methylphenidate or skin sensitivity to the methylphenidate transdermal system, and those with severe comorbid psychiatric disorders **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 27 % **Age mean:** 9.8 (1.8), 9.6 (1.8), 7.5, 10.3 (1.8) across groups **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** N/A	Thursday of each week, alternating wear times across 4 consecutive weeks with standard 9-hour wear time schedule Friday through Sunday, for duration of 4 weeks **Control:** NA **Comparator:** MedicationMethylphenidate transdermal 12 hours, 11 hours, 10 hours, 9 hours for 4 weeks, patch wear times maintained Monday through Thursday of each week, alternating wear times across 4 consecutive weeks with standard 9-hour wear time schedule Friday through Sunda **Follow-up:** 1 month	ADHD-RS-IV (Attention Deficit Hyperactivity Disorder Rating Scale-IV) There was no significant difference between groups (p=0.466). No significant effects of patch wear time on sleep latency (p=0.558) or total sleep time (p=0.382) were evident. No adverse event related treatment discontinuations were evident and no individuals reported a reaction greater than dark red and itchy.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Banaschewski, 2013[131] Coghill, 2013 [720]; Coghill, 2014[721]; Coghill, 2021[723]; Shire, 2008[1047]; Soutullo, 2013[1084]; Setyawan, 2015[1034]; Coghill, 2014[722] ID: NCT00763971 RCT Multicenter N = 336 Multiple countries Setting: Mixed	**Target:** Children and adolescents who meet DSM-IV criteria for ADHD diagnosis, with baseline ADHD-Rating Scale-IV total score of 28 or higher; no failure to respond to a previous course of OROS-MPH, no presence of a comorbid psychiatric diagnosis with significant symptoms (not including oppositional defiant disorder), effective control of ADHD symptoms with medications of acceptable tolerability **Other:** Parents reported some outcomes **ADHD presentation:** inattentive : 15.96,hyperactive : 3.01,combined : 80.72 **Diagnosis:** Confirmation by specialist DSM-IV-TR **Comorbidity:** N/A **Female:** 19.3 % **Age mean:** LDX 10.9 (2.9), placebo 11.0 (2.8), OROS-MPH 10.9 (2.6) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 1.20 % Black/African American : 0.30 % Asian : 0.30 % White : 97.0 Other : 2.41	**Intervention:** Lisdexamfetamine dimesylate once daily (30, 50, or 70 mg/day) for 7 weeks **Control:** Placebo Placebo pill identical to study drugs given daily at 07:00 to participants **Comparator:** MedicationOsmotic-release oral system methylphenidate (OROS) once daily, 18, 36, or 54 mg/day dose **Follow-up:** 2 months	CPRS-R (Conners Parent Rating Scale-Revised) change The intervention and comparator groups had significantly more improvement than the placebo group (p<0.001). ADHD-RS-IV change The intervention and comparator groups had significantly more improvement than control group (p<0.001). Weiss Functional Impairment Rating Scale-Parent Report (WFIRS-P) The intervention and comparator groups had significantly more improvement than control group (p<0.001). Decreased appetite Active treatments reported more appetite suppression than placebo, no difference between treatment medications.[720] Participants experiencing treatment emergent adverse events The rate was 72.1% for LDX, 64.9% for OROS-MPH, and 57.3% for placebo.[720] The proportion of patients who reported serious treatment emergent adverse events were low across all groups.[720]

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Bangs, 2007[132] ID: N/A RCT Multicenter N = 142 US Setting: N/A	**Target:** Adolescents who met the criteria for both ADHD and major depressive disorder per DSM–IV; no beginning structured psychotherapy for ADHD and/or depression less than 1 month before trial entry **Other:** **ADHD presentation:** inattentive : 57,combined : 43 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** Mood disorder **Female:** 27 % **Age mean:** ATX 14.6 (1.8), placebo 14.2 (1.5) **Minimum age:** 12 **Maximum age:** 18 **Ethnicity:** N/A	**Intervention:** Atomoxetine 1.2-1.8 mg/kg per day for 9 weeks **Control:** Placebo Placebo once daily **Comparator:** NA **Follow-up:** 2 months	ADHD-RS-IV-Parent: Inv scale Mean decrease was significantly greater in the intervention group (p=0.001). There were no significant differences between treatment groups in Children's Depression Rating Scale–Revised total scores at any time point. Decreased appetite Nausea and decreased appetite occurred significantly more often during the acute phase in the ATX treatment group compared with the placebo group. One serious adverse event, worsening of depression, occurred during the acute treatment phase in the placebo group and led to the patient discontinuing the study due to lack of efficacy.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
FDA-approved pharmacological	Bangs, 2008[133] ID: ID NA RCT Multicenter N = 226 Multiple countries Setting: Specialty care	**Target:** Children with ADHD and oppositional defiance disorder; those with serious psychiatric disorders or medical conditions were excluded **Other:** Parents reported some outcomes **ADHD presentation:** inattentive : 9.7,hyperactive : 5.8,combined : 84.5 **Diagnosis:** Confirmation by specialist DSM IV by an investigator's clinical assessment via structured interview (Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version) **Comorbidity:** ODD : 100% ODD **Female:** 6.6 % **Age mean:** 9.6 (1.9) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % White : 95.2	**Intervention:** Atomoxetine, 1.2 mg/kg per day for 8 weeks **Control:** Placebo Placebo daily for 8 weeks **Comparator:** NA **Follow-up:** 2 months	CGI-S (Clinical Global Impression - Severity) Atomoxetine group improved more on CGI-I (p 0.037) and CGI-Severity (p 0.013). ADHD impact module (child) Mean improvement in SNAP-IV ODD total score was not significantly different between groups (p 0.252). Mean improvement in SNAP-IV Combined, Inattentive, and Hyperactivity score was significantly greater in the intervention groups (p < 0.001, p < 0.001, a Decreased appetite Significantly more atom-oxetine patients reported decreased appetite (p < .001). Nausea and fatigue were significantly higher for atomoxetine than for placebo (p= 0.033 and p = 0.021, respectively).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Bedard, 2015[137] Mount Sinai, 2005[847] ID: NCT00183391 Crossover trial Unclear/Not reported N = 102 US Setting: Other	**Target:** Youth with ADHD as the primary diagnosis; no IQ below 75, non-English speaking parent or child, neurological dysfunction, systemic medical illness, uncorrected sensory impairments, and history of psychosis or bipolar disorder, comorbid conditions did not require medication treatment; nonresponders to atomoxetine and methylphenidate and must not have experienced disabling adverse effects with either medication **Other:** **ADHD presentation:** inattentive : 37,hyperactive : 3,combined : 60 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 25 % **Age mean:** 10.5 (2.7) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 20 % Black/African American : 31 % Asian : 1 % White : 36 % Multiracial : 12	**Intervention:** Atomoxetine 0.5 mg/kg, 1.0 mg/kg, 1.4 mg/kg, 1.8 mg/kg, administered each morning for 4-6 weeks **Control:** NA **Comparator:** MedicationMethylphenidate, 2 capsules of OROS MPH administered each morning, 18 mg, 36 mg, 54 mg, 72 mg **Follow-up:** 3.5 months	ADHD-RS Both medications produced significant improvement (p<0.001). For commission errors, there were no significant main effects of Drug or Time, and the Drug by Time was not significant. For omission errors, there was a significant Drug by Time interaction and a significant main effect of Time with no main effect of Drug, significant reduction in omission errors following MPH (p 0.001) but not ATX (p 0.69). There was a significant Drug by Time interaction such that youth treated with MPH had a greater speeding of RT than those treated with ATX. There was no main effect of Drug, but there was a main effect of Time. A post hoc paired t-test showed no significant change in RT for ATX (p = .99). There were main effects for Time and Drug on reaction time variability. There was also a significant Drug by Time interaction. MPH had a significantly larger impact than ATX.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Biederman, 2007[144] Childress, 2014[713]; New River Pharmaceuticals[986] ID: NCT00556296 RCT Multicenter N = 290 US Setting: N/A	**Target:** Children with inadequate treatment or no previous treatment of ADHD and an ADHD Rating Scale version IV score greater than or equal to 28 **Other:** **ADHD presentation:** hyperactive : 4,combined : 96 **Diagnosis:** No Unspecified interviewer **Comorbidity:** N/A **Female:** 30.7 % **Age mean:** 9 (1.8) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 17 % Black/African American : 24 % American Indian or Alaska Native : 0.7 % Asian : 1 % Native Hawaiian or Pacific Islander : 0.3 % White : 53	**Intervention:** Lisdexamfetamine dimesylate 70mg orally once per day for 4 weeks **Control:** Placebo Placebo **Comparator:** MedicationLisdexamfetamine dimesylate 30mg orally once per day for 4 weeks **Follow-up:** 1 month	Clinical Global Impression (CGI) scale Ratings were either very much improved or much improved in over 70% of patients in the active treatment groups, compared with 18% in the placebo group. ADHD Rating Scale The 70mg group had the greatest symptom improvement compared to the placebo (p<0.001). Decreased appetite Rates were 49.3% in the 70mg, 36.6% in the 30mg, 31.1% in the 50mg, and 4.2% in the placebo group (p<0.05). Number of participants that experienced any adverse events Rates were 83.6% in the 70mg, 67.6% in the 50mg, 71.8% in the 30mg, and 47.2% in the placebo group. Statistically significant different adverse events in treatment groups vs. placebo: decreased appetite, insomnia, irritability, vomiting, weight loss, dry mouth.

FDA-approved pharmacological	Biederman, 2008[145] Shire, 2003[1053] ID: NCT00152009 RCT Multicenter N = 345 US Setting: N/A	**Target:** Children with ADHD; no current, uncontrolled, comorbid psychiatric diagnosis (except oppositional defiant disorder) with significant symptoms, or when other symptomatic manifestations would contraindicate guanfacine extended release treatment or confound efficacy or safety assessments; patients who weighed<55 lb or were morbidly overweight or obese, pregnant, lactating, or hypertensive excluded; no QTc interval of >440 milliseconds, history of seizure during the past 2 years, tic disorder; family history of Tourette's disorder, positive urine drug screen, abnormal thyroid function not adequately treated, any cardiac condition or family history of cardiac condition , investigational drug use within 28 days, BP or heart rate medications, or were taking other medications that have central nervous system effects or affect performance **Other:** **ADHD presentation:** inattentive : 26.1,hyperactive : 2,combined : 71.9 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 25.5 % **Age mean:** 10.5 (6.0–17.0) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 9.9 % Black/African American : 13.3 % American Indian or Alaska Native : 0.3 % Asian : 0.6 % White : 70.1 Other : 5.8	**Intervention:** Guanfacine extended release 4 mg/day for 8 weeks **Control:** Placebo Matching placebo tablet **Comparator:** MedicationGuanfacine extended release 2mg/day group, began dosing at 1 mg/day, escalated weekly in 1-mg increments **Follow-up:** 2 months	CGI-I (Clinical Global Impression of Improvement) significant improvement Significant improvement in CGI-I scores at end point was shown in 25.64%, 55.95%, 50.00%, and 55.56% of patients in the placebo and GXR 2-mg, 3-mg, and 4-mg groups. ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale IV) total score Least-squares mean changes from baseline to the end point in Attention-Deficit/Hyperactivity Disorder Rating Scale IV total scores were significant in all groups of children taking guanfacine extended release compared with the placebo group. Appetite decreased The rate was 5.8% in the intervention, 2.3% in the placebo, 5.7% in the 2mg, and 9.3% in the 3mg group. Participants experiencing treatment emergent adverse events The rate as 87.2% in the intervention, 64% in the placebo, 77.0% in the 2mg and 88.4% in the 3mg group. Most of the commonly reported adverse events were mild or moderate in intensity. Severe treatment emergent adverse events were experienced by 24 patients, all of whom received GXR (sedation (n=7), somnolence (n=6), fatigue (n=4), headache (n=2), vomiting

FDA-approved pharmacological	Block, 2009[154] ID: N/A RCT Single center N = 288 US Setting: Primary Care	**Target:** Children who met DSM-IV-TR criteria for ADHD **Other:** **ADHD presentation:** inattentive_other : 16-26 across arms,hyperactive_other : 1-3% across arms,combined_other : 68-76% across arms **Diagnosis:** Confirmation by specialist clinical interview **Comorbidity:** N/A **Female:** 30 % **Age mean:** Across arms 8.8 (1.7), 9.1 (1.6), 8.9 (1.7) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** Other : 62-70% across arms	**Intervention:** Atomoxetine 1.25mg/kg/day each morning for 6 weeks **Control:** Placebo Placebo in the morning or evening for 6 weeks **Comparator:** MedicationEvening dosing, 1.26mg/kg/day of atomoxetine for 6 weeks **Follow-up:** 1.5 months	Daily Parent Rating of Evening and Morning Behavior–Revised (DPREMB-R) AM atomoxetine and PM atomoxetine showed significantly greater efficacy overall compared with placebo (p=0.048, p=0.004). CGI-ADHD-S Response rate CGI-ADHD-S decrease of 2 or more Morning dosing produced a 49% response rate compared with 32% for evening dosing and 22% for placebo (p<0.001). ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale IV)–Parent Version, investigator administered and scored Response rate (at least 25% decrease on ADHD-RS total score) Significantly greater improvement on the ADHD RS Total score (effect size 0.7) was observed for AM atomoxetine compared with placebo; evening-dosed atomoxetine also significantly decreased core ADHD symptoms relative to placebo; AM vs PM atomoxetine was e Significantly greater improvement on the CGIP-Evening Total (single-item rating of the clinician's assessment of the severity of ADHD symptoms) score (effect size 0.6) was observed for AM atomoxetine compared with placebo. Decreased appetite Decreased appetite were reported more often with AM atomoxetine than with placebo. Participants reporting at least 1 adverse event

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
				The rate was higher with AM atomoxetine than with PM atomoxetine or placebo (74.0%, 48.9%, 43.5%; p<0.001 for AM vs PM; p<0.001 for AM vs placebo; P = .552 for PM vs placebo). Abdominal pain, vomiting, somnolence, nausea, and stomach discomfort were reported more often with AM atomoxetine than with placebo; vomiting was reported more often with PM atomoxetine than with placebo; no significant differences between AM and PM atomo

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Brams, 2018[161] Shire, 2015[1051] ID: NCT02466425 RCT Multicenter N = 264 US Setting: Specialty care	**Target:** Children with ADHD **Other:** Clinician reported outcomes **ADHD presentation:** inattentive : 23.2,hyperactive : 1.1,combined : 75.7 **Diagnosis:** Confirmation by specialist DSM IV plus ADHD Rating Scale IV (ADHD-RS-IV) total scores >=28 **Comorbidity:** N/A **Female:** 38 % **Age mean:** 12.5 (3.24) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Black/African American : 28.5 % Asian : 0.3 % White : 61.2 % Multiracial : 8.0	**Intervention:** Amphetamine, SHP465 mixed amphetamine salts (12.5 or 25 mg) for 4 weeks **Control:** Placebo Placebo **Comparator:** NA **Follow-up:** 1 month	CGI-I (Clinical Global Impressions-Improvement) Intervention group improved significantly more than placebo group (p < 0.001). ADHD-RS-IV change Change from baseline significantly favored intervention over placebo (p<0.001). Appetite decrease Significantly more participants in the intervention group experienced decreased appetite than control group participants. Participants with any adverse event The rate was 67% for intervention and 47% for control. The frequency of treatment-emergent adverse events leading to discontinuation was greater with the intervention treatment than with placebo.

FDA-approved pharmacological	Buitelaar, 2007[164] Trzepacz, 2011[1122]; Michelson, 2004[926] ID: N/A RCT Multicenter N = 163 Multiple countries Setting: Other	**Target:** Children with ADHD and without bipolar disorder or psychotic illness or unstable medical illness or conditions requiring ongoing administration of a psychoactive medication (other than atomoxetine) **Other:** **ADHD presentation:** inattentive : 22.9,hyperactive : 4.5,combined : 72.6 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 10.6 % **Age mean:** 10.6 (2.3) **Minimum age:** 6 **Maximum age:** 15 **Ethnicity:** N/A	**Intervention:** Atomoxetine 0.5-1.8 mg/kg/d for 6 months **Control:** Placebo Placebo-controlled **Comparator:** NA **Follow-up:** 12 months	CGI-S (Clinical Global Impressions–Severity of Illness) change Statistically significant difference favoring atomoxetine (p 0.003). ADHD-RS-IV Total Score Relapse rate Atomoxetine was superior to placebo in maintaining symptom response (p 0.001). The relapse rate was 2.5% for atomoxetine and 12.2% for placebo. CHQ (Child Health Questionnaire) Psychosocial Summary Score No difference between groups. Effects on sexual development: Tanner stage: No statistically significant differences were observed between treatment groups either in sexual development (mean time, in days, to the first Tanner stage change, p=0.33) or in the duration of treatment exposure (p= 0.90).[1122] Weight increase in weight percentile Both groups showed an increase in weight percentile, but the increase was greater in the placebo group (p 0.001). Participants reporting at least 1 new or worsened adverse event The rate was 65.6% (intervention) vs 53.7% (placebo). Two adverse events were reported in more than 5% of subjects in both treatment groups, headache (atomoxetine, 8 [10.1%]; placebo, 7 [8.6%]) and nasopharyngitis (atomoxetine, 6 [7.6%]; placebo, 7 [8.6%]); all other adverse events were reported by <= 5% of

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
FDA-approved pharmacological	Cetin, 2015[175] ID: N/A RCT Single center N = 145 Turkey Setting: Specialty care	**Target:** Patients with ADHD without any comorbid psychopathologies **Other:** **ADHD presentation:** inattentive : 12.6,hyperactive : 0,combined : 87.4 **Diagnosis:** Confirmation by specialist DSM-IV-TR by child psychiatrists **Comorbidity:** N/A **Female:** 18.4 % **Age mean:** 9.47 (2.32) **Minimum age:** 7 **Maximum age:** 16 **Ethnicity:** Other : Ethnicity, Turkish patients but not sure of race	**Intervention:** Atomoxetine, mean dose 1.14±0.13 mg/kg/day, for 6 months **Control:** NA **Comparator:** MedicationOsmotic release oral system methylphenidate (OROS), mean dose of 0.73±0.22 mg/kg/day for 10 weeks **Follow-up:** 6 months	Conners Comprehensive Behavior Rating Scale-Behavior Problems, teacher There was no significant difference between groups (p=0.720). Weight loss The rate was 1.6% in both groups. Adverse effects The rate was 31.1% in the OROS-MPH and 27.1% in the ATX group. The most commonly encountered adverse effect was anorexia in both groups, and it was seen in 19.6% of the patients in the OROS- MPH group and 13.5% of the patients in the ATX group.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
FDA-approved pharmacological	Childress, 2009[195] ID: ID NA RCT Multicenter N = 253 US Setting: Specialty care	**Target:** Children with ADHD, drug naıve or not treated with any methylphenidate-related medication in the month prior to the study; those with serious psychological disorders were excluded **Other:** Parents and teachers provided outcome information **ADHD presentation:** inattentive : 21.7,hyperactive : 2.8,combined : 73.9 **Diagnosis:** Confirmation by specialist DSM-IV-TR based on a psychiatric examination and K-SADS PL **Comorbidity:** N/A **Female:** 35.6 % **Age mean:** 8.7 (1.84) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Black/African American % Asian : 0.8 % White : 57.7 Other : Other 12.6%	**Intervention:** Dexmethylphenidate hydrochloride extended-release (d-MPH XR; Focalin XR) methylphenidate, 30 mg extended release daily for 5 weeks **Control:** Placebo Placebo capsule daily **Comparator:** MedicationDexmethylphenidate hydrochloride extended-release (d-MPH XR; Focalin XR), 10 mg extended release daily, for 5 weeks **Follow-up:** 1 month	Clinical Global Impression - Improvement (CGI-I), number improved Significantly greater percentage of medication patients improved on CGI-I (p < . 001 for both groups). CGI-Severity ratings of each medication group was significantly better (p < 0.001) than placebo group. Conners' ADHD DSM-IV Scales (CADS), teacher report Patients in medication groups demonstrated a significant improvement as compared to placebo (p<0.001) on both CADS-T and CADS-P (parent report). Weight decrease Significantly more medication patients experienced appetite decease. Any adverse event Overall incidence of adverse events was generally higher in medication groups. Adverse events were mild to moderate in severity.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Childress, 2022[194] Shire, 2017[1052] ID: NCT03260205 RCT Multicenter N = 199 US Setting: N/A	**Target:** ADHD diagnoses per DSM-IV, baseline scores of 28 (boys) or 24 (girls) on the parent reported ADHD Rating Scale-IV Preschool version total scores and 4 on the Clinical Global Impression–Severity scale, undergone nonpharmacologic treatment or to have had symptoms severe enough to warrant enrollment without prior nonpharmacologic treatment, engaged in structured group activities that allowed for assessment of ADHD symptoms and impairment outside of the home, Peabody Picture Vocabulary Test standard score 70 and to have lived with the same parent/legally authorized representative for 6 months; no medications for central nervous system, concurrent illness, disability or comorbidity **Other:** **ADHD presentation:** combined : 91.6 **Diagnosis:** No **Comorbidity:** N/A **Female:** 32.3 % **Age mean:** 5.1 (6.54) **Minimum age:** 4 **Maximum age:** 5 **Ethnicity:** Other : depends on tx/placebo/pooled	**Intervention:** Lisdexamfetamine 30 mg/day for 6 weeks **Control:** Placebo Matching placebo for 6 weeks **Comparator:** MedicationTreatment with 5 mg lisdexamfetamine for 6 weeks **Follow-up:** 1.5 months	CGI Global Impression scale Rates were 41.7% across all active treatment groups and 24.3% with placebo (p 0.0857). ADHD-RS-IV-PS Scores decreased more with lisdexamfetamine than placebo (p 0.0074, effect size –0.52). Results for the sleep diary were variable across treatment groups, with no notable trends indicative of differential changes between active treatment and placebo. Decreased weight Weight decreased for two patients with 20 mg LDX but in no other group. Any treatment-emergent adverse event The rates were 57.9% in the intervention receiving 30mg, 33.3% in the 5mg group, 52.9% in the 20mg group, and 42.2% in the placebo group. Safety and tolerability assessments included treatment-emergent adverse events and changes in pulse (greater in all treatment group vs placebo) and blood pressure (greater in all treatment groups vs placebo).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Cho, 2011[196] ID: N/A RCT Multicenter N = 153 Korea Setting: N/A	**Target:** Children with a diagnosis of ADHD as defined by DSM-IV-TR, did not take any medication for ADHD treatment at least 2 weeks prior to randomization and at least 1 week prior to obtaining baseline ADHD-Rating Scale-IV-Parent: Investigator Rated and Clinical Global Impressions-Severity scores, had no significant laboratory abnormalities or clinical conditions that would preclude participation at study entry, had no impairment in intelligence as assessed clinically by the investigator, and were able to keep appointments for clinic visits and all examinations **Other:** **ADHD presentation:** **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 16.3 % **Age mean:** 9.8 (2.4) **Minimum age:** 6 **Maximum age:** 18 **Ethnicity:** % Asian : 100	**Intervention:** Atomoxetine 0.5-1.2 mg/kg/day for 6 weeks **Control:** NA **Comparator:** MedicationAtomoxetine at a target dose of 0.5 mg/kg/day and patients, 6 weeks total **Follow-up:** 1.5 months	CGI-S and CGI-I Atomoxetine 1.2 mg/kg/day was associated with greater improvement compared with atomoxetine 0.2 mg/kg/day (p 0.0025). ADHD-RS-IV-Parent:Inv total score The ANCOVA model for demonstrated a significantly greater improvement in mean change for atomoxetine 1.2 mg/kg/day in a pairwise comparison with atomoxetine 0.2 mg/kg/day (p=0.006). Decreased appetite Rates were 12.5% in the intervention vs 7.41% in the comparator group. Participants with at least one treatment emergent adverse event The rates were 58.33 in the intervention and 40.74 in the comparator. The majority of these events were mild or moderate, and no events related to suicide ideation or self-harm were reported.

FDA-approved pharmacological	Coghill, 2014[202] Banaschewski, 2014[673]; Shire, 2009[1049] ID: NCT00784654 RCT Multicenter N = 157 Multiple countries Setting: Specialty care	**Target:** All patients had ADHD of at least moderate severity, defined as an ADHD-Rating Scale-IV total score of 28 or higher at baseline **Other:** **ADHD presentation:** inattentive : 17.3,combined : 82.2,combined_other : 0.5% **Diagnosis:** Confirmation by specialist DSM-IV-TR by clinician **Comorbidity:** N/A **Female:** 21.7 % **Age mean:** 6-12 years 66.9%; 13-17years 33.1 % **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % White : 94.9	**Intervention:** Lisdexamfetamine dimesylate optimal dose orally for up to 6 weeks **Control:** Placebo Placebo identical in appearance for 6 weeks orally **Comparator:** NA **Follow-up:** 8.25 months	CGI-S treatment failure (at least 2-point increase) The rate was 17.1% in the intervention compared to 68.8% in the placebo group. ADHD-RS-IV Total Score Treatment failure (50% or greater increase in ADHD-RS-IV and 2-point increase in CGI-S) Significantly less participants in the intervention group met criteria for treatment failure compared to those in the control group (p<0.001). The difference between the LDX and placebo groups changes from baseline to endpoint was significant (p<0.001). CHIP-CE: PRF T-scores deteriorated in all domains in the placebo group, but not in the lisdexamfetamine dimesylate group. Weight, kg Decreased appetite The rate was 3.8% in the intervention compared to none in the placebo group. Participants with any treatment-emergent adverse events The rate was 39.7% in the intervention compared to 25.3% in the placebo group.
FDA-approved pharmacological	Concordia, 2011[205] ID: NCT01439126 RCT Multicenter N = 135 US Setting: Mixed	**Target:** Children and adolescents who meet DSM-IV-TR criteria for primary diagnosis for ADHD, IQ at least 70 or higher; no comorbid psychiatric conditions, other significant health conditions, pharmaceuticals used for ADHD treatment prior to 30 days before begin of study **Other:** **ADHD presentation:** N/A	**Intervention:** Clonidine hydrochloride 0.1 mg, 0.2 mg, 0.3 mg, or 0.4 mg taken daily for 26 weeks **Control:** Placebo Tapered off their optimal dose of KAPVAY at weekly intervals in decrements of 0.1 mg/day until reaching the dose of 0 mg/day,	CGI (Clinical Global Impressions-Severity of Illness) Intervention scores improved (mean 0.4, SD 1.40) when compared to placebo (mean 0.9, SD 1.28) ADHD-RS-IV (ADHD-Rating Scale-4th Edition)

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
		Diagnosis: Confirmation by specialist Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and Lifetime (MINI-Kid) **Comorbidity:** N/A **Female:** 30.4 % **Age mean:** 10.8 (2.88) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 23.7 % Black/African American : 27.4 % American Indian or Alaska Native : 0.0 % Asian : .7 % Native Hawaiian or Pacific Islander : 0.0 % White : 64.4 % Multiracial : 7.4	and then received only placebo for the remainder **Comparator:** NA **Follow-up:** 6.5 months	Intervention scores improved more (mean 3.0, SD 10.75) than the control (mean 7.0, SD 12.30). Weiss Functional Impairment Rating Scale-Parent (WFIRS-P) N/A Change in Epworth Sleepiness Scale for Children (ESS-C) from randomization to end of study period (mean, SD): intervention, -0.6 (3.18), placebo, -0.6 (4.09) Number of subjects that responded "Yes" to the question "Do you have a wish to be dead" in Columbia Suicide Severity Rating Scale (C-SSRS) at Visit 20; intervention 0 count, placebo 1 count Participants with at least 1 treatment emergent adverse event The rate was 50% for intervention and 46% for control.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Connor, 2010[207] Shire, 2006[1045] ID: NCT00367835 RCT Multicenter N = 217 US Setting: Specialty care	**Target:** Children with ADHD and oppositional symptoms and no other psychiatric co-morbidities **Other:** Parents provided some outcome data **ADHD presentation:** inattentive : 12.6,hyperactive : 3.3,combined : 84.1 **Diagnosis:** Confirmation by specialist DSM-IV-TR per Kiddie Schedule for Affective Disorders and Schizophrenia - Present and Lifetime **Comorbidity:** ODD **Female:** 31.3 % **Age mean:** 9.4 (1.84) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 16.8 % Black/African American : 22.4 % American Indian or Alaska Native : 2.8 % Native Hawaiian or Pacific Islander : 0.5 % White : 66.4 Other : 7.9% other	**Intervention:** Guanfacine extended release 1- 4 mg per day for 9 weeks **Control:** Placebo Placebo **Comparator:** NA **Follow-up:** 2 months	CGI-S A higher percentage of patients in the intervention group had improved on the CGI-S (p < .001). ADHD-RS-IV (ADHD Rating Scale IV) total score change, clinician rating Reduction in ADHD-RS-IV greater in intervention group than placebo group (p < .001). Medication Satisfaction Survey (MSS, number satisfied overall - agree or strongly agree) Greater percentage of intervention patients satisfied with treatment (p<0.001). Participants with any treatment emergent adverse event The rate was 83.8% in the intervention and 57.7% in the placebo group. Adverse events were more common in the intervention group. A higher percentage of intervention patients reported somnolence, sedation, dizziness, abdominal pain, fatigue, and irritability.

FDA-approved pharmacological	Daviss, 2008[217] Palumbo, 2008[976]; University of Cincinnati, 1999[1130] ID: NCT00031395 RCT Multicenter N = 122 US Setting: Other	**Target:** Participants of any ADHD subtype who had a designated parent in daily contact, had previously used methylphenidate or clonidine; with no history of tic disorder, major depression, pervasive developmental disorder, autism, psychosis, mental retardation, anorexia nervosa, bulimia, a serious cardiovascular or other medical disorder **Other:** **ADHD presentation:** inattentive : 19.9,hyperactive : 4.1,combined : 76.0,N/A **Diagnosis:** Confirmation by specialist DSM-IV by investigator **Comorbidity:** N/A **Female:** 19.7 % **Age mean:** 9.5 (1.6) **Minimum age:** 7 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 7 % Black/African American : 11 % White : 78 Other : 4	**Intervention:** Clonidine plus methylphenidate adjusted to optimal doses and continued, doses were titrated up to 0.6mg/day for clonidine and 60mg/day for methylphenidate in divided doses (up to four times per day for clonidine and up to three times per day for methylphenidate) for 8 weeks **Control:** Other Methylphenidate alone **Comparator:** NA **Follow-up:** 4 months	Childrens Global Assessment Scale (CGAS) Clonidine was not found to improve ADHD symptoms, whereas subjects treated with methylphenidate showed significant improvement compared to those not treated with methylphenidate. Conners Abbreviated Symptom Questionnaire for Teachers (ASQ-Teacher) Patients treated with clonidine had greater improvements compared with patients not treated with clonidine.[976] Pittsburgh Side Effect Scale (Drowsiness): Clon and Clon+MPH experienced initial drowsiness relative to others not taking clonidine. However, levels reached equivalent to those in placebo and MPH only. Quality of Life, as measured by Daily Hassles and Impact on Family instruments: in a general linear model repeated measures analysis, treatment groups improved compared to placebo; all treatment groups were combined for this analysis. Weight, kg All groups had mean weight gains during the 16 weeks period, but theses gains were significantly less when taking Methylphenidate than those that did not (p 0.0007).[217] Participants with any adverse event Rate was 75% in the combination group, 83.6% in the clonidine group, 58.6% in the methylphenidate group, and 40% in the placebo group.Subjects taking clonidine had higher rates of any AE reported (75%) than those not treated with clonidine (41%; p 0.0006

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
				Bradycardia on ECG (HR<60 bpm) significantly higher in subjects treated with clonidine than in subjects not treated with clonidine (p=0.02), somnolence: subjects treated with clonidine experienced higher rates of somnolence than subjects not treated with

FDA-approved pharmacological	Dell'Agnello, 2009[220] ID: NA RCT Multicenter N = 139 Italy Setting: Specialty care	**Target:** Children with ADHD with oppositional defiant disorder **Other:** Parents and teachers provided some outcome data **ADHD presentation:** inattentive : 5.8,hyperactive : 5.1,combined : 89.1 **Diagnosis:** Confirmation by specialist DSM-IV, in addition to Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version (K-SADS-PL) **Comorbidity:** ODD **Female:** 7.1 % **Age mean:** mean 9.9 **Minimum age:** 6 **Maximum age:** 15 **Ethnicity:** N/A	**Intervention:** Atomoxetine 1.2 mg/kg/day for 6 weeks **Control:** Placebo Placebo, once per day **Comparator:** NA **Follow-up:** 2 months	CGI-ADHD-S score Significant improvement in the intervention compared to control (p<0.001). ADHD subscale SNAP-IV (Swanson, Nolan and Pelham IV) Swanson, Nolan and Pelham (SNAP) IV ADHD subscale, at least 25% response Intervention group improved more (p < 0.001). A higher percentage of the intervention group had at least a 40% improvement (18.1% vs. 3.1%, p= 0.043). Children's Depression Rating Scale-Revised (CDRS-R), mean changes: Intervention -0.5 (4.4), Control -0.1 (5.0). Screen for Child Anxiety Related Emotional Disorders (SCARED)-Parent Version, mean changes: Intervention −2.1 (7.6), Control −1.7 (6.5). Health Related Quality of Life (HRQOL): Intervention 30.7, Control 28.2. SDs not reported. Higher score is better. p values not reported. Anorexia Small increase (+0.5 kg) in body weight with placebo and a small decrease (−1.2 kg) with atomoxetine (p , 0.001). Mean height increased more in placebo group (+ 1.5 cm) than in atomoxetine group (+1.0 cm) (p= 0.021).
FDA-approved pharmacological	Diamond, 1999[224] ID: ID NA RCT Unclear/Not reported N = 91 Canada Setting: N/A	**Target:** Children with pervasive ADHD (8 or more of the 14 DSM-III-R criteria for ADHD in one setting and at least 5 criteria in another setting), history of ADHD for more than 6 months and beginning before the age of 7, estimated Full Scale IQ greater than 80, no primary anxiety or affective disorder	**Intervention:** Methylphenidate (immediate release) 0.7 mg/kg twice daily with parental training/support for 4 months **Control:** Placebo Placebo with parental training/support	Telephone interview probe oppositional behavior, parent rating No statistically significant differences. No difference in the development of clinically significant side effects, only 1 or 2 children in each group developed those.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
		Other: **ADHD presentation:** N/A **Diagnosis:** No DSM-III-R, methods only state "interviewer" **Comorbidity:** Mood disorder **Female:** 0.2 % **Age mean:** 8.65 (1.8) and 8.07 (1.3) **Minimum age:** **Maximum age:** **Ethnicity:** N/A	**Comparator:** NA **Follow-up:** 4 months	

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Dittmann, 2011[226] ID: NA RCT Multicenter N = 181 Germany Setting: N/A	**Target:** Children with ADHD; no history of bipolar I or II disorder, psychosis, pervasive developmental disorder, or seizure disorder, at serious suicidal risk, or likely to require psychotropic medications or a structured psychotherapy **Other:** **ADHD presentation:** inattentive : 19.4,hyperactive : 5,combined : 75.6 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** ODD **Female:** 15.6 % **Age mean:** ATX 10.9(3.1), placebo 11.1 (2.8) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** N/A	**Intervention:** Atomoxetine fast titration, 0.5 mg/kg for 7 days, then 1.2 mg/kg once daily in the morning for 8 weeks **Control:** Placebo Placebo once daily for 9 weeks **Comparator:** MedicationAtomoxetine-slow 7 days each at 0.5 and 0.8 mg/kg, then 1.2 mg/kg; once daily for 9 weeks **Follow-up:** 2.25 months	Attention-Deficit and Disruptive Behavior Disorders (ADDB-Inv), disruptive behavior The intervention group had significantly reduced scores compared to the control group (p <0.001). There was no significant difference between intervention and comparator. CGI-Severity for ADHD ATX was significantly superior to placebo. ADHD Score SNAP-IV Intervention and comparator groups were significantly superior to the control group (p <0.001). There was no significant difference between intervention and comparator. The most commonly reported treatment-emergent AEs during intervention were fatigue (ATX-fast/slow 35.0%/21.3%; vs. placebo 10.2%), nausea (21.7/19.7% vs. 5.1%), headache (25.0/14.8% vs. 15.3%), vomiting (15.0/18.0% vs. 5.1%), upper abdominal pain (15.0/13

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Dittmann, 2013[225] Shire, 2010 [1050]; Dittmann, 2014[738]; ID: NCT01106430 RCT Multicenter N = 267 Multiple countries Setting: Mixed	**Target:** Male and female children and adolescents who satisfied DSM-IV-TR criteria for a primary diagnosis of ADHD of at least moderate severity as shown by a baseline ADHD Rating Scale IV total score of 28 or higher **Other:** **ADHD presentation:** inattentive : 16.8,hyperactive : 3.4,combined : 79.9 **Diagnosis:** Confirmation by specialist Yes - DSM-IV, Kiddie-Schedule for Affective Disorders and Schizophrenia for School Age Children—Present and Lifetime (KSADS-PL) **Comorbidity:** N/A **Female:** 24.81 % **Age mean:** 10.65 (2.79) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 18.7 % White : 88.95	**Intervention:** Atomoxetine, mean optimal dose 40.2 mg/day (SD 20.05) for 9 weeks **Control:** NA **Comparator:** MedicationLisdexamfetamine dimesylate, 30, 50 or 70 mg once daily for 9 weeks **Follow-up:** 2.25 months	CGI-I (Clinical Global Impressions-Improvement), days to first clinical response The median time to first clinical response was significantly shorter for patients in the lisdexamfetamine group than those in the atomoxetine group (p= 0.001) ADHD-RS-IV total score Improvement in ADHD-RS-IV from baseline to follow-up was significantly greater in the LDX group compared to the ADX group (p < 0.001). Decreased appetite The rate was 26.8% in the lisdexamfetamine dimesylate and 10.4% in the atomoxetine group. Any treatment-emergent adverse event The rate was 71.9% in the lisdexamfetamine dimesylate and 70.9% in the atomoxetine group. No deaths or serious treatment-emergent adverse event were reported.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Duke University, 2009[235] ID: NCT00889915 RCT Unclear/Not reported N = 228 US Setting: N/A	**Target:** Children with diagnosis of ADHD according to DSM-IV criteria, English-speaking, with no history cardiovascular diseases, may receive other medicinal and/or psychosocial interventions for other comorbid disorders; not inpatient status, cannot take another medication for ADHD (psychostimulant, atomoxetine, bupropion), no psychosis or autism spectrum disorder **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM IV **Comorbidity:** N/A **Female:** 31.6 % **Age mean:** 10.3 (3.1) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** N/A	**Intervention:** Mixed amphetamine salts extended release (Adderall) for 6 weeks **Control:** NA **Comparator:** MedicationMethylphenidate (Concerta, Osmotic-release Oral System Methylphenidate) **Follow-up:** 1.5 months	Weight loss The rate for weight loss was 5.66% for concerta and 5.13% for adderall. MAS 48% with events, concerta 34%.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Duke University, 2009b[236] ID: NCT00889915 RCT Unclear/Not reported N = 228 US Setting: N/A	**Target:** Children with diagnosis of ADHD according to DSM-IV criteria, English-speaking, with no history cardiovascular diseases, may receive other medicinal and/or psychosocial interventions for other comorbid disorders; not inpatient status, cannot take another medication for ADHD (psychostimulant, atomoxetine, bupropion), no psychosis or autism spectrum disorder **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM IV **Comorbidity:** N/A **Female:** 31.6 % **Age mean:** 10.3 (3.1) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** N/A	**Intervention:** Lisdexamfetamine dimesylate (vyvanse) for 6 weeks **Control:** NA **Comparator:** MedicationMethylphenidate transdermal system, optimal dose received for 6 weeks **Follow-up:** 1.5 months	Weight loss The rate for weight loss was 6.06% for transdermal system and 4.48% for lisdexamfetamine. Lisdexamfetamine dimesylate rate of other adverse events was 49% vs 49% methylphenidate transdermal system.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
FDA-approved pharmacological	Eli Lilly, 2004[247] ID: NCT00192023 RCT Single center N = 139 Italy Setting: Specialty care	**Target:** Children and adolescents with ADHD and comorbid Oppositional Defiant Disorder, no history of bipolar, psychosis or pervasive development disorder **Other:** Parents and teachers provided some outcomes. **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** ODD : 100% with ODD **Female:** 7.3 % **Age mean:** 9.8 (2.3) **Minimum age:** 6 **Maximum age:** 15 **Ethnicity:** % White : 97	**Intervention:** Atomoxetine 0.5 mg per kg per day for 1 week, then 1.2 mg/kg/day for 7 weeks **Control:** Placebo Placebo, daily for 8 weeks **Comparator:** NA **Follow-up:** 2 months	Clinical Global Impressions (CGI) Severity Greater improvement for intervention group (p<0.001) as measured by both CGI-S and Conners' Parent Rating Scale-Revised: Short Form, ADHD Index. Swanson, Nolan and Pelham Questionnaire (SNAP-IV) Intervention group improved more (p<0.001). Children's Depression Rating Scale-Revised: No difference in improvement between groups (p = 0.870). Decreased appetite Significantly higher proportion of intervention group experienced appetite decrease, anorexia, and weight loss. Adverse events Rate was 73.83% in the atomoxetine and 37.50 in the placebo group. No serious adverse events in either group.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Eli Lilly, 2006[248] N/A ID: NCT00406354 RCT Multicenter N = 181 Germany Setting: Specialty care	**Target:** Participants with ADHD and ODD, normal intelligence and able to swallow capsules **Other:** **ADHD presentation:** inattentive : 19.4,hyperactive : 5,combined : 75.6 **Diagnosis:** Confirmation by specialist DSM-IV criteria by unknown source **Comorbidity:** ODD **Female:** 15.6 % **Age mean:** 11.0 (3.01) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Black/African American : 1 % White : 99	**Intervention:** Atomoxetine 0.5 milligram per kilogram (mg/kg) daily dose taken orally for 1 week, then 1.2 mg/kg daily dose taken orally for 8 weeks **Control:** Placebo Matching placebo daily dose taken orally **Comparator:** MedicationAtomoxetine Slow Titration arm: 0.5 mg/kg daily dose taken orally for 1 week, then 0.8 mg/kg daily dose taken orally for 1 week, then 1.2 mg/kg daily dose taken orally for 7 weeks **Follow-up:** 2.25 months	Investigator-Rated Individual Target Behaviors (ITB-Inv): Intensity Score Intervention and comparator performed better than control group (p=0.010). CGI-S (Clinical Global Impressions - Severity) ADHD Score Intervention and comparator performed better than control group (p<0.001). ADHD Combined Score SNAP-IV (Swanson, Nolan & Pelham Rating Scale - Revised) Intervention and comparator scored better than control group (p<0.001). decreased appetite Participants with non-serious adverse events The rate was 80% for intervention, 54% for control and 70% for comparator.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Eli Lilly[249] ID: NCT00568685 RCT Multicenter N = 153 Korea Setting: N/A	**Target:** Patients with ADHD, based on the accepted criteria for that disease, must not have taken any medication used to treat ADHD for at least 2 weeks prior to study treatment, must be able to swallow capsules **Other:** **ADHD presentation:** N/A **Diagnosis:** No **Comorbidity:** N/A **Female:** 55.6 % **Age mean:** 9.41 (1.64) **Minimum age:** 6 **Maximum age:** 18 **Ethnicity:** N/A	**Intervention:** Atomoxetine hydrochloride for 6 weeks total, 0.5 mg/kg/day orally in 2 divided doses for 7 days, then 0.8 mg/kg/day orally in 2 divided doses for 7 days, then 1.2 mg/kg/day orally in 2 divided doses for 28 days **Control:** NA **Comparator:** MedicationAtomoxetine 0.2 mg/kg/day orally in 2 divided doses for 6-weeks **Follow-up:** 1.5 months	CGI-S (Clinical Global Impressions-ADHD Severity Scale) change The intervention group had more improvement than comparator group (p=0.0048). ADHD-RS-IV-Parent Total Score change The intervention group had more improvement than comparator group (p=0.024). No incidence of suicide or self-harm in either group. Decreased appetite Decreased appetite was more common in the high dose group. Participants with reported adverse events The rate was 56.25% in the higher dose compared to 29.41% in the lower dose. 8% irritability rate in high dose group, 4% in low dose group, 8% abdominal pain rate in high dose group, 0 in low dose group.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
FDA-approved pharmacological	Findling, 2001[271] ID: ID NA RCT Single center N = 177 US Setting: Specialty care	**Target:** Children and adolescents with ADHD **Other:** Parents and teachers provided outcomes **ADHD presentation:** inattentive : 46.9,hyperactive : 0,combined : 53.1 **Diagnosis:** Confirmation by specialist a computerized version of the Diagnostic Interview Schedule for Children and clinical interviews with a psychologist and a psychiatrist **Comorbidity:** N/A **Female:** 29.4 % **Age mean:** Age mean by age group; <8 years 6.35, 8-10.99 years 9.47, 11-17.59 years 13.64 **Minimum age:** 4 **Maximum age:** 17 **Ethnicity:** N/A	**Intervention:** Mixed amphetamine salts (Adderall), best dose (could be 5 mg, 10 mg or 15 mg per dose) for 4 weeks **Control:** Placebo Placebo in white gelatin capsules identical to the medication **Comparator:** MedicationMethylphenidate (5 mg, 10 mg, or 15 mg per dose) twice per day (in the morning and at lunch) **Follow-up:** 1 month	ASQ (Connors Abbreviated Symptoms Questionnaire), Parent and Teacher versions Similar efficacy was observed between the medications. Of the 195 youths who entered into this trial, 11 had their participation terminated because of adverse events. Dosage levels that led to discontinuation included placebo (n = 1), 5 mg (n = 3), 10 mg (n = 5), and 15 mg (n = 2). All youths who withdrew pre

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Findling, 2008[273] Noven Therapeutics, 2004[964]; Findling, 2009[776]; Findling, 2010[773] ID: NCT00444574 RCT Unclear/Not reported N = 282 US Setting: N/A	**Target:** Children who were diagnosed with ADHD according to DSM-IV-TR criteria (predominantly hyperactive/impulsive, inattentive, or combined type) **Other:** **ADHD presentation:** inattentive_other : 11-26% across groups,hyperactive_other : 1-2% across groups,combined_other : 71-86% across groups **Diagnosis:** Confirmation by specialist inclusive who were diagnosed with ADHD according to Diagnostic and Statical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) **Comorbidity:** N/A **Female:** 33.7 % **Age mean:** 8.7 (1.94) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Methylphenidate transdermal system 10, 15, 20, or 30 mg/9 hours (dose-optimized) plus placebo capsule for 7 weeks **Control:** Placebo Placebo capsule plus placebo patch **Comparator:** Medication18mg OROS capsules plus placebo patch for 5 weeks **Follow-up:** 1.25 months	CPR-S-R (Connors Parent Rating Scale-Revised Short Form) PGA (Parent Global Assessment) rated as improved Compared with placebo, both active treatments showed significant improvements (p<0.0001). ADHD-RS-IV The average magnitude of changes from baseline was a 2-fold greater improvement in active treatments compared to placebo. Compared with placebo, both active treatments showed significant improvements in ADHD-RS-IV scores (p<0.0001). Decreased appetite The rate of decreased appetite was 25.5% in the intervention, 18.7% in the OROS and 4.7% in the placebo group. Participants with at least 1 adverse event The rate was 75.5% for the intervention, 69.2% for the OROS, and 57.6% for the placebo group. The majority of treatment-emergent adverse events were mild or moderate.

FDA-approved pharmacological	Findling, 2010[272] ID: N/A RCT Multicenter N = 217 US Setting: Mixed	**Target:** Adolescent with diagnosis of ADHD according to DSM -IV-TR, total score of >=26 on the ADHD-Rating Scale-IV scale at baseline, IQ of >= 80; no conduct disorder or comorbid psychiatric illnesses that contraindicated treatment with methylphenidate transdermal system, history of cardiac problems, history of substance abuse, history of being nonresponsive to psychostimulant treatment; no clonidine, atomoxetine, antidepressants, sedatives, antipsychotics, anxiolytics, P450 enzyme altering agents, or other investigational medications within 30 days prior to screening **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version **Comorbidity:** N/A **Female:** 25.3 % **Age mean:** 14.6 (1.3) **Minimum age:** 13 **Maximum age:** 17 **Ethnicity:** % Black/African American : 40 % American Indian or Alaska Native : .5 % Asian : .5 % White : 77 Other : Other: 3.7%	**Intervention:** Methylphenidate transdermal system, patches applied to hips once daily (alternatinghips each day), worn for 9 hours per day, titrated to an optimal dose (10,15,20,30 mg) of medication (week 1-5) followed by a 2-week maintenance period, for total of 7 weeks **Control:** Placebo Matching placebo **Comparator:** NA **Follow-up:** 2 months	CGI-I (Clinical Global Impressions-Improvement) very much improved or much improved Intervention group had significantly more participants that improved compared to control group (p<0.001). ADHD-RS-IV (ADHD Rating Scale-IV) Intervention group had significantly more improvement compared to control group (p<0.001). Decreased appetite The rate was 25.5% in the intervention and 1.4% in the control group. Participants with treatment-emergent adverse events during the study period Adverse events were reported in 77.2% of intervention and 55.6% of placebo participants. A total of three serious adverse events were reported by two participants, one in each treatment group discontinued from the study due to the events (two episodes of syncope, both judged to be of moderate severity and related to study treatment by the inv
FDA-approved pharmacological	Findling, 2011[270] Shire, 2008[1046] ID: NCT00735371 RCT Multicenter N = 314 US	**Target:** Children with ADHD; no conduct disorder or a comorbid psychiatric diagnosis requiring medication, a concurrent chronic/acute medical condition that might confound efficacy/safety assessments or pose a safety risk, history of seizures, tic disorder or family history of Tourette disorder, family history of sudden cardiac	**Intervention:** Lisdexamfetamine dimesylate 70 mg/d for 4 weeks **Control:** Placebo Placebo for 4 weeks **Comparator:** MedicationLisdexamfetamine dimesylate 30 mg/d for 4 weeks **Follow-up:** 1 month	CGI-I (Clinical Global Impressions–Improvement) score of 1 or 2 A higher number of participants in the intervention and comparator groups were improved versus participants on placebo (p < 0.0001). ADHD-RS-IV A higher number of participants in the intervention and comparator groups

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
	Setting: N/A	death or arrhythmia, abnormal thyroid function, glaucoma, or those considered a suicide risk; BMI not in 5th or 97th percentile for age and gender; no positive test on urine drug screen (except current stimulant therapy) or recent history of suspected substance abuse; no pregnant/lactating females, with clinically significant electrocardiogram findings, who required medications with central nervous system effects, with failure to respond to and/or intolerance of amphetamine therapy, and/or who were well controlled on current ADHD medication with acceptable safety and efficacy **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist ADHD-RS-IV **Comorbidity:** N/A **Female:** 29.7 % **Age mean:** 14.6 (1.31) **Minimum age:** 13 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 14.8 % Black/African American : 14.8 % White : 79		were improved versus participants on placebo ($p < 0.0001$). YQOL-R changes at endpoint scores for LDX groups versus placebo were not significant. Decreased appetite The rate was 37.2% in the 70mg, 37.2% in the 30mg, and 2.6% in the placebo group. Participants with any treatment emergent adverse event The rate was 71.8% in the 70mg, 65.4% in the 30mg, and 58.4% in the placebo group. Commonly reported treatment emergent adverse events greater than or equal to 5% across all doses were decreased appetite, headache, insomnia, decreased weight, and irritability.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
FDA-approved pharmacological	Fuentes, 2013[281] Eli Lilly and Company, 2007[754] ID: NCT00447278 RCT Multicenter N = 398 Multiple countries Setting: Mixed	**Target:** Patients had to be pharmacologically naive for ADHD treatment **Other:** Parents provided some outcomes **ADHD presentation:** inattentive : 18.8,hyperactive : 2.8,combined : 78.4 **Diagnosis:** Confirmation by specialist ADHD-RS-IV **Comorbidity:** N/A **Female:** 20.6 % **Age mean:** 9.3 (2.60) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** N/A	**Intervention:** Atomoxetine oral once or twice daily, starting dose 0.5 mg/kg per day increasing to recommended target dose of 1.2 mg/kg per day, not exceeding a maximum dose of 1.8 mg/kg per day for 12 months **Control:** NA **Comparator:** MedicationThe OEST group defined as any ADHD medication except ATX, including long- and short-acting MPH and antidepressants; allowed switching between different formulations of a specific medication, specific doses were not mandated in the study protocol, but inve **Follow-up:** 12 months	Weiss Functional Impairment Rating Scale, Parent (WFIRS-P) There was no significant difference between groups (p=0.166). Significantly more patients of the ATX group reported fatigue (11.6% ATX vs 2.5% OEST; p= 0.001), somnolence (6.5% vs 1.0%; p = 0.006), and sedation (3.5% vs 0%; p = 0.015). In the OEST group, insomnia (12.6% OEST vs 2.0% ATX; p = 0.001) and irritability

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Gard, 2014[286] ID: CTRI/2011/08/001981 RCT Single center N = 84 India Setting: Specialty care	**Target:** Children diagnosed with ADHD and have moderate to severe illness as assessed by Clinical Global Impressions Severity Scale **Other:** **ADHD presentation:** inattentive : 21.7,hyperactive : 8.7,combined : 69.6 **Diagnosis:** No Not reported **Comorbidity:** N/A **Female:** 18.8 % **Age mean:** 8.47 (2.22) for methylphenidate, 8.66 (2.44) for atomoxetine **Minimum age:** **Maximum age:** **Ethnicity:** N/A	**Intervention:** Atomoxetine 1.2 mg/kg/day, once or twice daily based on response and tolerability for 8 weeks **Control:** NA **Comparator:** MedicationMethylphenidate (immediate release) 1 mg/kg/day **Follow-up:** 2 months	Clinical Global Impressions Severity Scale (CGI-S) Scores significantly improved for both groups, but there was no statistically significant difference between the groups (p=0.997). VADPRS (Vanderbilt ADHD Diagnostic Parent Rating Scale) Scores significantly improved for both groups, but there was no statistically significant difference between the two groups (p=0.500) in the parent or the teacher ratings. Decreased appetite Rate 33.3% in the atomoxetine, 43.8% in the methylphenidate group. Side effects 56% in the atomoxetine group developed side effects, 55% of the methylphenidate group (n.s.). 3 patients in each group dropped out due to adverse events.

FDA-approved pharmacological	Gau, 2006[289] ID: N/A RCT Single center N = 64 Taiwan Setting: Mixed	**Target:** Participants with diagnosis of ADHD, taking MPH on a total daily dose of 10-40 mg for the past 3 months; no significant gastrointestinal problems, a history of hypertension, known hypersensitivity to MPH, a co-existing medical condition or concurrent medication likely to interfere with the safe administration of MPH, glaucoma, Tourette's Syndrome, an active seizure disorder, a psychotic disorder, or girls who had reached menarche **Other:** Parents were also asked questions about the treatment and usage of ADHD within their children, but were not actively experimented on. **ADHD presentation:** inattentive : 18.8,hyperactive : 3.1,combined : 78.1 **Diagnosis:** Confirmation by specialist Chinese Kiddie-Schedule for Affective Disorders and Schizophrenia **Comorbidity:** N/A **Female:** 9.4 % **Age mean:** 10.5 (3.2) **Minimum age:** 6 **Maximum age:** 13 **Ethnicity:** N/A : Taiwanese children	**Intervention:** Methylphenidate OROS (Osmotic Release Oral System) with the treatment doses 18 mg or 36mg once daily for 28 days **Control:** NA **Comparator:** MedicationInstant release MPH at two different doses (5/10 mg/day) **Follow-up:** 1 month	CGI-I rating of 1 or 2 The OROS-MPH group had a significantly greater proportion of subjects being very much or much improved in the CGI-I scale than the IR MPH group (p = 0.014). ADHD Index Score Conner's Teacher Rating Scale-Revised: Short Form-C change Compared to the IR MPH group, the OROS MPH group showed a significantly greater slope of reductions in ADHD symptoms. SKAMP (Chinese Version of the Swanson, Kotin, Agler, M-Flynn, and Pelham Rating Scale) Attention score mean change (SD) from baseline at endpoint Difference in SKAMP Attention score mean change (SD) from baseline between OROS and IR MPH groups is statistically significant (p < 0.01). Difference in SKAMP Deportment score mean change (SD) from baseline between OROS (-4.65 SD 5.53) and IR (-4.41 SD 6. Decreased appetite The rate of decreased appetite was 46.9% in the OROS and 59.4% in the immediate release group (p=0.316). There was no difference in the rates of side effects between the two groups.
FDA-approved pharmacological	Gau, 2007[288] ID: N/A RCT Multicenter N = 106 Taiwan Setting: Other	**Target:** Children with ADHD, no ADHD treatment medication, or completion of the washout procedures before entering this study; did not weigh less than 20 kg or more than 60 kg; no serious medical illness, history of bipolar I or II disorder, psychosis, pervasive developmental disorder, anxiety disorder, history of any seizure disorder or prior EEG	**Intervention:** Atomoxetine once daily in the morning, maximal dose of 1.8 mg/kg per day, for 6 weeks **Control:** Placebo Placebo once daily in the morning **Comparator:** NA **Follow-up:** 1.5 months	CGI-S (Clinical Global Impressions–ADHD–Severity) Scores significantly decreased (mildly ill to moderately ill) for the atomoxetine group and (moderately ill to markedly ill) for the placebo group (p<0.001). ADHD-RS-IV (ADHD Rating Scale-IV Parents Version: Investigator

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
		abnormalities related to epilepsy, or taking anticonvulsants for seizure control, history of alcohol or drug abuse within the past 3 months, or if they might have to use psychoactive medications **Other:** **ADHD presentation:** inattentive : 27,combined : 73 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 11 % **Age mean:** Atomoxetine 9.1 (2.0), placebo 9.5 (2.4) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** N/A		Administered and Scored) total score change Mean total scores were significantly lower for the atomoxetine than placebo group (p<0.001). Decreased appetite The rate was 36.1% in the intervention compared to 17.4% in the control group. There was no other significant difference between the two treatment groups in the occurrence of adverse events other than decreased appetite, and no drug-related severe adverse event was reported.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Geller, 2007[292] ID: N/A RCT Multicenter N = 176 US Setting: Specialty care	**Target:** Children with ADHD according to DSM-IV and separation anxiety disorder, generalized anxiety disorder, or social phobia **Other:** Parents or legal representatives **ADHD presentation:** inattentive : 23.0,hyperactive : 1.2,combined : 75.9 **Diagnosis:** Confirmation by specialist Used the DSM-IV standard. "ADHD diagnoses were confirmed clinically, and anxiety and ADHD diagnoses were confirmed using the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL; Univers **Comorbidity:** Mood disorder **Female:** 37.9 % **Age mean:** Intervention 12.2 (2.8), placebo 11.8 (2.5) **Minimum age:** 8 **Maximum age:** 17 **Ethnicity:** Other : intervention 79% white, control 82%	**Intervention:** Atomoxetine 0.8-1.8 mg/kg/day divided into two doses daily for 12 weeks **Control:** Placebo Placebo has the same measurements as the treatment dosage **Comparator:** NA **Follow-up:** 3 months	CGI (Clinical Global Impression - Severity of Illness) change CGI results indicated overall symptom improvement. ADHD-RS-IV-P (Attention-Deficit/Hyperactivity Disorder Rating Scale-IV Parent Version) The mean change scores showed greater improvement with atomoxetine relative to placebo ($p<0.001$). Significant reduction in Multidimensional Anxiety Scale for Children (p 0.009). Decreased appetite Statistically significant decreased appetite associated with the intervention ($p=0.025$). No statistically significant difference in incidence of headache, upper abdominal pain, vomiting, irritability, nasopharyngitis, nausea, cough, influenza, sinusitis across groups.

FDA-approved pharmacological	Greenhill, 2006[305] ID: ID NA RCT Multicenter N = 103 US Setting: Mixed	**Target:** Children and adolescents with ADHD, attending school in a classroom setting with the same teacher for the duration of the study; no significant abnormalities in vital signs, physical examinations, or laboratory tests, no history of seizures or use of anticonvulsant medication, comorbid psychiatric conditions, any medical condition that could interfere with study participation or assessments or that may pose a danger with administration of methylphenidate, psychotropic medications, initiated psychotherapy within the past 3 months, positive urine drug screen or history of poor response or intolerance to methylphenidate **Other:** Teachers and parents provided outcomes **ADHD presentation:** inattentive : 21.4,hyperactive : 1.9,combined : 76.7 **Diagnosis:** Confirmation by specialist DSM IV per Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version) **Comorbidity:** N/A **Female:** 35.9 % **Age mean:** Intervention 9.76 (2.75), placebo 10.4 (2.70) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Black/African American : 23.3 % White : 60.2 Other : 16.5% other	**Intervention:** Dexmethylphenidate extended release, dose finding phase, 5, 10, 15, 20, or 30 mg/day once daily for 2 weeks, 7 weeks total **Control:** Placebo Placebo pills once daily **Comparator:** NA **Follow-up:** 2 months	Clinical Global Impressions - Improvement (CGI-I), number much improved or very much improved Significantly more medication group participants improved. Conners ADHD/DSM-IV Scale-Teacher version total score Statistically significant difference between groups favoring medication ($p<0.001$), effect size 0.79. Decreased appetite, number with The rate of decreased appetite was 30.2% in the intervention and 8.5% in the control group ($p = 0.007$) Participants with at least one adverse event reported The rate was 75.5% in the intervention and 57% in the placebo group; difference not statistically significant There were no deaths or serious adverse events

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Griffiths, 2018[306] ID: ANZCTR 12607000535471 Crossover trial Multicenter N = 136 Australia Setting: School	**Target:** Participants with ADHD, no current stimulant use, no contraindications to atomoxetine, no substance or alcohol abuse **Other:** **ADHD presentation:** inattentive : 45,hyperactive : 4,combined : 67 **Diagnosis:** Confirmation by specialist Patients were evaluated at the beginning of the study using the DSM-IV criteria **Comorbidity:** N/A **Female:** 20 % **Age mean:** 11.29 (2.5) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** N/A	**Intervention:** Atomoxetine dose based on body mass as per prescribing guidelines (mean dose was 1.35 mg.kg−1; range 1.0–1.4 mg.kg−1) taken daily for 6 weeks **Control:** Placebo Placebo, both groups switched and were evaluated again **Comparator:** NA **Follow-up:** 1.5 months	ADHD-RS Atomoxetine resulted in significant improvement of response inhibition ($p<0.001$) and fear identification ($p<0.04$), but not for sustained attention ($p<0.06$). The treatment improved ADHD symptoms ($p<0.001$) as well as anxiety symptoms ($p<0.043$). Atomoxetine significantly improved response inhibition, assessed using the Go-NoGo test ($p<0.001$; effect size 0.42). Atomoxetine was associated with significantly reduced symptom severity for anxiety ($p=0.043$).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Harfterkamp, 2012[317] ID: NCT00380692 RCT Multicenter N = 97 Netherlands Setting: Specialty care	**Target:** Children and adolescents dually diagnosed with autism spectrum disorders and ADHD **Other:** Teachers provided some outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM IV_TR **Comorbidity:** Autism **Female:** 14.4 % **Age mean:** 9.9 (10.8) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Black/African American : 1.0 % White : 99.9	**Intervention:** Atomoxetine titrated in 3 weeks to a fixed once daily dose of 1.2 mg/kg for 8 weeks **Control:** Placebo Placebo capsules identical to medication **Comparator:** NA **Follow-up:** 2 months	CGI-ADHD-I, number classified as much or very much improved Total ADHD score was not statistically difference between groups (p = 0.077); difference in those categorized as improved was not significant (p= 0.14). Decreased appetite The rate was 27.1% in the atomoxetine and 6.1% in the placebo group. At least one adverse event The rate was 81.3% in the intervention vs 653% in the placebo group. None of the patients had a serious adverse event.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
FDA-approved pharmacological	Hazell, 2003[321] ID: NA RCT Unclear/Not reported N = 67 Australia Setting: N/A	**Target:** Children with diagnosis of ADHD and comorbid Oppositional Defiant Disorder or Conduct Disorder based on DSM-IV, T scores for Attention problems and Aggressive behavior on the Child Behavior Checklist of ≥70, who had been treated for a minimum of 3 months with methylphenidate or dexamphetamine, IQ at least 70 **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist ADHD Rating Scale, assessment interviews by a qualified health professional **Comorbidity:** ODD **Female:** 8.96 % **Age mean:** 112.9 (19.8) and 125.4 (23.2) **Minimum age:** 6 **Maximum age:** 14 **Ethnicity:** N/A	**Intervention:** Clonidine added to ongoing psychostimulant therapy (either methylphenidate or dexamphetamine), 0.05 to 0.10 mg morning and evening for 6 weeks **Control:** Placebo Placebo syrup added to ongoing psychostimulant therapy, 0.05 mg during week 1; if the child is not experiencing daytime sedation or symptomatic hypotension at end of Week 1, dosage of placebo increased to 0.10 mg morning and evening for 5 more weeks; if **Comparator:** NA **Follow-up:** 1.5 months	Parent report conduct symptoms Number of patients achieving 38% reduction from baseline in conduct symptoms Results favored clonidine (p<0.01). Hyperactive index, parent report Number achieving 43% reduction from baseline There was no statistically significant difference between the groups (p = .16) A significant difference in Parent report conduct symptoms—no. achieving 38% reduction from baseline (p<.01) A significant difference in Parent report conduct symptoms—no. achi Mean height There were no statistically significant differences between groups. Transient increase in side effects in the clonidine-treated group compared with the control group for drowsiness and dizziness.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Hervas, 2014[326] ID: n/a RCT Multicenter N = 338 Multiple countries Setting: N/A	**Target:** Male and female children/adolescents with a diagnosis of ADHD of at least severity by a baseline ADHD-Rating Scale-IV with a total score of 32 or higher and a minimum Clinical Global Impression Severity score of 4; intellectual functioning, blood pressure measurements within the 95th percentile for age, sex and height; and the ability to swallow tablets or capsules **Other:** Parent/legal guardian had to be willing, able and likely to fully comply with the study procedures and restrictions **ADHD presentation:** inattentive : 10.7,hyperactive : 4.1,combined : 84.9 **Diagnosis:** No **Comorbidity:** N/A **Female:** 25 % **Age mean:** 10.8 (2.8) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** N/A	**Intervention:** Guanfacine (extended release), dose-optimized taken once daily in the morning for 6 weeks **Control:** Placebo Placebo tablets provided taken once daily, at a similar time, each morning for 6 weeks **Comparator:** MedicationAtomoxetine capsules for 6 weeks **Follow-up:** 2.25 months	Patients showing an improvement (CGI-I, very much improved or much improved) Compared with placebo, the difference in the percentage of patients showing improvement was significant for guanfacine (p<0.001) and atomoxetine (p 0.024). ADHD-RS-IV The change from baseline was greater for guanfacine and atomoxetine compared with placebo. Decreased appetite The rate was 13.2% in the guanfacine, 27.7% in the atomoxetine, and 10.8% in the placebo group. Treatment-emergent adverse events The rate was 77.2% in the guanfacine, 67.9% in the atomoxetine, and 65.8% in the placebo group. Three (1.1%) serious adverse events were reported: one in the placebo group (syncope [considered treatment related]) and two in the guanfacine group (syncope [considered treatment related] and appendicitis [occurred prior to randomization and not treatmen

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Ichikawa, 2020[337] Ichikawa, 2020[848] ID: NA RCT Multicenter N = 76 Japan Setting: N/A	**Target:** Children with ADHD per DSM-V; ADHD Rating Scale-IV total score>=28; without serious disorders of the blood or bone marrow, heart, kidneys, liver, lungs; psychiatric comorbidity (e.g., bipolar disorder, schizophrenia); Conduct Disorder (excluding Oppositional Defiant Disorder); current tics; history of seizures; low or high bodyweight; hypertension; QTc interval (Fridericia adjusted; QTcF) >430 mseconds; substance use disorder; and pregnancy or lactation **Other:** **ADHD presentation:** inattentive : 2.6,hyperactive : 34.2,combined : 63.2 **Diagnosis:** Confirmation by specialist DSM V plus ADHD-RS-IV **Comorbidity:** N/A **Female:** 17.1 % **Age mean:** 10.0 (2.8) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** N/A	**Intervention:** Lisdexamfetamine, 70 mg/day for 4 weeks, 1 week placebo, and 1 week of follow-up **Control:** Placebo Placebo pill **Comparator:** MedicationLisdexamfetamine 30 mg/day for 4 weeks **Follow-up:** 1 month	ADHD-RS-IV total score, parent, change from baseline All dosages had significantly greater improvements from baseline to all time points than placebo (p<0.0001). Participants with any adverse event The rate was 70% for intervention, 42% for control, and 68% for comparator.

FDA-approved pharmacological	Jain, 2011[341] Addrenex Pharmaceuticals, 2007[653] ID: NCT00556959 RCT Multicenter N = 236 US Setting: N/A	**Target:** Patients with a diagnosis of ADHD of the hyperactive or combined inattentive/hyperactive subtype, minimum score of 26 on the ADHD Rating Scale–IV, good health, be able to swallow tablets, be mentally competent, having a body mass index of at least the fifth percentile for the patients' age group, and having concomitant diagnosis of tics or oppositional defiant disorder eligible; no clinically significant illness or abnormality that would increase the safety risk of clonidine or if they had a clinically significant abnormality on electrocardiographic readings that were interpreted by a single entity, having a concomitant diagnosis or history of a psychiatric disorder that required psychotropic medication, and having a history of conduct disorders, syncopal episodes, or seizures **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 28 % **Age mean:** 9.4 (6–16), 9.6 (6–17) , 9.4 (6–17) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 8 % Black/African American : 27 % White : 59	**Intervention:** Clonidine hydrochloride extended release tablets of 0.4 mg/day: dose-escalating titration schedule of 0.1 mg/day per week to achieve the target dose for the patient (i.e., 0.2 mg/day at week 2 or 0.4 mg/day at week 4), followed by dose tapering in 0.1-mg/day/week intervals until cessation of treatment at the end of week 8 **Control:** Placebo Placebo for 8 weeks followed the same procedure as the intervention group **Comparator:** MedicationClonidine hydrochloride extended release 0.2 mg/day, forced dose-escalating titration schedule of 0.1 mg/day per week to achieve the target dose for the patient (i.e., 0.2 mg/day at week 2 or 0.4 mg/day at week 4), followed by dose tapering in 0.1-mg/day/ **Follow-up:** 2 months	Clinical Global Impression of Improvement (CGI-I) Significant improvement in both treatment groups versus placebo (p=0.0032). ADHD-RS-IV Statistically significant improvements in the intervention groups compared to control. Participants that reported an adverse event 83% of both intervention groups and 72% of placebo patients reported an adverse event. Adverse events that led to discontinuation occurred in 1% of patients in the placebo group, 7% of patients in the 0.2-mg/day group, and 19% in the 0.4-mg/day group. The most common reasons for discontinuation were somnolence and fatigue.
FDA-approved pharmacological	Johnson, 2020[348] Supernus Pharmaceuticals, 2016[1095] ID: NCT02633527 RCT Multicenter	**Target:** Children with ADHD per the DSM, medically healthy ,free of ADHD medication for at least 1 week prior to baseline, no history or presence of neuropsychiatric disease other than ADHD as the primary diagnosis, no history or presence of systemic diseases	**Intervention:** Viloxazine (SPN-812) , 400 mg/day of extended-release viloxazine for 8 weeks **Control:** Placebo Placebo titrated for the same period as the highest dose group	CGI-I Intervention scores but not comparator scores improved significantly compared to control (p<0.05). ADHD-RS-IV responders

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
	N = 234 US Setting: Mixed	or other neurologic or psychiatric diseases, no history of suicidal attempt or ideation 6 months prior to screening or at screening **Other:** **ADHD presentation:** inattentive_other : placebo 21.9 (4.7); 100mg/day: 22.1 (3.9); 200mg/day: 22.2 (3.6); 300mg/day 21.8 (3.8); 400mg/day: 21.0 (4.7),hyperactive_other : hyperactive/impulsivity mean(sd) for 4 groups: placebo: 20.5 (4.4); 100mg/day: 20.3 (5.2); 200mg/day: 21. **Diagnosis:** Confirmation by specialist MINI-KID **Comorbidity:** N/A **Female:** 33 % **Age mean:** Median 9.0 across all groups except 100mg group (median 8.0 years) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Black/African American : 38.3 % American Indian or Alaska Native : 0.97 % Asian : 0.97 % White : 56.8 % Multiracial : 2.43	**Comparator:** MedicationViloxazine (SPN-812), 100 mg/day of extended-release viloxazine for 8 weeks **Follow-up:** 2 months	Percent responders were 68.2% in 400mg group, 60% in 100mg group, and 45.8% in placebo. Decreased Appetite Adverse Event All groups had at least one participant experience decreased appetite as an adverse event. No deaths or serious treatment emergent adverse events were reported at any point during the study.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Kelsey, 2004[361] ID: ID NA RCT Multicenter N = 197 US Setting: N/A	**Target:** Children with ADHD; serious medical illness, a history of psychosis, or bipolar disorder were excluded **Other:** Parents provided some outcomes **ADHD presentation:** inattentive : 27.4,hyperactive : 3.6,combined : 69.0 **Diagnosis:** Confirmation by specialist DSM IV per Kiddie Schedule for Affective Disorders and Schizophrenia for School-Aged Children-Present and Lifetime Version **Comorbidity:** N/A **Female:** 29.4 % **Age mean:** 9.5 (1.8) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % White : 72.6	**Intervention:** Atomoxetine once per day in the morning (max 1.8 mg/kg per day, 120mg per day) for 8 weeks **Control:** Placebo Placebo once per day in the morning, for 8 weeks **Comparator:** NA **Follow-up:** 2 months	Conners' Global Index, Parent Significantly greater improvement in atomoxetine group. ADHD RS, parent ADHD RS, at least 25% re-duction from baseline Significantly greater improvement in atomoxetine group (62.7% vs 33.3%, p<0.001). Decreased appetite A significantly greater proportion of amoxetine patients experienced decreased appetite (17.6% vs 6.3%). 4.5% of atomoxetine and 1.6% of placebo patients discontinued as the result of adverse events.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Kollins, 2011[374] Shire, 2005[1055] ID: NCT00150592 RCT Multicenter N = 182 US Setting: N/A	**Target:** Participants without any current comorbid psychiatric diagnosis (except oppositional defiant disorder), weight <25 kg (55 lb), cardiac conditions that might have increased the safety risk to the subject, or a Pediatric Daytime Sleepiness Scale score 22 at screening and/or baseline **Other:** **ADHD presentation:** inattentive : 23.6,hyperactive : 1.7,combined : 74.7 **Diagnosis:** Confirmation by specialist DSM-IV-TR **Comorbidity:** N/A **Female:** 30.3 % **Age mean:** 12.6 (2.81) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 12.4 % Black/African American : 16.3 % White : 66.9	**Intervention:** Guanfacine extended release, optimal dose (1, 2, or 3mg/day) found in 3 week dose-findingphase, maintained for 2 weeks of maintenance; total duration of 5 weeks **Control:** Placebo Matching placebo **Comparator:** NA **Follow-up:** 2.5 months	CGI-I scale much improved or very much improved A significantly greater percentage in the intervention group was rated 'much improved' or 'very much improved' compared with placebo (p<0.007). ADHD-RS-IV total scores Reductions were significantly greater in the intervention than in the placebo group (p< 0.001). Reaction time as measured by the Choice Reaction Time (CRT) test indicated that treatment did not impair psychomotor functioning or alertness compared with placebo. Participants with treatment emergent adverse events reported Rate was 79.3% in intervention, 70.2% in placebo group. The majority of adverse events were mild to moderate; there were 2 serious events severe asthma and moderate loss of consciousness (neither was judged to be related to GXR).

FDA-approved pharmacological	Kollins, 2011[373] Addrenex Pharmaceuticals, Inc., 2008[654] ID: NCT00641329 RCT Multicenter N = 198 US Setting: N/A	**Target:** Children with inadequate stimulant medication response, total score 26 on the ADHD-Rating Scale-IV questionnaire after a minimum of 4 weeks on a stable stimulant regimen, estimated IQ to be 80, BMI in the 5th percentile for the patient's gender and age; no current diagnosis or history of a psychiatric disorder that required psychotropic medication or severe comorbid Axis I or Axis II disorder, history of conduct disorder, history of syncopal episodes or seizures (except for febrile seizures), current or past drug abuse, history of clonidine intolerance, or used any investigational drug within 30 days of the study initiation or had a positive drug test (except for ADHD medication) **Other:** Parents provided some outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 26 % **Age mean:** Intervention 10.4 (2.5), control 10.5 (2.5) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 11 % Black/African American : 27 % White : 54 Other : 8	**Intervention:** Clonidine hydrochloride extended-release tablets plus stimulant (methylphenidateor amphetamine): total daily doses of 0.1 to 0.4 mg per day, concomitant stimulant medication was prescribed by the patient's regular physician and was obtained from the patient's usual pharmacy, for duration of 8 weeks **Control:** Placebo Placebo plus stimulants for 8 weeks; methylphenidate or amphetamine prescribed by the patient's regular physician and was obtained from the patient's usual pharmacy **Comparator:** NA **Follow-up:** 1.25 months	CGI-I change from baseline Intervention group had greater improvement than the control group (p=0.006). ADHD-RS-IV (ADHD Rating Scale IV), change Intervention group had greater improvement than the control group (p=0.009). Participants with at least one treatment emergent adverse event Rate was 45% in the intervention and 41% in the concomitant placebo group. Statistical significance not reported. Somnolence, headache, fatigue, upper abdominal pain, and nasal congestion were the most commonly reported event in the CLON-XR plus stimulant group. Of the 96 patients in the placebo plus stimulant group, 3 (3%) discontinued because of TEAEs (ie, increase
FDA-approved pharmacological	Kratochvil, 2002[376] ID: NA RCT Multicenter N = 228 US	**Target:** Participants that were not girls older than 9 years or had history of bipolar or psychotic disorders, motor tics or a family history of Tourette syndrome, substance abuse, nonresponse to a previous trial of methylphenidate, and serious medical illness **Other:**	**Intervention:** Atomoxetine 1-2 mg/kg per day administered as a divided dose in the morning and late afternoon for 10 weeks **Control:** NA **Comparator:** MedicationMethylphenidate was	CGI ADHD Severity Both groups improved. ADHD-RS-IV No statistically significant differences between treatment groups (p = .66). Weight loss

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
	Setting: N/A	**ADHD presentation:** inattentive : 23,hyperactive : 1,combined : 76 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 7 % **Age mean:** 10.4 (2.1) **Minimum age:** 7 **Maximum age:** 15 **Ethnicity:** % White : 77	dosed beginning at 5 mg from one to three times daily with an ascending dose titration based on the investigator's assessment of clinical response and tolerability, total daily dose was not to exceed 60 mg, concomitant use of other psy **Follow-up:** 2.5 months	The rate of weigh loss was 2.7% in the atomoxetine and 5% in the methylphenidate group (p=0.611). Both atomoxetine and methylphenidate were well tolerated, with no statistically significant differences in discontinuations due to adverse events (atomoxetine 5.4%, methylphenidate 11.4%; p=.18); all atomoxetine patients who discontinued due to an adverse

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Kratochvil, 2011[378] University of Nebraska, 2007[1133] ID: NCT00561340 RCT Unclear/Not reported N = 101 US Setting: Other	**Target:** Young children with ADHD; no concurrent use of psychotropic or other medications with significant central nervous system effects, current effective treatment with atomoxetine, medical contraindication to atomoxetine, current diagnosis of adjustment disorder, autism, psychosis, bipolar disorder, or significant suicidality, history of abuse that may confound symptoms of ADHD, and failure to respond to an adequate previous trial of atomoxetine **Other:** **ADHD presentation:** inattentive : 8,hyperactive : 9,combined : 82 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 32 % **Age mean:** Placebo 6.1 (0.5) , Atomoxetine 6.1 (0.6) **Minimum age:** 5 **Maximum age:** 6 **Ethnicity:** % Black/African American : 1 % Native Hawaiian or Pacific Islander : 3 % White : 86	**Intervention:** Atomoxetine 0.5-1.8 mg/kg per day for 8 weeks **Control:** Placebo Placebo controlled **Comparator:** NA **Follow-up:** 2 months	CGI-I scores of very much improved or much improved rate 40% of atomoxetine and 22% of placebo participants had CGI-I scores of 1 (very much improved) or 2 (much improved) relative to baseline, which was not a significant difference after adjustment for age and study center (p = .1). A total of 62% of subjects ADHD-RS total score, parent Significant mean decreases in parent (P = .009) and teacher (P = .02) ADHD–IV Rating Scale scores with atomoxetine compared with placebo. Decreased appetite The rate was 30% in the intervention compared to 8% in the placebo group. There were no significant differences in the mean change in systolic blood pressure with atomoxetine treatment compared with placebo (p=.09) , in the change in diastolic blood pressure (p=.8), or heart rate (p=.07) with atomoxetine. There was a significan

FDA-approved pharmacological	Kurowski, 2019[383] Childrens Hospital Medical Center, Cincinnati, 2013[709] ID: NCT01933217 Crossover trial Single center N = 26 US Setting: Specialty care	**Target:** Children with hospital admission for blunt head trauma and confirmed diagnosis of moderate to severe traumatic brain injury (Glasgow Coma Scale≤ 8); at least 6 of 9 current symptoms on at least one subscale of the Vanderbilt Attention Deficit Hyperactivity Disorder Parent Diagnostic Rating Scale; no preinjury diagnoses of developmental or neurological disorders, hospitalization for psychiatric reasons in the past 12 months; not involved in active behavioral and/or medication treatments for attention problems and/or who had contraindications to methylphenidate use or were on medications that had potentially severe interactions with methylphenidate **Other:** **ADHD presentation:** inattentive : 69.2,hyperactive : 7.7,combined : 23.1,N/A **Diagnosis:** Confirmation by specialist K-SADS-P/L **Comorbidity:** Other : Traumatic brain injury **Female:** 23.1 % **Age mean:** 11.5 (2.8) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % White : 73.1	**Intervention:** Methylphenidate long-acting (Concerta), initial dose of 18 mg, subsequent 3 weeks, titrated based on response and side effects for week 4; <25kg = 18mg (low), 27mg (medium), and 36mg (high) dosages, 25kg = 18mg (low), 36mg (medium), 54mg (high) dosages; total duration of 4 weeks **Control:** Placebo Identical capsules filled with placebo (inert white capsules) for 4 weeks, then switching to the intervention drug **Comparator:** NA **Follow-up:** 2 months	ADHD total symptom score VADPRS (Vanderbilt ADHD Parent Diagnostic Rating Scale) On optimal dose of medication, greater reductions were found for the medicated condition than for placebo (p 0.022, effect size 0.59). Mean number of participants with change in appetite side effect Compared to the placebo condition, the medication condition was associated with lower weight at the second, third, and fourth week (p<.0001). Methylphenidate was associated with weight loss (~ 1 kg), increased systolic blood pressure (~3–6 point increase), and mild reported changes in appetite versus the placebo condition. At the last visit, suicidal ideation was reported by one participant whi
FDA-approved pharmacological	Law, 1999[387] ID: ID NA RCT Single center N = 91 Canada Setting: Other	**Target:** Children with pervasive ADHD, estimated IQ greater than 80, no primary anxiety or affective disorder; no history of prior treatment for ADHD or tics, severe motor or vocal tic disorder or Tourette's disorder, regularly received medication for a medical problem, had a chronic medical condition, or attended a full time residential or day treatment program	**Intervention:** Methylphenidate (immediate release) 0.7mg/kg twice daily for 1 year **Control:** Placebo Placebo **Comparator:** NA **Follow-up:** 12 months	Onset or worsening severity of tics: clinically significant tics developed in 19.6% of the subjects without preexisting tics receiving MPH and in 16.7% of those receiving the placebo (p 0.59); deterioration of tics was observed in 33% of subjects with pre

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
		Other: Parents, teachers, and research assistants; research assistants were trained to achieve high consistency in measurements of tics under supervision of study psychiatrist **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-III-R **Comorbidity:** N/A **Female:** 18.68 % **Age mean:** MPH group 8.4 (1.6), Placebo group 8.3 (1.5) **Minimum age:** **Maximum age:** **Ethnicity:** N/A		

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Lilly, 2008[250] ID: NCT00760747 RCT Multicenter N = 112 Multiple countries Setting: Mixed	**Target:** Children 6-16 years old who meet DSM-IV diagnostic criteria for ADHD and unsatisfactory symptom response to stimulant therapy or experience of adverse events while on stimulant therapy; no previous participation in an atomoxetine study and not taking anticonvulsants, antihypertensive agents, medication with sympathomimetic activity, psychotropic medications, monoamine oxidase inhibitor **Other:** **ADHD presentation:** inattentive : 28.2,hyperactive : 3.6,combined : 66.7,combined_other : Not categorized: 1/111 **Diagnosis:** No Not mentioned **Comorbidity:** N/A **Female:** 16.2 % **Age mean:** 11.5 (2.38) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** % Hispanic or Latino : 18,9 % Black/African American : 0.9 % White : 80.2	**Intervention:** Slow switching group (switch from full stimulant dose to atomoxetine, 1.2 mg/kg/day, orally, during 10 weeks then continue treatment up to 1.8 mg/kg/day, to 14 weeks **Control:** NA **Comparator:** MedicationFast switching group (switch from full stimulant dose to atomoxetine 1.2 mg/kg/day, PO, during 2 weeks then continue treatment up to 1.8 mg/kg/day, PO to 14 weeks **Follow-up:** 2.5 months	CGI-S (Clinical Global Impression Severity) rating scale change There was no significant difference between groups (p=0.898). ADHD-RS-IV (Attention Deficit Hyperactivity Disorder-Rating Scale) Parent Version change There was no significant difference between groups (p=0.692). Treatment Satisfaction Preference Serious adverse events The rate was 1.8% in the intervention group and 1.9% for comparator group.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Martenyi, 2010[414] Eli Lilly and Company, 2004[751] ID: NCT00386581 RCT Multicenter N = 105 Russia Setting: N/A	**Target:** Participants with a DSM-IV diagnosis of ADHD, a minimum score of 25 for boys and 22 for girls, or > 12 for their diagnostic subtype on the Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent Version: Investigator-Administered and Scored, score of >= 4 on Clinical Global Impressions-ADHD Severity scale, had not taken any medications for ADHD; excluded weight <20 kg or >60 kg, history of bipolar disorder, anxiety disorder, psychosis, developmental disorder, or suicidal **Other:** **ADHD presentation:** inattentive : 22.9,hyperactive : 4.8,combined : 72.4 **Diagnosis:** Confirmation by specialist Kiddie Schedule for Affective Disorders and Schizophrenia for School-aged Children-Present and Lifetime Version (K-SADS-PL) **Comorbidity:** N/A **Female:** 14.3 % **Age mean:** 9.8 (2.8) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** % White : 100	**Intervention:** Atomoxetine 1.2 mg/(kg/day) as a single dose in the morning for 6 weeks **Control:** Placebo Identical placebo treatment **Comparator:** NA **Follow-up:** 1.5 months	CGI-ADHD-S (Clinical Global Impression-ADHD-Severity) change The intervention group had significantly more improved scores compared to control group (p=0.035). ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent Version) change The intervention group had significantly more improved scores compared to control group (p=0.013). Weight loss Rate was 8.3 in the intervention group with none in placebo. Treatment emergent signs and symptoms Rate was 41.9% in the intervention and 33.3% in the control group. No serious adverse events (including deaths or suicidal ideation) were reported in either treatment group. One patient (in the atomoxetine group) discontinued the study due to an adverse event (mild skin itch and eruptions).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Matthijssen, 2019[418] ID: 5252 Dutch trial registry RCT Multicenter N = 94 Netherlands Setting: Mixed	**Target:** Children using methylphenidate as prescribed in clinical practice in any dosage or form for 2 years or longer; if the period of not using methylphenidate had not exceeded 2 continuous months during the past 2 years **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist ADHD-RS **Comorbidity:** N/A **Female:** 22 % **Age mean:** 13.8 (2.2) and 13.6 (2.2) **Minimum age:** 8 **Maximum age:** 18 **Ethnicity:** % White : 98.9	**Intervention:** Gradual withdrawal of methylphenidate OROS (osmotic-controlled release oral delivery system) to placebo over a 3-week period followed by 4 weeks of complete placebo, total study of 7 weeks **Control:** NA **Comparator:** MedicationContinued extended-release methylphenidate OROS (osmotic-controlled release oral delivery system) for 7 weeks, 54 or 36 mg/day **Follow-up:** 2.75 months	CGI-I (Clinical Global Impressions improvement scale) not worsened CGI-I indicated worsening in 40.4% of the discontinuation group compared with 15.9% of the continuation group. ADHD-RS (ADHD Rating Scale) A significant between-group difference in change over time of in favor of the group that continued methylphenidate treatment. Strengths and Difficulties Questionnaire (SDQ), total score, parent, change from baseline The intervention group improved significantly compared to comparator group (p=0.03). Change in appetite The rate of patients with changes in appetite was 9.6% in the discontinuation group and 7.4% in the continuation group. Participants with at least one adverse event reported In the discontinuation group, 13.5% reported at least one adverse event, compared with 10.6% in the continuation group (p=0.46). None of the participants had a serious adverse event.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Mattingly, 2020[419] Shire, 2017[1059] ID: NCT03325881 RCT Multicenter N = 89 US Setting: Specialty care	**Target:** Children with Diagnostic and Statistical Manual of Mental Disorders, Fifth edition—defined ADHD; baseline ADHD-Rating Scale, Fifth Edition, Child, Home Version total scores ≥ 28 and baseline Clinical Global Impressions-Severity scores ≥ 4 **Other:** **ADHD presentation:** inattentive : 13.6,hyperactive : 13.6,combined : 72.8 **Diagnosis:** Confirmation by specialist ADHD-Rating Scale, Fifth Edition, Child, Home Version **Comorbidity:** N/A **Female:** 40 % **Age mean:** 8.8 (2.20) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Black/African American : 24.4 % American Indian or Alaska Native : 0 % White : 66.7 % Multiracial : 8.9	**Intervention:** Mixed amphetamine salts extended-release (SHP465), 6.25 mg once daily for 4 weeks **Control:** Placebo Placebo capsules were identical in appearance to maintain blinding **Comparator:** NA **Follow-up:** 1 month	CGI-I (Clinical Global Impressions-Improvement) Difference between groups was not statistically significant (p=0.597). ADHD-RS-5-HV-TS (ADHD-Rating Scale, Fifth Edition, Child, Home Version total scores, hyperactivity/impulsivity and inattention) Difference between groups was not statistically significant. Decreased appetite The rate was 2.2% in the intervention and 4.7% in the placebo group. Participants with treatment emergent adverse events The rate was 16.3% in the placebo and 24.4% in the treatment group. There were no serious or severe treatment emergent adverse events, nor events or leading to discontinuation or death.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	McCracken, 2016[425] Bilder, 2016[688]; Sayer, 2016[1022]; University of California, Los Angeles, 2007[1128] ID: NCT00429273 RCT Single center N = 212 US Setting: Specialty care	**Target:** Male or female individuals; DSM-IV ADHD (any subtype) diagnosed by Kiddie-Schedule for Affective Disorders and Schizophrenia -Present and Lifetime version and clinical interview and Clinical Global Impression Severity score 4 for ADHD **Other:** **ADHD presentation:** inattentive : 44,hyperactive : 2,combined : 51 **Diagnosis:** Confirmation by specialist DSM-IV ADHD by clinician **Comorbidity:** N/A **Female:** 32 % **Age mean:** 10.0 (2.1) **Minimum age:** 7 **Maximum age:** 14 **Ethnicity:** % Hispanic or Latino : 21.3 % Black/African American : 17 % Asian : 8 % White : 69 Other : 6	**Intervention:** Guanfacine (1-3 mg/day) plus d-methylphenidate extended-release (5-20 mg/day), with fixed-flexible dosing, for 8 weeks **Control:** Placebo Placebo plus d-methylphenidate extended-release (5-20 mg/day) **Comparator:** NA **Follow-up:** 2 months	CGI-I treatment response (very much improved or much improved) There were significant differences in treatment response for the 3 treatment sequences, with rates of 81% for methylphenidate alone, 69% for guanfacine alone, and 91% for guanfacine plus methylphenidate (p 0.01). ADHD-RS-IV (ADHD-Rating Scale-IV) total score Guanfacine plus methylphenidate showed superiority versus guanfacine alone (p 0.049), but did not differ statistically from methylphenidate (p 0.066). Any adverse event The rate was 98.6% for the combination, 95.7% for DMPH, and 97.1% for guanfacine.

FDA-approved pharmacological	Michelson, 2001[432] Matza, 2004[913] ID: NA RCT Multicenter N = 297 US Setting: Other	**Target:** Children with ADHD from the DSM-IV by clinical assessment and structured interview **Other:** **ADHD presentation:** inattentive : 31,hyperactive : 2,combined : 67 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** ODD **Female:** 29 % **Age mean:** 11.2 (2.3) **Minimum age:** 8 **Maximum age:** 18 **Ethnicity:** % Hispanic or Latino : 2 % Black/African American : 17.9 % Asian : 1 % White : 75.8	**Intervention:** Atomoxetine 1.8 mg/kg/day for 8 weeks **Control:** Placebo Placebo-controlled **Comparator:** MedicationAtomoxetine 0.5 mg/kg/day **Follow-up:** 2 months	Behavior rating, Psychological Summary Score Atomoxetine groups were statistically significantly better than placebo. CGI-S Outcomes in the 1.2 and 1.8 mg/kg/day groups were superior to placebo on almost all measures but for the 0.5 mg/kg/day group CGI-S scale outcomes were not statistically significantly different from those of the placebo group. ADHD-RS, parent Atomoxetine groups were statistically significantly better than placebo. Psychosocial summary score Atomoxetine groups were statistically significantly better than placebo. Reduction in affective symptoms, as measured by the CDRS-R, was greater among those in the 2 higher dose groups of atomoxetine compared with placebo. Anorexia The rate of anorexia was 12% in the high dose, 6.8% in the low dose, and 4.8% in the placebo group. Atomoxetine was well tolerated at all doses. No adverse event was statistically significantly more frequent among either of the 1.2 mg/kg/day or 1.8 mg/kg/day atomoxetine dose groups compared with placebo.
FDA-approved pharmacological	Michelson, 2002[431] ID: NA RCT Multicenter N = 171 US	**Target:** Children and adolescents with ADHD **Other:** Parents and teachers provided outcome data **ADHD presentation:** inattentive : 40.6,hyperactive : 1.8,combined : 57.6 **Diagnosis:** Confirmation by specialist	**Intervention:** Atomoxetine 1-1.5 mg/kg per day at 4 weeks **Control:** Placebo Placebo, once per day **Comparator:** NA **Follow-up:** 1.5 months	CGI-S Intervention group improved more (p < .001). ADHD-RS-IV (ADHD Rating Scale IV), total score, parent report Intervention group improved more (p < .001).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
	Setting: Specialty care	DSM-IV, assessed by clinical interview and confirmed by Schedule for Affective Disorders and Schizophrenia for School-aged Children (K-SADS-PL) **Comorbidity:** N/A **Female:** 29.4 % **Age mean:** 10.3 (2.4) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** N/A		Decreased appetite More intervention patients reported decreased appetite (p=0 .02).

FDA-approved pharmacological	Montoya, 2009[442] Escobar, 2009[761] ID: NCT00191945 RCT Multicenter N = 151 Spain Setting: Specialty care	**Target:** Medication naive children and adolescents with ADHD and no psychiatric comorbidities **Other:** Parents provided some outcome data **ADHD presentation:** inattentive : 32.9,hyperactive : 4.0,combined : 63.1 **Diagnosis:** Confirmation by specialist Diagnosed per DSM-IV-TR). Confirmed by Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime version (K-SADS-PL). **Comorbidity:** N/A **Female:** 20.5 % **Age mean:** 10.3 (2.5) **Minimum age:** 6 **Maximum age:** 15 **Ethnicity:** % Hispanic or Latino : 3.3 % Black/African American : 0.7 % White : 96	**Intervention:** Atomoxetine, target dose of 1.2 mg/kg/day taken once daily for 12 weeks **Control:** Placebo Placebo **Comparator:** NA **Follow-up:** 3 months	CPRS-R:S (Conners' Parent Rating Scale-Revised: Short Form), Total CGI-S (Clinical Global Impression - Severity) severely ill Total Conners score was significantly lower in intervention group at 12 weeks. A significantly lower percentage of intervention group participants were determined to be 'severely ill' compared to the control group. ADHD-RS-IV (ADHD-Rating Scale-IV) total score, parent report Statistically significant improvements with atomoxetine compared to placebo from baseline to follow up on total and subscale scores of the ADHD- RS-IV (p < .001). Atomoxetine improved Health Related Quality of Life risk avoidance (p < .001) and achievement (p = .042) domains compared to placebo, as assessed by parents. Difference in satisfaction, comfort, and resilience domains not statistically significant. Number with decreased appetite Significantly lower percentage of placebo patients experienced appetite decrease (p = 0.006). Participants with at least one adverse event The rate was 65% for intervention and 37% for control.
FDA-approved pharmacological	Morell, 2019[504] ID: ID NA RCT Single center N = 45 Spain Setting: Specialty care	**Target:** Children with ADHD and poor performance in executive functions or delay aversion; IQ ≥85; absence of sensory, psychiatric and/or other neurological disorders; no previous ADHD medications; absence of concomitant psychotropic medication **Other:**	**Intervention:** Atomoxetine, effective clinical dose, titration initiated with a standard dose based on weight (0.8–1.5 mg /kg/day for ATX) and adjusted by clinical response until an optimal clinical response with minimum	Risk taking behavior evaluated by the Cambridge Gambling Task No significant difference between groups. Both MPH and ATX significantly improved scores in verbal working memory, spatial working memory, planning, decision making, and

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
		ADHD presentation: N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 26 % **Age mean:** Intervention: 10.46 (0.66), comparator: 10.0 (0.40) **Minimum age:** 9 **Maximum age:** 12 **Ethnicity:** N/A	side effects was reached, mean dose 40 mg/day, for 6 months **Control:** NA **Comparator:** MedicationModified-release methylphenidate (long-acting), dose titration initiated with a standard dose based on weight (1 mg/kg/day for MPH) and adjusted by clinical response until an optimal clinical response with minimum side effects was reached, mean dose was 3 **Follow-up:** 6 months	inhibition, but difference between groups was not significant. No beneficial effect on delay aversion and risk taking was found with MPH or ATX. No ADHD participant dropped out due to adverse effects or other any other reason.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Mount Sinai, 2012[539] N/A ID: NCT01678209 RCT Single center N = 127 US Setting: Specialty care	**Target:** Children and adolescents with primary diagnosis of ADHD, any subtype, determined by Kiddie Schedule for Affective Disorders and Schizophrenia for School-Aged Children-Present and Lifetime Versions, ADHD Rating Scale-IV-Parent Version: Investigator Administered total score ≥ 1.5 SD above age and gender means for subtype, Clinical Global Impressions-ADHD-Severity score > 4, Wechsler Intelligence Scale for Children ≥ 75, treatments offered in the study must not be contraindicated for the comorbid disorder **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Diagnosis of ADHD, any subtype, determined by Kiddie Schedule for Affective Disorders and Schizophrenia for School-Aged Children-Present and Lifetime Versions (K-SADS-PL) **Comorbidity:** N/A **Female:** 27.3 % **Age mean:** 11 (2.94) **Minimum age:** 7 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 56.8 Other : 43.2 not Hispanic or Latino	**Intervention:** Atomoxetine, flexible-dose titration for 6-8 weeks **Control:** NA **Comparator:** MedicationMethylphenidate, flexible-dose titration with Concerta for 6-8 weeks **Follow-up:** 1.5 months	CGI-S (Clinical Global Impressions-Severity) Intervention scores improved when compared to comparator. ADHD-RS Intervention scores improved compared to comparator. Percentage of correct inhibition in the Go-No go task favored methylphenidate (81.81%) compared to atomoxetine (80.72%). Decreased appetite The rate was 9.09% for atomoxetine and 18.18 for methylphenidate. Participants with adverse events The rate was 27.7% for atomoxetine and 18.18% for methylphenidate.

FDA-approved pharmacological	Nasser, 2020[453] Supernus Pharmaceuticals, 2017[1096] ID: NCT03247530 RCT Single center N = 477 US Setting: Other	**Target:** Children with ADHD according to the DSM-5, no diagnosis of a major psychiatric/neurologic disorder other than ADHD (excluding oppositional defiant disorder, or major depressive disorder if the subject was free of major depressive episodes both currently and for the 6 months before screening), significant systemic disease, history of allergic reaction to viloxazine, any food allergy or intolerance that can impede treatment, and/or evidence of suicidality within 6 months of screening **Other:** **ADHD presentation:** inattentive_other : mean(sd) 22.7 (3.5),hyperactive_other : hyperactive/impulsivity mean(sd) 21.5 (4.9) **Diagnosis:** Confirmation by specialist DSM-5, MINI-KID **Comorbidity:** N/A **Female:** 37 % **Age mean:** 8.5 (1.7) **Minimum age:** 6 **Maximum age:** 11 **Ethnicity:** % Black/African American : 43.7 % American Indian or Alaska Native : 0.4 % Asian : 0.2 % White : 51.3 % Multiracial : 4.3	**Intervention:** Viloxazine (SPN-812) 200 mg/day, viloxazine extended-release daily in the morning, with or without food, for 6-weeks **Control:** Placebo Placebo, 2 capsules daily for 6 weeks **Comparator:** MedicationViloxazine (SPN-812), one 100-mg SPN-812 and one placebo capsule daily for 6 weeks **Follow-up:** 1.5 months	Conners-3 Composite Score (inattention, hyperactivity, learning problems, executive functioning, defiance/aggression, peer relations), parent Significant improvement for Conners 3-PS Composite T-score (P =0.0003 and P =0.0002) when compared to placebo. ADHD-RS-5 Statistically significant improvements in ADHD-RS-5 Total score were observed in both the 100- and 200-mg/day SPN-812 treatment groups compared to placebo at week 1 of treatment (P=0.0004 and P=0.0244, respectively), which was maintained through EOS (P=0. Weiss Functional Impairment Rating Scale - Parent, change from baseline Significant improvement was shown in both the intervention and comparator groups compared to the placebo (p=0.0019 for comparator, p=0.0002 for intervention). Decreased appetite There was no incidence of decreased appetite in the placebo group but a rate of 7.5 in the 200mg group and 4.5 in the 100mg group. Participants with at least 1 adverse event The rate was 48% for intervention, 30% for control, and 48% for comparator Discontinuations due to AEs were infrequent with 1.3% in the placebo, 1.2% in the 200mg, and 3.2% in the 100mg group discontinuing the trial.

FDA-approved pharmacological	Nasser, 2021[454] Supernus Pharmaceuticals, 2017[1100] ID: NCT03247556 RCT Multicenter N = 297 US Setting: Mixed	**Target:** Adolescents with diagnosis of ADHD according to DSM-5, weight>= 35 kg, have an ADHD-Rating Scale-5 Total score >= 28, and a Clinical Global Impression-Severity of Illness score >= 4, without a current diagnosis of a major psychiatric disorder, no major neurological disorder, no significant systemic disease, no evidence of suicidality, no intolerance or allergic reaction to viloxazine, not received any investigational drugs within 30 days of trial **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID) **Comorbidity:** N/A **Female:** 32.2 % **Age mean:** 13.8 (1.6) **Minimum age:** 12 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 33.2 % Black/African American : 29.1 % American Indian or Alaska Native : 0.7 % Native Hawaiian or Pacific Islander : 0.3 % White : 66.1 % Multiracial : 3.8	**Intervention:** Viloxazine extended-release (SPN-812), 600 mg/day group, one 200-mg capsule and two placebo capsules daily during week 1, two 200-mg capsules and one placebo capsule daily during week 2, followed by three 200-mg capsules daily for the remaining 5 weeks **Control:** Placebo Three placebo capsules daily for 7 weeks **Comparator:** MedicationViloxazine, 400-mg/day viloxazine extended-release taken daily for 7 weeks **Follow-up:** 2 months	CGI-I (Clinical Global Impression-Improvement) There was a higher proportion of responders for each week of treatment in both the intervention and comparator groups compared to the placebo group. This difference was statistically significant in the intervention group at Week 3 and in the comparator g ADHD-RS-5 (ADHD Rating Scale-5) change ADHD-RS-5 responders The difference in mean improvement was statistically significant for comparator vs control group (p<0.05), as was the proportion of responders (p < 0.0340). Weiss Functional Impairment Rating Scale (WFIRS-P), parent, change from baseline Total scores were improved in intervention and comparator groups compared to the placebo group, but this difference was not statistically significant for either the 600-mg/ day or 400-mg/day SPN-812 treatment arms (p = 0.9756 and p =0.0698, respectively). Stress Index for Parents of Adolescents (SIPA) scores were lower in the comparator arm compared to placebo (p 0.1259). Appetite changes The rate was 6.1% in the intervention, 6.0% in the comparator, and 2.1% in the control group. Participants with at least one adverse event The rate was 55.6% in the intervention, 58.0% in the

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
				comparator, and 40.2% in the placebo group. The most common treatment-related adverse events that occurred in at least 5% of subjects in any of the active treatment groups were somnolence (15.1%), fatigue (10.6%), headache (8.0%), nausea (6.5%), and decreased appetite (6.0%),

FDA-approved pharmacological	Nasser, 2021[455] Supernus Pharmaceuticals, Inc., 2017[1101] ID: NCT03247543 RCT Multicenter N = 313 US Setting: Mixed	**Target:** Male and female children with a body weight of at least 20 kg and a primary diagnosis of ADHD as defined in the DSM-5, confirmed using the Mini International Neuropsychiatric Interview for Children and Adolescents, and an ADHD-Rating Scale-5 score of at least 28 and a Clinical Global Impression-Severity of Illness score of at least 4 **Other:** Parents/guardians of children with ADHD completed parent rating scales and clinicians completed clinician rating scales **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist primary diagnosis of ADHD as defined in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5), confirmed using the Mini International Neuropsychiatric Interview for Children and Adolescents, and an ADHD-RS-5 score of 28 or higher **Comorbidity:** N/A **Female:** 35.5 % **Age mean:** 8.4 (1.7) **Minimum age:** 6 **Maximum age:** 11 **Ethnicity:** % Hispanic or Latino : 30.2 % Black/African American : 41.5 % American Indian or Alaska Native : 1.0 % Asian : 0.3 % White : 52.8 % Multiracial : 4.3	**Intervention:** Viloxazine, 400 mg FDA-approved viloxazine extended-release, once daily for 8 weeks (including 3 weeks titration period) **Control:** Placebo Four matching placebo capsules daily **Comparator:** MedicationViloxazine, 200 mg mg FDA-approved viloxazine extended-release, once daily for 8 weeks (including 3 weeks titration period) **Follow-up:** 2 months	CGI-I (Clinical Global Impression-Improvement) Intervention and comparator groups had significantly more improvement compared to the control group (p=0.009, p=0.0028). ADHD-RS-5 (ADHD Rating Scale -5) ADHD-RS-5 responders (patients who had a reduction in total score of 50% Intervention and comparator groups had significantly more improvement compared to the control group (p=0.0063, p=0.0038). Weiss Functional Impairment Rating Scale-Parent (WFIRS-P) There was no significant difference between comparator and placebo (p=0.065) or between intervention and placebo (p=0.168). Decreased Appetite Treatment Related Adverse Event Both intervention and comparator group participants had a higher percentage of participants experiencing decreased appetite compared to control group participants. No participants in any treatment group were noted to misuse or overuse medication. The rate of discontinuations due to adverse events in both SPN- 812 treatment groups combined was <5%. All groups had at least 1 or greater adverse events that led to discontinuation of the study.

FDA-approved pharmacological	Nasser, 2021[452] Supernus Pharmaceuticals, Inc., 2016[1099] ID: NCT03247517 RCT Multicenter N = 310 US Setting: N/A	**Target:** Participants with ADHD-Rating Scale-5 Total score ≥28 and a Clinical Global Impression—Severity of Illness core ≥4; refrain from taking other ADHD medications for a minimum of 1 week before randomization and for the study duration; considered medically healthy via assessment of physical examination, medical history, clinical laboratory tests, vital signs, and electrocardiogram; females of childbearing potential had to either be sexually inactive (abstinent) or agree to use one of the acceptable birth control methods beginning 30 days before the first dose and throughout the study **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-V **Comorbidity:** N/A **Female:** 32.4 % **Age mean:** 200mg 13.9 (1.48), 400mg 14.0 (1.59) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** Other : Reported for 200mg= 28.7% / 400mg=31.1% Other : Reported for 200mg=39.4% / 400mg=40.8% Other : reported for 200mg= 1.1% / 400mg=1.9% Other : Reported for 200mg=1.1% / 400mg=1.0% Other : Reported for 200mg=56.4% / 400mg=53.4% Other : reported for 200mg= 2.1% / 400mg=2.9%	**Intervention:** Viloxazine, 400 mg viloxazine extended-release capsules, taken once daily for 6 weeks; one 200-mg Viloxazine extended-release capsule and one placebo capsule daily during week 1, followed by two 200-mg capsules daily for the remaining 5 weeks **Control:** Placebo Capsules were identical in appearance, 2 placebo capsules daily for 6 weeks **Comparator:** MedicationViloxazine, 200-mg viloxazine extended-release capsules for 6 weeks **Follow-up:** 3 months	CGI-I The scores were significantly better in each VLX-ER treatment group compared with placebo (p<0.05). ADHD-RS-5 (ADHD Rating Scale Edition 5) At least 50% reduction ADHD-RS-5 Intervention and comparator groups had significantly greater improvement compared to the control group (p<0.05). Weiss Functional Impairment Rating Scale—Parent (WFIRS-P) There were no significant differences between groups. Decreased appetite The rate was 8.6% in the 400mg, 5.1% in the 200mp, and 0 in the placebo group. Participants with at least 1 adverse event The rate was 53.3% in the 400mg, 43.4% in the 200mg, and 36.5% in the placebo group. The most common treatment-related adverse events were somnolence, headache, decreased appetite, nausea, and fatigue. The adverse event–related discontinuation rates were <5% in all groups.

FDA-approved pharmacological	Newcorn, 2005[461] ID: NA RCT Multicenter N = 297 US Setting: Mixed	**Target:** Children and adolescents with clinical diagnosis of ADHD according to DSM-IV, have a symptom severity score of >=1.5 standard deviations above age and gender norms on the Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent version, have a IQ >= 80 according to the full Wechsler Intelligence Scale for Children-III; no serious medical illness, comorbid psychosis or bipolar disorder, history of a seizure disorder, or ongoing use of psychoactive medications other than the study drug **Other:** **ADHD presentation:** inattentive : 31.4,hyperactive : 1.7,combined : 66.9 **Diagnosis:** Confirmation by specialist Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime versions (K-SADS-PL) **Comorbidity:** N/A **Female:** 28.3 % **Age mean:** ODD 11.2 (2.1), non-ODD 11.1 (2.4) **Minimum age:** 8 **Maximum age:** 18 **Ethnicity:**	**Intervention:** Atomoxetine 1.8 mg/kg/day administered equally divided doses in themorning and late afternoon for 8 weeks **Control:** Placebo Matching placebo for 8 weeks **Comparator:** MedicationAtomoxetine 1.2 mg/kg/day **Follow-up:** 2 months	CGI-S (Clinical Global Impressions of Severity) Tests for a linear dose-response showed a statistically significant effect, suggesting increased efficacy as a function of increasing atomoxetine dose. ADHD-RS-IV-Parent, investigator rated and scored Atomoxetine at 1.8 mg/kg/day, but not 1.2 mg/kg/day, was superior to placebo in reducing symptoms of ADHD among youths with ADHD and ODD, effect sizes were ADHD + ODD (placebo versus ATMX1.2 = 0.49; placebo versus ATMX1.8 = 0.69; placebo versus ATMX1.2 + CHQ Psychosocial Summary scale Changes in ADHD and oppositional symptoms were associated with improvements in broader functioning for youths with ADHD with and without ODD. There was significant improvement on the CPRS-R:S Oppositional subscale for patients with ADHD and ODD receiving atomoxetine doses 0.5 and 1.8 mg/kg/day (effect sizes, ODD: placebo versus ATMX1.2 = 0.39; placebo versus ATMX1.8 = 0.68; placebo versus ATMX1.2 + ATMX1.8 = 0.56; non-ODD: placebo versus ATMX1.2 = 0.55; placebo versus ATMX1.8 = 0.40; placebo versus ATMX1.2 + ATMX1.8 = 0.46.
FDA-approved pharmacological	Newcorn, 2008[460] ID: ID NA Crossover trial Multicenter N = 516 US	**Target:** Children and adolescents with ADHD; no seizures, bipolar disorder, a psychotic illness, a pervasive developmental disorder or who were taking concomitant psychoactive medications, anxiety and tic disorders, nonresponders to methylphenidate or	**Intervention:** Atomoxetine 0.8–1.8 mg/kg per day for 6 weeks **Control:** Placebo Placebo - identically appearing capsules	Daily Parent Ratings of Evening and Morning Behavior—Revised, Evening score, change from baseline There was no difference between comparator and intervention (p=0.21). CGI ADHD severity scale, change in

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
	Setting: N/A	amphetamine or had intolerable adverse events; other concurrent psychiatric diagnoses permitted as long as ADHD was the primary diagnosis **Other:** Parents provided some outcomes **ADHD presentation:** inattentive : 28,hyperactive : 2,combined : 70 **Diagnosis:** Confirmation by specialist DSM-IV via KSADS-PL **Comorbidity:** N/A **Female:** 26 % **Age mean:** Atomoxetine: 10.3 (2.2) Osmotically Released Methylphenidate: 10.2 (2.5) Placebo: 10.1 (2.7) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** N/A	**Comparator:** MedicationOsmotically released methylphenidate, 18–54 mg/day, initiated at 18 mg/day, with increases to 36 mg and 54 mg allowed at the first and second visits **Follow-up:** 1.5 months	Patients on methylphenidate changed more than patients on atomoxetine (p = 0.004) or placebo ADHD-RS (ADHD Rating Scale) total score, change in Osmotically released methylphenidate group improved more than atomoxetine group (p=0.02) Change in weight (kg) Difference from placebo was statistically significant for both active interventions (p<0.05). Adverse events occurring in at least 5% of the patients in any group or that occurred significantly more often for either drug than for placebo: Insomnia was more common for patients assigned to methylphenidate than for those taking placebo; Somnolence wa

FDA-approved pharmacological	Newcorn, 2016[459] Shire, 2010[1057] ID: NCT01081145 RCT Multicenter N = 316 Multiple countries Setting: Mixed	**Target:** Primary diagnosis of ADHD, any subtype, based on a detailed psychiatric evaluation by a licensed clinician using the ADHD-Rating Scale-IV and the Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime version who had age-appropriate intellectual functioning **Other:** **ADHD presentation:** inattentive : 12.1,hyperactive : 3.8,combined : 84.1 **Diagnosis:** Confirmation by specialist DSM-IV-TR detailed psychiatric evaluation by a licenced clinician **Comorbidity:** N/A **Female:** 25.7 % **Age mean:** 10.8 (2.67) **Minimum age:** **Maximum age:** **Ethnicity:** % White : 79.5 Other : 20.5	**Intervention:** Guanfacine hydrochloride extended-release 1-7 mg/day for 13 weeks before withdrawal for 26 weeks **Control:** Placebo Placebo **Comparator:** NA **Follow-up:** 9 months	CGI-S, rated as normal or bordeline mentally ill A larger proportion of participants in the GXR group was rated as normal or borderline mentally ill compared with placebo (p = 0.001). ADHD-RS-IV (ADHD Rating Scale-IV) total score The difference between GXR and placebo was significant (p < 0.001), indicating that the effect of treatment was better maintained with GXR than placebo. Weiss Functional Impairment Rating Scale, Parent (WFIRS-P) There was no difference between groups in global domain score. Treatment failure (defined as (≥50% increase in ADHD Rating Scale version IV total score and ≥2-point increase in Clinical Global Impression-Severity compared with baseline) occurred in 49.3% of the GXR and 64.9% of the placebo group(p = 0.006). Treatment-emergent adverse events The rate was 56.7% in the intervention, and 48.1% in the placebo group. TEAEs led to discontinuation in 1.9% in the GXR group (grand mal convulsion, sedation, somnolence) and 1.3% in the placebo group (one with irritability, the other with chest pain, dizziness, dyspnoea, nausea and tremor). Six participants (GXR, n = 2; plac

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Prasad, 2007[481] ID: NA RCT Multicenter N = 201 UK Setting: Specialty care	**Target:** Children and adolescents with ADHD; no history of bipolar disorder, psychotic disorders, pervasive development disorder, any seizure disorder or alcohol/drug abuse, with significant prior/current medical conditions or at serious suicidal risk, or taking medication that could potentially interfere with study outcomes **Other:** Parents supplied some outcome data **ADHD presentation:** inattentive : 7.5,hyperactive : 2.0,combined : 90.5 **Diagnosis:** Confirmation by specialist DSM-IV criteria by clinical investigator and confirmed by the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Aged Children-Present and Lifetime Versions (K-SADS-PL) **Comorbidity:** N/A **Female:** 11.4 % **Age mean:** 10.9 (2.2) **Minimum age:** 6.9 **Maximum age:** 15.9 **Ethnicity:** % Black/African American : 0.5 % Asian : 0.5 % White : 99.0	**Intervention:** Atomoxetine 0.5 to 1.8 mg/kg/day for 10 weeks **Control:** TAU Standard current therapy **Comparator:** NA **Follow-up:** 2.5 months	CGI-I (Clinical Global Impression Improvement) much improved The intervention group had significantly more improvement compared to the control group ($p<0.001$). ADHD-RS (ADHD Rating Scale), investigator rated ADHD RS, number showing at least 25% improvement Percent improving at least 25% on investigator-rated ADHD-RS total score was statistically superior for atomoxetine group ($p< 0.001$). Weight decreased, number No statistical differences in percent with weight decrease or decreased appetite. There were no deaths and no serious adverse events.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Sallee, 2009[511] Shire, 2004[1054] ID: NCT00150618 RCT Multicenter N = 324 US Setting: Specialty care	**Target:** Children with ADHD; no co-morbid psychological disorders (other than Oppositional Defiant Disorder), medications that might affect blood pressure, morbid obesity or abnormal vital signs, or prior treatment with guanfacine **Other:** **ADHD presentation:** inattentive : 26,hyperactive : 2,combined : 73 **Diagnosis:** Confirmation by specialist DSM IV - TR per psyc evaluation **Comorbidity:** N/A **Female:** 28 % **Age mean:** 11 (3.0) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 9 % Black/African American : 17 % American Indian or Alaska Native : 0.003 Other : 0.3% Asian or Pacific Islander % White : 67 Other : "Other" 4.3%	**Intervention:** Guanfacine extended-release (SPD503) 4 mg g for 9 weeks **Control:** Placebo Placebo **Comparator:** MedicationGuanfacine extended-release (SPD503) 1 mg g for 9 weeks **Follow-up:** 4 months	Child Health Questionnaire-Parent Form (CHQ-PF50), psychosocial score CGI-I (Clinical Global Impressions-Improvement) showing clinical improvement Intervention and comparator groups had significantly more improvement compared to control group (p = 0.0237). ADHD-RS-IV total score change, parent report Intervention and comparator groups had significantly more improvement compared to control group (p 0.003, p 0.01). Medication was not associated with abnormal changes in height or weight. No specific data or p value reported. Adverse events occurring in 5% or greater in participants taking medication were somnolence, headache, fatigue, sedation, dizziness, irritability, upper abdominal pain, and nausea.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Sangal, 2006[512] ID: NA Crossover trial Multicenter N = 85 US Setting: Other	**Target:** Children with ADHD and no pre-existing sleep disorders or serious medical conditions **Other:** **ADHD presentation:** inattentive : 29.8,hyperactive : 2.4,combined : 67.9 **Diagnosis:** Confirmation by specialist DSM IV diagnosis a. Diagnosis per investigator's clinical evaluation and by the administration of several modules of the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version structured interview **Comorbidity:** N/A **Female:** 24.7 % **Age mean:** 10.1 (2.0) **Minimum age:** 6 **Maximum age:** 14 **Ethnicity:** % White : 72.9 Other : 27.1% non-white	**Intervention:** Atomoxetine 1.0-1.8 mg/kg/day divided into twice daily doses for 7 weeks **Control:** NA **Comparator:** MedicationMethylphenidate, three times per day **Follow-up:** 1.8 months	Daily Parent Ratings of Evening and Morning Behavior (DPREMB) There were statistically significant differences in favor of atomoxetine (p=0.003). Clinical Global Impression-Severity (CGI-S) There was no significant difference between groups at follow up. ADHD-RS-IV (ADHD rating scale-IV), parent report There was no significant difference between groups (p = 0.427). Methylphenidate increased sleep-onset latency significantly more than did atomoxetine (p<0.001). Child diaries indicated better sleep (p=0.045), ease to get up in the morning (p=0.004), and less time to fall asleep (p=0.001) with atomoxetine. Number of patients with decreased appetite Greater incidence of decreased appetite with methylphenidate (p=0.03). No significant difference in percent reporting headache, irritability, congestion, cough, and intestinal pain. More methylphenidate patients reported insomnia (p < .001).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
FDA-approved pharmacological	Seattle Children's, 2015[193] ID: NCT02293655 RCT Multicenter N = 109 US Setting: Specialty care	**Target:** Children with ADHD with normal physical exam and ECG findings; those with serious psychological co-morbidities or participating in ADHD-related behavioral interventions were excluded **Other:** Parents and teachers provided some outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-V **Comorbidity:** N/A **Female:** 33.9 % **Age mean:** all 18 or under **Minimum age:** 7 **Maximum age:** 11 **Ethnicity:** % Hispanic or Latino : 8.3 % Black/African American : 7.3 % American Indian or Alaska Native : 0 % Asian : 2.8 % Native Hawaiian or Pacific Islander : 0 % White : 80.7 % Multiracial : 9.2	**Intervention:** Methylphenidate, OROS, 4-week titration, followed by 4-week MPH maintenance phase, followedby 4-week MPH continuation phase; total duration of 8 weeks **Control:** Placebo Methylphenidate titration 4-weeks, followed by 4-week MPH maintenance phase, followed by 4-week MPH discontinuation phase using placebo **Comparator:** NA **Follow-up:** 1 month	ADHD RS, Total, parent report Maintenance group had lower symptoms than discontinuation group (p 0.01) Inhibitory Control Reaction Time, measured by Go-No Go test: discontinuation group scored significantly worse (p 0.001). Math Computation - Number of Problems Completed Correctly: no significant difference (p 0.07). Decreased appetite Sustained MPH patients had higher rate of decreased appetite. 1 discontinuation patient had a serious adverse event (suicidal ideation).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Shang, 2020[525] Shang, 2015[1037]; Wu, 2021[1180]; Shih, 2019[1041]; Hospital, National Taiwan University, National Science Council, 2009[953] ID: NCT00916786 RCT Single center N = 168 Taiwan Setting: Specialty care	**Target:** Drug naive children with ADHD; no comorbid psychiatric conditions, including psychosis, bipolar disorders, autism spectrum disorders, substance use disorders, intellectual disability (IQ<80), or had a history of major medical or neurological problems **Other:** Parents **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DMS IV, Chinese version of the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children–Epidemiological Version (K-SADS-E) to confirm ADHD **Comorbidity:** N/A **Female:** 13 % **Age mean:** 8.7 (2.56) **Minimum age:** 7 **Maximum age:** 16 **Ethnicity:** % Asian : 100	**Intervention:** Atomoxetine: an initial dosage of 0.5 mg/(kg per day), administered as once-daily dose, titrated at visits 2–7 (weeks 2–24) according to clinical response and adverse effects; max dose 1.2 mg/kg daily, total duration of 24 weeks **Control:** NA **Comparator:** MedicationMethylphenidate, initial dosage of 18 mg/day, administered as a single morning dose, titrated at visits 2–7 (weeks 2–24) according to clinical response and adverse effects, max dose 54 mg/day **Follow-up:** 8 months	Home Behaviors subcale of the Social Adjustment Inventory for Children and Adolescents (SAICA), parent, change from baseline There was no significant difference between groups (p=0.097). CBCL (Child Behavior Checklist) The intervention group improved more on aggressive behavior subscale (p = 0.032) and somatic complaint subscale (0.008) than the comparator group but none of the other subscales. Both treatment groups showed improvement in executive functions (p-value <0.05 for the major indices of each domain). Magnitude of increasing detectability (p< 0.01) and reducing commission errors (p<0.05) was significantly greater in the intervention group vs comparator group.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Shaywitz, 2017[526] Eli Lilly and Company, 2008[755] ID: NCT00607919 RCT Multicenter N = 124 US Setting: Other	**Target:** Children with ADHD per DSM-IV-TR criteria; met criteria for dyslexia; IQ>=80; no history of bipolar I or bipolar II disorder, psychosis, autism, Asperger's syndrome, or pervasive developmental disorder, or were currently taking anticonvulsants for seizure control **Other:** **ADHD presentation:** inattentive : 46,hyperactive : 2.4,combined : 51.6 **Diagnosis:** Confirmation by specialist DSM-IV-TR criteria for ADHD diagnosis confirmed during the first screening visit **Comorbidity:** Learning disability : Dyslexia alone group and dyslexia + ADHD subgroup **Female:** 36.3 % **Age mean:** Intervention mean age 12.2, control mean age 12.3 **Minimum age:** 10 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 15.3 % Black/African American : 13 % Asian : 2.4 % White : 69.4	**Intervention:** Atomoxetine 1.0–1.4mg/[kg*day] once daily for 16 weeks **Control:** Placebo Placebo once daily for 16 weeks **Comparator:** NA **Follow-up:** 4 months	ADHD-RS-IV-Parent:Inv scores ADHD symptom decreases were significantly greater for patients treated with atomoxetine. Reading abilities change from baseline measured using Gray Oral Reading Tests-4. N of participants intervention group (51). Academic rating scale least-squares mean change scores intervention group (-2.19). N of participants control group (55). Academic r

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Simonoff, 2013[538] ID: N/A RCT Single center N = 122 UK Setting: Specialty care	**Target:** Children with a diagnosis of ICD-10 hyperkinetic disorder and a full-scale IQ of 30–69 **Other:** **ADHD presentation:** N/A : 100% with a diagnosis of ICD-10 hyperkinetic disorder **Diagnosis:** Confirmation by specialist Diagnosis of hyperkinetic disorder was made using the Child and Adolescent Psychiatric Assessment **Comorbidity:** Learning disability : Full-scale IQ of 30–69 **Female:** 30 % **Age mean:** 13.4 (28) **Minimum age:** 7 **Maximum age:** 15 **Ethnicity:**	**Intervention:** Methylphenidate (equasym), dose titration comprised at least 1 week each of low (0.5 mg/kg/day), medium (1.0 mg/kg/day) and high dose (1.5 mg/kg/day), taken for 16 weeks **Control:** Placebo Placebo medication, offered active medication after the trial **Comparator:** NA **Follow-up:** 4 months	CGI-I improved 40% of participants receiving methylphenidate compared to 7% of placebo were rated as improved. ADHD Index Conners Rating Scale-Short Version-Parent Methylphenidate was superior to placebo for the parent Conners ADHD index. Methylphenidate was superior to placebo for the teacher Conners ADHD index. Poor appetite 15% of patients receiving methylphenidate compared to 2% on placebo reported poor appetite. 16 withdrew from the trial, 5 were due to adverse events following methylphenidate; 21% vs 3% had trouble getting to sleep (P<0.01) but there was no difference in looks sad/miserable, crying, looks anxious, meaningless repetitive behavior, talks less with

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
FDA-approved pharmacological	Singer, 1995[540] ID: N/A RCT Single center N = 37 US Setting: N/A	**Target:** Children with Tourette's Syndrome and ADHD of normal intellect **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** Tic disorder **Female:** 8 % **Age mean:** mean age 10.6 **Minimum age:** 7 **Maximum age:** 13 **Ethnicity:** % Black/African American : 3 % White : 89	**Intervention:** Clonidine 0.05 mg 4 times daily for 6 weeks **Control:** Placebo Uniform-appearing capsule **Comparator:** MedicationDesipramine (25 mg four times daily), each child started with one capsule per day (evening) and added 1 additional capsule every week to a maximum daily dose of one capsule 4 times a day; patients then were maintained on the highest daily dose for an addi **Follow-up:** 1.5 months	Hyperactivity scale CBCL (Child Behavior Checklist) Desipramine was significantly better than placebo and clonidine (p <0.05). A global linear analogue comparing the child's current tics to tics anytime in the past, showed a statistically significant drug effect (P < .05), with orthogonal contrasts demonstrating that desipramine was superior to clonidine (P < .01). Results with clonidine did not differ from placebo, whereas desipramine significantly reduced tics compared to placebo (P <.05). Participants with at least one drug-related problem The rate was 82% for intervention, 44% for control, and 76% for comparator.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Spencer, 2002[554] ID: Study 1 RCT Multicenter N = 144 US Setting: Specialty care	**Target:** Children with ADHD, patients who weighed less than 55 pounds, were on psychoactive medication, or had a history of psychosis or bipolar disorder were excluded; those who were prognosed to be poor metabolizers of medication based on a genetic test were excluded **Other:** Parents provided some outcomes **ADHD presentation:** inattentive : 18,hyperactive : 1,combined : 81 **Diagnosis:** Confirmation by specialist DSM IV assessed by clinical interview and the Kiddie Schedule for Affective Disorders & Schizophrenia **Comorbidity:** N/A **Female:** 20.6 % **Age mean:** 9.8 (1.55) **Minimum age:** 7 **Maximum age:** 12 **Ethnicity:**	**Intervention:** Atomoxetine 3 times per day, drug dosage based on weight, for 12 weeks **Control:** Placebo Placebo 3 times per day, for 12 weeks **Comparator:** NA **Follow-up:** 2 months	CGI-Severity Significantly greater mean improvement in CGI-S scores (p<0.001) and Conners Parent Rating Scale in atomoxetine patients than placebo patients. ADHD RS total, mean improvement ADHD RS, response (25% decrease in total score) Atomoxetine patients had greater mean improvement than placebo patients (p<0.001) and a significantly greater rate of response.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Spencer, 2002[555] ID: Study 2 RCT Multicenter N = 147 US Setting: Specialty care	**Target:** Children with ADHD, stimulant naive patients, who weighed less than 55 pounds, were on psychoactive medication, or had a history of psychosis or bipolar disorder were excluded; those who were prognosed to be poor metabolizers of medication based on a genetic test were excluded **Other:** Parents provided some outcomes **ADHD presentation:** inattentive : 18,hyperactive : 1,combined : 81 **Diagnosis:** Confirmation by specialist DSM IV assessed by clinical interview and the Kiddie Schedule for Affective Disorders & Schizophrenia **Comorbidity:** N/A **Female:** 20.6 % **Age mean:** 9.8 (1.55) **Minimum age:** 7 **Maximum age:** 12 **Ethnicity:**	**Intervention:** Atomoxetine 3 times per day, drug dosage based on weight, for 12 weeks **Control:** Placebo Placebo 3 times per day, for 12 weeks **Comparator:** MedicationMethylphenidate in the morning and midday and placebo dose in the evening, titrated to 1.5 mg/kg/day or total daily dose of 60mg, based on therapeutic response, for 12 weeks **Follow-up:** 2 months	CGI-Severity Significantly greater mean improvement in CGI-S scores (p<0.001) and Conners Parent Rating Scale in atomoxetine patients than placebo patients. ADHD RS total, mean improvement ADHD RS, response (25% decrease in total score) Atomoxetine patients had greater mean improvement than placebo patients (p<0.001) and a significantly greater rate of response.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Spencer, 2006[557] ID: NA RCT Unclear/Not reported N = 287 US Setting: Specialty care	**Target:** Adolescents with ADHD, known to be nonresponsive to stimulants or naive to stimulant treatment; no comorbid psychiatric diagnosis except oppositional defiant disorder, hypertension, history of seizure disorder within the last 2 years, tic disorder, Tourette's syndrome, abnormal thyroid function, cardiac disorder, and significant laboratory abnormalities **Other:** **ADHD presentation:** inattentive : 41.0,hyperactive : 2.5,combined : 56.5 **Diagnosis:** Confirmation by specialist DSM-IV-TR **Comorbidity:** N/A **Female:** 34.5 % **Age mean:** 14.2 (1.2) **Minimum age:** 13 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 6.8 % Black/African American : 15.8 % White : 73.7 Other : Other 3.6	**Intervention:** Mixed amphetamine salts extended release 40 mg per day for 4 weeks **Control:** Placebo Placebo **Comparator:** MedicationMixed amphetamine salts extended release (Adderall MX) 10 mg per day **Follow-up:** 1 month	CGI-I (Clinical Global Impression – Improvement scale) improved A higher percentage of patients in the medication groups were considered improved compared with those receiving placebo (p< 0.001). ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale-IV) Statistically significant (p < 0.001) improvement in mean ADHD-RS-W total scores in medication groups compared with placebo. Anorexia/decreased appetite, number of patients Significantly more medication patients experienced decreased appetite and weight loss compared to placebo patients. p value not reported. Insomnia and abdominal pain more prevalent in medication patients. p value not reported.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Spencer, 2008[556] ID: N/A RCT Multicenter N = 117 US Setting: N/A	**Target:** Children with Tourette's syndrome and scoring 1.5 standard deviations above sex norm for their diagnostic subtype at enrollment and at randomization for the Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent version **Other:** **ADHD presentation:** inattentive : 30.8,hyperactive : 3.4,combined : 65.8 **Diagnosis:** Confirmation by specialist met the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for ADHD and concurrent TS. Subjects' scores on the Attention-Deficit/Hyperactivity Disorder Rating Scale- IV-Parent Version:Investigator-administered and -scored (ADHDRS-IV-P **Comorbidity:** Tic disorder **Female:** 12.8 % **Age mean:** 11.2 (2.4) **Minimum age:** 7 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 4.3 % Black/African American : 4.3 % Asian : 0.9 % White : 88.0	**Intervention:** Atomoxetine 0.5-1.5 mg/kg/day, as a divided dose, for 15 weeks **Control:** Placebo Placebo **Comparator:** NA **Follow-up:** 3 months	CGI-ADHD/Psych-S ADHD-RS-IV, parent Intervention participants showed significantly greater improvement compared to controls (p=0.011). The intervention group showed a significantly greater decrease from baseline in tic severity relative to control (p=0.027). Body weight change Decreased appetite The rate was 18% in the atomoxetine vs 10.3% in the placebo group. Discontinuations because of an adverse event were rare, with 2 in the atomoxetine group (headache, vomiting) and 1 in the placebo group (upper abdominal pain).

FDA-approved pharmacological	Steele, 2006[561] ID: n/a RCT Multicenter N = 147 Canada Setting: Specialty care	**Target:** Children with ADHD; medication naïve, Clinical Global Impression Severity score of 4 or greater and with behavioral difficulties **Other:** Parents reported some outcomes **ADHD presentation:** inattentive : 18.37,hyperactive : 2.04,combined : 78.23 **Diagnosis:** Confirmation by specialist DSM IV by clinical and structural interview **Comorbidity:** N/A **Female:** 16.6 % **Age mean:** 9.0 (2.1) and 9.1 (1.8) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Black/African American : 3.4 % Asian : 0.6 % White : 85.7 Other : 8.8% other	**Intervention:** Methylphenidate OROS (osmotic release oral system), 18-54 mg once daily for 8 weeks **Control:** NA **Comparator:** MedicationImmediate release methylphenidate initiated at what ever dose the clinician felt was appropriate and over the weeks each individual dose was titrated weekly by 5mg or 10mg increments, according to manufacturer's recommendations and the investigator's clin **Follow-up:** 2 months	Homework visual analog scale There was no statistically significant difference between groups CGI-I Clinical Global Severity, change Statistically significant difference favoring intervention group (p < .001) SNAP-IV, 26 item score, parent report, reduction There was a statistically significant reduction in scores favoring OROS (p = .004) Parent satisfaction with current ADHD medication There was a statistically significant difference in parent satisfaction favoring OROS (p = 0.003) Parent Stress Index scores showed significant differences in favor or OROS (p = 0.008) Decreased appetite Rates were similar in both groups. Participants with any adverse event The rate was 82% for both intervention and comparator. Adverse events (any possible medication related event, headache, insomnia, abdominal pain, nervousness, emotional lability, agitation, fatigue, flu-like symptoms, sleep disorder) were similar between groups.
FDA-approved pharmacological	Su, 2016[568] Peking University, 2010[980]; Yang, 2012[1183] ID: NCT01065259 RCT Single center N = 237	**Target:** Youth with ADHD, either treatment naive or untreated for at least 6 months; no history of poor response with adequate treatment or intolerance to either treatment medication; no medical contraindications to stimulants or who had seizure disorder or an abnormal EEG associated with epilepsy, bipolar disorder, psychosis, anxiety disorder, depression disorder, tic disorder,	**Intervention:** Atomoxetine initiated at a dose of 0.5 mg/kg/day, which could increase to 0.8mg/kg/day for week 2, and 1.2mg/kg/day for weeks 3 and 4; initially administered once daily in the morning and could be switched to being administered twice daily when adverse events	CGI-ADHD-S Remission Rate There was no significant difference between groups (0.972). ADHD-RS Remission Rate There was no significant difference between groups (p 0.777). Both OROS-MPH and ATX significantly improved the parent- and

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
	China Setting: N/A	pervasive developmental disorder, or an IQ less than 70, children taking concomitant psychoactive medications including dietary supplements with central nervous system activity in the past 30 days **Other:** **ADHD presentation:** inattentive : 48,hyperactive : 3,combined : 49 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 17 % **Age mean:** 9.5 (1.9) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** N/A	were intolerable, with follow-up up to 1 year **Control:** NA **Comparator:** MedicationOsmotic Release Oral System Methylphenidate optimized dose (18, 36, or 54 mg/day) for 4 weeks **Follow-up:** 12 months	teacher-rated BRIEF and the groups did not differ significantly. Appetite change No statistically significant differences between the two groups (p=0.455). Adverse events rated as severe occurred in 14% of the OROS MPH group and 18.7% of the ATX group (p > 0.05).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Svanborg, 2009[573] Svanborg, 2009[1102] ID: NA RCT Single center N = 92 Sweden Setting: Specialty care	**Target:** Male and female children and adolescents that met the criteria for ADHD of the DSM- IV **Other:** **ADHD presentation:** inattentive_other : 18.2% across all arms,hyperactive_other : 4% across all arms,combined_other : 77.8% across all arms **Diagnosis:** Confirmation by specialist clinical interview **Comorbidity:** N/A **Female:** 19.2 % **Age mean:** Mean 12.8 **Minimum age:** 7 **Maximum age:** 15 **Ethnicity:** Other : 0-1%across all arms Other : 3% across all arms Other : 93.9% across all arms Other : 2.2% across all arms	**Intervention:** Atomoxetine plus psychoeducation for caregivers, 1.2 mg/kg day (70 kg) or 80 mg/day (>70 kg) for 10 weeks **Control:** Placebo Placebo capsules plus psychoeducation for caregivers for 10 weeks **Comparator:** NA **Follow-up:** 2.75 months	CGI-I (Clinical Global Impression Improvement), change from baseline An improvement was observed in the atomoxetine group whereas in the placebo group the score changed only slightly ($p < 0.001$). ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale IV)–Parent Version: Investigator Administered and Scored Treatment responders Statistically significant between-treatment differences in favor of atomoxetine at each visit ($P < 0.001$) from visit 4 (week 3) onwards. The global parental assessment of most aspects of psychoeducation was very positive; items were mostly rated as very good/very satisfied or rather good/satisfied. Decreased appetite The rate was 6.1% in the intervention and 0 in the placebo group (p 0.117). Patients with at least 1 treatment emergent adverse event The rate was 89.8% in the intervention, and 74% in the placebo group (p 0.066). No serious adverse events occurred in either group.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Takahashi, 2009[575] ID: NA RCT Multicenter N = 245 Japan Setting: Mixed	**Target:** Children and adolescents with DSM-IV diagnosis of ADHD, Clinical Global Impressions-ADHD-Severity score of >= 3, have symptom severity score at least 1.5 standard deviations above Japanese pediatric age and gender norms on the Attention-Deficit-Hyperactivity Disorder Rating Scale-IV–Parent Version: Investigator Administered and Scored, IQ >= 80; no antipsychotic medication within 26 weeks of study visit 1, history of bipolar disorder or psychosis, or at suicidal risk **Other:** **ADHD presentation:** inattentive : 61.2,hyperactive : 4.5,combined : 34.5 **Diagnosis:** Confirmation by specialist Kiddie Schedule for Affective Disorders and Schizophrenia for School- Aged Children–Present and Lifetime Versions (KSADS-PL) **Comorbidity:** N/A **Female:** 14.7 % **Age mean:** 10.53 (2.52) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Asian : 100	**Intervention:** Atomoxetine 1.8 mg/kg per day for 8 weeks **Control:** Placebo Placebo pills 2 times a day for 8 weeks **Comparator:** MedicationAtomoxetine 0.5 mg/kg per day for 8 weeks **Follow-up:** 2 months	ADHD RS-IVJ:I (Attention-Deficit Hyperactivity Disorder Rating Scale-IV–Parent Version: Investigator Administered and Scored-Translated and Validated in Japanese) 1.8 mg per day atomoxetine was superior to placebo (p 0.010). Decreased appetite The rate was 21.3% in the intervention, 4.8% in the comparator, and 3.2% in the placebo group. Participants with one or more treatment-emergent adverse event The rate was 78.7% for the intervention, 79.0% for the comparator, and 69.4% for placebo. Two serious adverse events occurred, both in the same patient in the intervention group (hospitalization due to headache and vomiting).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Tris Pharma, 2014[588] ID: NCT02083783 RCT Multicenter N = 108 US Setting: Other	**Target:** Children with ADHD who require pharmacologic treatment for ADHD, no other serious illnesses or conditions that would put the patient at particular risk for safety events or would interfere with treatment/assessment of ADHD **Other:** **ADHD presentation:** inattentive : 20,hyperactive_other : impulsive 1,combined : 78 **Diagnosis:** No **Comorbidity:** N/A **Female:** 31 % **Age mean:** 9.4 (1.86) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 39 % Black/African American : 34 % White : 55 % Multiracial : 10	**Intervention:** TRI102 formulation containing active moiety (amphetamine), i.e amphetamine extended-release oral suspension, 10 to 20 mg/day for 5 weeks **Control:** Placebo Placebo formulation without active moiety **Comparator:** NA **Follow-up:** 1.25 months	Swanson, Kotkin, Agler, M-Flynn, and Pelham Scale (SKAMP), change from baseline The intervention significantly improved compared to control group (p<0.0001). PERMP (Permanent Product Measure of Performance) - The PERMP consists of 400 math questions and each are scored. PERMP scores are expressed as the number of questions correct. Predose PERMP Tests are compared with post-dose PERMP scores at prespecfied tim Significant improvement compared to placebo (p<0.0001). In the intervention group, 3.85% reported pain in the upper abdomen, 3.85% epistaxis,3.85% rhinitis; only one person (2.08%) in the placebo group reported pain in the upper abdomen.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	TS SG, 2002[380] ID: NA RCT Multicenter N = 65 US Setting: N/A	**Target:** Children meeting the DSM-IV criteria for ADHD and for Tourette disorder, chronic motor tic disorder or chronic vocal tic disorder; excluded if there was evidence of secondary tic disorder, major depression, pervasive developmental disorder, autism, psychosis, mental retardation, anorexia nervosa, bulimia, a serious cardiovascular or other medical disorder that would preclude the safe use of the medication, impaired renal function, or pregnancy **Other:** **ADHD presentation:** inattentive : 71,hyperactive : 2,combined : 27 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** Tic disorder **Female:** 15 % **Age mean:** Placebo 9.7 (1.8), Combination 10.6 (1.9) **Minimum age:** 7 **Maximum age:** 14 **Ethnicity:** % White : 72	**Intervention:** Methylphenidate plus alpha agonist, 60mg/day ritalin plus 0.6mg/day clonodine for 8 weeks **Control:** Placebo Placebo **Comparator:** Medication **Follow-up:** 4 months	Classroom observation disruptive behavior MPH (but not CLON) improved "on task" behavior. CGI (Clinical Global Impression) investigator judged improvement of ADHD Combined intervention had 87.5% improvement, placebo 32.3%. Children's Global Assessment Scale (C-GAS) Intervention and comparator groups significantly improved over control group (p 0.002, p 0.0005). A similar pattern of treatment effects was found when analyzing secondary outcome measures for ADHD, including Iowa Conners. 20% with MPH reported a worsening of tics as an adverse event (8 when used alone, 6 when given in combination with CLON) compared with 26% treated with CLON alone and 22% receiving placebo. Tics were reported to limit further dosage increases more often f

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	TS SG, 2002b[381] ID: ID NA RCT Multicenter N = 71 US Setting: N/A	**Target:** Children meeting the DSM-IV criteria for ADHD and for Tourette disorder, chronic motor tic disorder or chronic vocal tic disorder; excluded if there was evidence of secondary tic disorder, major depression, pervasive developmental disorder, autism, psychosis, mental retardation, anorexia nervosa, bulimia, a serious cardiovascular or other medical disorder that would preclude the safe use of the medication, impaired renal function, or pregnancy **Other:** **ADHD presentation:** inattentive : 71,hyperactive : 2,combined : 27 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** Tic disorder **Female:** 15 % **Age mean:** MPH 10.7 (2.0), CLON 9.7 (1.8) **Minimum age:** 7 **Maximum age:** 14 **Ethnicity:** % White : 72	**Intervention:** Clonodine (alpha agonist), 0.6mg/day for 8 weeks **Control:** NA **Comparator:** MedicationMethylphenidate, 60mg/day ritalin for 8 weeks **Follow-up:** 4 months	Classroom observation disruptive behavior MPH but not CLON improved “on task” behavior. CGI (Clinical Global Impression) investigator judged improvement of ADHD MPH 80.6%, CLON 60.6% improvement. Children’s Global Assessment Scale (C-GAS) Intervention and comparator groups significantly improved over control group (p 0.002, p 0.0005). A similar pattern of treatment effects was found when analyzing secondary outcome measures for ADHD, including Iowa Conners. 20% with MPH reported a worsening of tics as an adverse event (8 when used alone, 6 when given in combination with CLON) compared with 26% treated with CLON alone. Tics were reported to limit further dosage increases more often for subjects assigned to MP

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	van Stralen, 2020[598] JPM van Stralen Medicine Professional, 2013[872] ID: NCT01985581 Crossover trial Single center N = 50 Canada Setting: Specialty care	**Target:** Children with a diagnosis of inattentive, hyperactive, or combined subtype of ADHD, being treated with stimulant medication and presenting with suboptimal executive function **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV-TR diagnosed via clinical assessment and ADHD-RS-IV **Comorbidity:** N/A **Female:** 16.0 % **Age mean:** Meds then placebo group; 9.4 (1.6) / Placebo then meds; 9.0 (1.4) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Guanfacine extended-release 4 mg/day plus usual stimulant therapy for 8 weeks **Control:** Placebo Placebo plus usual stimulant therapy **Comparator:** NA **Follow-up:** 2 months	CGI-S (Clinical Global Impressions - Severity) Intervention group had significantly lower severity at follow-up (p =.0007). ADHD-RS-IV, total score Intervention had significantly lower symptom score at follow-up (p < .001). Participants with any adverse event The rate was 87% in the intervention and 85% in the control group. Intervention group reported more abdominal pain, fatigue, affect lability, and somnolence.

FDA-approved pharmacological	Wang, 2007[604] ID: N/A RCT Multicenter N = 330 Multiple countries Setting: N/A	**Target:** Eligible participants included outpatient children and adolescents, 6-16 years of age, weighing between 20 and 60 kg with a symptom threshold of >=25 for boys or >=22 for girls, or >12 for a specific subtype, on the Attention Deficit Hyperactivity Disorder Rating Scale-IV-Parent Version: Investigator-Administered and -Scored, as well as a Clinical Global Impressions Attention Deficit Hyperactivity Disorder-Severity (CGI-ADHD-S) score of >=4. Exclusion criteria included any history of bipolar, psychotic or pervasive developmental disorders; suicidal risk; or ongoing use of psychoactive medications other than the study drug. Patients with motor tics, a diagnosis or family history of Tourette's syndrome or those who met DSM-IV criteria for anxiety disorder as assessed by the investigator and confirmed by the K-SADS-PL were also excluded **Other:** **ADHD presentation:** inattentive : 38,hyperactive : 3,combined : 59 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 18 % **Age mean:** Atomoxetine 9.4 (2.0) Methylphenidate 9.9 (2.3) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** % Hispanic or Latino : 8 % Asian : 92	**Intervention:** Atomoxetine 0.8-1.8 mg/kg/day for 8 weeks **Control:** NA **Comparator:** MedicationMethylphenidate, began therapy at 0.2 mg kg^(-1) day^(-1) administered twice daily (in the morning and at lunch), which was titrated to 0.4 mg kg^(-1) day^(-1) on Day 5, and could be either maintained or titrated upward or downward within the final range **Follow-up:** 2 months	CGI-ADHD-S (Clinical Global Impressions-Attention Deficit Hyperactivity Disorder-Severity) scale Both groups improved. ADHD-RS-IV (Attention Deficit Hyperactivity Disorder Rating Scale-IV-Parent Version), investigator-administered, change Similar improvement between the treatment groups. Weight loss Decreased appetite The rate for appetite suppression was 28% in the atomoxetine and 19% in the methylphenidate group (p 0.070). Atomoxetine reported -1.2 kg vs. methylphenidate -0.4 kg weight loss (p 0.001). Participants experiencing treatment emergent adverse events A significantly greater percentage of patients in the atomoxetine treatment group (87%) experienced events compared with methylphenidate (67%; p<0.001). No deaths were reported, a simple partial seizure was reported for a patient in the atomoxetine group (discontinued from the study).

FDA-approved pharmacological	Wehmeier, 2012[608] Eli Lilly and Company, 2007[753] ID: NCT00546910 RCT Multicenter N = 128 Germany Setting: Mixed	**Target:** Girls and boys with a diagnosis of ADHD according to the DSM 4th edition TR **Other:** **ADHD presentation:** inattentive : 22.4,hyperactive : 7.2,combined : 70.4 **Diagnosis:** Confirmation by specialist **Comorbidity:** N/A **Female:** 22.4 % **Age mean:** 9.0 (1.79) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % White : 99.2	**Intervention:** Atomoxetine 0.5-1.2 mg/kg per day once daily in the morning for 8 weeks **Control:** Placebo Placebo-controlled **Comparator:** NA **Follow-up:** 2 months	Weekly Ratings of Evening and Morning Behavior (WREMB) The severity of ADHD symptoms was reduced to a statistically significantly greater degree in the treatment group compared to placebo (p<0.001). CGI-S The severity of ADHD symptoms was reduced to a statistically significantly greater degree in the treatment group compared to placebo (p<0.001). ADHD-RS-IV The severity of ADHD symptoms was reduced to a statistically significantly greater degree in the treatment group compared to placebo (p<0.0001). Treatment was significantly superior to placebo in reducing hyperactivity, inattention, and impulsivity as measured by q-scores of 10 primary variables of the cb-CPT/MT (infrared motion-tracking devise). Decreased appetite The rate of decreased appetite was 1.6 in the intervention and 3.2 in the placebo group. Participants with treatment emergent adverse events The rate of participants with adverse events was 51% in the intervention and 44% in the control group. No serious treatment emergent adverse event or death occurred.
FDA-approved pharmacological	Weiss, 2005[611] Brown, 2006[696] ID: N/A RCT Multicenter N = 153	**Target:** Children with a standard deviation score of 1.0 for ADHD-Rating Scale-IV-Teacher Version and score at least 1.5 standard deviations above age and sex norm for the Conners Parent Rating Scale-Revised: Short Form ADHD Index	**Intervention:** Atomoxetine up to 1.8 mg/kg/day for 7 weeks **Control:** Placebo Identical in appearance, once-daily for 7 weeks **Comparator:** NA	Connors Global Index-Teacher, change from baseline Statistically significant change favored the treatment group change compared to the placebo group (p=0.008).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
	Multiple countries Setting: Mixed	**Other:** Teachers had to be available for telephone interviews and updates on the progress **ADHD presentation:** inattentive : 26.8,hyperactive : 0.7,combined : 72.5 **Diagnosis:** Confirmation by specialist Followed the DSM-IV: "Diagnostic criteria were evaluated by clinic assessment and confirmed using a structured parent interview, the behavioral module of the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime V **Comorbidity:** N/A **Female:** 19.6 % **Age mean:** 9.9 (1.3) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** N/A : Not mentioned or brought up.	**Follow-up:** 1.75 months	ADHD-RS-IV-Teacher (Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Teacher) total score change Only the standardized symptoms scores for the continuous data is available. Treatment group responded with a reduction in score by 20% compared to the placebo group (Fisher exact test p 0.003). Decreased appetite Decreased appetite was 24.0% vs 3.8% (p 0.001). 5.9% in the atomoxetine group discontinued due to adverse events, including abdominal pain, emotional disturbance, feeling abnormal, irritability, and vomiting; no patients in the placebo group discontinued due to adverse events.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Weiss, 2007[610] ID: N/A Crossover trial Multicenter N = 90 Canada Setting: Mixed	**Target:** Children with ADHD, score of 1.5 or greater standard deviation from the norm on the Conners' ADHD Index; no allergy to methylphenidate or amphetamines or history of serious adverse reactions to methylphenidate or lack of response to methylphenidate, serious or unstable medical illness, co-morbid psychiatric illness of sufficient severity to require treatment, or currently receiving psychotropic medications or herbal treatments, a history of drug abuse, alcohol abuse, disorders of the sensory organs, autism, psychosis, or any unstable psychiatric conditions **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 18 % **Age mean:** 11.0 (2.5) **Minimum age:** 6.4 **Maximum age:** 17.5 **Ethnicity:** % Black/African American : 6 % Asian : 4 % White : 83 Other : 7	**Intervention:** Methylphenidate long-duration multilayer-release, once daily based on weight (10 mg for 20 kg, 20 mg for between 20 and 35 kg, and 30 mg for greater than 35 kg) for 2 weeks **Control:** Placebo Placebo in the morning and at midday **Comparator:** MedicationImmediate-release MPH administered daily at 08:00 hour +/- 1 hour and 12:00 hour +/- 1 hour, initial daily dose was based on body weight (10 mg for <= 20 kg, 20 mg for between 20 and 35 kg, and 30 mg for greater than 35 kg), daily dose was titrated in 10- **Follow-up:** 2.75 months	Home Situations Questionnaire (HSQ), number of problem situations Both groups improved significantly form baseline but there was no difference between groups. CGI (Clinical Global Impressions), investigator rating No difference between active groups. ADHD Index, CPRS (Conners' Parent and Teacher Rating Scales) Both active groups improved compared to baseline ($p<0.05$). PSS (Parent Satisfaction Survey), satisfied or very satisfied with treatment 77% of parents were satisfied or very satisfied with MLR-MPH treatment and 82% with IR-MPH. Decrease in ADHD Index and oppositional scales, which was of similar magnitude for MLR- and IR-MPH in patients. Decreased appetite There was no statistically significant difference between active treatment groups. There were no significant differences between treatments in the adverse effects.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Weiss, 2021[612] Rhodes Pharmaceuticals, 2014[1000]; Rhodes Pharmaceuticals, 2014[1001] ID: NCT02139111, NCT02168127 RCT Multicenter N = 367 Multiple countries Setting: Specialty care	**Target:** Children diagnosed with of any presentations of ADHD (hyperactive/impulsive, inattentive, or combined); either treatment naıve or dissatisfied with their current ADHD pharmacotherapy; age-appropriate intellectual functioning (IQ ≥80 based on the Wechsler Abbreviated Scale of Intelligence or Kaufman Brief Intelligence Test); provide a negative pregnancy test (if female); demonstrate that they could successfully swallow the largest capsule size **Other:** **ADHD presentation:** inattentive : 26.2,hyperactive : 1.9,combined : 71.5 **Diagnosis:** Confirmation by specialist DSM-5 criteria by clinician **Comorbidity:** N/A **Female:** 33.0 % **Age mean:** 14.2 (1.58) **Minimum age:** 12 **Maximum age:** 17 **Ethnicity:** N/A	**Intervention:** Methylphenidate long-acting formulation (PRC-063, Adhansia) 85 mg/day for 4 weeks **Control:** Placebo Identical in appearance **Comparator:** MedicationLong-acting methylphenidate formulation (PRC-063, Adhansia) 25 mg/day for 4 weeks **Follow-up:** 1 month	CGI-I (Clinical Global Impression-Improvement) responders (much or very much improved) About 52.7% of participants randomized to PRC-063 were responders versus 32.4% on placebo (p 0.0004). ADHD-5-RS Treatment groups showed a statistically significant improvement compared to placebo. Decreased appetite Across doses, 20.1% of participants reported decreased appetite (none in placebo). Participants with any treatment related adverse event Across doses, the rate was 48.6% for placebo and 65.6% across all doses. Two serious adverse events (both during the open-label study), one of which (aggressive behavior) was assessed as related to study drug.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Wietecha, 2009[616] Saylor, 2010[1023]; Eli Lilly and Company, 2004[752] ID: NCT00191035 RCT Multicenter N = 267 US Setting: Mixed	**Target:** Adolescents who met DSM-IV criteria for ADHD, score of at least1.5 standard deviation above age and gender normative sample for ADHD-Rating Scale-IV Parent version, score of 70 or more on Kaufman Brief Intelligence Test; no patients currently taking psychotropic medications, have a history of bipolar disorder, psychosis, autism, Asperger's syndrome, pervasive developmental disorder, patients who previously participated in a study of atomoxetine **Other:** **ADHD presentation:** inattentive : 49.8,hyperactive : 2.2,combined : 47.9 **Diagnosis:** Confirmation by specialist DSM-IV-TR via Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version (K-SAD-PL: Behavioral) **Comorbidity:** N/A **Female:** 35.95 % **Age mean:** 14,6 **Minimum age:** 13 **Maximum age:** 16 **Ethnicity:** % Hispanic or Latino : 7.49 % Black/African American : 12.0 % White : 74.5 Other : Other: 5.62%	**Intervention:** Atomoxetine slow titration group had starting dose 0.5 mg/kg/day for 7–9 days, followed by 1.0 mg/kg/day for 7–9 days, then 1.2 mg/kg/day for remainder of the 8-week period; fast titration group received atomoxetine at starting dose of 0.5 mg/kg/day for a minimum of 3 days followed by 1.2 mg/kg/day for the remainder of the 8-week study period; all received low dose of 0.8 mg/kg/day for 40 week maintenance **Control:** NA **Comparator:** MedicationAtomoxetine slow titration group had starting dose 0.5 mg/kg/day for 7–9 days, followed by 1.0 mg/kg/day for 7–9 days, then 1.2 mg/kg/day for remainder of the 8-week period; fast titration group received atomoxetine at starting dose of 0.5 mg/kg/day for a **Follow-up:** 12 months	Youth Risk Behavior Surveillance (YRBS) Total scores of the highest quartile patients did not improve significantly from baseline (p=0.116) CGI-ADHD-S (Clinical Global Impressions-Attention-Deficit-Hyperactivity Disorder-Severity), clinician Significant benefit was demonstrated with both titration schedules (p <0.001) and there was no significant difference between groups (p=0.205). ADHD-RS (ADHD Rating Scale), clinician rating Significant benefit was demonstrated with both titration schedules and there was no significant difference between groups. Decreased appetite (8 week acute period) No statistically significant differences were observed in any of the vital signs or in weight between the 0.5=1.2 mg=kg=day and 0.5=1.0=1.2 mg=kg=day groups.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Wigal, 2004[617] ID: NA RCT Multicenter N = 132 US Setting: Specialty care	**Target:** Children with ADHD, female subjects were premenarche, without other psychological disorders, not taking antidepressants, sedatives/hypnotics, neuroleptics/antipsychotics, mood stabilizers, anticonvulsants, beta-blockers, α2-agonists, thyroid medications, and chronic oral steroids **Other:** **ADHD presentation:** inattentive : 34.8,hyperactive : 0.8,combined : 64.4 **Diagnosis:** Confirmation by specialist DSM IV diagnosis, confirmed by NIMH Diagnostic Interview Schedule for Children (DISC-IV) administered to parents **Comorbidity:** N/A **Female:** 12 % **Age mean:** 9.8 (2.65) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Black/African American : 13.6 % White : 78.0 Other : Other race: 8.3	**Intervention:** Dexmethylphenidate hydrochloride (d-MPH, Focalin) twice daily, withtitration of the dose based on weekly clinic visits, a maximum of 10 mg twice daily for 4 weeks **Control:** Placebo Placebo, twice daily for 4 weeks. **Comparator:** Medicationd,l-threo-Methylphenidate Hydrochloride twice daily for 4 weeks, with titration of the dose based on weekly clinic visits. **Follow-up:** 1 month	CGI-I, proportion much improved or very much improved The percentage of patients with a therapeutic response was significantly higher in the group treated with d-MPH (p = .0010) and the group treated with d,l-MPH (p = .0130) than placebo. SNAP-ADHD (abbreviated version of the full SNAP-IV Rating Scale) change, teacher reported Treatment with either d-MPH (p = .0004) or d,l-MPH (p = .0042) significantly improved Teacher SNAP ratings compared with placebo. The d-MPH group showed significant improvements compared with placebo on afternoon Parent SNAP ratings (p = .0003) as did the Anorexia 4 intervention patients, 2 placebo patients, and 6 comparator patients had clinically significant weight losses ranging from 5% to 18% of baseline values. Four intervention patients, 0 placebo patients, and 5 comparator patients had anorexia. P values n 70% of patients experienced at least one adverse event, more medication patients experienced headache and nausea.

FDA-approved pharmacological	Wigal, 2011[618] Ortho-McNeil Janssen Scientific Affairs, 2008[972] ID: NCT00799409 Crossover trial Multicenter N = 78 US Setting: School	**Target:** Participants receiving medication to treat their ADHD exhibited an inadequate response to stimulant dose, completed a washout equivalent to 5 half-lives of the given medication before completing baseline assessments, attendance of regular school, the ability to read and understand English; no history or current diagnosis of epilepsy, severe anxiety, conduct, psychotic disorders, pervasive developmental, eating, obsessive compulsive, sleep, major depressive, bipolar, chronic tic, or disorders **Other:** **ADHD presentation:** inattentive : 19,hyperactive : 0,combined : 81 **Diagnosis:** Confirmation by specialist K-SADS-PL **Comorbidity:** N/A **Female:** 30 % **Age mean:** 10.1 (1.08) **Minimum age:** 9 **Maximum age:** 12 **Ethnicity:** % Black/African American : 28 % White : 58 Other : Other: 14%	**Intervention:** Methylphenidate OROS (Osmotic-Release Oral System) optimized dose of 18, 36,or 54 mg/day for 6 weeks **Control:** Placebo In the crossover design, subjects who completed both laboratory school assessments served as their own control and provided data for both OROS MPH and placebo **Comparator:** NA **Follow-up:** 1.5 months	Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) - Composite score Intervention group had significantly better scores than control group (p<0.0001). Permanent Product Measure of Performance (PERMP) - Correct Answers Intervention group had significantly better scores than control group (p<0.0001). Children taking OROS MPH had significantly better scores than placebo-treated children on the Reaction Time, and Reaction Time Variability scores of the TOVA (p< 0.0001 for all). OROS MPH significantly improved performance on tests of visual working memory as demonstrated on both the Finger Windows forward and backward subtests. Overall, 20 participants had appetite loss. The study reported only the overall number of adverse events . A total of 39 subjects (50%) reported at least one treatment-emergent AE during the study. The types of AEs reported were consistent with those previously reported with the use of stimulant medications in the management of ADHD. There were no deaths or se
FDA-approved pharmacological	Wilens, 2005[621] ID: N/A RCT Unclear/Not reported N = 138 US Setting: Specialty care	**Target:** Participants with IQ score ≥ 80; blood pressure measurements within the 95th percentile for age, gender, and height; electrocardiogram findings within the normal range; history of response to stimulant medication **Other:** **ADHD presentation:** N/A : for 6 months open-label MAS XR arm	**Intervention:** Mixed amphetamine salts extended-release 50mg per day for 6 months **Control:** Placebo Placebo, no other description noted.	Changes in BP and QTcB (Bazett's formula) intervals at 4 weeks with MAS XR were not significantly different from the placebo group. Pulse increased by 5.0 and 8.5 bpm after 3 weeks with MAS XR 20 and 50 mg/day, respectively (P<.002). After 6 months of ope

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
		Diagnosis: Confirmation by specialist DSM-IV by either a child psychiatrist or psychologist **Comorbidity:** N/A **Female:** 29 % **Age mean:** Open-label mixed amphetamine salts extended release (MAS XR) mean age (year) at 14.4. No SD provided. **Minimum age:** 13 **Maximum age:** 17 **Ethnicity:** % White : 72.0 N/A : no other info provided	**Comparator:** Medication60 mg of MAS XR (mixed amphetamine salts extended-release) **Follow-up:** 6 months	

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Wilens, 2008[619] Noven Therapeutics, 2005[965] ID: NCT00151970 Crossover trial Multicenter N = 117 US Setting: Specialty care	**Target:** Children with ADHD; no children with conduct disorder or comorbid illnesses that contraindicated or could confound medication treatment, or a history of failing to respond to psychostimulant treatment **Other:** Parents provided some outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Diagnosed per DSM-IV-TR criteria. Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version interview was also conducted **Comorbidity:** N/A **Female:** 35.9 % **Age mean:** 8.8 (0.2) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Black/African American : 15.4 % American Indian or Alaska Native : 0 % Asian : 0 % Native Hawaiian or Pacific Islander : 0 % White : 63.2	**Intervention:** Methylphenidate transdermal patch, 6 hour patch, dose optimized over 5 weeks **Control:** Placebo Placebo transdermal patch **Comparator:** MedicationMethylphenidate transdermal patch, dose optimized over 5 weeks, 4 hour patch **Follow-up:** 2 months	CPRS-R (Conners Parent Rating Scale-Revised) Mean total score decreased by >67% from baseline to follow-up when patients wore the patch (p <.0001). ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale-IV) change, clinician rating Mean total score decreased at follow-up when patients wore the patch (p <.0001). Permanent Product Measure of Performance (PERMP) math problem score A significant increase in the number of attempted math problems was seen during the 4- and 6-hour medicated patch wear times compared with placebo patch (p < .0001). Correct scores for the 4- and 6-hour medicated patch wear times were significantly high 326 treatment-emergent adverse events were reported during the entire study for subjects in the safety population, majority were mild (62%) or moderate (37%) in intensity; there were no serious adverse events.

FDA-approved pharmacological	Wilens, 2012[622] Wilens, 2017[1176]; Shire, 2008[1048] ID: NCT00734578 RCT Multicenter N = 461 US Setting: Specialty care	**Target:** Children and adolescents with ADHD with suboptimal but partial response to stimulant medication **Other:** Parents provided some outcome data **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV-TR per Kiddie Schedule for Affective Disorder - Present and Lifetime (K-SADS-PL) **Comorbidity:** N/A **Female:** 28.4 % **Age mean:** 10.8 (2.4) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 13.4 % Black/African American : 22.0 % American Indian or Alaska Native : 0.2 % Asian : 1.3 % Native Hawaiian or Pacific Islander : 0.7 % White : 67.7	**Intervention:** Guanfacine extended release 1-4mg in morning as adjunct to usual stimulant medication for 9 weeks **Control:** Placebo Placebo plus usual stimulant medication daily **Comparator:** MedicationGuanfacine extended release in evening plus usual stimulant medication **Follow-up:** 2 months	Oppositional symptoms, measured by oppositional subscale of the Conners' Parent Rating Scale-Revised: Long Form (CPRS-R:L) GXR + stimulant taken in AM (p<0.001) or PM (p<0.003) led to significantly greater improvement in oppositional symptoms than versus placebo + psychostimulant. CGI-I (Clinical Global Impression - Improvement) much or very much improved A higher proportion of intervention and comparator group aprticipants classified as much or very much improved on compared to placebo group (p =0.024 and p = 0.003). ADHD-RS-IV (Attention Deficit Hyperactivity Disorder Rating Scale IV) , clinician rating The intervention and the comparator group had greater decrease in ADHD symptoms at follow up than placebo (p 0.002 and p 0.001). Before-School Functioning Questionnaire (BSFQ) Participants who received GXR + psychostimulant showed significantly greater improvement compared with participants who received placebo + psychostimulant (p 0.002). Participants with decreased appetite Significantly more patients in the medication groups experienced appetite decrease compared to the placebo group. Participants reporting any adverse event The rates were 77.3% in the AM, 76.3% in the PM, and 63.4% in the placebo group.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
				Similar findings for somnolence, headache, abdominal pain, and fatigue.
FDA-approved pharmacological	Wilens, 2015[623] Shire, 2011[1058] ID: NCT01081132 RCT Multicenter N = 314 US Setting: Mixed	**Target:** Adolescents with ADHD; no co-morbid psychological disorder other than ODD or serious medical issues **Other:** Parents reported function outcome **ADHD presentation:** inattentive : 29.17,hyperactive : 2.89,combined : 67.95 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** **Female:** 35.03 % **Age mean:** 14.5(1.39) **Minimum age:** 13 **Maximum age:** 17 **Ethnicity:** % Black/African American : 16.88 % American Indian or Alaska Native : 0.63 % Asian : 1.59 % White : 72.29 Other : 8.0% other	**Intervention:** Guanfacine extended-release once-daily less than or equal to 7mg for 13 weeks **Control:** Placebo Placebo ratio 1:1 same as baseline of 1 mg depending on weight group and was allowed to increase 1mg weekly **Comparator:** NA **Follow-up:** 3 months	CGI-S, number responded (score = 1 or 2) More intervention participants showed improvement than control participants (p=0.01). ADHD-RS-IV Intervention participants showed improvement compared to control group (p<0.001). Weiss Functional Impairment Rating Scale, parent (WFIRS-P) No significant difference between groups. Treatment emergent adverse events Proportion of adverse events was 93.6% in the intervention and 77.4% in the placebo group No clinically meaningful differencew between intervention and placebo on hematology, clinical chemistry, or urine analyses

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
FDA-approved pharmacological	Wolraich, 2001[626] Faraone, 2005[767]; Spencer, 2006[1085]; Baren, 2000[675] ID: N/A RCT Multicenter N = 282 US Setting: Specialty care	**Target:** Children with ADHD who were taking methylphenidate or had taken it in the past; a total daily methylphenidate dose of at least 10 mg but not more than 60 mg; no glaucoma, Tourette's syndrome, an ongoing seizure disorder, or a psychotic disorder, no girls who had reached menarche **Other:** Parents and teachers provided outcome data **ADHD presentation:** inattentive : 19.5,hyperactive : 7.1,combined : 73.4 **Diagnosis:** Confirmation by specialist DSM diagnosed confirmed by Diagnostic Interview Schedule for Children (Version 4) **Comorbidity:** N/A **Female:** 17.4 % **Age mean:** 9.0 (1.8) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 3.5 % Black/African American : 7.4 % Asian : 0.4 % White : 84.4 Other : Other 4.3%	**Intervention:** Methylphenidate extended-release OROS tablets, 18 to 54 mg per day for 28 days **Control:** Placebo Placebo **Comparator:** MedicationImmediate release methylphenidate, 5 to 15 mg per day **Follow-up:** 1 month	CGI (Clinical Global Impression) much improved or very much improved Both medications groups had more improvement in mean teacher (p < .05) and parent (p < .05) Conners ratings than placebo group. OROS MPH and immediate release MPH did not differ significantly (p < .539). Inattention SNAP-IV, teacher report The medication groups improved more than the placebo on SNAP-IV Inattention - Teacher Report, SNAP-IV Hyperactivity/Impulsivity - Teacher Report, SNAP-IV Inattention - Parent report and SNAP-IV Hyperactivity/Impulsivity - Parent Report p < .001 for all s Proportion of patients eating less than usual The percentage of patients eating less than usual was significantly higher (p < .001) for the 2 medication groups compared with placebo. There was not difference between the medication groups. Participants experiencing at least one adverse event The rate was 43% for intervention, 35% for control, and 47% for comparator.

FDA-approved pharmacological	Young, 2014[634] Newcorn, 2013[959]; Stein, 2015[1087] ID: N/A RCT Multicenter N = 340 Multiple countries Setting: N/A	**Target:** Children with a primary diagnosis of ADHD according to DSM-IV-TR; a baseline ADHD-RS-IV total score 28 and a Clinical Global Impressions–Severity of Illness Scale score 4; no current diagnosis of controlled or uncontrolled comorbid psychiatric disorders; no previous or present risk for suicide; no history or active presence of cardiac abnormalities or a primary sleep disorder **Other:** Parents **ADHD presentation:** inattentive : 2.1,hyperactive : 1.8,combined : 96.1 **Diagnosis:** Confirmation by specialist ADHD diagnosis according to DSM-IV-TR based on psychiatric assessment **Comorbidity:** N/A **Female:** 29.4 % **Age mean:** Intervention 9.1 (1.77), control 8.9 (1.78), comparator 9.3 (1.76) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Black/African American : 36 % American Indian or Alaska Native : 0.3 % Asian : 0.6 % White : 57.1	**Intervention:** Guanfacine extended release administered in the morning and placebo administeredin the evening, 1-4 mg/day based on dose optimization, for 8 weeks **Control:** Placebo Placebo administered in the morning and evening for 8 weeks **Comparator:** MedicationGuanfacine extended release administered in the evening and placebo administered in the morning for 8 weeks; 5 week dose-optimization period, 3 week dose-maintenance period, and 9 day dose-taper period, dose optimization starting dose of 1 mg/day was titr **Follow-up:** 2 months	CPRS-RS total score Intervention group and comparator group had a significantly greater improvement from baseline in total score than control group (p<0.001). ADHD-RS-IV score At end of treatment, participants receiving guanfacine had a significantly greater reductions in mean ADHD-RS-IV total scores compared with the placebo group, regardless of the time of administration (p < .001 for all intervention groups versus placebo). Weiss Functional Impairment Rating Scale–Parent Report (WFIRS-P) Both medication groups showed significantly greater improvement in mean WFIRS-P Total scores versus placebo (p < 0.001). No significant correlations were found between change from baseline to last visit in pediatric daytime sleepiness scale (PDSS) total scores by treatment group. Decreased appetite Rate of decreased appetite was 4% in the active arms and 2.7% in the placebo arm. Participants with treatment-emergent adverse events The rate of events was 79% in the active groups and 57% in placebo. 4.1% reported severe adverse events (4 in the AM, 5 in the PM group, 0 in placebo).
FDA-approved	Zhu, 2017[645] ID: ID NA RCT Single center	**Target:** Patients who met the ADHD diagnostic criteria of the DSM5, fourth edition **Other:**	**Intervention:** Atomoxetine with initial dose 0.5 mg/kg per day then gradually increased to 1.2 mg/kg according to the participant's condition and	CGI-ADHD-S Both groups improved but there was no statistical significance in difference values between the two groups.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
	N = 104 China Setting: Other	**ADHD presentation:** inattentive : 49.03,hyperactive : 29.80,combined : 21.15 **Diagnosis:** Confirmation by specialist Confirmed by clinician using DSM 5. **Comorbidity:** N/A **Female:** 20.19 % **Age mean:** Atomoxetine 9.92 (2.98), methylphenidate 9.75 (3.14) **Minimum age:** 6 **Maximum age:** 14 **Ethnicity:** N/A	tolerance, taken after breakfast for 2 months **Control:** NA **Comparator:** MedicationMethylphenidate with initial dose 0.2 mg/kg per day and then gradually increased to 0.5 mg/kh., taken after breakfast every day for 2 months **Follow-up:** 2 months	ADHD-RS (ADHD rating scale for parent version) total score At the end of treatment, a significant decrease from baseline was observed in two groups in scores of ADHDRS-IV-Parent: Inv, 2 subscales and CPRS-R: S (ADHD index, learning problems, hyperactivity-impulsion and confrontation), with considerable clinical s Loss of appetite There was no statistically significant difference in loss of appetite between groups (p=0.239). The incidence of lethargy of atomoxetine group was significantly higher than that of methylphenidate group (p=0.027).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Neurofeedback	Arnold, 2022[126] Kerson, 2020[880] ID: ID NA RCT Multicenter N = 144 US Setting: Specialty care	**Target:** Children with ADHD; comorbid diagnoses were allowed if they did not require psychiatric medication; exclusions were serious physical illness, convergence insuf-ficiency, vitamin D deficiency/insufficiency, more than 5 previous neurofeedback sessions, seizures, sleep apnea, restless legs, or current/recent psychoactive drug use other than stimulants for ADHD **Other:** Parents and teachers provided outcomes **ADHD presentation:** inattentive : 37.5,combined : 62.5 **Diagnosis:** Confirmation by specialist DSM per Child Interview for Psychiatric Syndromes (CHIPS) **Comorbidity:** N/A **Female:** 23.3 % **Age mean:** 8.6 (1.14) **Minimum age:** 7 **Maximum age:** 10 **Ethnicity:** % Hispanic or Latino : 10.83 % Black/African American : 7.63 % Asian : 4.24 % White : 76.3 % Multiracial : 8.47 Other : Other: 3.39	**Intervention:** Theta-beta ratio neurofeedback protocol in which theta power was down-trained and beta power was reinforced at scalp site Cz or Fz, 38 sessions total, at 3 times per week for 13 weeks **Control:** Placebo Treatment of identical appearance, intensity/frequency, and duration, differing only in that reinforcement for controls was based on a pre-recorded EEG of another child **Comparator:** NA **Follow-up:** 25 months	Aggression, parent rating Aggression score were more reduced in the intervention than control group. Clinical Global Impression (CGI) global index, parent Clinical Global Impression (CGI) - Severity >2 The proportion of scores above 2 was 78% in the intervention and 86% in the control group. ADHD Symptom Remission Decreases in both groups. Functional Assessment Checklist, teacher rating Function improved in both groups without statistical difference between them. Percentage of participants with ADHD medication decrease/discontimuation was 7.1% for neurofeedback and 4.0% for control.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Neurofeedback	Bakhshayesh, 2011[130] ID: NA RCT Unclear/Not reported N = 35 Germany Setting: N/A	**Target:** Children with a primary diagnosis of hyperkinetic disorder (disturbance of activity and attention (ICD-10:F90.0); or attention deficit without hyperactivity (ICD-10:F98.8); an IQ of >80; no known neurological or gross organic diseases, hyperkinetic conduct disorders (ICD-10:F90.1) or pervasive developmental disorders **Other:** Parents, teachers; assessed the behavior of pre-and post-treatment **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist ICD-10:F90.0; (ICD-10:F98.8 **Comorbidity:** N/A **Female:** 26 % **Age mean:** 9.34 (1.92) **Minimum age:** 6 **Maximum age:** 14 **Ethnicity:** N/A	**Intervention:** EEG neurofeedback: each session lasted 30 min with a 30-s break between the different games, each game consisted of three trials lasting 3 min each, total of 30 sessions over 10-15 weeks **Control:** NA **Comparator:** OtherEMG biofeedback (BF) aiming at forehead muscle relaxation: Both groups experienced similar treatment conditions except for the location of electrodes. Children received instructions on a computer screen to familiarize them with the exercises based on thei **Follow-up:** 6 months	FBB-HKS (German ADHD rating scales) total scores, parent report Improvement of the NF group in total score was superior to EMG group and approached statistical significance (p=0.062; effect size -.77); no significant differences between treatment groups in teacher ratings Computer Continuous Performance Test: Commission Errors: No significant difference between groups

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Neurofeedback	Bluschke, 2022[156] ID: ID NA Clinical trial Single center N = 129 Germany Setting: Specialty care	**Target:** Children and adolescents with ADHD according to ICD-10 criteria **Other:** Parents reported one outcome measure **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist determined according to standard clinical guidelines by a team of experienced child and adolescent psychiatrists and psychologists **Comorbidity:** N/A **Female:** % N/A **Age mean:** 10.76 (0.37) **Minimum age:** **Maximum age:** **Ethnicity:** N/A	**Intervention:** Neurofeedback, downregulation of theta and upregulation of beta, 2 one-hours sessions per week for 8 weeks **Control:** No intervention No neurofeedback **Comparator:** NeurofeedbackNeurofeedback, upregulation of beta, 2 one-hours sessions per week for 8 weeks **Follow-up:** 2 months	ADHD Symptom Checklist inattention scale, parent rating No significant difference in effect by group. Flanker test: the no neurofeedback group demonstrated significantly faster reaction times than those in the intervention (p=0.007) or comparator (p=0.033) group.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Neurofeedback	Dashbozorgi, 2021[215] Faculty of Rehabilitation, 2018[764] ID: IRCT20160717028964N2 RCT Single center N = 40 Iran Setting: Specialty care	**Target:** Male elementary school children with ADHD with IQ>90, no history of cerebral trauma/injuries, learning disability, and behavioral disorders, taking a stable dose of psychostimulant under the supervision of a child psychiatrist, no history of receiving any other types of non-medical therapies **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV per Child Psychiatrist **Comorbidity:** N/A **Female:** 0 % **Age mean:** 11.17 (0.97) **Minimum age:** **Maximum age:** **Ethnicity:** N/A,Other : 100% Persian	**Intervention:** Neurofeedback 60 minute training sessions, twice a week, for a total of 12 sessions, for 6 weeks **Control:** Placebo Sham neurofeedback group that watched animations which had no therapeutic potency; they waited to receive neurofeedback training sessions after the study **Comparator:** NA **Follow-up:** 1.5 months	Buss-Perry Aggression Questionnaire (BPAQ) Intervention group had significantly greater decrease in aggression (p=0.01) BIS (Barrat Impulsiveness Scale) Intervention group (NF) had significantly greater decrease in impulsivity (p=0.01)

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Neurofeedback	Duric, 2017[240] Duric, 2014[748] ID: NCT01252446 RCT Unclear/Not reported N = 130 Norway Setting: N/A	**Target:** Children with ADHD using the ICD-10 criteria; IQ>70; no involvement in another intervention group, including CBT and Stop Now And Plan; no co-morbid disorders other than Oppositional Defiant Disorder or anxiety disorder; no presence of a neurological and/or cardiovascular condition **Other:** Parents, teachers **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Child psychiatrist using ICD-10 diagnostic criteria consistent with DSM-IV **Comorbidity:** N/A **Female:** 20 % **Age mean:** 11.2 (2.8), 11.4 (3.1), 10.9 (2.4) across groups **Minimum age:** 6 **Maximum age:** 18 **Ethnicity:** N/A	**Intervention:** Neurofeedback plus methylphenidate, 3 times a week, at a dosage of 1mg/kg/day in the form of long-acting methylphenidate capsules between 20–60mg, with a total of 30 sessions for 3 months **Control:** Other Methylphenidate, 3 times a week, of 1mg/kg/day in the form of long-acting methylphenidate capsules between 20–60mg, for 6 months **Comparator:** NA **Follow-up:** 6 months	ADHD core symptoms, Barkley's Defiant Children rating scale, parent All groups improved over time but no difference was found between groups (p=0.385). School performance in the neurofeedback group did show a significant improvement (mean difference 1.5, CI 0.1 to 0.29).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Neurofeedback	Fuchs, 2003[280] ID: ID NA Cohort study Single center N = 34 Germany Setting: Specialty care	**Target:** Treatment naive children with ADHD, Wechsler intelligence quotient >80; and at least one substandard score(<85) on the Test of Variables of Attention **Other:** Teachers and parents reported outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV by : a child neurologist or pediatrician and a psychologist specialized in child and adolescent clinical psychology **Comorbidity:** N/A **Female:** 2.9 % **Age mean:** 9.7 (1.25) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** EEG neurofeedback, 3 training sessions per week using the Neurocybernetics EEG BiofeedbackSystem; neurofeedback training consisted of 30–60 min of visual and auditory feedback per session, interrupted for short breaks if required; for 12 weeks **Control:** NA **Comparator:** MedicationMethylphenidate on school days only, dosages were adjusted during the treatment period and varied between 10 and 60 mg/day, for 12 weeks **Follow-up:** 3 months	Conners Behavior Rating Scale, total, parent report No significant difference in effect between groups on parent or teacher ratings. No main effects of group or interactions for the three subscales of the d2 Attention Endurance Test. No main effect of group on Variables of Attention (TOVA). No effect of group on Wechsler Intelligence Scale for Children-Revised.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Neurofeedback	Gelade, 2017[291] Gelade, 2016[788]; Janssen, 2016[857]; Janssen, 2016[858]; Janssen, 2017[859]; Janssen, 2020[860]; Gelade, 2018[789]; van Mourik, 2011 [1140]; van Mourik, 2010[1140] ID: NCT01363544 RCT Multicenter N = 112 Netherlands Setting: Specialty care	**Target:** Children with confirmed ADHD, free of stimulant use for 1 month, IQ>80, no comorbidity restrictions **Other:** Parents and teachers provided outcome data **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV-TR diagnosis required; parent- and teacher ratings on the Disruptive Behavior Disorders Rating Scale (DBDRS) confirmed diagnosis **Comorbidity:** N/A **Female:** 24.1 % **Age mean:** 9.63 (1.76) **Minimum age:** 7 **Maximum age:** 13 **Ethnicity:** N/A	**Intervention:** Theta/beta neurofeedback training with the aim to inhibit theta (4–8 Hz) andreinforce beta (13–20 Hz) activity at Cz, three 45 minute individual training sessions a week, for 10–12 weeks **Control:** Attention-matched control Physical activity consisting of three 45 minute individual training sessions a week, over a period of 10–12 weeks **Comparator:** MedicationShort-acting methylphenidate; during the 4 weeks titration phase, children received in pseudo-random order 5 mg, 10 mg, 15 mg, 10 mg MPH, or placebo for 1 week, twice daily **Follow-up:** 6 months	Inattention score, SWAN, parent report SWAN Inattention score, Parent report: MPH group had better score at follow-up than neurofeedback (p = .002). SWAN Hyperactivity / Impulsivity score, Parent report: MPH group had better score at follow-up than neurofeedback (p = .005). SWAN Inattention sc Response speed at follow-up as measured by stop-signal reaction time (SSRT) and mean reaction time (MRT) was better for intervention compared to neurofeedback and physical activity (p < .001 for all).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Neurofeedback	Gevensleben, 2010[294] Gevensleben, 2009[790]; Wangler, 2011[1161] ID: ISRCTN87071503 RCT Multicenter N = 102 Germany Setting: Specialty care	**Target:** Children with ADHD; vast majority (over 90%) were medication naive; included comorbid conduct disorder, emotional disorders, tic disorder, and dyslexia; lacked gross neurological, other organic disorders, and comorbidities not specified above **Other:** Parents provided some outcome data **ADHD presentation:** inattentive : 29.8,combined : 70.2 **Diagnosis:** Confirmation by specialist Diagnoses were based on a semi-structured clinical interview (CASCAP-D [6]) and confirmed using the Diagnostic Checklist for Hyperkinetic Disorders/ADHD [7] by a child and adolescent psychiatrist or a clinical psychologist **Comorbidity:** N/A **Female:** 18.1 % **Age mean:** 9.9 (1.25) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Neurofeedback system SAM ('self-regulation and attention management') with 36 units of 50 minutes each, divided in two blocks of 18 units, the units were combined in 9 sessions which took place 2-3 times a week, break of 2–3 weeks between the two treatment blocks over 8-11 weeks **Control:** NA **Comparator:** Cognitive trainingComputerized attention skills training which primarily exercises visual and auditory perception, vigilance, sustained attention, and reactivity; 36 units of 50 minutes each, divided in 2 blocks of 18 units; the units were combined in 9 sessions which too **Follow-up:** 6 months	Problem behavior during homework, Homework Problem Checklist No statistically significant difference. FBB-HKS (German ADHD rating scale) total score At one week post 8 week treatment, improvement in German ADHD rating scale (FBB-HKS) total score , parent rating, was greater for neurofeedback group compared to attention training group (p < .005). Improvement in teacher rating was also greater for neur SDQ (Strength and Difficulties Questionnaire) Effect size was 0.32 indicating a small positive effect of the intervention. For the problem situations in family (HSQ-D) questionnaire, no significant effects were seen.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Neurofeedback	Gonzalez-Castro, 2016[302] ID: ID NA Clinical trial Unclear/Not reported N = 131 Spain Setting: Mixed	**Target:** Children with ADHD and an IQ of 80 or higher **Other:** Parents report ADHD symptoms outcome **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Neuro-pediatrician **Comorbidity:** N/A **Female:** 37 % **Age mean:** 9.61 (1.11) **Minimum age:** 8 **Maximum age:** 11 **Ethnicity:** N/A	**Intervention:** Neurofeedback plus pharmacological support, neurofeedback consisted of a 15 minsession, 3 days per week, methylphenidate administered according to neuropediatricians' recommendations, for 3 months **Control:** Other Pharmacalogical support, methylphenidate administered according to neuropediatricians' recommendations **Comparator:** NA **Follow-up:** 3 months	ADHD Scale of Assessment of Attention Deficit with Hyperactivity (EDAH) Significant difference between neurofeedback plus pharma vs pharma alone. Test of Variables of Attention (TOVA): Differences between combined intervention group and the pharmacological support only group were statistically significant (p 0.005)

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Neurofeedback	Hasslinger, 2021[320] Karolinska Institutet, 2013[875] ID: NCT01841151 RCT Single center N = 217 Sweden Setting: Other	**Target:** Individuals with ADHD as primary diagnosis, IQ>80, had sufficient Swedish proficiency, and stable pharmacologic treatment **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Kiddie Schedule for Afective Disorders and Schizophrenia Interview **Comorbidity:** N/A **Female:** 24 % **Age mean:** 12.21 and 12.61 (2.30 and 2.74) **Minimum age:** 9 **Maximum age:** 17 **Ethnicity:**	**Intervention:** Slow cortical potentials neurofeedback plus pharmacotherapy, intentionally creating negative or positive slow cortical potentials, each trial lasted 10s, each session consisted of 144 trials split into 4 blocks (36 trial per block), lasted around 60 min, 5 sessions per week for 5 weeks **Control:** TAU Treatment as usual in accordance with regional guidelines for treatment of ADHD, pharmacotherapy, many of the children's parents underwent psychoeducational parent group-training **Comparator:** Cognitive trainingWorking Memory Training plus pharmacotherapy, computerized software program with visuospatial and auditory tasks called Minneslek Flex (based on CogMed); participants could choose between a Junior and a Senior version that differed in the thematic content **Follow-up:** 6 months	Inattention, Conners 3 Swedish Version, parent Intervention and comparator were significantly superior to control. There were no significant differences between intervention and comparator. Live Z-score neurofeedback outperformed slow cortical potential for teacher-rated hyperactivity (p 0.028; effect No severe adverse events were reported during the trial, whereas transient stress-related problems were quite frequent.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Neurofeedback	Korfmacher, 2022[375] ID: NCT 01879644 RCT Single center N = 115 Germany Setting: Specialty care	**Target:** Children with ADHD; disorders or conditions that may mimic ADHD such as autism, brain disorders, epilepsy, hyperthyreosis, and any genetic or medical disorder associated with externalizing behavior were excluded **Other:** Parents and teachers provided some outcomes **ADHD presentation:** inattentive : 34,hyperactive : 11,combined : 55 **Diagnosis:** Confirmation by specialist DSM-III-R and DSM-IV via semi-structured diagnostic interview (K-SADS-PL) **Comorbidity:** N/A **Female:** 23 % **Age mean:** mean 9.1 **Minimum age:** 7.0 **Maximum age:** 11.8 **Ethnicity:** N/A	**Intervention:** Slow cortical potential neurofeedback training aims at first learning to controland self-regulate certain brain activity parameters (via real-time feedback and operant principles), and as the next step utilizing this ability (by transfer) to improve everyday life functioning; 3 booster sessions 6 months after end of therapy; 3 training sessions per week over 3 months **Control:** NA **Comparator:** BehavioralSelf management training addressing selective attention, inhibitory control, and self-regulation (e.g., stopping and checking), planning skills, and self-instruction; 3 sessions per week over 3 months; 3 booster sessions 6 months after end of therapy **Follow-up:** 12 months	Conners Parent Rating Scale No significant differences between groups in any Conner's Parent or Teacher Rating Scales (p > 0.34). Conners parent-rated ADHD-index Qb-Test (quantified behavior test) for core ADHD symptoms Self-management decreased ADHD-index more than neurofeedback. No differences between the groups in the Qb subscales. Quality of life assessed via KINDL-R self-report showed SMT superior to neurofeedback regarding quality of life in school.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Neurofeedback	Lim, 2019[398] National Healthcare Group, Singapore, 2011[951] ID: NCT01344044 RCT Single center N = 172 Singapore Setting: Specialty care	**Target:** Children with ADHD; without intellectual disability, epilepsy and severe sensorineural deficits or co-existing psychiatric disorder **Other:** One parent and one clinician per child completed outcome assessments **ADHD presentation:** inattentive : 41.7,combined : 58.3 **Diagnosis:** Confirmation by specialist Computerized Diagnostic Interview Schedule for Children Version IV (CDISC-IV) **Comorbidity:** N/A **Female:** 15.3 % **Age mean:** 8.6 (1.54) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Brain-computer interface-based attention training program, first 8 weeks 3 sessions per week, next 12 weeks 4 sessions per week, each training session consists of 10 minutes gameplay, 10 minutes break, 10 minutes game play (30 minutes total), for 20 weeks **Control:** Wait list Wait list who received the intervention after the first group **Comparator:** NA **Follow-up:** 6 months	CBCL (Child Behavior Checklist) - Externalizing reduction The intervention group had significantly greater reductions than the control group (p<0.001). ADHD-RS, clinician-rated The intervention group had significantly greater reductions on the inattentive symptom score on the clinician-rated ADHD-RS than control group (p=0.017). A total of 11 children across groups reported at least one adverse event. Only 1 participant reported 2 different adverse events–headache and trouble paying attention/concentrating–on one occasion. None of these adverse events required medical treatment o

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Neurofeedback	Luo, 2022[409] ID: ChiCTR 1900021891 RCT Single center N = 121 China Setting: Specialty care	**Target:** Children with ADHD, those with other serious neuropsychiatric diseases or IQ<80 were excluded **Other:** Parents provided outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSMIV criteria by a qualifed psychiatrist **Comorbidity:** N/A **Female:** 20 % **Age mean:** 8.8 (1.5), 8.8 (1.2), 9.1 (1.0) in the different groups **Minimum age:** 7 **Maximum age:** 12 **Ethnicity:** % Asian : 100,Other : assumed; conducted in China	**Intervention:** Neurofeedback plus computerized cognitive training; Focus Pocus training program includes neurofeedback games and cognitive training games, each training session consisted of 14 randomly ordered mini-games, each 1 min, total time per session 15 minutes; neurofeedback games to promote awareness and control of brain activity with EEG recorded via a portable Bluetooth device that provided the participant with real-time feedback; cognitive training games to train and improve inhibitory control and working memory abilities; 3-5 sessions per week online at home, for 3 months **Control:** Other Computerized cognitive training only; cognitive training games to train and improve inhibitory control and working memory abilities; 3-5 sessions per week online at home, for 3 months **Comparator:** NA **Follow-up:** 3 months	ADHD Rating Scale IV (ADHD-RS IV), parent All groups improved; no significant difference in change among groups. Weiss Functional Impairment Scale-Parent Report All groups improved; no significant difference in change among groups. Behavior Rating Inventory of Executive Function (BRIEF): no significant difference in change among groups.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Neurofeedback	Minder, 2018[435] Zuberer, 2018[1194]; University of Zurich, 2015[1135] ID: NCT02358941 RCT Multicenter N = 102 Switzerland Setting: Mixed	**Target:** Children with ADHD, with or without hyperactivity; no severe comorbidities, autism, tics, or other psychiatric disorders; medication dose kept stable over duration of study **Other:** Parents and teachers provided outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 35 % **Age mean:** Mean (SD) by group: 10.58 (2.3), 11.37 (1.7), 10.40 (2.0), 10.83 (1.8) **Minimum age:** 8 **Maximum age:** 15 **Ethnicity:** N/A	**Intervention:** Slow cortical potential neurofeedback with the Theraprax training device where patients were supposed to steer a feedback item on the screen downward or upward by changing brain activity; in 50% of the trials, the task was to decrease brain activity and in the other 50% to increase brain activity; in school setting, training began with two to three double sessions (2 × 45–60 min) per week and continued with one to two sessions per week, over a period of 10–14 weeks; in clinical setting, daily double sessions over 2 weeks, usually followed by a short therapy break and five double sessions over 5–8 weeks **Control:** NA **Comparator:** Cognitive trainingCognitive training with CogniPlus, a software program developed for the rehabilitation of neurological patients consisting of adaptive game-like training tasks that target neuropsychological functions such as alertness, sustained attention, working memory **Follow-up:** 3.5 months	Conners-3 ADHD DSM–IV inattention, parent report Conners-3 ADHD DSM-IV indices responder rate Parent rated inattention score improved significantly more in cognitive training group than neurofeedback group. No significant differences between groups in other Conners scores. % responding: A greater % of neurofeedback patients "responded" - improve BRIEF indices of Metacognition and Behavior Regulation, parent & teacher report: no significant differences in effect between intervention and comparator.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Neurofeedback	NF Coll. Group, 2021[458] Ohio State University, 2014[969] ID: NCT02251743 RCT Multicenter N = 144 US Setting: N/A	**Target:** Children with ADHD and IQ>=80; an eyes-open theta/beta power ratio greater than or equal to 4.5 at Cz or Fz; stimulants discontinued for 5 days before major assessments; no comorbid disorder requiring psychoactive medication other than psychostimulant; no medical disorder requiring systemic chronic medication with confounding psychoactive effects **Other:** **ADHD presentation:** inattentive : 35.9,combined : 64.1 **Diagnosis:** Confirmation by specialist DSM-V **Comorbidity:** N/A **Female:** 21.8 % **Age mean:** 8.58 (1.14) **Minimum age:** 7 **Maximum age:** 10 **Ethnicity:** % Black/African American : 7.9 % Asian : 3.6 % White : 76.3 % Multiracial : 9.4	**Intervention:** EEG biofeedback treatment, 5 training periods per training session, each period lasted 5 minutes at the beginning and gradually increased to 9 minutes per period in later sessions, 38 sessions in 14 weeks **Control:** Placebo Prerecorded electroencephalograms instead of the live electroencephalograph to determine rewards; participants were also counseled about the importance of sleep and nutrition, especially breakfast, and were given an "Eat Smart" list of recommended breakfa **Comparator:** NA **Follow-up:** 13 months	Conners 3 Aggression, teacher rating The difference between groups was not statistically significant. CGI-I (Clinical Global Impression-Improvement) improvement of more than 2 Responders were 61% in the intervention and 54% in the control group (p =0.36). DSM Inattentive Symptoms on Conners 3 Long Version (average of teacher and parent ratings), change from baseline Both groups improved and there was no significant difference between groups (p 0.412) Functional assessment checklist, parent rating The difference between groups was not statistically significant. Appetite decrease The rate was 26.2% in the intervention and 13.8% in the control group. Adverse events that were possibly attributable to treatment were distributed proportionally between the treatments, with no significant difference in any.

Neurofeedback	Purper-Ouakil, 2021[483] Mensia Technologies SA, 2016[920] ID: NCT02778360 RCT Multicenter N = 186 Multiple countries Setting: Mixed	**Target:** Children diagnosed with an inattentive or combined presentation of ADHD; without established diagnosis of autism, schizophrenia, severe generalized anxiety disorder, major depression, tics, epilepsy, or other neurological disorders; no antecedents of treatment with neurofeedback or medications for ADHD; no systemic chronic medication; IQ>80 **Other:** **ADHD presentation:** N/A : Inattentive and combined presentation but no breakdown **Diagnosis:** Confirmation by specialist Made by a clinician using Kiddie-SADS (K-SADS) **Comorbidity:** N/A **Female:** 15.3 % **Age mean:** 9.8 (1.8) **Minimum age:** 7 **Maximum age:** 13 **Ethnicity:** N/A	**Intervention:** At-home neurofeedback training consisted of five 4-minute-long active blocks (withreal-time feedback) and two 2.5 minute-long transfer blocks (with only intermittent feedback), 2 treatment phases of 16 to 20 sessions (4 per week), for 90 days **Control:** NA **Comparator:** MedicationMethylphenidate, open titration period of 3 weeks and a treatment period with titration started at 10 mg of extended-release methylphenidate per day and a maximum possible dose of 60 mg/day; treatment lasted 2 months **Follow-up:** 3 months	CGI improvement The comparisons between neurofeedback and medication were significant, indicating a better CGI Improvement in the medication group; 76.3% were much or very much improved with medication and 21.1% with neurofeedback. ADHD-Rating Scale-Clinician-rated total score The study failed to demonstrate noninferiority of neurofeedback vs methylphenidate (mean between-group difference 8.09; 90% CI 8.09, 10.56). Executive functions (BRIEF) showed significant decreases in both groups, the comparison showed greater effects in the medication group (p=0.002). Participants with spontaneous reporting or Pediatric Adverse Event Rating Scale adverse events 91% of patients in the MPH group versus 21.6% in the NF group had at least one adverse event related to treatment with a significant between-group difference (chi-square test (1) = 80.71, p < .0001); Severe adverse events occurred in 20.9% of patients in the MPH vs 29.7% in the NF group (p=0.195).
Neurofeedback	Qian, 2018[484] ID: ID NA RCT Single center N = 29 Singapore Setting: Specialty care	**Target:** ADHD participants who had combined or inattentive subtypes on medicine after at least 1 month of washout **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A	**Intervention:** Brain-computer-interface training: each session lasting 30 minutes with breaks included,3 sessions per week for 8 weeks **Control:** No intervention MRI scan and clinical assessment were performed in the control	CBCL (Child Behavior Checklist) The reduction of internalizing problems in the intervention group was slightly greater than that in the control group, but not significant (p = 0.44). ADHD-RS, clinician rated inattention The intervention group had significantly greater reduction in the

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
		Female: 0 % **Age mean:** 9 (1.5) and 9.45 (1.29) in the groups **Minimum age:** **Maximum age:** **Ethnicity:** N/A	group although no intervention was done **Comparator:** NA **Follow-up:** 2 months	ADHD-RS clinician inattention scores compared to the control group (p=0.038).
Neurofeedback	Rahmani, 2022[490] ID: IRCT20190602043790N1 RCT Single center N = 112 Iran Setting: Specialty care	**Target:** Children with ADHD; those with serious medical conditions or using psychotropic medication were excluded **Other:** Parents and teachers provided outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM V by psychiatrist **Comorbidity:** N/A **Female:** % N/A **Age mean:** 11.3 (1.94) **Minimum age:** 6 **Maximum age:** 15 **Ethnicity:** N/A	**Intervention:** Neurofeedback, one 30-min session 2 days per week, for 12 weeks **Control:** No intervention No intervention **Comparator:** NA **Follow-up:** 3 months	ADHD-RS-IV, total, parent rating Effect was more significant in the intervention group (p<0.001). ADHD-RS-IV, total, teacher rating showed similar results (p<0.05). The rate of reported side effects was not different across all groups for 12 weeks. No dangerous side effect was reported in any of the patients during 12 weeks. All reported side effects ranged from mild to moderate.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Neurofeedback	Rajabi, 2020[492] ID: ID NA RCT Single center N = 32 Iran Setting: School	**Target:** Children diagnosed with ADHD, IQ > 85, no comorbid disorder other than oppositional defiant disorder, depression, and anxiety disorder **Other:** **ADHD presentation:** inattentive : 15.6,hyperactive : 25.0,combined : 59.4 **Diagnosis:** Confirmation by specialist DSM-V **Comorbidity:** N/A **Female:** 0 % **Age mean:** intervention 10.20 (1.3), control 10.05 (0.83) **Minimum age:** **Maximum age:** **Ethnicity:** N/A	**Intervention:** Monopolar neurofeedback training, 3 times a week during thirty 45-min sessions, for 3 months **Control:** Wait list Waiting list control **Comparator:** NA **Follow-up:** 2.5 months	Attention, CPRS-R (Conners Parent Rating Scales-Revised) There was a statistically significant effect favoring the intervention group. The intervention significantly improved total attention and total response control (impulsivity) measured by the Integrated Visual and Auditory Continuous Performance compared to the control group (p <0.05).

Neurofeedback	Steiner, 2014[562] Steiner, 2014[1088]; Tufts Medical Center, 2012[1124] ID: NCT01583829 RCT Multicenter N = 104 US Setting: School	**Target:** Children with ADHD, IQ of 80 or higher; with no coexisting diagnosis of conduct disorder, autism spectrum disorder, or other serious mental illness **Other:** Parents provided some outcome data **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist clinical diagnosis of ADHD made by the child's clinician, **Comorbidity:** N/A **Female:** 26.0 % **Age mean:** 8.57 (1.0) **Minimum age:** 7 **Maximum age:** 10 **Ethnicity:** % Black/African American : 6.7 % Asian : 18.3 % White : 73.1	**Intervention:** Neurofeedback training (Play Attention) in-school 45- minute intervention sessions 3 times per week, monitored by a trained research assistant for 40 sessions over 5 months **Control:** No intervention No intervention **Comparator:** Cognitive trainingCognitive training via computer (Captain's Log, BrainTrain) with 14 auditory and visual exercises targeting areas of attention and working memory; each exercise is interactive and lasts ~5 minutes; in-school 45-minute intervention sessions 3 times per we **Follow-up:** 6 months	Behavioral Observation of Students in Schools (BOSS), Off-task, teacher Significant improvements were found in the intervention condition compared with the control (p 0.04) but there were no differences found between the intervention and comparator. Inattention score Conners 3, parent report Intervention participants had significantly greater than gains than control group on the Connor's 3 Inattention, Executive Functioning and Hyperactivity/Impulsivity scales ($p < .01$ for all). Swanson, Kotkin, Agler, M-Flynn and Pelham scale (SKAMP) total score No significant differences between groups in SKAMP total score at follow up. Intervention (neurofeedback) group had greater improvement at follow-up compared to control group on the following Behavior Rating Inventory of Executive Function (BRIEF) rating summary scales: Behavior Regulation ($p < .03$), Metacognition ($p < .04$), and Global Executive Composite ($p < .01$). No adverse side effects of either intervention were reported on the standardized session checklists.
Neurofeedback	Strehl, 2017[567] Holtmann, 2014[837]; Aggensteiner, 2019[657] ID: ISRCTN76187185 RCT Multicenter N = 150	**Target:** Children diagnosed with ADHD combined type according to the DSM-IV; no diagnosis of bipolar disorder, obsessive compulsive disorder, psychosis, chronic severe tics, Tourette syndrome, major physical or neurological illness, and IQ of less than 80 **Other:** **ADHD presentation:** combined : 100	**Intervention:** Neurofeedback where participants were prompted to either produce negative (reducingthe excitability threshold of the underlying cortex) or positive shifts (inhibition of excitation) in a randomized order; after session 12, ratio of negativity to positivity trials increased from	ADHD Symptom Severity, parent-rated Neurofeedback showed a significant superiority over EMG (treatment difference 0.17, 95% CI 0.02–0.3, p = 0.02); yielding an effect size (ES) of d = 0.57 without and 0.40 with baseline observation carried forward

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
	Germany Setting: School	**Diagnosis:** Confirmation by specialist Diagnosis confirmed by licensed psychologist/clinical psychiatrists **Comorbidity:** N/A **Female:** 16.7 % **Age mean:** mean (SD) Neurofeedback group 8.6 (0.92), EMG feedback 8.57 (0.88) **Minimum age:** 7 **Maximum age:** 9 **Ethnicity:** N/A	50 to 80%, total of 25 training sessions with 2-3 sessions per week, for 3 months **Control:** Placebo Semi-active control condition EMG feedback of coordination in the supraspinatus muscles where participants were instructed either to contract or to relax the left relative to the right supraspinatus muscle to induce differential EMG control corresponding **Comparator:** NA **Follow-up:** 6 months	(BOCF); the sensitivity analysis confirmed In the safety population (N = 140) 119 AE were reported.; at least one AE was reported in 33% of NF participants and 35% of EMG participants; children reported headaches (N = 4, both groups), skin reactions (n = 3, NF), myalgia (n = 1, EMG), and nausea (n

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Neurostimulation	Schertz, 2022[517] ID: MOH_2018-07-24_002209 RCT Single center N = 27 Israel Setting: Specialty care	**Target:** Children with ADHD; those with history of seizure or presence of brain implant device or score above 70 on the anxiety/depression subtest of the Child Behavior Checklist were excluded **Other:** Parents provided some outcomes **ADHD presentation:** inattentive : 56,hyperactive : 12,combined : 32 **Diagnosis:** Confirmation by specialist DSM -V by a specialist in pediatric neurology and child development or a pediatrician with formal training **Comorbidity:** N/A **Female:** 28 % **Age mean:** 10.83 (1.79) **Minimum age:** 8 **Maximum age:** 16 **Ethnicity:** N/A : Israel	**Intervention:** Transcranial Direct Current Stimulation, 12 sessions, 20 minutes each, combined with cognitive therapy 3 times per week, for 4 weeks **Control:** Other Sham Transcranial Direct Current Stimulation, 12 sessions, 20 minutes each, combined with cognitive therapy 3 times per week, for 4 weeks **Comparator:** NA **Follow-up:** 2 months	Child Behavior Checklist (CBCL) overall score No significant difference in total score or any subscore other than social problems (p 0.035). Vanderbilt ADHD Rating Scales total score, parent report Group difference not significant (p 0.475). No effect of group on Cambridge Neuropsychological Test Automated Battery (CANTAB). Any adverse event No group differences in number of adverse events. 3 children, all receiving active stimulation, reported notable headaches, resulting in removal from the study for one child and temporary suspension of intervention for two children.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Aevi Genomic Medicine, 2016[113] ID: NCT02777931 RCT Single center N = 101 US Setting: Specialty care	**Target:** Children and adolescents with diagnosis of ADHD based on DSM-V criteria, ADHD-Rating Scale-5 score > 28 at baseline, IQ at least 79, have disruptive mutations in genes within the glutamate receptor metabotropic-network, no substance use, no comorbid psychiatric disorders, no serious chronic or physical health conditions **Other:** Parent reported symptoms outcome **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM V **Comorbidity:** Other : Genetic disorders **Female:** 37.1 % **Age mean:** 14.1 (1.58) **Minimum age:** 12 **Maximum age:** 17 **Ethnicity:** % Black/African American : 29.9 % American Indian or Alaska Native : 2.1 % Asian : 1.0 % White : 56.7 % Multiracial : 9.3 Other : Unknown: 1 count (1.0%)	**Intervention:** NFC-1 (Fasoracetam) 100-400 mg twice daily as capsules (size 2 hard gelatin capsules);dosing was be optimized during the first 4 weeks of treatment, based on clinical response and tolerability, and maintained for an additional 2 weeks; total duration of 6 weeks **Control:** Placebo Matching placebo capsules **Comparator:** NA **Follow-up:** 1.5 months	CGI-S, number responding (Very much improved" or Much improved") Intervention group performed better than placebo. ADHD-RS-5, parent report, decrease from baseline Symptoms were reduced more in the intervention group compared to control. Non serious adverse events, number with The rate was 70% for intervention and 56% for control. Statistical tests not conducted. No serious adverse events in either group.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
New pharmaceutical agent	Aevi Genomic Medicine, 2018[114] ID: NCT03609619 RCT Multicenter N = 108 US Setting: Mixed	**Target:** Children with diagnosis of ADHD according to DSM-V criteria, minimum score of 28 on ADHD-Rating Scale-5; those with autism spectrum disorder or significant cardiovascular conditions, any of the specific gene mutation of interest implicated in glutamatergic signaling and neuronal connectivity; no other medications except for medications intended to treat ADHD within 28 days prior to screening visit **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM V **Comorbidity:** N/A **Female:** 35.2 % **Age mean:** 10.4 (2.86) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 18.5 % Black/African American : 14.8 % American Indian or Alaska Native : 0.9 % Asian : 0.00 % White : 75.9 % Multiracial : 4.6 Other : Not reported: 4/108 (3.7%)	**Intervention:** AEVI-001 (fasoracetam monohydrate) 100 mg, 200 mg or 400 mg administered orally twice daily for 6 weeks **Control:** Placebo Oral doses of placebo administered twice daily **Comparator:** NA **Follow-up:** 1.5 months	CGI-I (Clinical Global Impression) - Global Improvement scale, response (very much improved or much improved) No significant difference between groups. ADHD-RS-5 (Attention Deficit Hyperactivity Disorder Rating Scale) change No difference in rates of improvement. Non serious adverse events The intervention rate was 6% and the comparator rate was 17%. No serious adverse events in both treatment groups.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
New pharmaceutical agent	Amiri, 2008[122] ID: N/A RCT Single center N = 60 Iran Setting: Other	**Target:** Children with ADHD; no history or current diagnosis of pervasive developmental disorders, schizophrenia or other psychiatric disorders, any current psychiatric comorbidity that required pharmacotherapy, any evidence of suicide risk and mental retardation (I.Q.<70), a clinically significant chronic medical condition, current abuse or dependence on drugs within 6 months, hypertension, hypotension and habitual consumption of more than 250 mg/day of caffeine **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV-TR **Comorbidity:** N/A **Female:** 22 % **Age mean:** Modafinil 9.20 (2.53), methylphenidate 8.96 (2.34) **Minimum age:** 6 **Maximum age:** 15 **Ethnicity:** N/A	**Intervention:** Modafinil film coated tablet in doses of 200–300 mg/day depending on weight (200 mg/day for <30 kg and 300 mg/day for >30 kg) for 6 weeks **Control:** NA **Comparator:** MedicationMethylphenidate (in doses of 20–30 mg/day) depending on weight (20 mg/day for <30 kg and 30 mg/day for >30 kg), titrated up: week 1: 10 mg/day (5 mg in the morning and 5 mg at midday); week 2: 20 mg/day (10 mg in the morning and 10 mg at midday) and week **Follow-up:** 1.5 months	ADHD-RS-IV (ADHD Rating Scale-IV) parent and teacher report Responders (at least 40% decrease in ADHD-RS scores) Both groups showed a significant improvement over the 6 weeks of treatment for the parent and teacher ratings. Decreased appetite Observed more frequently in the methylphenidate group (p 0.03). Ten side effects were observed over the trial that all of them were mild to moderate and tolerable. The difference between the modafinil and methylphenidate groups in the frequency of side effects was not significant except for decreased appetite and diff

New pharmaceutical agent	Biederman, 2005[147] ID: NA RCT Multicenter N = 248 US Setting: Mixed	**Target:** Patients with ADHD according to DSM-IV, have a Clinical Global Impressions-Severity rating of 4 or higher, have a teacher-/investigator-rated Attention-Deficit/ Hyperactivity Disorder Rating Scale-IV School Version total and/or subscale score at least 1.5 standard deviations above normal values for age and gender, between 5-9th percentile for weight and health, IQ of at least 80 based on Wechsler Intelligence Scale for Children–Third Edition, and have a score of at least 80 on the Wechsler Individual Achievement Test–Second Edition–Abbreviated; no history or current diagnosis of pervasive developmental disorder, schizophrenia, DSM IV Axis I disorders, evidence of suicide risk, current psychiatric comorbidity that required pharmacotherapy, have well-controlled ADHD, history of substance abuse **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Psychiatric/clinical evaluation and the Diagnostic Interview Schedule for Children, Fourth Edition **Comorbidity:** N/A **Female:** 29.3 % **Age mean:** Modafinil 10.4 (6-17), placebo 10.1 (6-17) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** N/A	**Intervention:** Modafinil film–coated tablets 170-425 mg/day for 9 weeks **Control:** Placebo Matching placebo pills for 9 weeks **Comparator:** NA **Follow-up:** 2.5 months	CGI-I (Clinical Global Impressions Scale-Improvement) responders Proportion of participants who were classified as responders based on CGI-I rating (rating of 1 or 2) at final visit between modafinil and placebo groups were statistically significant (p<0.0001). Modafinil showed significantly greater improvement than pa ADHD-RS-IV School Version total score Difference between Modafinil and placebo groups in ADHD-RS-IV School Version total score at final visit was statistically significant (p < 0.0001). Decreased appetite The rate was 16% in the intervention and 4% in the placebo group (p=<0.05). Serious adverse events were reported for 2 patients in the modafinil group (Stevens-Johnson syndrome possibly related to study; duodenitis, peptic ulcer, and hypertonia unrelated to study drug).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Biederman, 2006[146] ID: NA RCT Multicenter N = 248 US Setting: N/A	**Target:** Children with diagnosis of ADHD according to DSM-IV, stimulant-naive or who had manifested an unsatisfactory response to stimulant therapy, IQ of at least 80, a score of 80 or higher on the screener version of the Wechsler Individual Achievement Test, Clinical Global Impressions-Severity score of 4 or more at baseline visit **Other:** **ADHD presentation:** inattentive : 20.6,hyperactive : 2.0,combined : 76.6 **Diagnosis:** Confirmation by specialist Psychiatric evaluation and the Diagnostic Interview Schedule for Children, Fourth Edition **Comorbidity:** N/A **Female:** 26.6 % **Age mean:** 8.8 (2.0), 8.8 (2.1), 9.2 (2.1), 10.5 (1.6), 8.9 (2.0) across groups **Minimum age:** 6 **Maximum age:** 13 **Ethnicity:** % White : 81.5 Other : Other: 46/248 (18.5%)	**Intervention:** Modafinil 400 mg total, 200mg twice daily (morning and midday) for 4 weeks **Control:** Placebo 5 placebo pills daily **Comparator:** MedicationModafinil 100 mg followed by 200 mg at midday (modafinil 100/200-mg divided dose) **Follow-up:** 1 month	CGI-I (Clinical Global Impressions of Improvement) much improved or very much improved The intervention and comparator groups had significantly greater improvement compared to the control group (p=0.04 and p=0.01). Both the intervention and comparator groups had a higher percentage of participants rated as improved compared to the placebo, ADHD-RS-IV (ADHD Rating Scale-IV), school version The intervention group had significantly greater improvement compared to the control group (p=0.006). Decreased appetite The rates were 2% in the intervention and the placebo group and 12% in the comparator. Insomnia was the only adverse event that occurred with significantly greater prevalence in a group assigned to modafinil (200/100-mg divided dose) than in the placebo group (p 0.03). One child who received modafinil 400 mg experienced serious dehydration,

New pharmaceutical agent	Blader, 2021[151] Joseph Blader, 2008[870] ID: NCT00794625 RCT Multicenter N = 175 US Setting: Specialty care	**Target:** Children with ADHD (any subtype) and either oppositional defiant disorder or conduct disorder according to DSM-IV-TR; Retrospective Modified Overt Aggression Scale total score >24; recent or current treatment with stimulant medication at a minimum daily total dose equivalent of 30 mg of immediate-release methylphenidate for at least 30 days; no current or previous major depressive disorder, bipolar I or II disorder, Tourette's disorder, autism spectrum disorder, or any psychotic disorder as defined by DSM-IV-TR; IQ>=70; no seizure disorders; no pregnancy; no contraindications to treatment with stimulants **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Completion of the Schedule of Affective Disorders and Schizophrenia for School-Age Children (K-SADS) with a parent and the child by a clinical child psychologist or a child and adolescent psychiatrist. A second clinician (child and adolescent psychiatrist **Comorbidity:** ODD **Female:** 19 % **Age mean:** 9.63 (2.02) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 30.29 % Black/African American : 16.57 % White : 46.29 Other : 6.86 other	**Intervention:** Stimulant medication and behavioral therapy plus risperidone, dose started at 0.25 mg each evening for 3 days, with a morning dose of 0.25 mg added on the fourth day, dose adjustments were elective and based on response and tolerability, duration of 8 weeks **Control:** Placebo Stimulant medication and behavioral therapy plus placebo **Comparator:** Medication + behavioralStimulant medication and behavioral therapy plus divalproex sodium, aimed to achieve approximately 18 mg/kg by the end of the first week; when permitted by valproic acid level, dose increases by 125 mg or 250 mg occurred based on clinical response through **Follow-up:** 2 months	Retrospective Modified Overt Aggression Scale (R-MOAS), parent % in remission from aggression (R-MOAS <15) Intervention and comparator had larger reductions in aggression relative to the placebo group (risperidone p <0.003; divalproex sodium p<0.046). Percent in remission from aggression-remission was met by 69% of the risperidone group, 40% of the divalproex There were no instances of serious adverse events.
New pharmaceu	Blumer, 2009[155] Sanofi, 2006[1021] ID: NCT00318448 RCT	**Target:** Patients with latency to persistent sleep of 30 minutes and a sleep disturbance not attributable to direct physiologic effects of an abused drug or misused prescription medication,	**Intervention:** Zolpidem, recommended dose of 0.25 mg/kg, prepared as an oral formulation at 2.5 mg/mL, once per day at night for 8 weeks	CGI-I (Clinical Global Impressions Scale), parent There was no significant difference between groups (p=0.076). ADHD Rating Scale-IV

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
	Multicenter N = 201 US Setting: Other	no other sleep disorders diagnosed with baseline polysomnography, other major psychiatric disorders (but not obsessive-compulsive disorder), or a history of substance abuse and/or dependence, no previous adverse experience with zolpidem, no use of pharmacologic sleep aids that the patient was unwilling to discontinue or current use of rifampicin and/or sertraline **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** % N/A **Age mean:** N/A **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** N/A	**Control:** Placebo Placebo was matched with respect to color and flavor **Comparator:** NA **Follow-up:** 2 months	Baseline-adjusted mean changes did not differ between groups. No significant difference between treatment groups in latency to persistent sleep of more than 30 minutes was detected. Participants with at least one treatment emergent adverse event Rate of 62.5% in treatment and 47.7% in placebo group. Administration was terminated because of adverse events for 7.4% in the intervention and none in the placebo group; the main reason was hallucination.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Bostic, 2000[158] ID: N/A Crossover trial Unclear/Not reported N = 21 US Setting: Other	**Target:** Children with ADHD and no clinically significant medical conditions or abnormal baseline laboratory liver function tests, mental retardation, organic brain disorders, unstable psychiatric conditions, bipolar disorder, psychosis, drug or alcohol abuse or dependence within the prior 6 months, or active pregnancy or nursing **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 14 % **Age mean:** 14.14 (1.6) **Minimum age:** 12 **Maximum age:** 17 **Ethnicity:** % White : 90	**Intervention:** Pemoline, morning and after school dosing as 18.75-mg and 37.5-mg tablets(3mg/kg/day) for 4 weeks **Control:** Placebo Identical appearing and tasting 18.75-mg and 37.5-mg tablets morning and after school dosing **Comparator:** NA **Follow-up:** 2.5 months	CGI score very much improved or much improved A significantly higher proportion experienced improvement on pemoline relative to placebo (60% versus 11%, p 0.013). Hyperactivity, Inattentiveness, Impulsivity, DSM-IV-derived ADHD rating scale Progressive improvement in the intervention group compared to placebo (p 0.001). Using standard cutoff points for depression (HAM-D . 16, BDI . 19) and anxiety (HAM- A.21), no subjects had scores indicative of clinical depression or anxiety. Furthermore, none of the three depression or anxiety measures changed to a clinically or statistically significant degree over the course of this study (all p . 0.05). Loss of appetite Rates were 38% in intervention and 10% in placebo (p 0.014). The only adverse effects specifically associated with pemoline relative to placebo were mild insomnia (62% versus 5%, p < 0.001) and mild loss of appetite (38% versus 10%, p 0.014).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Buitelaar, 1996[165] ID: N/A Crossover trial Unclear/Not reported N = 52 Netherlands Setting: N/A	**Target:** Children with ADHD according to DSM-III-R criteria, scores in the clinical range on both the Child Behavior Checklist and Conners' Teacher Rating Scale hyperactivity factors, deficits in attention performance on either a reaction-time task or a continuous performance task; no previous treatment with psychotropic medication, a clinical indication for drug treatment, diagnosis of tic disorder or pervasive developmental disorder, a family history of tic disorder, and the usual contra-indications for treatment with j9-blockers such as cardiac diseases, hypotension, obstructive pulmonary diseases, and insulin-dependent diabetes **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 12 % **Age mean:** 109.8 (20.2) and 113.2 (19.1) **Minimum age:** 6 **Maximum age:** 13 **Ethnicity:** N/A	**Intervention:** Pindolol 20 mg twice per day for 4 weeks **Control:** Placebo Matching placebo administered at breakfast and at noon **Comparator:** MedicationMethylphenidate 10 mg b.i.d, during the first 3 days a single dose of 10 mg, then treated in a fixed-dosage schedule 10 mg b.i.d at breakfast and at noon **Follow-up:** 1 month	CGI-S No difference between the two active treatments Hyperactivity scale CPRS (Conners Parent Rating Scale) No difference between groups. Anorexia The rate was 15% for pindolol, 24% for methylphenidate, and 25% for placebo. Paresthesias were significantly more often reported with pindolol than with methylphenidate or with placebo; for all other adverse effects the frequencies did not differ significantly across drug status.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Ceresoli-Borroni, 2021[174] Supernus Pharmaceuticals, 2011[1098] ID: NCT01364662 RCT Multicenter N = 121 US Setting: Specialty care	**Target:** ADHD participants with persistent impulsive aggression **Other:** **ADHD presentation:** N/A : aggressive subtype 100% **Diagnosis:** Confirmation by specialist DSM-4 by psychiatrist investigator **Comorbidity:** ODD **Female:** 12.9 % **Age mean:** 9.0 (0.34) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 16.9 % Black/African American : 30.5 % White : 63.6 N/A : 6.0	**Intervention:** Molidone SPN-810, extended-release, 36mg/54mg, alongside existing monotherapy (stimulants/nonstimulants) and behavioral therapy, ~2.5-week titration, 3-week maintenance; total duration of 6.5 weeks **Control:** Placebo Placebo **Comparator:** MedicationSPN-810, 12 mg/18 mg extended-release molindone (low dose) **Follow-up:** 1.5 months	Rate of remission for aggressive behavior (Retrospective-Modified Overt Aggression Scale (R-MOAS) scale score ≤. 10) Rates of remission for aggressive behavior were greater in intervention and comparator groups compared with placebo. CGI Global Impression scale There was no significant difference between any groups. Weight and BMI All treatment groups exhibited increases in mean weight and BMI. Participants with adverse events The intervention group had 68% of participants with any adverse events, the comparator group had 38%, and the placebo group had 58%.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Conners, 1996[206] ID: ID NA RCT Multicenter N = 109 US Setting: Specialty care	**Target:** Children with ADHD in good physical health with no lab abnormalities **Other:** Parents and teachers provided data **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM III **Comorbidity:** N/A **Female:** 10.0 % **Age mean:** 66% in 3rd grade or lower **Minimum age:** **Maximum age:** **Ethnicity:** % White : 75	**Intervention:** Bupropion 50 mg or 75 mg, depending on body weight, twice daily at 7 AM and 7 PM. for 4 weeks **Control:** Placebo Placebo tablet **Comparator:** NA **Follow-up:** 1 month	Clinical Global Impression The pooled results from the sites failed to demonstrate a significant treatment effect. Conners Parent Questionnaire, hyperactive-immature, restless-impulsive, and conduct disorder Improvements in the intervention group. Significant treatment effects for the continuous performance test and memory retrieval. Bupropion appeared to be well tolerated in most children; dermatological reactions were twice as frequent in the drug group than the placebo group with 4 reactions prompting discontinuation.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Dehbozorghi, 2019[219] Roozbeh Psychiatric Hospital, 2018[1016] ID: IRCT20090117001556N108 RCT Unclear/Not reported N = 53 Iran Setting: N/A	**Target:** Participants with the diagnosis of ADHD based on DSM-5, the Kiddie Schedule for Affective Disorders and Schizophrenia 25, and medical history; patients with history or current diagno-sis of a psychiatric comorbidity except for oppositional defiant disor-der, pervasive develop mental disorders, mental retardation; history or allergy to tipepidine or methylphenidate hydrochloride; use or any medication or supplement for psychotropic disorders; presence or uncontrolled seizures; abnormal systolic blood pressure, resting pulse rate, or liver function; neurological or cardiac disorders were excluded **Other:** **ADHD presentation:** inattentive_other : Intervention: 19.54 (5.83); Control: 18.89(5.35),hyperactive_other : Intervention: 18.00(5.18); Control: 18. 22(5.00) **Diagnosis:** Confirmation by specialist DSM-V **Comorbidity:** N/A **Female:** 25 % **Age mean:** 8.57(1.81) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Tipepidine (Asverin) at a dose of 15- 30 mg/day divided into 3 doses before breakfast, supper, and bedtime plus 0.3-1.5 mg/kg/day of methylphenidate hydrochloride divided into two separate doses at 30 min before breakfast and lunch, treatment over a period of 8 weeks **Control:** Placebo Starch as placebo (at a dose or 15- 30 mg/day) for 8 weeks **Comparator:** NA **Follow-up:** 2 months	CGI-S Score The effect for time by treatment interaction was not significant (p=0.182). ADHD-IV-RS, parent On general linear model repeated measures analysis a significant effect was seen for time by treatment interaction (p=0.049). Increased appetite The rate was 4.16% in the intervention compared to none in the control group. The frequencies of adverse events were similar between the groups.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Dreakhshanpour, 2022[232] ID: IRCT2015123025768N1 RCT Single center N = 55 Iran Setting: Specialty care	**Target:** Children with ADHD; those with morbid obesity, excessive polyphagia, or unstable physical conditions that prevented drug intake, using any psychotropic drug during the two prior weeks or with co-psychiatric disorders such as bipolar mood disorder, mental retardation, and autism excluded **Other:** Parents provided some outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM V TR **Comorbidity:** N/A **Female:** 23.6 % **Age mean:** 3.98 (0.93) **Minimum age:** 3 **Maximum age:** 6 **Ethnicity:** N/A	**Intervention:** Risperidone daily, started at 0.25 mg/day in 1 dose and increased based on response and tolerance by 0.25 mg weekly increments, to a maximum dose of 1.25 mg/day for 12 weeks **Control:** NA **Comparator:** OtherAripiprazole started at 2.5 mg per day and gradually increased by 1.25 mg every week based on response and tolerance, to a maximum dose of 6.25 mg/day for 12 weeks **Follow-up:** 3 months	Strengths and Difficulties Questionnaire (SDQ), pro-social behavior Aripiprazole group improved more than risperidone group (p 0.031). ADHD-RS, parent report Aripiprazole group improved more than risperidone group (p 0.019). No difference in improvement in emotional symptoms or peer problems based on the SDQ score. No statistically significant differences between the adverse effects of the two drugs.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Farmer, 2017[264] Aman, 2008[952]; Findling, 2017[775]; Joseph, 2019[871]; Grondhuis, 2020[806]; Farmer, 2015[770] ID: NCT00796302 RCT Unclear/Not reported N = 165 US Setting: N/A	**Target:** Children with a DSM-4 diagnosis of any subtype of ADHD and evidence of severe physical aggression, either conduct disorder or oppositional defiant disorder, and a Clinical Global Impressions Severity score >=4, IQ >70, no condition that was a contraindication for medication, no family history of type-2 diabetes, not using any psychotropic medications that would cause risk to the participant if stopped, no suicidal ideation, eating disorder, autism disorder diagnosed using the DSM-4 criteria, or a mood disorder **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-4 diagnosis was required for participation **Comorbidity:** ODD **Female:** 22 % **Age mean:** 8.94 (2.01) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Black/African American : 41 % White : 61 Other : Non-Hispanic 93%	**Intervention:** Risperidone plus psychostimulant (usually osmotic release oral system [OROS] methylphenidate) titrated to an optimal dose for 6 weeks **Control:** Other Psychostimulant alone (usually osmotic release oral system [OROS] methylphenidate; STIM) plus placebo for 6 weeks titrated to an optimal dose **Comparator:** NA **Follow-up:** 2.25 months	No difference in h Conners' Continuous Performance Test (CPT-II) or Digit Span performance was observed between groups.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Findling, 2019[269] Sunovion, 2015[1094]; Sunovion, 2015[1093] ID: NCT02457819, NCT02428088 RCT Multicenter N = 342 US Setting: N/A	**Target:** Children meeting DMS-V criteria, ADHD Rating Scale version IV-Home Version score >28, Clinical Global Impression-Severity Scale score >4; without bipolar or major depressive disorder, conduct disorder, obsessive compulsive disorder, disruptive mood dysregulation disorder, intellectual disability, psychosis, autism, Tourette's syndrome, central nervous system disorder, or any other unstable medical condition **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist participants were evaluated based on the DSM-V criteria at the beginning of the trial **Comorbidity:** N/A **Female:** 33.3 % **Age mean:** 2mg/day dose 8.9 (1.7), 4mg/day dose 9.1 (1.9), placebo 9.2 (2.1) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Black/African American : 29.5 % White : 62.9 % Multiracial : 7.6	**Intervention:** Dasotraline 4 mg administered once-daily in the morning for 6 weeks **Control:** Placebo Placebo for 6 weeks **Comparator:** MedicationDasotraline 2 mg administered once-daily in the morning for 6 weeks **Follow-up:** 1.5 months	CGI Severity The reduction compared to placebo was statistically significant for the 4mg (p 0.04) but not the 2mg dose (n.s.). ADHD-RS-IV (ADHD Rating Scale-IV) Home Version total score change There was a significant difference in 6 week change from baseline between the placebo and 4mg/day group (p<0.001), but not when compared to the 2mg/day. This significance was also observed between the placebo and 4mg/day groups in the CGI-S score (p 0.04) Weight change Decreased appetite The rate was 21.7% in the 4mg, 15.3% in the 2mg, and 4.3% in placebo. Discontinuation rates were higher in the 4mg/day (12.2%) than 2mg/day (6.3%) and placebo (1.7%) groups. Psychosis symptoms were reported in 7 participants. For events with a higher incidence on dasotraline compared with placebo, the most frequent were ins

New pharmaceutical agent	Greenhill, 2006[304] ID: NA RCT Multicenter N = 200 US Setting: Mixed	**Target:** Participants with clinical diagnosis of ADHD, a Clinical Global Impressions-Severity rating of 4+, weight and height between 5-95th percentile, IQ at least 80, no learning disabilities, attending school full-time, have a investigator-rated ADHD-Rating Scale-IV School Version score of at least 1.5 standard deviations above the norm for the patient's age and gender; no history or current diagnosis of pervasive developmental disorder, schizophrenia, DSM-IV axis I disorder, any current psychiatric comorbidity that required pharmacotherapy, presence of suicide risk, ADHD symptoms well controlled on current therapy with tolerable side effects, or failed 2+ courses of stimulant therapy for ADHD **Other:** **ADHD presentation:** inattentive : 23.7,hyperactive : 5.1,combined : 70.2 **Diagnosis:** Confirmation by specialist the National Institute of Mental Health Diagnostic Interview Schedule for Children, Fourth Edition (DISC-IV) was used to establish the patients' diagnosis of ADHD using the full DSM-IV diagnostic criteria. **Comorbidity:** N/A **Female:** 27.3 % **Age mean:** Modafinil 9.9 (6-16), placebo 9.9 (6-16) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Black/African American : 18.2 % White : 71.7 Other : Other: 20/198 (10.1%)	**Intervention:** Modafinil film-coated tablets 170-425mg once daily in the morning for 9 weeks **Control:** Placebo Matching placebo tablets once daily in the morning for 9 weeks **Comparator:** NA **Follow-up:** 2.5 months	CGI-I rated 1 or 2 52% of modafinil and 18% of placebo met criteria for responder on the CGI-I (p<0.0001). ADHD-RS-IV School Version change Modafinil produced significant reductions in ADHD-RS-IV total scores at school compared with placebo (p<0.0001). Decreased appetite The rate of decreased appetite as 18% in the intervention and 3% in the placebo group. Modafinil was associated with significantly more insomnia, headache, decreased appetite, and weight loss than placebo, but discontinuation attributed to adverse events did not differ statistically between treatment groups (modafinil, 5%; placebo, 6%).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
New pharmaceutical agent	Kahbazi, 2009[354] ID: NA RCT Single center N = 46 Iran Setting: Specialty care	**Target:** Children newly diagnosed with ADHD; no history or current diagnosis of pervasive developmental disorders, schizophrenia, or other psychiatric disorders or a clinically significant chronic medical condition **Other:** Parents and teachers provided outcome data **ADHD presentation:** combined : 100 **Diagnosis:** Confirmation by specialist DSM-IV-TR diagnosis confirmed by psychiatrist **Comorbidity:** N/A **Female:** 23.9 % **Age mean:** 9.07 (2.03) **Minimum age:** 6 **Maximum age:** 15 **Ethnicity:** N/A	**Intervention:** Modafinil, 200–300 mg/day (once daily) depending on weight for 6 weeks **Control:** Placebo Placebo **Comparator:** NA **Follow-up:** 1.5 months	ADHD-RS-IV (ADHD Rating Scale-IV) change, parent report ADHD Rating Scale-IV (ADHD-RS-IV), parent report, % responding (at least 40% decrease in score) Change in ADHD Rating Scale-IV (ADHD-RS-IV) total, teacher report favored intervention (p < 0.001), as did ADHD-RS-IV total score, parent report (p < 0.001). The difference in % responding (at least 40% decrease in score) was significantly higher in the Decreased appetite More children in the modafinil group reported decreased appetite (p=0.05). No statistically significant differences between groups regarding abdominal pain, anxiety or nervousness, sadness, difficulty falling asleep, weight loss, nausea, dry mouth , irritability, or headaches.

New pharmaceutical agent	Kratochvil, 2005[377] ID: ID NA RCT Multicenter N = 173 US Setting: Mixed	**Target:** Children and adolescents with ADHD and comorbid anxiety or depression symptoms; no history of psychosis, bipolar disorder, serious medical illness, or history of substance abuse **Other:** **ADHD presentation:** inattentive : 23.2,hyperactive : 2.9,combined : 73.8 **Diagnosis:** Confirmation by specialist DSM IV Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime version **Comorbidity:** Mood disorder **Female:** 27.7 % **Age mean:** Atomoxetine + Fluoxetine 11.2 (2.7), Atomoxetine + Placebo 11.6 (2.4) **Minimum age:** 7 **Maximum age:** 17 **Ethnicity:** % White : 83.8 Other : Other: 16.2%	**Intervention:** Fluoxetine 20 mg administered once daily plus atomoxetine 1.8mg/kg/dayevenly divided into two doses for the final 5 weeks of treatment for total of 8 weeks **Control:** Other Atomoxetine alone plus placebo, after 3 weeks of placebo, atomoxetine was added for the final 5 weeks of treatment, initiated at 0.5 mg/kg/day and increased at weekly intervals to 0.8 mg/kg/day and then to 1.2 mg/kg/day; maximum dose of atomoxetine up to **Comparator:** NA **Follow-up:** 2 months	CGI-S (Clinical Global Impressions-Severity) change Difference in CGI-S score mean change from baseline between groups were not statistically significant (p 0.065). ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale-IV) total, change Difference in ADHD-RS-IV Total T-score mean change from baseline between groups was not statistically significant (p 0.121); difference in ADHD-RS-IV Total score mean change from baseline not significant (p =0.101) Children's Depression Inventory (CDI) score mean (SD) change from baseline favors intervention group (p =0.043) CDRS-R (Children's Depression Rating Scale-Revised) total score mean (SD) change from baseline - group difference not significant (p =0.342) Multidimensional Anxiety Scale for Children (MASC) score mean (SD) change from baseline: - group difference not significant (p =0.489). Decreased appetite The rate was 20% in intervention vs 6.8% in placebo approaching significance (p=0.055); patients in the combined treatment group also experienced greater weight loss (mean [SD] weight change in kilograms: A/F –1.0 [1.7], A/P –0.4 [1.3], p = .009). The proportion of patients who discontinued because of an adverse

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
				event was low and similar between groups (A/F 2.4%, A/P 2.2%); Mean heart rate increased more in the A/F group as compared with the A/P group (mean [SD] change in beats/minute: A/F 11.9 [11

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Lin, 2014[399] Eli Lilly and Company, 2009[756] ID: NCT00922636 RCT Multicenter N = 340 Multiple countries Setting: N/A	**Target:** Female and male patients with ADHD **Other:** **ADHD presentation:** inattentive : 24.16,hyperactive : 3.68,combined : 72.18 **Diagnosis:** Confirmation by specialist DSM-IV-TR **Comorbidity:** N/A **Female:** 29 % **Age mean:** mean age 11.46 **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % White : 72.6%	**Intervention:** Edivoxetine 0.3mg/kg administered daily for 8 weeks **Control:** Placebo Placebo-controlled **Comparator:** MedicationOROS MPH was administered at the label-recommended doses **Follow-up:** 2 months	Clinical Global Impressions-Attention-Deficit/Hyperactivity Disorder-Improvement (CGI-ADHD-I): Scores at the end-point for the edivoxetine 0.3 mg/kg/day arm was significantly lower relative to the placebo arm (lower score indicating greater clinical impro ADHD-RS-IV The edivoxetine 0.2 mg/kg/day and 0.3 mg/kg/day arms had statistically significantly greater improvement than the placebo arm in mean ADHD-RS total score change at end-point (placebo - 10.35; edivoxetine 0.2 mg/kg/day - 16.09, p < 0.010; edivoxetine 0.3 m Statistically significant differences relative to placebo were observed for all edivoxetine dose arms with respect to changes in weight. (p< 0.05) Edivoxetine dose arms demonstrated statistically significantly greater mean increases in sitting heart rates, and sitting systolic and diastolic blood pressure, than the placebo arm (p<0.05). Edivoxetine and placebo treatment arms did not differ in the nu

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Mohammadi, 2010[439] Tehran University, 2010[1113] ID: NCT01099059 RCT Single center N = 40 Iran Setting: Mixed	**Target:** Participants with a diagnosis of ADHD based on DSM-IV criteria, have ADHD-Rating Scale-IV School version score of at least 1.5 SD above the norm for patient's gender and age; no history of pervasive developmental disorders, schizophrenia or other psychiatric disorders, any current psychiatric comorbidity that required pharmacotherapy, IQ <70, have a significant chronic medical condition **Other:** **ADHD presentation:** combined : 100 **Diagnosis:** Confirmation by specialist Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime diagnostic interview **Comorbidity:** N/A **Female:** 30 % **Age mean:** Amatadine 9.60 (1.98), methylphenidate 9.25 (1.80) **Minimum age:** 6 **Maximum age:** 14 **Ethnicity:** N/A	**Intervention:** Amantadine, dose of 100–150 mg/day depending on weight, 50 mg twiceper day for <30 kg and 50 mg three times per day for >30 kg, for 6 weeks **Control:** NA **Comparator:** MedicationMethylphenidate at a dose of 20–30 mg/day depending on weight (20 mg/day for <30 kg and 30 mg/day for >30 kg), titrated up: week 1: 10 mg/day (5 mg in the morning and 5 mg at midday); week 2: 20 mg/day (10 mg in the morning and 10 mg at midday) and week 3 **Follow-up:** 1.5 months	ADHD-RS (ADHD Rating Scale) Total Score change, parent rating No significant differences were observed between the two groups on the Parent and Teacher Rating Scale scores. Decreased appetite The rate was 45% in the amantadine group and 84% in the methylphenidate group (p=0.01). All side effects were mild to moderate and tolerable. The difference between the amantadine and methylphenidate groups in the frequency of side effects was not significant except for decreased appetite and restlessness that were observed more frequently i

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Saito, 2020[507] Taisho Pharmaceutical, 2016[1111] ID: JapicCTI-163244 RCT Multicenter N = 216 Japan Setting: N/A	**Target:** Children with ADHD according the DSM-5; a total ADHD Rating Scale-IV score ≥23; Clinical Global Impressions severity score of ≥3; no history or current diagnosis of schizophrenic disorder or any psychiatric disorder (diagnosed by DSM-5), comorbid of reactive attachment disorder, and intellectual disabilities (IQ <70) **Other:** **ADHD presentation:** inattentive : 41.2,hyperactive : 0.5,combined : 58.3 **Diagnosis:** No Any existing diagnosis was required but nothing was done in the trial **Comorbidity:** N/A **Female:** 15.2 % **Age mean:** 9.5 (2.3) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** N/A	**Intervention:** Tipepidine, 60 mg twice a day of tipepidine hibenzate (Asverin, non-opioid antitussive), 2 weeks of observation with 8 weeks of treatment **Control:** Placebo Placebo dose **Comparator:** MedicationTipepidine, 30mg/day tipepidine hibenzate (Asverin) **Follow-up:** 16 months	ADHD RS-IV-J:I (ADHD Rating Scale IV Japanese version) Mean Changes No significant difference was observed between the placebo and treatment groups, and no dose-response was observed; 30mg vs placebo (p=0.183) 120mg (p=0.748) No clinically significant changes in body weight were observed Adverse Events Total Count Incidence of AEs: 36.5% (placebo); 51.9% (30mg); 46.2 (60mg); 49.1% (120mg); no significant differences amongst treatment groups (p= 0.420) Incidence of side-effects: 3.8% (placebo); 5.6% (30mg); 17.3% (60mg); 3.8% (120mg); no significant differences (p= 0.050). No clinically significant changes in laboratory tests or vital signs were observed amongst treatment groups.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Salardini, 2016[508] ID: NA RCT Single center N = 54 Iran Setting: Specialty care	**Target:** ADHD patients with blood pressure, pulse rate, and liver function tests within clinically normal range **Other:** **ADHD presentation:** combined : 100 **Diagnosis:** Confirmation by specialist ADHD-RS-IV diagnosed by psychiatrist **Comorbidity:** N/A **Female:** 22 % **Age mean:** 10.47 (2.13) **Minimum age:** 6 **Maximum age:** 15 **Ethnicity:** % White : 100	**Intervention:** Agomelatine was started as 15 mg/day in participants with weight 30 kg and 25 mg/day in patients with weight 45 kg in the morning and followed by placebo at lunch time for 6 weeks **Control:** NA **Comparator:** MedicationRitalin (methylphenidate hydrochloride) 10 mg tablet twice daily for 6 weeks, participants who weighed more than 30 kg received a 10 mg methylphenidate hydrochloride tablet thrice daily **Follow-up:** 1.5 months	ADHD-RS-IV, parent, change from baseline Changes from baseline were not significantly different between the agomelatine group and the MPH group (p=0.44). The frequency of side effects was not significantly different between the agomelatine and MPH groups.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Sangal, 2014[513] Sunovion, 2009[1091]; Sunovion, 2009[1092] ID: NCT00856973, NCT00857220 RCT Multicenter N = 486 US Setting: Specialty care	**Target:** Children and adolescents with ADHD and insomnia; exclused another primary sleep disorder, other major psychiatric disorders, alcohol or substance abuse, and nicotine use **Other:** Parents supplied some outcome data **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV criteria and confirmed by the M.I.N.I. Inter-national Neuropsychiatric Interview for Children and Adolescents **Comorbidity:** Sleep **Female:** 36.2 % **Age mean:** 11.4 (3.0) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 15.5 % Black/African American : 19.3 % White : 74.5	**Intervention:** Eszopiclone high dose (2 mg for children, 3 mg for ado-lescents), participantscontinued on whatever stimulant medication they were on prior to trial enrollment, for duration of 12 weeks **Control:** Placebo Placebo plus whatever stimulant medication patients were on prior to trial enrollment **Comparator:** MedicationEszopiclone low dose (1 mg for children, 2 mg for ado-lescents), patients also continued on whatever stimulant medication they were on prior to trial enrollment **Follow-up:** 3 months	CGI, parent The intervention group improved significantly over the control group (p=0.009), but the comparator did not (p=0.238). Inattention score, Conners Comprehensive Behavior Rating Scale (CBRS) change, parent report No significant difference between groups (p 0.238 for high dose vs placebo, p 0.352 for low dose vs placebo). No significant differences between intervention, comparator, and placebo group in change from baseline to week 12 in latency to persistent sleep based on polysomnography (p 0.375 for high dose, p 0.999 for low dose). Participants with any adverse event The rate was 61% for intervention, 59.5% for comparator, and 46% for placebo. A dose-response relationship was observed for dysgeusia, abdominal discomfort, dizziness, and nasal congestion.

New pharmaceutical agent	Supernus, 2016[572] ID: NCT02618408 RCT Multicenter N = 333 US Setting: Specialty care	**Target:** Children with ADHD and comorbid impulsive aggression already using monotherapy treatment with FDA-approved optimized ADHD medication, no current or lifetime diagnosis of epilepsy, major depressive disorder, bipolar disorder, schizophrenia or a related disorder, personality disorder, Tourette's disorder, or psychosis **Other:** Parents provided some outcomes. **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-5 confirmed by the Schedule for Affective Disorders and Schizophrenia for School-aged Children - Present and Lifetime Version 2013 **Comorbidity:** ODD : Impulsive agression **Female:** 24.9 % **Age mean:** 9.0 (1.84) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 14.2 % Black/African American : 26.5 % American Indian or Alaska Native : 2.2 % Asian : 0.3 % White : 65.8 Other : Categories not mutually exclusive	**Intervention:** Molindone Hydrochloride Extended-Release (SPN-810) high dose (36 mg) twice each day, in the morning and in the evening, in addition to usual ADHD medication, for total of 7 weeks **Control:** Placebo Placebo twice each day, in the morning and in the evening, in addition to usual ADHD medication **Comparator:** MedicationMolindone Hydrochloride Extended-Release (SPN-810) 18 mg twice each day, in the morning and in the evening, in addition to usual ADHD medication **Follow-up:** 1 month	Clinical Global Impression-Improvement (CGI-I) Scale Investigator Rated No significant difference (p = 0.0742) in improvement measured by investigator rated CGI-I or CGI-S (p = 0.1729). Significantly greater improvement on parent rated CGI-I for high dose medication group (p = 0.0384). Swanson, Nolan, Pelham Rating Scale- Revised (SNAP-IV) Rating Scale, parent No significant difference between groups (p= 0.1418). Increased appetite None of 65 low dose patients experienced appetite increase, compared to 9 of 137 high dose patients. and 6 of 126 in placebo group. Adverse events Rates were 18.98% in the high dose, 15.38% in the low dose, and 14.29% in the placebo group. 2/13 participants experienced a serious adverse event (eye disorder, appendicitis perforated) in the high dose group, none in the other groups.
New pharmaceutical agent	Swanson, 2006[574] ID: N/A RCT Multicenter N = 190 US Setting: Specialty care	**Target:** Participants with ADHD; Clinical Global Impressions-Severity of Illness scale rating of 4 or higher, total and/or subscale scores on the Attention-Deficit/Hyperactivity Disorder Rating Scale-IV School Version 22 at least 1.5 standard deviations above norm, and IQ of at least 80 as estimated by the Wechsler Intelligence Scale for Children-Third Edition, and a score of at least 80	**Intervention:** Modafinil 340 or 425 mg/day (depending on weight) for 7 weeks **Control:** Placebo Placebo **Comparator:** NA **Follow-up:** 2.25 months	ADHD-RS-IV (Attention-Deficit/ Hyperactivity Disorder Rating Scale-IV) Home Version Modafinil significantly improved symptoms of ADHD as shown by reductions in ADHD-RS-IV School Version total scores compared with placebo at all visits (p ≤ .009), including the final visit of the double-blind phase (p < .0001).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
		on the Wechsler Individual Achievement Test, Second Edition, Abbreviated **Other:** **ADHD presentation:** inattentive : 27,hyperactive : 6,combined : 67 **Diagnosis:** Confirmation by specialist DSM-IV-TR **Comorbidity:** N/A **Female:** 30 % **Age mean:** 11.6 (2.6) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:**		Decreased appetite The rate was 14% in the intervention vs 2% in the placebo group. Two patients receiving modafinil experienced 3 serious adverse events (asthma attack, influenza syndrome, dehydration), these events resolved spontaneously and were considered to be not related or unlikely related to the study medication.

New pharmaceutical agent	Wilens, 2011[105] ID: NCT00640419 RCT Multicenter N = 121 US Setting: N/A	**Target:** Participants with DSM-IV diagnosis of any ADHD subtype, confirmed by the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version 15 and a rating of 4 or higher on the Clinical Global Impression-ADHD-Severity Scale; no history of current or past diagnosis of bipolar I, II, or not otherwise specified disorder; psychotic disorder; autism, Asperger's syndrome or pervasive developmental disorder; tics or Tourette syndrome; seizure disorder; traumatic brain injury; current diagnosis of obsessive-compulsive disorder, eating disorder, anxiety disorder, or depressive disorder requiring treatment of any kind; psychotropic medications within 14 days or 5 half-lives (7 days for stimulants) **Other:** **ADHD presentation:** inattentive,inattentive_other : %s broken down by meds,hyperactive,hyperactive_other : %s broken down by meds,combined,combined_other : %s broken down by meds **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 33 % **Age mean:** 8.5 **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** Other : % race is broken down by med dosage	**Intervention:** ABT-089 (neuronal nicotinic receptor partial agonist) 1.4 mg/kg taken daily for 6 weeks **Control:** Placebo Placebo **Comparator:** MedicationABT-089 (neuronal nicotinic receptor partial agonist) 0.7 mg/kg taken daily for 6 weeks **Follow-up:** 1.5 months	CGI-ADHD-S There was no statistically significant difference between any ABT-089 dose and placebo for the mean change from baseline to final evaluation for the CGI-ADHD-S (Table 2), or on the mean change from baseline to each evaluation. ADHS-RS-IV There was no statistically significant difference between ABT-089 and placebo in the primary efficacy analysis of mean change from baseline to final evaluation of the ADHD-RS-IV (HV) Total Score (Table 2), or on the secondary analysis of mean change from Any adverse event The rates were 60% in the intervention, 69% in the placebo, and 67.6% in the low dose group.

New pharmaceutical agent	Willens, 2011[620] ID: NCT00528697 RCT Multicenter N = 278 US Setting: N/A	**Target:** Participants with DSM-IV diagnosis of any ADHD subtype, confirmed by the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version, a rating of 4 or higher on the Clinical Global Impression-ADHD-Severity Scale; no history of current or past diagnosis of bipolar I, II, or not otherwise specified disorder, psychotic disorder, autism, Asperger's syndrome or pervasive developmental disorder, tics or Tourette syndrome, seizure disorder, traumatic brain injury, current diagnosis of obsessive-compulsive disorder, eating disorder, anxiety disorder, or depressive disorder requiring treatment of any kind, psychotropic medications within 14 days or 5 half-lives (7 days for stimulants), atomoxetine within 3 months of randomization or not a suitable candidate to receive atomoxetine **Other:** **ADHD presentation:** inattentive_other : %s broken down by meds,hyperactive_other : %s broken down by meds,combined_other : %s broken down by meds **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 33 % **Age mean:** mean 8.6 **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:**	**Intervention:** ABT-089 of 0.085 mg/kg, 0.260 mg/kg, 0.520 mg/kg, or 0.700 mg/kg once per day, treatment period of 8 weeks **Control:** Placebo Placebo **Comparator:** MedicationAtomoxetine 1.2 mg/kg/day once per day, treatment period of 8 weeks **Follow-up:** 2 months	CGI-ADHD-S There was no statistically significant difference between any ABT-089 dose and placebo for the mean change from baseline to final evaluation for the CGI-ADHD-S, or on the mean change from baseline to each evaluation, with the exception of the 0.520 mg/kg ADHD-RS-IV There was no statistically significant difference between ABT-089 and placebo in the primary efficacy analysis of mean change from baseline to final evaluation of the ADHD-RS-IV (HV) Total Score, or on the secondary analysis of mean change from baseline t In the atomoxetine group, mean weight and BMI decreased by 0.1 kg and 0.2 kg/m2 (mean difference from placebo −1.3 CI-1.99, −0.69 and −0.6 CI −0.96, −0.19] Any adverse event The rate were 82% in the intervention, 76.1% in the placebo, and 82% in the atomoxetine group. ABT-089 was generally safe and well tolerated, with no statistically significant difference between any ABT-089 dose and placebo in the overall incidence of any specific AE, and no clinically significant changes in other safety measures

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Zarinara, 2010[636] ID: N/A RCT Single center N = 38 Iran Setting: Other	**Target:** Children with combined subtype of ADHD and newly diagnosed (drug naive); no history or current diagnosis of pervasive developmental disorders, schizophrenia or other psychiatric disorders, any current psychiatric comorbidity that required pharmacotherapy, any evidence of suicide risk, mental retardation (IQ<70), clinically significant chronic medical condition, seizures or current abuse or dependence on drugs in the last 6 months, hypertension or hypotension **Other:** **ADHD presentation:** combined : 100 **Diagnosis:** Confirmation by specialist DSM-IV-TR **Comorbidity:** N/A **Female:** 29 % **Age mean:** 9.42 (2.19) and 9.57(1.86) **Minimum age:** 6 **Maximum age:** 13 **Ethnicity:** N/A	**Intervention:** Venlafaxine (antidepressant) at doses of 50–75 mg/day depending on weight (25 mg twice per day for <30 kg and 25 mg three times per day for >30 kg), treatment for 6 weeks **Control:** NA **Comparator:** MedicationMethylphenidate at a dose of 20–30 mg/day depending on weight, titrated up: week 1: 10 mg/day (5 mg in the morning and 5 mg at midday); week 2: 20 mg/day (10 mg in the morning and 10 mg at midday); and week 3: 30 mg/day for children >30 kg (10 mg in the m **Follow-up:** 1.5 months	ADHD-RS-IV, parent rating Responder (at least 40% decrease in ADHD-RS-IV) No significant difference was observed in the two groups (p 0.33). No significant difference was observed on the reduction of scores of the Teacher ADHD Rating Scale (p 0.30). Decreased appetite The reported rates were 10.52% in the venlafaxine and 10.52% in the methylphenidate group. Nine side effects were observed over the trial, but all of them were mild to moderate and tolerable. The difference between the venlafaxine and methylphenidate groups in the frequency of side effects was not significant except for headaches and insomnia t

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
New pharmaceutical agent	Zavadenko, 2019[637] NA ID: NA RCT Multicenter N = 100 Russia Setting: Mixed	**Target:** Children with ADHD diagnosis based on ICD-10 criteria, presence of hyperdynamic (hyperkinetic) syndrome with attention deficit; severity of ADHD on the Clinical Global Impressions-Severity scale of 3–6 points; total score on the ADHD-DSM-IV scale is at least 25 for boys and 22 for girls; patients with comorbid diseases that would require the use of barbiturate, anticonvulsants, or any other nootropic agents were excluded **Other:** **ADHD presentation:** inattentive : 61.8,hyperactive : 7.9,combined : 30.3 **Diagnosis:** No **Comorbidity:** N/A **Female:** 18.0 % **Age mean:** Intervention 8.7 (2.1). placebo 8.24 (1.63) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Hopantenic acid (pantogam) was given as tablets containing 250 mg at the pediatric therapeutic dose of 30 mg/kg, divided into two split doses taken after meals, for 4 months **Control:** Placebo Placebo as tablets with external appearance, packaging, and labeling identical to those of the study drug, taken in two split doses after meals, for 4 months **Comparator:** NA **Follow-up:** 4 months	CGI-S (Clinical Global Impressions Scale- Severity) The intervention produced a decrease in disease severity from the placebo level (p=0.014). Proportions of patients with clinical improvements (decreases in total points scores on the DSM-IV ADHD scale by 25% or more from baseline) There was no significant difference between groups. Weiss Functional Impairment Rating Scale (WFIRS-P); Family Section-Parent There were significant decreases in impairment in the intervention compared to the control (p<0.01). Total adverse events The rate was 68% for intervention and 48% for control. Statistical analysis did not identify any significant differences between groups in clinical or biochemical blood tests or measures of urinalysis; results of clinical and neurological examination, the state of major organs or organ systems revealed no sig

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Abbasi, 2011[104] ID: N/A RCT Single center N = 40 Iran Setting: Other	**Target:** Children with combined subtype of ADHD and newly diagnosed (drug naive); no history or current diagnosis of pervasive developmental disorders, schizophrenia or other psychiatric disorders, any current psychiatric comorbidity that required pharmacotherapy, any evidence of suicide risk, mental retardation (IQ<70), clinically significant chronic medical condition, seizures or current abuse or dependence on drugs in the last 6 months, hypertension or hypotension **Other:** **ADHD presentation:** combined : 100 **Diagnosis:** Confirmation by specialist DSM-IV-TR **Comorbidity:** N/A **Female:** 30 % **Age mean:** 8.84(2.03) and 8.36(1.53) **Minimum age:** 7 **Maximum age:** 13 **Ethnicity:** N/A	**Intervention:** Acetyl-L-Carnitine plus methylphenidate, doses ranging from 500 to 1,500 mg/day depending on the weightof the child (13.5–30 kg = 0.5 g twice per day;>30–50 kg = 1.0 g twice per day; and >50 kg = 1.5 g twice per day) plus methylphenidate at a dose of 20–30 mg/day depending on weight (20 mg/day for <30 kg and 30 mg/day for>30 kg), treatment for 6 weeks **Control:** Placebo Placebo plus methylphenidate at a dose of 20–30 mg/day depending on weight (20 mg/day for <30 kg and 30 mg/day for >30 kg). Methylphenidate was titrated up: week 1: 10 mg/day (5 mg in the morning and 5 mg at midday), week 2: 20 mg/day (10 mg in the mornin **Comparator:** NA **Follow-up:** 1.5 months	ADHD-RS-IV, parent rating The difference between groups was not significant (p 0.74). The difference between the two protocols was not significant for the teacher ratings (p 0.63). Decreased appetite The rate was 35% in the intervention and 40% in the control group. Fourteen side effects were observed, all mild to moderate and tolerable. The difference in the frequency of side effects was not significant except for headache and irritability that were observed more frequently in the methylphenidate plus placebo group.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Akhondzadeh, 2004[116] ID: ISRCTN64132371 RCT Single center N = 44 Iran Setting: Specialty care	**Target:** Children with newly diagnosed with ADHD combined subtype and had not yet received any stimulant medication prior to enrollment **Other:** **ADHD presentation:** combined : 100.0 **Diagnosis:** Confirmation by specialist Diagnosed by psychiatrist **Comorbidity:** N/A **Female:** 40.9 % **Age mean:** 7.88 (1.67) **Minimum age:** 5 **Maximum age:** 11 **Ethnicity:** Other : Persian: 100%	**Intervention:** Zinc sulfate 55 mg/day (15mg elemental zinc) plus methylphenidate 1 mg/kg/day twice daily for 6 weeks **Control:** Other Methylphenidate 1 mg/kg/day twice daily **Comparator:** NA **Follow-up:** 1.5 months	Parent ADHD rating scale Both groups showed significant improvement and the zinc+methylphenidate group improved significantly more than the placebo+methylphenidate group (p<0.001). Decreased appetite No difference between groups. Metallic taste was experienced more in the zinc group (p=0.0001).
Nutrition, supplements	Arnold, 2007[125] ID: RCT Multicenter N = 112 US Setting: N/A	**Target:** Children with ADHD **Other:** **ADHD presentation:** N/A **Diagnosis:** No **Comorbidity:** N/A **Female:** 26 % **Age mean:** placebo mean 8.3 (2.2), ALC mean 8.4 (2.3) **Minimum age:** 5 **Maximum age:** 12 **Ethnicity:** % White : 68.75	**Intervention:** Acetyl-L-Carnitine, metabolite necessary for energy metabolism and essential fatty acid anabolism, 500-1500mg depending on weight, for 16 weeks **Control:** Placebo Identical-appearing and tasting **Comparator:** NA **Follow-up:** 4 months	CGI-I responder 17% improved in the interention, 14% in the placebo group. Conners'-Revised Both groups improved (p 0.291) Height Hight increased more in placebo group.

Nutrition, supplements	Baziar, 2019[136] Tehran University of Medical Sciences, 2017[1114] ID: IRCT201701131556N94 RCT Single center N = 54 Iran Setting: Other	**Target:** Children with a subscale scores on Attention-Deficit/Hyperactivity Disorder Rating Scale-IV of at least 1.5 standard deviations above norms; exclusion criteria were psychiatric comorbidities, mental retardation, clinically significant chronic medical condition, systolic blood pressure over 125 mmHg and/or resting pulse below 60 or over 110 beats/min, history of allergy to saffron, psychotropic medication use in the past 2 weeks, females who were likely to go through pregnancy or lactation, use of any medication that might have adverse reactions with saffron, and patients who were going to undergo surgery within 36 hours to 14 days **Other:** **ADHD presentation:** N/A : Baseline ADHD-RS-IV Parent version total, mean(SD): Control=34.20(4.69) Intervention=33.56(6.48) Baseline ADHD-RS-IV Teacher version total, mean(SD): Control=24.16(8.32) Intervention=23.64(8.16) **Diagnosis:** Confirmation by specialist DSM-V **Comorbidity:** N/A **Female:** 20 % **Age mean:** Intervention 9.08 (2.23), control 8.28 (1.59) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** N/A	**Intervention:** Saffron (crocus sativus L.) capsules at a dosage of 20–30 mg/d depending on weight (20 mg/d for <30 kg and 30 mg/d for >30 kg) for 6 weeks **Control:** NA **Comparator:** MedicationMethylphenidate (ritalin), 0.3–1 mg/(kg*d), titrated up during the trial: 10 mg/d (5 mg in the morning and 5 mg at midday) in week 1; 20 mg/d (10 mg in the morning and 10 mg at midday) in week 2; 20 mg/d for children <30 kg and 30 mg/d for children >30 kg **Follow-up:** 1.5 months	ADHD-RS-IV total, parent and teacher No significant difference between the two groups on Parent and Teacher Rating Scale scores. Decreased appetite The rate of decreased appetite was 8% in the saffron group compared to 20% in the methylphenidate group. No serious adverse event was observed in any of the patients and all noticed adverse effects were mild to moderate and tolerable, the frequency of side effects was not significantly different between the saffron and MPH groups.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Behdani, 2013[138] ID: ID NA RCT Single center N = 75 Iran Setting: Specialty care	**Target:** Children and adolescents with ADHD; those with co-morbid psychological diagnoses or serious medical conditions were excluded **Other:** Teachers and parents reported outcomes **ADHD presentation:** inattentive : 21.7,hyperactive : 37.7,combined : 40.6 **Diagnosis:** Confirmation by specialist DSM-IV-TR by board-certified psychiatrists **Comorbidity:** N/A **Female:** 20.3 % **Age mean:** 8.7 (1.7) **Minimum age:** 7 **Maximum age:** 15 **Ethnicity:** Other : 100% Persian	**Intervention:** Omega 3 plus methylphenidate, final dose of 1mg/kg (maximum dose 60mg/day), in 2or 3 divided doses, plus Omega-3, two 1000-miligram capsules (containing 240 mg of DHA and 360 mg of EPA), per day in 2 divided doses for 8 weeks **Control:** Placebo Placebo plus methylphenidate; final dose of 1mg/kg (maximum dose 60mg/day), in 2or 3 divided doses plus placebo **Comparator:** NA **Follow-up:** 2 months	ADHD Rating Scale-IV, parent Difference between groups in terms of parent's and teacher's ADHD rating scale scores were not significant. 1/75 dropped out due to side effects of omega 3, including nausea, vomiting, and abdominal pain.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Nutrition, supplements	Bilici, 2004[149] ID: N/A RCT Single center N = 400 Turkey Setting: Specialty care	**Target:** Children with ADHD who have no other mental or medical illness **Other:** Teachers supplied some outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV by psychiatrists, pediatrician, and psychologist **Comorbidity:** N/A **Female:** 20 % **Age mean:** 9.4 (1.5) **Minimum age:** 6 **Maximum age:** 14 **Ethnicity:** Other : Turkish	**Intervention:** Zinc sulfate (150 mg/day) for 12 weeks **Control:** Placebo Placebo (sucrose, 150 mg) for 12 weeks **Comparator:** NA **Follow-up:** 3 months	ADHDS (Attention Deficit Hyperactivity Disorder Scale) change Therapeutic response Intervention patients showed greater improvement than placebo patients (p=.002). Intervention group also showed significantly more improvement in ADHDS-H (p=.01), ADHDS-I (p=.03), and ADHDS-S (p = .03) subscales compared with placebo groups. Therapeutic Significantly more intervention patients than placebo patients reported metallic taste (p = .01). No significant difference in nausea, vomiting, abdominal pain, and diarrhea.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Carucci, 2022[171] ID: ID NA RCT Multicenter N = 160 Italy Setting: Specialty care	**Target:** Drug naive children with mild to moderate ADHD-inattentive type; those with serious medical or serious psychiatric conditions were excluded **Other:** Parents reported some outcomes **ADHD presentation:** inattentive : 100 **Diagnosis:** Confirmation by specialist DSM IV based on psychiatric evaluation and Schedule for Afective Disorders and Schizophrenia for school-age children-present and lifetime version **Comorbidity:** N/A **Female:** 26 % **Age mean:** 9.7 (1.9) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Omega 3/6, 2 capsules containing 279 mg EPA, 87 mg DHA, 30 mg GLA (gamma linolenic acid) per day, to be taken with a meal for 6 months **Control:** Placebo Placebo, 2 capsules per day, to be taken with a meal **Comparator:** NA **Follow-up:** 6 months	Clinical Global Impression, Severity score (CGI-S) No significant differences between the two groups in CGI-S or Conner's Parent and Rating Scale-Revised. ADHD RS IV, total, clinician administered ADHD-RS- Inattention score, number "responders" Intervention group improved more than control on total score (p 0.036); no significant difference in the percent categorized as responders on Inattention scale. No effect was found on mood and anxiety symptoms measured by Multidimensional Anxiety Scale for Children (MASC). Number reporting an adverse event 2 in intervention group reported diarrhoea, 3 on placebo reported one each respectively abdominal pain, itch, and somnolence. No severe adverse events.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Chang, 2019[178] Hospital, China Medical University, National Science Council, 2016[715] ID: NCT03542643 RCT Single center N = 103 Taiwan Setting: Specialty care	**Target:** Children and adolescents with ADHD who were drug naïve or had no medication for the past 6 months, without comorbid psychiatric disorders, such as autism spectrum disorder, anxiety disorder, and conduct disorder **Other:** ADHD symptoms were rated by parents and teachers **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM V diagnoses were confirmed by a child and adolescent psychiatrist **Comorbidity:** N/A **Female:** 14.1 % **Age mean:** 9.49 (3.05) **Minimum age:** 6 **Maximum age:** 18 **Ethnicity:** % Asian : 100	**Intervention:** Omega 3 eicosapentaenoic acid (EPA) 1.2 g per day for 12 weeks **Control:** Placebo Placebo **Comparator:** NA **Follow-up:** 3 months	SNAP IV total score, parent version There was no difference between groups in changes in parent or teacher reported inattention (p=.072, .066), hyperactivity (p=.075, .766) and ODD (p=.207, .759) subscale scores. Continuous Performance Test (CPT) variability score (measures focused attention). Intervention group had significantly greater decrease from baseline to 12 weeks (p = 0.041).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Cornu, 2018[209] ID: ID NA RCT Multicenter N = 162 France Setting: Specialty care	**Target:** Children and adolescents with hyperactivity-impulsivity symptoms for 6 months or more and/or at least one of six inattention symptoms for six months or more, with certain symptoms which were present before age 7 and with a functional impairment in 2 or more environments and clinically significant alteration in social, school, or family functioning **Other:** Staff, parents **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist child psychiatrist **Comorbidity:** N/A **Female:** 0 % **Age mean:** 6.9 (2.9) **Minimum age:** 6 **Maximum age:** 15 **Ethnicity:** N/A	**Intervention:** Omega 3 dietary supplement, aged 6–8 eicosatetraenoic acid 336mg, aged 9–11 eicosatetraenoic acid 504mg, aged 12–15 eicosatetraenoic acid 672mg, capsules also contained 100 µg vitamin A, 1.25 µg vitamin D, and 3.5 mg vitamin E, during which other hyperactivity treatments and other omega-3 supplements or psychotropic drugs were not allowed, for 3 months **Control:** Placebo Placebo capsules indistinguishable from active capsules, composedof olive oil, the same amount of vitamin A, D, and E, with traces of marine lipid concentrate: EPA (18%), DHA (12%), totaling 4.83 mg, to give the capsules a similar taste and smell and stra **Comparator:** NA **Follow-up:** 3 months	Connors total score No beneficial effect of omega-3 supplement. ADHD-RS-IV No beneficial effect of omega-3 supplement. There was no significant change in reading skills (L'Aloutte) in both groups (p=0.28). Participants experiencing adverse events 15% vs 11% adverse events favoring placebo. 2/80 patients in the DHA–EPA group experienced a severe adverse event (hospitalisation for worsening ADHD symptoms).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Crippa, 2019[212] Crippa, 2018[726]; IRCCS Eugenio Medea, 2012[849] ID: NCT01796262 RCT Single center N = 50 Italy Setting: Specialty care	**Target:** Children with ADHD who were drug-naïve and had not consumed omega-3/omega-6 supplements during the 3 months prior to the recruitment **Other:** **ADHD presentation:** inattentive : 15.7,hyperactive : 33.3,combined_other : 51 **Diagnosis:** Confirmation by specialist DSM-IV by child neuropsychiatrist **Comorbidity:** N/A **Female:** 8.7 % **Age mean:** 11.1 (1.85) **Minimum age:** 7 **Maximum age:** 14 **Ethnicity:** % White : 100	**Intervention:** Omega 3 supplement of 500 mg algal docosahexaenoic acid (DHA) per day for 6 months **Control:** Placebo Placebo, 2 pearls per day of 500mg wheat germ oil, stabilized with low concentration of Vitamin E **Comparator:** NA **Follow-up:** 6 months	Behavior in Child Health Questionnaire Only the intervention group improved. CGI-S Difference between groups was not significant (p > 0.05). ADHD-RS-IV (ADHD rating scale IV) Parent Version, total Difference between groups was not significant (p>0.05). Word Reading Accuracy (errors) difference between groups was not significant (p>0.05). Higher impact of symptoms on functioning evaluated by SDQ in DHA group (p=0.045). Participants with adverse events No adverse events in both groups. Over the course of the 6 months, no instances of either major or minor adverse events were reported.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Fallah, 2018[262] Shahid Sadoughi University of Medical Sciences, 2016[1036] ID: IRCT201604212639N18 RCT Single center N = 56 Iran Setting: Specialty care	**Target:** Children with ADHD and refractory epilepsy **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** Other : Epilepsy **Female:** 41.0 % **Age mean:** 9.24 (0.15) **Minimum age:** 7 **Maximum age:** 11 **Ethnicity:** % White : 100	**Intervention:** Omega 3 plus risperidone, plus antiepileptic drug, 1000 mg of omega 3 fish oil, 180 mg of eicosapentaenoic acid and 120 mgdocosahexaenoic acids) 1 capsule per day plus 0.5 mg of risperidone per day and an antiepileptic drug for 3 months **Control:** Other Risperidone 0.5 mg and an antiepileptic drug alone **Comparator:** NA **Follow-up:** 6 months	Monthly seizure frequency was lower in intervention group compared to control group (p=0.03). The rate of good response, defined as a 50% decrease in seizures, was higher in the intervention group (p 0.001). Participants with side effects No significant difference between groups (p 0.50).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Ghajar, 2018[295] ID: IRCT201601031556N84 RCT Single center N = 56 Iran Setting: Specialty care	**Target:** Participants who met criteria of DSM-V, no previously diagnosed psychiatric comorbidity (except for Oppositional Defiant Disorder) or developmental or physiological disorders, IQ>70, without receiving any supplemental medication, or having an allergy to L-carnosine or methylphenidate **Other:** **ADHD presentation:** combined : 100 **Diagnosis:** No **Comorbidity:** N/A **Female:** 16 % **Age mean:** 9.12 (2.18) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** Other : All patients were reported as persian	**Intervention:** L-carnosine (800mg/d) plus methylphenidate hydrochloride (20 mg/d in 2 divided doses, 30 mg/d in three divided doses) for 8 weeks **Control:** Other Methylphenidate alone, 0.5-1.5mg;/kg, titrated up: 10mg/d (2 divided doses) for the first week followed by 20mg/d (2 divided doses) from the second week till the rest of the trial; weight >30kg received 30mg/d (3 divided doses) from the third week of the **Comparator:** NA **Follow-up:** 2 months	ADHD-RS-IV Significant time by treatment interaction on total and inattention subscales indicating beneficial effects of the adjunct. Seven side effects were recorded during the course of the study; no serious adverse event was observed in any of the patients; the most common side effects were abdominal pain (28%), headache (20%), and insomnia (16%) in the l-carnosine group; and abdomi

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Ghanizadeh, 2015[296] ID: IRCT201311303930N29 RCT Single center N = 106 Iran Setting: Specialty care	**Target:** Children with ADHD; those with serious medical conditions were excluded **Other:** Parents **ADHD presentation:** inattentive_other : Mean inattentiveness score at basline = 15.75 on ADHD Checklist **Diagnosis:** Confirmation by specialist DSM-IV diagnostic criteria supported by KSADS **Comorbidity:** N/A **Female:** 26.4 % **Age mean:** 8.45 (2.1) **Minimum age:** 5 **Maximum age:** 14 **Ethnicity:** Other : 100% Persian	**Intervention:** Dietary recommendations plus methylphenidate, mean dose 12.7(5.4) mg/day. parents received a lists of foods which were recommended (diary, homemade fruit juices, vegetables, low-fat meat) and another list of the foods which were recommended to be eaten as less as possible; parents were encouraged to provide their children with 3 regular meals per day, for 1 month **Control:** Other Methylphenidate alone, mean dose 11.9(4.6) mg/day **Comparator:** NA **Follow-up:** 1 month	ADHD Checklist, Hyperactivity / Impulsivity Score No significant difference between groups.

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Nutrition, supplements	Gustafsson, 2010[310] Hela Pharma AB, 2004[828] ID: EudraCT No. 2004-003853-13 RCT Multicenter N = 92 Sweden Setting: Specialty care	**Target:** ADHD patients with no medical conditions requiring intervention and no neurological or psychological comorbidity **Other:** Parents and teachers provided outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** % N/A **Age mean:** NA **Minimum age:** 7 **Maximum age:** 12 **Ethnicity:** % White : 100	**Intervention:** Omega 3, one eicosapentaenoic acid capsule PlusEPA, 500 mg EPA +2.7 mg DHA and 10 mg Vitamin E mixed tocopheroles, 1 capsule per day for 15 weeks **Control:** Placebo Placebo, mixture of rape seed oil and medium-chain triglycerides containedin a capsule identical to the PlusEPA containing <10% of the PlusEPA content of omega-3 LCPUFA **Comparator:** NA **Follow-up:** 3.75 months	Conners Rating Parent rating scale total No significant difference between groups (p > .05). There were only mild adverse events observed, most of them classified as not related or unlikely to have been related to the drug. Events possibly related to drug treatment, such as abdominal symptoms and nose bleeding did not differ between groups.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Hariri, 2012[318] ID: N/A RCT Single center N = 120 Iran Setting: Other	**Target:** ADHD patients taking Ritalin with Conners' Abbreviated Questionnaires scores for hyperactivity greater than 14; no infectious diseases, diabetes, hyperthyroidism, convulsion, epilepsy and consumption of n-3 fatty acids supplements **Other:** Parents provided outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Conners' Abbreviated Questionnaires (ASQ-P) **Comorbidity:** N/A **Female:** 38 % **Age mean:** 7.90 (1.5) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:**	**Intervention:** Omega 3 plus ritalin (any dose); soft gel capsules of n-3 fatty acids with a total daily dose of 900mg n-3 fatty acids (635mg eicosapentaenoic acid, 165mg docosahexaenoic acid and 100mg other n-3 fatty acids), for 8 weeks **Control:** Other Placebo plus ritalin (any dose), olive oil capsules **Comparator:** NA **Follow-up:** 2 months	ASQ-P (Conners' Abbreviated Questionnaires) Intervention group improved more than control group (p < .001). 2 intervention group patients withdrew because of steatorrhoea.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Hemamy, 2021[324] Hemamy, 2020[829] ID: ID NA RCT Single center N = 66 Iran Setting: Mixed	**Target:** Children with serum level of 25-hydroxyvitamin D3 less than 30 ng/dL, a diagnosis of ADHD based on the presence of at least 6 out of 9 cases of inattention and also at least 6 out of 9 cases of hyperactivity based on DSM IV and serum magnesium levels less than 2.3 mg/dL **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV diagnosed by unknown source **Comorbidity:** N/A **Female:** 30.3 % **Age mean:** 9.06 (1.76) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % White : 100	**Intervention:** Vitamin D (50,000 IU/week with lunch meal) and an oral tablet of magnesium (6 mg/kg/day with lunch meal) for a duration of 8-weeks **Control:** Placebo Placebo, similar in appearance, color, and taste to the supplements (edible paraffin oil as a placebo for vitamin D, microcrystalline cellulose, and stearic acid as a placebo for magnesium) **Comparator:** NA **Follow-up:** 2 months	Conduct problems Significant reduction in conduct problems (p 0.0002). Strength and difficulties questionnaire (SDQ), total difficulties The intervention group showed a significant reduction in total difficulties compared to control group (p 0.001). Significant reduction in emotional problems (p 0.001), peer problems (p 0.001), prosocial score (p 0.007), externalizing score (p 0.001), and externalizing score (p 0.001) compared with placebo. No adverse effects of Vitamin D and magnesium supplementation were reported at the end of this study.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Hirayama, 2014[328] ID: ID NA RCT Single center N = 36 Japan Setting: Community	**Target:** Children with ADHD **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist diagnosed by child's own psychiatrist **Comorbidity:** N/A **Female:** 5.6 % **Age mean:** 9.1 (1.7) for intervention group; 8.7 (3.0) for placebo group **Minimum age:** **Maximum age:** **Ethnicity:** N/A	**Intervention:** Phosphatidylserine (soy-derived) 100mg chewable tablet, 2 chews per day for 2 months **Control:** Placebo Identical-appearing placebo chewable tablets, 2 chews per day **Comparator:** NA **Follow-up:** 2 months	Inattention Go/No-Go task No difference between groups (p 0.29). DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th edition) criteria score ADHD symptoms were statistically significantly lower in the phosphatidylserine treated group compared to the placebo group ($p<0.01$). Working memory: phosphatidylserine 0.3, placebo -0.7 (n.s.).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Johnson, 2009[349] ID: N/A RCT Multicenter N = 75 Sweden Setting: Specialty care	**Target:** Children and adolescents with ADHD; no autism, psychosis, bipolar disorder, mental retardation, uncontrolled seizure disorder, hyper- or hypothyroidism, significant other medical conditions, weight below 20 kg, alcohol or drug abuse, or the use of any psychoactive drugs or omega 3 preparations in the past 3 months **Other:** Parents reported some outcomes **ADHD presentation:** inattentive : 53,combined : 47 **Diagnosis:** Confirmation by specialist DSM-RS-IV **Comorbidity:** N/A **Female:** 15 % **Age mean:** Intervention 11.8 (2.14), control 12.2 (2.19) **Minimum age:** 8 **Maximum age:** 18 **Ethnicity:** N/A	**Intervention:** Omega 3/6 in a dose of three capsules twice daily, corresponding to a daily dose of 558 mg eicosapentaenoic acid, 174 mg docosahexaenoic acid (both are omega-3 fatty acids), 60 mg gamma linoleic acid (an omega 6 fatty acid), and 10.8 mg Vitamin E for 3 months **Control:** Placebo Placebo, identical capsules containing olive oil **Comparator:** NA **Follow-up:** 3 months	CGI (Clinical Global Impression) scale change Intervention group improved more than placebo group (p 0.02). ADHD-RS-IV (ADHD Rating Scale IV), parent reported change Number responding (defined as 25% improvement in ADHD symptoms on ADHD RS IV) Difference in mean improvement at follow-up not significant. Higher percentage of intervention group classified as responders. 11 (3 active, 8 placebo) withdrawals during Study Period (7 were unmotivated to continue or had problems swallowing the capsules [1 active, 6 placebo], 3 had side effects in the form of dyspepsia, vomiting, or diarrhea [2 active, 1 placebo]), and 1 patien

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Johnstone, 2022[350] Johnstone, 2019[869]; Oregon Health Science University, 2018[971] ID: NCT03252522 RCT Multicenter N = 135 US Setting: Specialty care	**Target:** Children with ADHD not on medication; exclusion criteria were neurological disorders, serious medical conditions, and known allergy to any ingredient in either intervention **Other:** Parents provided outcome data **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-V **Comorbidity:** N/A **Female:** 27 % **Age mean:** 9.8 (1.7) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Black/African American : 3 % Asian : 3 % White : 88	**Intervention:** Vitamins and known essentialminerals, amino acids and antioxidants, total of 9 to 12 capsules per day accumulated to doses above the recommended dietary allowance but below the upper tolerable intake level, for 8 weeks **Control:** Placebo Visually identical placebo capsules containing cellulose filler and 0.1 mg of riboflavin per capsule to mimic the color of urine as when supplemented with B-vitamins **Comparator:** NA **Follow-up:** 2 months	CGI-S severity reduced 56% of micronutrient group vs 22% of placebo group had illness severity reduced by at least 1 category ($p < .001$). Inattention CASI-5 (Child and Adolescent Symptom Inventory-5), parent-rated Between-group difference was not significant. Impairment scale CASI teacher rating No statistically significant difference between groups ($p=0.22$). Height (cm) Intervention patients gained more height (p 0.002). Participants with any adverse event Rate was 32% in the intervention and 45% in the placebo group. No between-group differences for treatment-emergent adverse events were detected.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Katz, 2010[360] Etz-HaChayim Clinic (Israel), 2007[762] ID: ISRCTN10628149 RCT Single center N = 120 Israel Setting: Specialty care	**Target:** Treatment naïve children with ADHD and without medical conditions, psychiatric comorbid conditions, or ongoing use of any medications **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 15 % **Age mean:** Intervention 9.72 (1.58), control 9.20 (1.82) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** PaeoniaeAlba, Withania Somnifera , Centella Asiatica, Spirulina Platensis, Bacopa Monieri, and Mellissa Officinalis compound herbal preparation, 3 ml of the compound herbal preparation taken 3 times daily before meals diluted in 50 to 60 ml of water for 4 months **Control:** Placebo Placebo home administered by parents who were instructed how to prepare (dilute in water) the daily dosage for the entire day **Comparator:** NA **Follow-up:** 4 months	Test of Variables of Attention (TOVA), composite score Improvement for overall TOVA (p < .001) as well as omission (p = .016), commission (p = .026), response time (p < .001) and variability (p < .001) scales was greater for intervention group than placebo group. Decreased appetite Decreased appetite reported by 2 people in the control group and only 1 in the intervention group. No serious adverse events were reported, and the rate of even mild adverse events among intervention patients was less than that of placebo. None of the adverse events were more frequent in the intervention than in the placebo group.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Khaksarian, 2021[363] Khoram-Abad University of Medical Sciences, 2020[882] ID: IRCT20190602043790N2 RCT Single center N = 70 Iran Setting: Specialty care	**Target:** Children and adolescents with ADHD **Other:** Parents and teachers provided outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM V by Child Psychiatrist **Comorbidity:** N/A **Female:** % N/A **Age mean:** Methylphenidate group: 11.03 (2.31) and for Methylphenidate and Saffron group: 10.57 (2.56) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** N/A	**Intervention:** Saffron plus methylphenidate: 20 mg/d (for <30 kg and 30 mg/d for > 30 kg, 10 mg for morning, midday, and evening equally) plus 20-30 mg/d saffron capsules according to the BMI (20 and 30 mg/d for <30kg and > 30kg), for 8 weeks **Control:** Other Methylphenidate alone; in week one, initial dose 10mg/d (5mg for morning and midday equally); week 2 dose 20 mg/d (10 mg for morning and midday equally), 20 mg/d (for <30 kg and 30 mg/d for > 30 kg, 10 mg for morning, midday, and evening, for 8 weeks **Comparator:** NA **Follow-up:** 2 months	ADHD-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale-IV) scores, total, parent report Intervention group improved more on all ADHD IV parent and teacher reported scales ($p < .001$). No significant difference between groups in side effects.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Khoshbakht, 2021[364] Nutrition and Food security research center, 2018[966] ID: IRCT20130223012571N6 RCT Single center N = 86 Iran Setting: Specialty care	**Target:** Treatment naive children with ADHD **Other:** Parents and teachers provided outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV by psychiatrist **Comorbidity:** N/A **Female:** 0 % **Age mean:** N/A **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Dietary Approaches to Stop Hypertension (DASH) diet, dietcontains higher amounts of whole grains, fruits, vegetables, low-fat dairy products, nuts, and beans, as well as low amounts of saturated fats, cholesterol, refined grains, sweets, and red meat, for 3 months (12 weeks) **Control:** Attention-matched control Control diet was similar to the usual diet of Iranian children, allowing for refined grains, full-fat dairy, and meats; it had lower amounts of fruits and vegetables, simple sugars were also allowed **Comparator:** NA **Follow-up:** 3 months	SNAP-IV, combined, parent report Intervention group improved more on both parent reported SNAP IV (p = 0.007) and teacher reported SNAP IV (p = 0.03). SDQ-P (strengths and difficulties questionnaire, parent reported) total score After adjustment for confounders, parent, teacher, and child reported SDQ hyperactivity, emotional symptoms, and total scores significantly improved in the DASH group compared with the control group (p < 0.05).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Manor, 2012[411] Manor, 2012[908]; Enzymotec, 2007[760] ID: NCT00418184 RCT Single center N = 200 Israel Setting: Specialty care	**Target:** Participants with confirmed DSM-IV-ADHD diagnosis, no girls who reached menarche, no history or current diagnosis of any serious systemic or neurological condition, no pervasive developmental disorder or nonverbal learning disability, no psychotic disorder, no current psychiatric comorbidity that required psychiatric pharmacotherapy, no history of alcohol or substance abuse. **Other:** Parents, teachers reported outcomes **ADHD presentation:** inattentive : 32,hyperactive : 2,combined : 66 **Diagnosis:** Confirmation by specialist DSM-IV ADHD diagnosis confirmed **Comorbidity:** N/A **Female:** 29.3 % **Age mean:** 9.2 (1.9) **Minimum age:** 6 **Maximum age:** 13 **Ethnicity:** N/A	**Intervention:** Omega 3, 4 capsules (2 capsules twice a day) of Phosphatidylserine-Omega3daily; daily dosage provided 300 mg of Phosphatidylserine, 120 mg of Eicosapentaenoic acid + Docosahexaenoic acid (Eicosapentaenoic acid/Docosahexaenoic acid ratio of 2:1); for duration of 15 weeks **Control:** Placebo Placebo, 4 capsules (2 capsules twice a day) of cellulose as placebo, for 15 weeks **Comparator:** NA **Follow-up:** 4 months	CTRS/L (Conners' Teacher Rating Scale Revised Long-Hebrew Version) No significant difference between the intervention and control group (p=0.898). Strengths and Difficulties Questionnaire (SDQ) No significant difference between the intervention and control group. BMI change following 15 weeks of treatment P=0.301 Participants with adverse events No significant differences were detected between the placebo and the intervention group in the incidence or number of adverse events recorded (p = 0.848 and p = 0.982, respectively).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Nutrition, supplements	Mohammadi, 2012[440] ID: N/A RCT Single center N = 50 Iran Setting: N/A	**Target:** Children diagnosed with ADHD (combined form) by a child and adolescent psychologist, no use any confounding drugs or supplements; no history of major prenatal complications such as prematurity, low birth weight, any past or present psychosis, comorbid Tourette syndrome, celiac, phenylketonuria, autism, other persistent developmental disorders, or narcotics use **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 28 % **Age mean:** Intervention 9.57(1.65), control 8.83(1.82) **Minimum age:** 7 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Melatonin (3 or 6mg) plus methylphenidate (ritalin) (1mg/kg) for 8 weeks **Control:** Placebo Placebo plus methylphenidate (ritalin) (1mg/kg) for 8 weeks **Comparator:** NA **Follow-up:** 2 months	ADHD-RS (ADHD Rating Scale) The mean attention deficiency scores of two groups based on ADHD rating scale at 8 weeks after the treatment showed no statistically significant difference (p=0.974; mean for melatonin was 11.11 and mean for placebo was 11.29). SDSC (Sleep Disturbance Scale for Children): The mean sleep latency and total sleep disturbance scores were reduced in melatonin group, while the scores increased in the placebo group (p≥0.05). Loss of appetite The rates were 70% in the melatonin and 61% in the placebo group. Mean scores of side effects based on the stimulant drug side effects questionnaire were 11.35 (SD 8.81) in melatonin group and 10.16 (SD 9.05) in placebo group (p=0.686).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Mohammadzadeh, 2019[441] Kurdistan University of Medical Sciences, 2017[891] ID: IRCT2016060128182N2 RCT Single center N = 66 Iran Setting: Specialty care	**Target:** Children with ADHD, no omega-3 use in at least the last6 months, without any physical illness or psychological disorder **Other:** Parents provided some outcomes **ADHD presentation:** N/A : "Patients were from all ADHD subtypes and new ones." **Diagnosis:** Confirmation by specialist DSM-IV-TR, diagnosis made by a child & adolescent psychiatrist **Comorbidity:** N/A **Female:** 25.8 % **Age mean:** Methylphenidate + placebo: 8.20 (1.72), Methylphenidate + omega-3: 7.7 (1.65) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Omega-3 plus methylphenidate, eicosapentaenoic acid capsules (180 mg) and docosahexaenoic acid (120mg) plus optimal dose of methylphenidate up to 30 mg, supplement and medication taken twice a day for 8 weeks **Control:** Other Placebo plus methylphenidate for 8 weeks **Comparator:** NA **Follow-up:** 2 months	ADHD-RS-IV (ADHD Rating Scale-IV parents), total score There was no statistically significant difference between groups (p=0.75). There were also no significant intergroup differences between the Inattention (p=0.48) and hyperactivity/impulsivity (p=0.80) subscale scores on the Parents ADHD Rating Scale. Anorexia No difference between groups (p>0.05). There was no statistically significant difference in incidences of nausea, vomiting, diarrhea, stomach ache, dry mouth, drowsiness, insomnia, anxiety, restlessness, irritability, or seizure between the groups.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Mostajeran, 2020[443] Mostajeran, 2018[1186] ID: IRCT20180303038930N1 RCT Single center N = 64 Iran Setting: Specialty care	**Target:** Children with ADHD on medication; no significant physical impairment, history of a pervasive developmental disorder, schizophrenia, bipolar disorder, severe depressive episode, epilepsy or heart disease **Other:** Parents provided some outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Pediatrician by DSM-V **Comorbidity:** N/A **Female:** 12.5 % **Age mean:** 9.38 (2.18) **Minimum age:** 6 **Maximum age:** 13 **Ethnicity:** N/A	**Intervention:** Ma'aljobon (whey protein) powder plus medication, 25 g in 100 cc water, once daily after breakfast, participants continued their previous standard conventional ADHD medications, for 2 months **Control:** TAU Medication alone, standard conventional ADHD medications continued **Comparator:** NA **Follow-up:** 2 months	Hyperactivity scale Strengths and Difficulties Questionnaire (SDQ), parent-report Intervention group improved more on hyperactivity scale (p = 0.04). No significant difference in improvement on emotional symptoms (p= .88), conduct problems (p = .55), peer problems (p = .66), or prosocial behavior (p = .62). Regarding teacher report SD

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Motaharifard, 2019[444] Vice Chancellor for research of Tehran university of Medical Sciences, 2015[1142] ID: IRCT2015050922165N1 RCT Single center N = 59 Iran Setting: Primary Care	**Target:** Children diagnosed with mild or moderate ADHD according to DSM-5, no significant chronic medical condition, no development disorders, no other psychiatric disorders, no intellectual disabilities (IQ<70), not clinically current drug abusers or dependent on drugs within the last 6 months **Other:** Parents and teachers of children with ADHD **ADHD presentation:** combined : 100 **Diagnosis:** Confirmation by specialist Child and adolescent psychiatrist confirmed diagnosis of ADHD according to DSM-5 **Comorbidity:** N/A **Female:** 34 % **Age mean:** 7.1 (1.36) **Minimum age:** 6 **Maximum age:** 14 **Ethnicity:**	**Intervention:** Sweet almond syrup 5 cc/day three times a day for 8 weeks **Control:** NA **Comparator:** MedicationMethylphenidate 1 mg/kg/day, dose 5 mg twice daily in the first week, followed by a 10-mg tablet twice daily, participants weighing beyond 30 kg received a 10-mg tablet thrice daily from the third week of the study, tablets mixed into 5 cc/day of therapeu **Follow-up:** 2 months	ADHD-RS-IV (ADHD Rating Scale-IV), parent- Hyperactivity Subscale There was no significant difference between groups (p=0.78). Decreased appetite Intervention group had significantly more participants with decreased appetite (p<0.001). Reported side effects of sweet almond syrup: insomnia 8%; increased sleep 16%; difficulty falling asleep 12%; abdominal pain 8%; impulsiveness 4%) irritability 4%; nausea 4%. Side effects of MPH: insomnia 24%; increased sleep 4%; difficulty falling asleep

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Pelsser, 2011[472] Wageningen University (The Netherlands), 2008[1147] ID: ISRCTN76063113 Crossover trial Unclear/Not reported N = 100 Netherlands Setting: Mixed	**Target:** Children with ADHD; not receiving drugs or behavioural therapy for ADHD, children already following a diet, or family circumstances that were likely to prevent completion of the study **Other:** Parents & teachers supplied some outcomes. **ADHD presentation:** inattentive : 6,hyperactive : 9,combined : 85 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 14 % **Age mean:** 6.9 (1.3) **Minimum age:** 4 **Maximum age:** 8 **Ethnicity:**	**Intervention:** Elimination diet, individually designed, consisting of the few- foodsdiet (ie, rice, meat, vegetables, pears, and water) complemented with specific foods such as potatoes, fruits, and wheat for 5 weeks **Control:** Attention-matched control Healthy food advice according to the guidelines of the Dutch NutritionCentre. Parents continued to keep an extended diary until the end of the trial **Comparator:** NA **Follow-up:** 3 months	ADHD-RS (ADHD rating scale), total score, teacher report Intervention group improved more than control group on both teacher ($p < .001$) and parent ($p < .001$) scales.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Nutrition, supplements	Pongpitakdamrong, 2021[478] ID: ID NA RCT Single center N = 52 Thailand Setting: Specialty care	**Target:** Children and adolescents with ADHD and iron deficiency treated with a steady dosage of methylphenidate for at least 1 month **Other:** Parents & teachers supplied outcomes **ADHD presentation:** inattentive : 21.2,hyperactive : 1.9,combined : 76.9 **Diagnosis:** Confirmation by specialist DSM-V **Comorbidity:** Other : Iron deficiency **Female:** 13.5 % **Age mean:** 9.6 (2.0) **Minimum age:** 6 **Maximum age:** 18 **Ethnicity:** % Asian : 100	**Intervention:** Iron in the form of ferrous fumarate, 200mg capsules of ferrous fumarate, participantswho weighed less than or equal to 30kg received 1 capsule of ferrous fumarate per day, participants who weighed > 30kg received 2 capsules per day (2–4 mg of elemental iron/kg/d), methylphenidate continued as already prescribed; duration of 12 weeks **Control:** Placebo Placebo that tasted and looked similar to the ferrous fumarate capsules, participants who weighed less than or equal to 30kg received 1 capsule of placebo per day for 12 weeks, whereas participants who weighed >30kg received 2 capsules per day for 12 wee **Comparator:** NA **Follow-up:** 3 months	Vanderbilt ADHD total score Intervention group improved more (p 0.037). No significant difference between groups regarding change in teacher ADHD RS total score. Participants with any adverse event No reported adverse events in either group.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Rafeiy-Torghabeh, 2021[488] Roozbeh Psychiatric Hospital, 2018[1015] ID: IRCT20090117001556N115 RCT Single center N = 66 Iran Setting: Specialty care	**Target:** Children 6 to 12 with ADHD per DSM 5; excluded if any psychiatric comorbidity except oppositional defiant disorder **Other:** Guardians (usually parents) and teachers **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM 5 **Comorbidity:** N/A **Female:** 28.3 % **Age mean:** 8.7 (1.7) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Antioxidant resveratrol 250mg two times a day in addition to methylphenidate 20mg/day, participants weighing more than 30kg received methylphenidate 30mg/day for 8weeks **Control:** Placebo Placebo plus methylphenidate 20mg/day for 8 weeks, participants weighing more than 30kg received methylphenidate 30mg/day **Comparator:** NA **Follow-up:** 2 months	ADHD-RS-IV parent version Significant of intervention on parent ADHD-RS (total p 0.015; inattention p 0.032; hyperactivity/impulsivity p 0.036). No significant differences on teacher version of ADHD-RS (total p 0.401; inattention p 0.507; hyperactivity/impulsivity p 0.466). Reduced appetite No group difference in decreased appetite (p = 0.76). The frequencies of adverse events in the groups were similar.

Nutrition, supplements	Rucklidge, 2018[505] ID: ACTRN12613000896774 RCT Single center N = 93 New Zealand Setting: Specialty care	**Target:** Medication-free children with ADHD **Other:** Parents and teachers provided some outcome data **ADHD presentation:** inattentive : 28.0,hyperactive : 5.4,combined : 66.6 **Diagnosis:** Confirmation by specialist DSM IV plus Kiddie Schedule for Affective Disorders and Schizophrenia Lifetime Version (KSADS-PL) plus parent and teacher Conners Rating Scales (CRS-R:L; T score > 65 on parent form and >60 on teacher form) **Comorbidity:** N/A **Female:** 23.7 % **Age mean:** 9.75 (1.5) **Minimum age:** 7 **Maximum age:** 12 **Ethnicity:** % Native Hawaiian or Pacific Islander : 21.5%,Other info : Maori or Tongan % White : 78.5%	**Intervention:** Vitamin capsules, multivitamin containing a comprehensive range of micronutrients (13 vitamins, 17 minerals, and four amino acids), 15 capsules a day for 10 weeks **Control:** Placebo Placebo **Comparator:** NA **Follow-up:** 2.5 months	SDQ - Conduct problems, teacher No statistically significant difference between groups (p=0.055). CGI-I (Clinical Global Impressions-Improvement) CGI-I improved or very much improved Intervention group had greater improvement in mean score (p=0.029) and had a higher percentage showing improvement (p<0.05). ADHD-RS-IV, clinician report No between-group differences (p=0.415). Intervention group improved more on Teacher BRIEF–Behavioural Regulation Index (p 0.05) and BRIEF emotional control scale (p 0.01). No difference in Child Mania Rating Scale -Parent report (p 0.10). No difference in Strengths and Difficulties Questionnaire (SDQ) total problem score as reported by parents (p 0.062) or teachers (p 0.064). Intervention group scored better on SDQ conduct problems scale in the parent (p 0.015) but not teacher report (p 0.055). Weight (kg) change from baseline The change in weight was not statistically significant (p=0.6.08). Across a large number of assessed outcomes, micronutrients had minimal side effects.
Nutrition, supplements	Salehi, 2010[509] Roozbeh Psychiatric Hospital, 2009[1014] ID: IRCT138711151556N6 RCT	**Target:** Children with ADHD; no comorbid psychiatric diagnosis that would contraindicate guanfacine extended-release treatment or confound efficacy or safety assessments	**Intervention:** Ginkgo biloba dose of 80–120 mg/day depending on weight, 40 mg twice per day for < 30 kg and 120 mg three times per day for > 30kg, treatment for 6 weeks	ADHD-RS-IV Total Score changes, parent MPH group improved more on parent (p=0.047) and teacher (p =0.05) ADHD-RS-IV total score.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
	Single center N = 50 Iran Setting: Specialty care	**Other:** Parents & teachers provided outcomes **ADHD presentation:** combined : 100 **Diagnosis:** Confirmation by specialist Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime diagnostic interview **Comorbidity:** N/A **Female:** 22 % **Age mean:** Ginko 9.12 (1.61), methylphenidate 9.61 (2.26) **Minimum age:** 6 **Maximum age:** 14 **Ethnicity:** Other : Persian	**Control:** NA **Comparator:** MedicationMethylphenidate 20–30 mg/day depending on weight (20 mg/day for < 30kg and 30 mg/day for > 30 kg) for 6 weeks; titrated in week 1: 10 mg/day (5 mg in the morning and 5 mg at midday), week 2: 20 mg/day (10 mg in the morning and 10 mg at midday) and week 3: **Follow-up:** 1.5 months	Decreased appetite, number of patients Decreased appetite more common in MPH group (p = 0.0002). Side effects were mild to moderate and tolerable, the difference in the frequency of side effects was no significant except for decreased appetite, headache, and insomnia that were more frequent in the methylphenidate group.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Salehi, 2016[510] ID: IRCT20110416201N1 RCT Single center N = 150 Iran Setting: Specialty care	**Target:** Children with ADHD with no history of psychiatric drug usage and no history of other psychiatric disorders, no limitation or sensitivity for the use of zinc sulfate and omega-3, and absence of mental retardation **Other:** Parents & teachers supplied outcomes **ADHD presentation:** inattentive : 28.7,hyperactive : 29.3,combined : 42 **Diagnosis:** Confirmation by specialist Psychiatrist DSM-IV-TR **Comorbidity:** N/A **Female:** 26 % **Age mean:** 9.07 (2.13) **Minimum age:** 6 **Maximum age:** 15 **Ethnicity:** Other : Persian	**Intervention:** Omega 3 plus methylphenidate, eicosapentaenoic fatty acid (100 mg for children <25 kg, 200 mg for 26–35kg, and 400 mg for children >35 kg/day) with daily methylphenidate, prescribed based on child's weight (10 mg daily for children under 20 kg; 10 mg, twice a day for children over 20 kg) for 8 weeks **Control:** Other Placebo plus methylphenidate, whitish color capsule containing sugar, as the sameshape and volume of omega-3 capsules **Comparator:** Nutrition, supplementsZinc sulfate capsule (containing 22 mg zinc sulfate) administered with daily MPH **Follow-up:** 2 months	Conners' Parent and Teacher Rating Scales average No difference among groups (p=0.581).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Tan, 2016[579] ID: NCT01855984 RCT Multicenter N = 146 Malaysia Setting: Specialty care	**Target:** Children with ADHD; those with syndromes, inborn errors of metabolism, structural brain lesions, co-existing chronic liver disease and those on concurrent anticoagulants or antiplatelet drugs were excluded as were children who were unable to swallow the capsule **Other:** Parents and teachers provided outcomes **ADHD presentation:** inattentive : 10.3,hyperactive : 0,combined : 89.7 **Diagnosis:** Confirmation by specialist DSM-IV by physicians **Comorbidity:** N/A **Female:** 15 % **Age mean:** 9.4 (1.8) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Asian : 100,Other : Malaysian	**Intervention:** Antioxidant tocotrienol-rich fractions (from the natural Vitamin E family), 2 softgel capsules containing 100 mg per day, for 6 months **Control:** Placebo Two placebo capsules per day for 6 months **Comparator:** NA **Follow-up:** 6 months	Vanderbilt ADHD Parent Rating Scale, Total No significant group differences in parent or teacher ratings. There were 14 adverse events in the intervention and 24 in the placebo group, all were mild.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Trebaticka, 2006[586] Chovanova, 2006[716] ID: NA RCT Single center N = 61 Slovakia Setting: Specialty care	**Target:** Children with ADHD with at least 6 months of symptoms, general disposition as restless, inattentive, distractible and disorganized; acute inflammatory diseases, renal and cardiovascular disorders, diabetics, and co-morbid psychiatric conditions were excluded **Other:** Parents and teachers provided some outcomes **ADHD presentation:** N/A **Diagnosis:** No ADHD according to ICD-10 with following diagnoses: Hyperkinetic Disorder, Hyperkinetic Conduct Disorder, Attention Deficit without Hyperactivity **Comorbidity:** N/A **Female:** 18 % **Age mean:** mean 9.5 **Minimum age:** 6 **Maximum age:** 14 **Ethnicity:** N/A : Slovakian	**Intervention:** Pycnogenol (extract from the bark of the French maritime pine, consisting of phenolic acids, catechin, taxifolin and procyanidins), 1 mg/kg/day for 4 weeks **Control:** Placebo Placebo **Comparator:** NA **Follow-up:** 1 month	CAP (Child Attention Problems), teacher Intervention group scores improved significantly compared to placebo on hyperactivity (p=0.044) and inattention (p= 0.0067) scores. CPRS (Conner's Parent Rating Scale) No significant difference in reduction between intervention and placebo.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Tzang, 2016[590] Mackay Memorial Hospital, 2012[905] ID: NCT01725737 RCT Single center N = 116 Taiwan Setting: Primary Care	**Target:** Children with a clinical diagnosis of ADHD as defined by DSM-IV; children were deemed healthy by means of medical history, physical examination, vital-sign measurements, and laboratory assessments; children had to be naïve to all treatments for ADHD **Other:** **ADHD presentation:** inattentive : 34.5,hyperactive_other : Treatment: 14.0%; Placebo 15.1%,combined : 65.5,N/A : ODD comorbidity in treatment group: 72.4% and placebo: 74.1% **Diagnosis:** Confirmation by specialist The diagnoses of ADHD and other mental disorders were confirmed by a child-and adolescent psychiatrist by using a structured parent interview according to the National Institute of Mental Health Diagnostic Interview Schedule for Children (version 4.0). **Comorbidity:** N/A **Female:** 44.8 % **Age mean:** Treatment group: 9.3 (2.7) Placebo Group: 9.0 (2.2) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Sarcosine (dietary supplement, glycine transporter-1 inhibitor), 0.3 g of 1 capsule daily if body weight 10±5 kg, twice a day for 20±5 kg, thrice a day for 30±5 kg, or 2 capsules twice a day for 40±5 kg, no other psychotherapy was provided, including family or group therapy, for 6 weeks **Control:** Placebo Identically appearing capsules of placebo **Comparator:** NA **Follow-up:** 6 months	SNAP ODD: Swanson, Nolan, Pelham oppositional defiance disorder scores The sarcosine group had lower mean values on all three subscales compared to placebo. Decreased appetite The difference between groups was not significant (p=0.677). Rates of adverse events

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Van der Heijden, 2007[596] ID: ISRCTNR47283236 RCT Multicenter N = 107 Netherlands Setting: Specialty care	**Target:** Children with diagnosed ADHD and chronic sleep-onset insomnia **Other:** **ADHD presentation:** inattentive : 21.0,hyperactive : 3.8,combined : 73.3 **Diagnosis:** Confirmation by specialist Psychologist and psychiatrist **Comorbidity:** Sleep : chronic sleep-onset insomnia **Female:** 25.7 % **Age mean:** 9.1 (2.3) treatment, 9.3 (1.8) placebo **Minimum age:** **Maximum age:** **Ethnicity:** N/A	**Intervention:** Melatonin, fast-release, 3mg if body weight <40mg, 6mg if body weight > 40kg for 4 weeks **Control:** Placebo Identical-appearing placebo tablets **Comparator:** NA **Follow-up:** 1 month	CBCL (Child Behavior Checklist) The melatonin group had significantly smaller improvements compared to the placebo group. TACQOL-P (TNO-AZL Questionnaire for Children's Health-Related Quality of Life, Parent form) showed no statistically significant changes in scores between groups. Adverse events There were no statistically significant differences between the intervention and placebo group (p=1.00)

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Voigt, 2001[601] ID: ID NA RCT Single center N = 63 US Setting: Specialty care	**Target:** Children with ADHD treated with stimulant medication; no treatment with other psychotropic medications, diagnosis of other childhood psychiatric disorders, use of dietary supplements other than vitamins, occurrence of a significant life event within 6 months, a history of head injury or seizures, receipt of special education services for mental retardation or a pervasive developmental disorder, premature birth, exposure to tobacco, alcohol, or other drugs in utero, chronic medical condition **Other:** None **ADHD presentation:** inattentive : 9.4,combined : 90.6 **Diagnosis:** Confirmation by specialist DSM-IV per diagnostic interview with a neurodevelopmental pediatrician **Comorbidity:** N/A **Female:** 22 % **Age mean:** 9.3 (1.9) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % White : 92.5	**Intervention:** Omega 3 plus stimulant medication, docosahexaenoic acid (DHA), algae-derived triglyceride capsule, 345mg DHA per day for 4 months **Control:** Placebo Placebo plus stimulant medication, 1 capsule once a day for 4 months **Comparator:** NA **Follow-up:** 4 months	Test of Variables of Attention (TOVA), a computer administered measure of sustained attention: No significant difference in improvement in any of the four TOVA scores (errors of omission, errors of commission, total response time, response time variability). No participant withdrew because of adverse effects of treatment.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Nutrition, supplements	Weber, 2008[606] National Center for Complementary and Integrative Health (NCCIH), 2004[950] ID: NCT00100295 RCT Single center N = 54 US Setting: Other	**Target:** Children and adolescents with ADHD that scored more than 1.5 standard deviations above age and sex norms on the ADHD Rating Scale-IV; no psychiatric co-morbidities **Other:** Parents **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM IV criteria based on the Kiddie Schedule for Affective Disorders and Schizophrenia–Epidemiologic Version (K-SADS) **Comorbidity:** N/A **Female:** 37 % **Age mean:** 9.8 (2.0) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 14.8 % Black/African American : 0 % American Indian or Alaska Native : 1.9 % Asian : 0 % White : 85.2 % Multiracial : 13.0	**Intervention:** St. John's wort, 300 mg of H perforatum standardized to 0.3% hypericin 3 timesdaily for 8 weeks **Control:** Placebo Placebo 3 times daily **Comparator:** NA **Follow-up:** 2 months	CGI-I (Clinical Global Impression - Improvement Scale) much or very much improved There was no significant difference between groups (p=0.59). ADHD RS-IV (ADHD Rating Scale–IV), parent report No significant difference between the 2 groups in the change in scores from baseline to follow up (p = 0.68). No significant difference was seen in change in height between the groups during the 8-week trial. Participants with any adverse event The rate was 41% for intervention and 44% for comparator, which was no significantly different between groups.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Parent education	Abikoff, 2015[110] NYU Langone Health, 2011[968] ID: NCT01320098 RCT Single center N = 164 US Setting: Specialty care	**Target:** Preschool, daycare or nursery school students diagnosed with ADHD, not currently taking medication for ADHD **Other:** Parents were trained **ADHD presentation:** inattentive : 33.5,hyperactive : 15.2,combined : 50.6 **Diagnosis:** Confirmation by specialist DSM IV diagnosis confirmed by confirmed by clinical evaluation conducted by a psychologist with child and parent **Comorbidity:** N/A **Female:** 26.2 % **Age mean:** N/A **Minimum age:** 3 **Maximum age:** 4 **Ethnicity:** % Hispanic or Latino : 25.6 % Black/African American : 16.4 % Asian : 8.8 % White : 69.2	**Intervention:** New Forest Parenting Package, weekly 1-to-1.5-hour sessions, home-based intervention which fosters constructive parenting to target ADHD-related dysfunctions in attention and impulse control for 8 weeks **Control:** Wait list Wait list **Comparator:** Parent trainingHelping the Noncompliant Child, clinic-based parenting intervention for treating noncompliant behavior **Follow-up:** 24 months	New York Parent Rating Scale - Physical Aggression Subscale, parent, post-tx Comparator group participants, but not intervention group, were rated better than control (p < 0.003) at 6 months. There was no significant difference between intervention and comparator at 2 years. CPRS (Conners Parent Rating Scale) total Intervention and comparator groups significantly improved score compared to control (p <. 001); there was no significant difference between intervention and control . Parent treatment satisfaction Treatment satisfaction was equally high for intervention and comparator. P value not reported. There were no adverse effects with either NFPP or HNC.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Parent education	Chacko, 2009[176] ID: NA RCT Single center N = 120 US Setting: Other	**Target:** Children living with single mothers **Other:** Single mothers of children with ADHD **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist diagnosis was determined through completion of parent and teacher rating scales of DSM IV, completion of semistructured interviews with the parent, and assessment of cross-situational impairment through completion of parent and teacher rating scales (Imp **Comorbidity:** N/A **Female:** 29.3 % **Age mean:** 7.85 (2.14) **Minimum age:** 5 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 12.7 % Black/African American : 21.0 % White : 53.3 % Multiracial : 13.0	**Intervention:** Strategies to Enhance Positive Parenting (STEPP), a manualized, program heldfor 2.5 hours each week, for 9 weeks **Control:** Wait list Wait list **Comparator:** Parent trainingTraditional manualized behavioral parent training program; meets for one 2.5 hour session per week for 9 weeks; sessions included videotapes of parenting errors whereby single mothers identified these errors and then formulated alternative parenting strat **Follow-up:** 3 months	Inattentive score, Disruptive Behavior Disorders rating scale Benefits of the combined parent training groups compared to the waitlist control group were observed on on DBD ODD symptoms ($p < .009$) at treatment end but not follow-up. No significant differences in Disruptive Behavior Disorders Inattentive and Hype Impairment Rating Scale (IRS) The intervention group was significantly more improved than the control group, while the comparator group was not significantly different from the control group.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Parent education	Churchill, 2018[200] ID: ID NA RCT Unclear/Not reported N = 174 US Setting: Other	**Target:** Children and adolescents with ADHD; child must live with mother or primary female caregiver; English or Spanish speaking; lack of comorbid intellectual disability, autism, or psychosis **Other:** Mother or primary female caregiver of child with ADHD **ADHD presentation:** inattentive : 16.7,hyperactive : 23.55,combined : 33.35,combined_other : % unknown 26.4 **Diagnosis:** Confirmation by specialist Diagnosed by County Health Department, unclear method **Comorbidity:** N/A **Female:** 33.9 % **Age mean:** Intervention group mean age (10.6) and SD (3.2). Control group mean age (10.8) and SD (3.4). **Minimum age:** 4 **Maximum age:** 18 **Ethnicity:** % Hispanic or Latino : 8.6 % Black/African American : 14.35 % American Indian or Alaska Native : 7.5 % Asian : 6.95 % White : 79.35	**Intervention:** In-home nurse visits with families with variable frequency based onparticipant family needs, participant families given a resource guide and received a newsletter every 6 months with up-to-date information about ADHD, duration of 1 year **Control:** NA **Comparator:** Parent trainingParenting book on ADHD and same newsletter every 6 months with up-to-date information about ADHD **Follow-up:** 18 months	CBCL (Child Behavior Checklist) No significant difference between groups (p=0.374). Longitudinal family function: Family Systems Scale No difference between groups (p = 0.154).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Parent education	Dose, 2017[228] University of Cologne, Shire, 2012[1131] ID: NCT01660425 RCT Single center N = 103 Germany Setting: Other	**Target:** Children with ADHD taking methylphenidate for at least 2 months and had to show functional impairment in at least 1 of the domains of the Weiss Functional Impairment Rating Scale – Parent Report **Other:** Parents were the intervention target and provided some outcome data **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Diagnosis by psychologist or psychiatrist required. **Comorbidity:** N/A **Female:** 18.5 % **Age mean:** 9.78 (1.60) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Telephone-assisted self-help program for parents, reading 8 self-helpbooklets, then parents receive 10 telephone consultations of about 30 min each during the first 6 months and four booster telephone consultations during the second 6-month period; children received also methylphenidate but no specific dose was required, duration of 1 year **Control:** TAU Usual care plus children received methylphenidate, but no specific dosage was required **Comparator:** NA **Follow-up:** 12 months	FBB-ADHS (German symptom checklist for ADHD), total score No difference in German ADHD scale, total score, at follow-up (p = 0.12). Intervention group performed better on German symptom checklist for Oppositional Deviant Disorder at follow-up (p = .03). Weiss Functional Impairment Rating Scale – Parent Report There was no significant difference between groups (p = 0.30).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Parent education	Ercan, 2014[257] ID: NA Clinical trial Single center N = 120 Turkey Setting: Specialty care	**Target:** Children diagnosed with ADHD and oppositional defiant disorder or conduct disorder by psychiatrists, no other comorbid disorders **Other:** Parents, teachers **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM IV per KSADS-PL **Comorbidity:** ODD **Female:** 31.7 % **Age mean:** 9.07 (1.92) **Minimum age:** 6 **Maximum age:** 13 **Ethnicity:** N/A	**Intervention:** Parent-training program plus methylphenidate, optimal methylphenidate dose takendaily, parent-training program consisted of 4 consecutive weekly meetings that started at the beginning of the 2nd month and 10 monthly meetings that took place during the remaining 10 months of the treatment with each parent-training group consisted of 10 to 15 members, total duration of 12 months **Control:** Other Methylphenidate only, initial dose was 7.5 mg/day for children between 7 and 10 years of age and 10 mg/day for children between 11 and 13, dose was adjusted in response to continuous feedback from the parents, mean (SD) dose throughout the 12-month study **Comparator:** NA **Follow-up:** 12 months	CPRS (Conners' Parent Rating Scale) No significant effect of parent training on CPRS or Conners' Teacher Rating Scale. Hyperactivity-impulsivity scale, T-DSM-IV-S, parent rating No significant effect of group on T-DSM-IV-S Hyperactivity / Impulsivity - Parent (p = .60), T-DSM-IV-S Attention - Parent (p = .89), T-DSM-IV-S OD - Parent (p = .39), or T-DSM-IV-S CD - Parent (p = .39). No significant effect of group on T-DSM-IV-S

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Parent education	Ferrin, 2014[265] ID: N/A RCT Single center N = 81 Spain Setting: Other	**Target:** Female and male participants with diagnosis of ADHD any subtype according to the DSM-IV; the diagnosis was confirmed by clinical interview with a child psychiatrist, supplemented with structured interview using the validated Spanish version of the semi-structured clinical interview of the Schedule for Affective Disorders and Schizophrenia for school age children, clinical ADHD symptoms stabilization for at least 1 month before entering the study **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist KSADS-PL **Comorbidity:** N/A **Female:** 20 % **Age mean:** Intervention 11.25(2.96), control 9.94(3.04) **Minimum age:** 5 **Maximum age:** 18 **Ethnicity:** N/A	**Intervention:** Psychoeducation program composed of 5 successive groups of 8–10 families who received 90 min weekly sessions for 12 weeks **Control:** NA **Comparator:** Parent trainingParent counselling and support intervention, 5 successive groups of 8–10 families who received 12-week 90 min weekly sessions, families were reunited and encouraged to comment on their thoughts and share their experiences in a nondirective, nonthreatening **Follow-up:** 12 months	ADHD Index, CPRS-R (Conners' Parent Rating Scale Revised 27-items), parent There was no significant difference between groups. Strengths and Difficulties Questionnaire (SDQ), parent There was no statistically significant interaction effect of time by group.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Parent education	Ferrin, 2020[266] ID: ISRCTN 26270684 RCT Single center N = 69 UK Setting: Specialty care	**Target:** Children and adolescents with ADHD on stabilizing medication for 1 month prior to baseline assessment, without severe learning disabilities (IQ <70), autistic spectrum disorder as primary diagnosis, any clinically significant or unstable medical or psychiatric condition, and children whose families had received any similar school-based individual and/or group treatments at any point in time **Other:** Parents **ADHD presentation:** combined : 69.6 **Diagnosis:** Confirmation by specialist DSM-IV confirmed by clinical interview with a child psychiatrist **Comorbidity:** N/A **Female:** 13 % **Age mean:** Intervention 10.86 (3.04), control 10.56 (3.20) **Minimum age:** 5 **Maximum age:** 18 **Ethnicity:** % Black/African American : 10.14% % White : 50.7% % Multiracial : 24.6	**Intervention:** Psychoeducation with 5 successive groups of 7-10 families who received six sessionsof 2 hr at weekly intervals; a handout was delivered and parents were assigned some short additional homework to prepare for the next session, total duration of 6 weeks **Control:** TAU Treatment as usual group, families continued routine medical care as usual with their clinicians; they were offered the opportunity to join the psychoeducation group once their collaboration with the study had ended; control participants received monthly **Comparator:** NA **Follow-up:** 6 months	CGI-I (Clinical Global Impression - Improvement) change, clinician rating Intervention improved significantly more than control (p=.038) ADHD Index, Conners' Parent Rating Scale: Short Form (CPRS-R:S) Intervention group improved more than control on overall Index (p = .034) and cognitive/inattention (p = .037) and the hyperactive/impulsive (p = .025) subdomains. Difference on Conners Teacher Rating Scale, total, not statistically significant (p = .210 Strengths and Difficulties Questionnaire, teacher rating No statistically significant differences (p=0.67) in teacher rating, parent rating, or child rating. There were no statistically significant differences in parental stress across groups (p=0.521).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Parent education	Herbert, 2013[325] ID: ID NA RCT Single center N = 31 US Setting: Specialty care	**Target:** Preschool age children with developmentally deviant levels of hyperactivity /impulsivity; children with mental retardation, autism, Asperger's, or cerebral palsy were excluded **Other:** Parents **ADHD presentation:** hyperactive : 100 **Diagnosis:** Confirmation by specialist DISC-IV **Comorbidity:** N/A **Female:** 25.8 % **Age mean:** 4.42 (0.90) **Minimum age:** 2 **Maximum age:** 6 **Ethnicity:** % Hispanic or Latino : 3.2 % Black/African American : 6.5 % White : 83.9 % Multiracial : 6.5	**Intervention:** Parenting Your Hyperactive Preschooler pro-gram delivered via one 90-minute sessionper week; first 8 sessions focus on traditional parenting strategies shown to be effective in managing child behavior and tailoring these strate-gies for use with hyperactive preschoolers; the last 6 sessions focus on emotion socialization strategies designed to improve children's emotion regulation; for duration of 14 weeks **Control:** Wait list Wait list **Comparator:** NA **Follow-up:** 3 months	DBRS (Disruptive Behavior Rating Scale), hyperactivity-impulsivity Intervention group improved more on DBRS hyperactivity/ impulsivity (p 0.008), inattention (p 0.002), and oppositional defiance disorder (p 0 .046) scales. Behavior Assessment System for Children 2 (BASC 2), Parent Report , externalizing behavior scale Intervention group improved more on BASC-2 externalizing scale (p 0.035) but not on internalizing scale (p 0.203).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Parent education	Hosainzadeh Maleki, 2014[333] ID: ID NA RCT Single center N = 36 Iran Setting: Specialty care	**Target:** Children with ADHD taking ritalin **Other:** One group received parent training; all had parents report some outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-TR by child psychiatrist **Comorbidity:** N/A **Female:** % primarily boys **Age mean:** mean N/A **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** Other : 100% Persian	**Intervention:** Barkley's parent training plus children's working memory training plus ritalin, 10 training sessions for mothers, a coupon-based economy at home for behavior modification, child computer working memory training and learning strategies and feedback from a therapist, 1 session for mothers and 1 for the children per week for 8 weeks **Control:** Other Working memory training plus ritalin alone, computerized, for child, for 8 weeks **Comparator:** NA **Follow-up:** 2 months	SNAP IV total score Intervention group (combined treatment) improved most (p<0.001).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Parent education	Lange, 2018[384] University of Aarhus, 2012[1127] ID: NCT01684644 RCT Multicenter N = 164 Denmark Setting: Specialty care	**Target:** Children with clinical ADHD diagnosis supported by the Development and Well-Being Assessment; Danish as a first language spoken at home; IQ>=70; no autism spectrum disorder diagnosis; not in receipt of pharmacologic or psychosocial treatment for ADHD; no severe parental psychiatric disorder; no severe social adversity in the home **Other:** Parents and teachers of children with ADHD **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist ADHD diagnosis was made by specialist child and adolescent psychiatrists based on results from all clinical assessments and Development and Well-Being Assessment profiles, which were conducted by trained raters. Development and Well-Being Assessment desig **Comorbidity:** N/A **Female:** 27 % **Age mean:** 57% of children were aged 3-5; 43% of children were aged 6-7 **Minimum age:** 3 **Maximum age:** 7 **Ethnicity:** N/A	**Intervention:** New Forest Parenting Programme consisted of personalized weekly homework assignments and 8 2-hour sessions (6 sessions in the clinic and 2 in the home), includes 5 elements: psychoeducation to enhance parents' understanding of child's behavior, scaffolding to help parents work from the child's level of development, enhancing parent-child interaction, relieving the child's ADHD symptoms through play and games, guiding parents in use of behavioral strategies; intervention for 12 weeks **Control:** TAU Treatment as usual typically consisted of a package of psychoeducation delivered to groups of individual parents by specialized staff; information about ADHD as a developmental disorder; how ADHD symptoms affect normal play and the development of preschoo **Comparator:** NA **Follow-up:** 9 months	Directly observed ADHD behaviors during solo play "index of attention/ engagement" using the Child Solo Play instrument No significant difference. ADHD-RS-IV (ADHD Rating Scale) symptom severity, parent ratings After treatment, the parent training program was superior to treatment as usual on parent-rated ADHD symptoms (p=0.009; effect size d=0.30). The parent training program was superior to treatment as usual on parenting self-efficacy and family strain.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Parent education	Mehri, 2020[428] Department of Research and Technology, 2013[734] ID: IRCT2013042112990N1 RCT Single center N = 56 Iran Setting: Specialty care	**Target:** Children with ADHD, only taking methylphenidate for 6 months prior to study, with a fixed dose of drug in the last 30 days prior to start of study; at least one sleeping issue; no physical or mental comorbidities **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist diagnosed by psychiatrist based on DSM-IV criteria **Comorbidity:** Sleep **Female:** 14.3 % **Age mean:** 8.50 (1.79) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Behavioral parental training on sleep problems, including information, sleep hygiene and nutrition health, control of environmental stimuli, cognitive behavioral therapy strategies, conducted in 2 groups of 14 parents per week in week 1, 3, and 5 of the study; children also received methylphenidate treatment; for 5 weeks **Control:** Other Methylphenidate treatment only **Comparator:** NA **Follow-up:** 2 months	Intervention group experienced a significantly greater improvement in total sleep scores compared to the control group (p = 0.03). Also the intervention group had a significantly greater decline in total sleep problem compared to the control group (p = 0.01).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Parent education	Schorr-Sapir, 2021[520] ID: ID NA RCT Unclear/Not reported N = 101 Israel Setting: Mixed	**Target:** Children with primary DSM-5 ADHD diagnosis and scores above 55 on the Conners' Scale for ADHD; no psychotic symptoms and no concurrent psychotherapy **Other:** Parents **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-5 **Comorbidity:** N/A **Female:** 21 % **Age mean:** 8.8 (1.77) **Minimum age:** 5 **Maximum age:** 13 **Ethnicity:** Other : 100% Jewish	**Intervention:** Nonviolent resistance parent training with clinical psychologist,12 sessions (1 involving the parents and members of the school staff); 2 weekly telephone conversations with undergraduate student; special emphasis was given to psychoeducation on ADHD, parental emotion regulation and self-control, and the development of a collaborative relationship with the school; for 4 months **Control:** Wait list Waiting period is 12 weeks, given nothing during waiting period **Comparator:** NA **Follow-up:** 4 months	Child Behavior Checklist (CBCL), Externalizing symptoms Difference in externalizing symptoms not significant (p<0.08); significant difference in internalizing symptoms (p<0.001). Conners' Rating Scale - ADHD index, parent Difference between groups not statistically significant (p<0.08)

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Parent education	Smit, 2021[544] Mikami, 2020[928] ID: NA RCT Multicenter N = 172 Canada Setting: Specialty care	**Target:** Children with ADHD who children scored ≥3 on parent or teacher reports on the Strengths and Difficulties Questionnaire Peer Problems subscale **Other:** Parents were trained to coach children in friendship skills **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM V diagnosis required. Children required to have ≥6 symptoms of inattention and/or hyperactivity/impulsivity endorsed by either the parent on the K-SADS (Kiddie-Schedule for Affective Disorders and Schizophrenia) or the teacher on the CSI (Child Sympt **Comorbidity:** N/A **Female:** 30 % **Age mean:** 8.54 (1.55) **Minimum age:** 6 **Maximum age:** 11 **Ethnicity:** % Hispanic or Latino : 1.2 % Black/African American : 0.6 % Asian : 5.8 % White : 72.7 % Multiracial : 18.6	**Intervention:** Parental Friendship Coaching: behavioral parent training where parents learn to be friendship coaches by teaching their children friendship skills and facilitating opportunities for children to make real-life friends; weekly, 90-min sessions for parents over 10 weeks **Control:** NA **Comparator:** Parent trainingPsychoeducation and social support (Coping with ADHD through Relationships and Education), weekly, 90-min sessions for parents over 10 weeks **Follow-up:** 8 months	Child Behavior Checklist (CBCL) - Aggressive Behavior Subscale, parent and teacher score composite There were no significant differences between treatment and comparator groups. Intervention group had greater score improvement than comparator for Child Behavior Checklist (CBCL) - Withdrawn / Depressed Subscale, parent and teacher score composite

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Parent education	Sonuga-Barke, 2001[550] ID: N/A RCT Single center N = 78 UK Setting: Community	**Target:** Children born between January 1992 and September 1993, parents had to take the Parental Account of Childhood Symptoms examination **Other:** Parents **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist They followed the American Psychiatric Association, DSM-IV standard. **Comorbidity:** N/A **Female:** 38.5 % **Age mean:** All age 3 **Minimum age:** 3 **Maximum age:** 3 **Ethnicity:** N/A	**Intervention:** Parent training group received coaching in child management techniques, 1-hour weekly sessions for 8 weeks **Control:** Wait list Waiting-list control **Comparator:** Parent trainingParent counseling and support, non-directive support and counseling for parent of children with ADHD **Follow-up:** 3.75 months	Observation of ADHD behavior during 10 minute play with multipurpose toy Significant effects seen for the intervention in direct observation measures (p<.05). Parental Account of Childhood Symptoms (PACS) to assess core symptoms of ADHD, parent Recovery (Jacobson & Truax criteria) Significant effects were seen for the intervention (p<0.001).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Parent education	Sonuga-Barke, 2004[551] Sonuga-Barke, 2002[1083] ID: NA RCT Unclear/Not reported N = 89 UK Setting: Other	**Target:** Children with ADHD **Other:** Parents receiving training and providing outcome measures **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Children met cut-offs on the Werry-Weiss-Peters Activity Scale and the Parental Account of Childhood Symptoms Structured Clinical Interview and their parents reported significant clinical impairment. **Comorbidity:** N/A **Female:** % N/A **Age mean:** 3 years old at time of enrollment **Minimum age:** 3 **Maximum age:** 3 **Ethnicity:** N/A	**Intervention:** Parent training of mothers, conducted in home with 1 hour per week for 8 weeks **Control:** Wait list Wait list **Comparator:** NA **Follow-up:** 3.75 months	BCL (Behaviour checklist) Difference in Behavior Checklist not significant between intervention and control. AD/HD score PACS (Parental Account of Childhood Symptoms) No difference in follow-up ADHD symptoms between intervention and control groups.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Parent education	Sonuga-Barke, 2018[552] ID: NA RCT Multicenter N = 307 UK Setting: Mixed	**Target:** Children positive for ADHD symptoms (score≥ 20) on the Werry-Weiss-Peters Activity Rating Scale, were given an ADHD research diagnosis of any sub-type based on the parent Diagnostic Interview Schedule for Children-IV-ADHD Scale; not taking ADHD medication **Other:** Parent and/or caregiver aged 18 years or over **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Werry-Weiss-Peters Activity Rating Scale and DISC-IV-ADHD Scale **Comorbidity:** N/A **Female:** 27 % **Age mean:** mean 42.7 (6.75) months **Minimum age:** 3 **Maximum age:** 5 **Ethnicity:** N/A	**Intervention:** New Forest Parenting Programme parent training intervention delivered at home for 1.5 hour sessions for 12 weeks **Control:** TAU Standard patterns of preschool ADHD care available in the parents' region; in two regions, there was little provision for preschool ADHD while in one region provision might include parenting education and training **Comparator:** Parent trainingIncredible Years, developmentally based interventions, delivered weekly for 12 weeks, sessions were 2-2.5 hours long **Follow-up:** 6 months	Directly Observed Attention No difference between arms. SNAP-IV (Swanson Nolan and Pelham - IV - Parent) Small, non-significant, benefits of New Forrest program over TAU were seen (p 0.053). Slightly better results for Incredible Years compared to New Forrest. No difference between active programs and treatment as usual. One adverse event was reported—an accidental minor head injury in the New Forrest program.

Parent education	Sugaya 2022[569] ID: NCT02807870 RCT Single center N = 153 Brazil Setting: Specialty care	**Target:** Children with moderate or severe ADHD; those with affective, psychotic, or autism spectrum disorders, used psychotropic medications during the previous 30 days, a major clinical condition; a history of neurological disorder or head trauma with loss of consciousness were excluded **Other:** Parents provided outcomes - one group of parents received training **ADHD presentation:** inattentive : 7,hyperactive : 22,combined : 71 **Diagnosis:** Confirmation by specialist DSM V by psychiatrists experienced in preschool mental health **Comorbidity:** N/A **Female:** 16 % **Age mean:** 5.0 (0.63) **Minimum age:** 3.0 **Maximum age:** 5.9 **Ethnicity:** N/A	**Intervention:** Parent behavioral training session, Helping the Noncompliant Child based on social learning and behavior modification principles designed to teach parents how to manage children's behavior, improve parent–child relationships, and parental competencies one 90 minute session per week for 8 weeks **Control:** Placebo Placebo plus sham parent behavioral training for 8 weeks **Comparator:** MedicationMethylphenidate plus sham parent training (education), immediate release, for 8 weeks **Follow-up:** 2 months	Multidimensional Assessment Profile of Disruptive Behavior (MAP-DB) Time-by-group interaction significant only for Temper Loss scale: methylphenidate plus sham intervention vs placebo plus behavioural parent training group (p = 0.026); placebo plus behavioural parent training vs placebo plus sham intervention group (p=0· Clinical Global Impressions Severity (CGI-S) scale Significant difference between methylphenidate plus sham intervention and placebo plus sham intervention group (p 0·0088). SNAP-IV, average scores across parent and teacher ratings Significant difference between methylphenidate plus sham intervention and placebo plus sham intervention groups (p 0·049). Conners Kiddie Continuous Performance Test (KCPT-2), a cognitive measure: detectability and hit reaction time results were superior for methylphenidate plus sham intervention compared to both placebo plus behavioural parent training and placebo plus sham intervention. Decreased appetite Significantly more common in more frequently in the methylphenidate plus sham intervention group than in the other two groups. Number with any adverse event No significant difference among groups. Insomnia occurred more frequently in the methylphenidate plus sham l

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
				intervention group than in the other two groups,

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Parent education	Tiwawatpakorn, 2021[585] ID: TCTR20180516002 RCT Unclear/Not reported N = 80 Thailand Setting: Other	**Target:** Participants diagnosed with ADHD by a developmental behavioral pediatrician or child and adolescent psychiatrist, receiving stable medication for at least 3 months, and living with their primary caregivers for at least 5 days a week **Other:** Parents **ADHD presentation:** inattentive_other : Intervention: 1.7 (0.6); Control: 1.6 (0.6),hyperactive_other : 1.8 (0.6); Control: 1.6 (0.8) **Diagnosis:** Confirmation by specialist Vanderbilt ADHD Diagnostic Parent Rating Scale (VADPRS) **Comorbidity:** N/A **Female:** 18 % **Age mean:** 8.3 (1.1) **Minimum age:** **Maximum age:** **Ethnicity:**	**Intervention:** Parental training plus routine clinical care, routine clinical care included psychoeducation, problem-oriented counseling, prescription of standard medications, and child evaluation, visits were scheduled every 3–6 months and took 15–30 minutes for each visit, parenting training consisting of six 120-minute weekly sessions consisting of general knowledge about ADHD and quality time, functional behavioral analysis, effective communication, positive and negative reinforcement, punishment, and time and school management; for 6 weeks **Control:** Other Routine clinical care only: psychoeducation, problem-oriented counseling, prescription of standard medications, and child evaluation, visits were scheduled every 3–6 months and took 15–30 minutes for each visit **Comparator:** NA **Follow-up:** 2 months	VADPRS (Vanderbilt ADHD Diagnostic Parent Rating Scale) subscales The scores of inattention, hyperactivity/impulsivity, and oppositional-defiant behavior showed a noticeable reduction in both groups; no significant interactions were found between time and treatment arm (P > 0.05) indicating that the improvement in score Treatment arm was not associated with changes in parenting style.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Parent education	Vaidyanathan, 2023[593] ID: ID NA RCT Single center N = 56 India Setting: Specialty care	**Target:** Children with ADHD per DSM-5, without visual and hearing impairment, comorbid autism spectrum disorder, or social quotient under 50 **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Diagnosis was made by the team in the clinic consisting of a paediatrician, child psychiatrist, and senior resident in child psychiatry based on the DSM-5 criteria **Comorbidity:** N/A **Female:** 16.1 % **Age mean:** mean 57.82 (15.12) months **Minimum age:** 2.5 **Maximum age:** 6 **Ethnicity:** N/A	**Intervention:** Behavior parent training in groups of 4-8 members per group, educating parents about their child's disorder, necessary investigations as planned by the treating team, if indicated: pharmacotherapy, occupational therapy, speech therapy; training for 12 weeks **Control:** NA **Comparator:** Parent trainingBehavior parent training on an individual basis, plus educating parents about their child's disorder, necessary investigations as planned by the treating team; if indicated: pharmacotherapy, occupational therapy, speech therapy **Follow-up:** 3 months	Conner's abbreviated behaviour rating scale Both groups improved from baseline ($p<0.001$) and there was no significant interaction between group and time (p 0.468).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Physical exercise	Chang, 2022[180] ID: ID NA RCT Multicenter N = 48 Taiwan Setting: School	**Target:** Children with ADHD and handwriting difficulties; those with history of any medical, neurological, or pervasive developmental disorders were excluded, as were those taking medication other than stimulant for ADHD **Other:** None **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist **Comorbidity:** N/A **Female:** 18.8 % **Age mean:** mean 8.36 **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Asian : 100	**Intervention:** Table tennis training designed to improve to general executive attention with a special focus on short- and long-duration visuomotor control, 3 one-hour sessions per week for 12 weeks **Control:** No intervention No intervention **Comparator:** Physical exerciseSimulated table tennis training with Nintendo Wii Sport, 3 one-hour sessions per week for 12 weeks **Follow-up:** 3 months	Wisconsin Card Sorting Test, total errors: Intervention group improved more than comparator or control groups (p <0.01). No differences in improvement in Stroop Color Test among groups, intervention and comparator groups improved more than control group on Stroop Word test (p 0.017).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Physical exercise	Durgut, 2020[239] University, Bezmialem Vakif, University, Medipol, 2018[683] ID: NCT03469180 RCT Single center N = 30 Turkey Setting: Specialty care	**Target:** Treatment naive children with ADHD; without history of chronic and severe systemic disease or a seizure-like neurological disorder or vision, speech and hearing problems; any contraindications for physical activity; comorbid conditions such as autism spectrum disorders or intellectual disability **Other:** Teachers and parent provided some outcome data **ADHD presentation:** inattentive : 16.7,hyperactive : 3.3,combined : 80.0 **Diagnosis:** Confirmation by specialist diagnosed by psychiatrists via DSM V **Comorbidity:** N/A **Female:** 20 % **Age mean:** 8.13 (1.19) **Minimum age:** 7 **Maximum age:** 11 **Ethnicity:** N/A	**Intervention:** Treadmill training plus whole body vibration training 3 days per week, treadmill training for 45 minutes, 5 minutes rest, whole body vibration training for 15 minutes, for 8 weeks **Control:** Other Treadmill training alone **Comparator:** NA **Follow-up:** 2 months	CPRS-R/L (Conners' Parent Rating Scale-Revised/Long Form) Intervention group had more improvement in CPRS-R/L-total (parent report) but did not reach statistical significance (p = .055). Intervention group had significantly more improvement in CTRS-R/L-total (teacher report) p = .041. No difference between groups in Behavior Rating Inventory of Executive Function (BRIEF) - Parent report (p = 0.816) at follow-up. Intervention groups scored significantly better on BRIEF- teacher report (p = 0.023).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Physical exercise	Ji, 2023[345] ID: KCT0008239 RCT Single center N = 30 Korea Setting: Specialty care	**Target:** Children with mild to moderate ADHD, absence of diseases other than ADHD, right-hand dominance, normal or corrected-to-normal vision, and the absence of physical impairment to perform exercise **Other:** **ADHD presentation:** N/A **Diagnosis:** No Korean Attention-Deficit/Hyperactivity Disorder Diagnostic Scale **Comorbidity:** N/A **Female:** 13 % **Age mean:** Intervention: 9.00 (1.46), Comparator: 8.85 (1.63) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** % Asian : 100	**Intervention:** Exergaming using using ExerHeart devices consisting of a running or jumping board with a connected screen; participants run or jump in place with their avatars, using the front, back, left, and right sensors on the mat to avoid obstacles and acquire items; 3 days/week, 50 min/day, for 4 weeks **Control:** Attention-matched control Attention matched control - stationary bike exercise using commercial Fit Elite-Whole body exerciser 1000, with resistance of 0.5~3 kiloponds; 3 days/week, 50 min/day, for 4 weeks **Comparator:** NA **Follow-up:** 1 month	FAIR (Frankfurt Attention Inventory) Both groups increased selective attention and continuous attention ($p<.001$) and self-control ($p<.05$) but no significant difference between groups. No significant group × time interaction on the changes in Response Time to Go and No-go stimulations.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Physical exercise	Kadri, 2019[353] University of Genova, 2018[1132] ID: NCT03678844 RCT Single center N = 40 Tunesia Setting: Other	**Target:** Children with ADHD, no consumption of any diet supplements or drugs; no history of chronic disease, bronchospasm or atopy; not color blind or vision-impaired **Other:** **ADHD presentation:** N/A **Diagnosis:** No Participants with ADHD were recruited from Tunis and Sidi Bouzid mental centers, but DSM criteria not mentioned. **Comorbidity:** N/A **Female:** 10 % **Age mean:** Intervention group 14.5 (3.5), control group 14.2 (3.0) **Minimum age:** **Maximum age:** **Ethnicity:**	**Intervention:** Taekwondo exercises practiced for 50-minutes twice weekly, 10-minute general warm-up before each session and 10-minute recovery after each session, for a year and a half **Control:** Other Engaged in physical activities, including athletics, handball and gymnastic, during two sessions of physical education per week at school **Comparator:** NA **Follow-up:** 18 months	Processing speed measured using total time in seconds to complete the Ruff's test 2 and 7; intervention mean 240.3 (SD 19.7), control group 288.1 (SD 12.5).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Physical exercise	Liang, 2022[396] ID: ChiCTR2200056126 RCT Single center N = 80 China Setting: Specialty care	**Target:** Children with ADHD without comorbid psychological disorders **Other:** **ADHD presentation:** inattentive : 51.25,hyperactive : 16.25,combined : 32.5 **Diagnosis:** Confirmation by specialist DSM 5 by psychiatrist using K-SADS-PL **Comorbidity:** N/A **Female:** 22.6 % **Age mean:** 8.46 (1.5) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Asian : 100	**Intervention:** Aerobic and neurocognitive exercise, 3 sessions per week, 60-minutes per session, for 12 weeks **Control:** Wait list Wait list control group **Comparator:** NA **Follow-up:** 3 months	Intervention group decreased reaction time as measured by Arrow Flanker Task for Inhibitory Control, compared to wait list group. Intervention group also increased working memory as measured by the Tower of London task, compared to wait list group. Intervention group also improved cognitive flexibility measured by the Trail Making Test for Cognitive Function compared to the wait list group. Sleep quality also improved significantly. However, the significant differences in all measures disappeared 1 month after intervention ended.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Physical exercise	Ludyga, 2022[406] ID: DRKS00020125 RCT Multicenter N = 63 Multiple countries Setting: Community	**Target:** Right-handed children with ADHD undergoing pharmacotherapy with methylphenidate or dexamphetamine for at least three months **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-5 **Comorbidity:** N/A **Female:** % N/A **Age mean:** 10.4 (1.2) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Judo training in a group setting, 2 weekly 60-min sessions per week, for 3 months **Control:** Wait list Wait list **Comparator:** NA **Follow-up:** 3 months	No group difference in Movement Assessment Battery for Children-2. Intervention group performed better on a Change Detection Task (p 0.003).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Physical exercise	Rothe, 2023[503] ID: ID NA Cohort study Single center N = 58 Germany Setting: Specialty care	**Target:** Children with ADHD, majority with below average motor skills; those with neurological disorders, head injury, metabolic disorder or below average intelligence (IQ<85) were excluded **Other:** None **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist by child and adolescent psychiatrists/psychotherapist **Comorbidity:** Coordination disorder : majority had below average motor coordination **Female:** 17.2 % **Age mean:** 9.52 (1.91) **Minimum age:** **Maximum age:** **Ethnicity:** N/A	**Intervention:** Physiotherapeutic treatment designed to treat and train children's fine and grossmotor skills, 2 sessions per week with physiotherapist, for8 weeks **Control:** NA **Comparator:** MedicationMethylphenidate, 10–40 mg per day, for 8 weeks **Follow-up:** 2 months	General motor testing (handwriting, drawing movements) no significant differences among groups.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Provider	Elmaadawi, 2022[252] ID: ID NA Cohort study Single center N = 136 US Setting: Specialty care	**Target:** Children and adolescents with ADHD **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM IV by board certified child psychiatrists **Comorbidity:** N/A **Female:** % N/A **Age mean:** 13.8 (3.6) **Minimum age:** 4 **Maximum age:** 18 **Ethnicity:** N/A	**Intervention:** Pharmacogenetic testing to enable genomically assisted prescribing for 6 months **Control:** TAU Treatment as usual, without genetic testing or treatment guidance **Comparator:** NA **Follow-up:** 6 months	Clinical Global Impression Scale-, Improvement Component (CGI-I) Significantly more improvement in intervention group. Intervention group required almost twice as many medication changes compared to control (1.8 changes vs 1.1 in control; p<0.001).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Provider	Enns, 2017[254] ID: NA Cohort study Single center N = 2369 Canada Setting: Community	**Target:** Children and adolescents with ADHD **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Manitoba Population Research Data Repository **Comorbidity:** N/A **Female:** 15.37 % **Age mean:** 16% of the intervention cohort were 6 years old or younger, 13% were 13 years old or older; 17% of the control cohort were 6 years old or younger, 10% were 13 years old or older **Minimum age:** 5 **Maximum age:** 17 **Ethnicity:** N/A	**Intervention:** ADHD intervention service, participants and their families receive a range of servicesthat can include assessment, treatment, and consultative services (e.g. individual therapy, parent support, group therapy, education, and medication management) from multiple providers; the typical participation length in the program ranges from 3-6 months (extended based on participant needs) **Control:** No intervention No contact with the ADHD Service matched on age, sex, year of ADHD diagnosis, and income quintile; matches were identified separately in urban and rural income quintiles **Comparator:** NA **Follow-up:** 24 months	Adjusted rate ratios (95% CI) for health and social services use outcomes for intervention (n =485) and control (n = 1884): Hospital admissions (rate of): 1.29 (0.68 to 2.46) (p = 0.43) Visits to emergency department (rate of): all 1.03 (0.75 to 1.41) (p = 0.87), injury-related 1.00 (0.68 to 1.46) (p =1.00) Medication use (proportion of participants who were dispensed 1 or more medications): 1.21 (1.08 to 1.36) (p < 0.01) Medication adherence (proporton of participants who have a medication possession ratio of at least 0.8): 1.42 (1.03 to 1.96) (p < 0.05) Children with child welfare contact: 1.34 (0.54 to 3.35) (p = 0.53) Children in age-appropriate grade: 1.33 (1.09 to 1.63) (p < 0.01).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Provider	Epstein, 2007[256] ID: NA Cluster RCT Multicenter N = 377 US Setting: Primary Care	**Target:** Children who met DSM-IV criteria for ADHD, stimulant-naive **Other:** Pediatricians and associated healthcare professionals (27 men, 25 women) from 12 practices **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Conners Rating Scale **Comorbidity:** N/A **Female:** 36.3 % **Age mean:** 7.8 (1.5) **Minimum age:** 6 **Maximum age:** 10 **Ethnicity:** % Hispanic or Latino : .68 % Black/African American : 16.4 % American Indian or Alaska Native : .68 % White : 79.5 % Multiracial : .68	**Intervention:** Collaborative consultation services: pediatricians were encouraged to and assisted in using titration trials to determine optimal dosages, taught to prescribe 4 different weekly dosages of methylphenidate hydrochloride during a titration trial (placebo, 18 mg, 36 mg, 54 mg) and the order of weekly dosages was blinded but standardized across all patients (week 1, 18 mg; week 2, placebo; week 3, 36 mg; week 4, 54 mg); participants followed for 12 months **Control:** TAU Patients in control group received treatment as usual alone, practices assigned to control group do not have access to consultative services **Comparator:** NA **Follow-up:** 12 months	DSM-IV symptomatology, Conners Parent Rating Scale Children in the intervention group demonstrated a 27% reduction in DSM-IV symptomatology compared with an 18% reduction in the control group (p=.008).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Provider	Epstein, 2016[255] Childrens Hospital Medical Center, Cincinnati, 2010[710] ID: NCT01143701 Cluster RCT Multicenter N = 577 US Setting: Primary Care	**Target:** Children presenting for ADHD evaluation, ADHD medication naive **Other:** Pediatric practices with ≥2 physicians, uses an electronic billing system, office has Internet access, must not have co-located mental health care **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV by research staff **Comorbidity:** N/A **Female:** 29.5 % **Age mean:** 7.8 (1.4) **Minimum age:** **Maximum age:** **Ethnicity:** Other : 36.7% were Non-white - unspecified	**Intervention:** Training sessions for providers, office flow modification, guided quality improvement, and an ADHD Internet portal to assist with treatment monitoring, for at least 4 weeks **Control:** No intervention Control practices **Comparator:** NA **Follow-up:** 12 months	ADHD symptoms parent ratings Intent-to-treat analyses examining outcomes of all children assessed for ADHD were not significant (P=0.08) but among the 373 children prescribed ADHD medication, there was a significant intervention effect (P=0.04) indicating greater reductions in parent ADHD treatment care around medication was significantly better at intervention practices compared with control practices.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Provider	Guevara, 2021[308] Children's Hospital of Philadelphia, 2016[712] ID: NCT02716324 RCT Multicenter N = 303 US Setting: Primary Care	**Target:** Participant had an ADHD diagnosis code (InternationalClassification of Diseases, Ninth Revision [ICD-9] code 314) recorded at an ambulatory visit in the past year **Other:** **ADHD presentation:** **Diagnosis:** Confirmation by specialist International Classification of Diseases, Ninth Revision **Comorbidity:** N/A **Female:** 31 % **Age mean:** 8.5 **Minimum age:** 5 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 5 % Black/African American : 45.9 % White : 26.4 Other : 9.2	**Intervention:** Portal combined with an ADHD care manager to enhance communication and promote greater shared decision-making ; designed to (1) collect and share patient and family treatment preferences and goals with a clinician; (2) trend ADHD symptoms, performance impairment ratings, medication side effects, treatment receipt, and medication side effects by using electronically submitted parent and teacher reports; (3) provide a repository of ADHD educational materials; and (4) support information sharing between parents and teachers. ADHD care managers were bachelor's-trained individuals who were responsible for communicating information and facilitating coordination of care; total duration of 12 months **Control:** Other Electronic Health Record portal alone **Comparator:** NA **Follow-up:** 9 months	ADHD symptoms VPRS (Vanderbilt Parent Rating Scale) In multivariate models, VPRS scores decreased over time (Adjusted b 5 .015; 95% confidence interval 0.023 to 0.07) in both groups, but there were no intervention-by-time effects (Adjusted b 5 .000; 95% confidence interval 0.011 to 0.012) between groups. There were no adverse effects from either intervention identified, and interactions of intervention by race or income were not significant, suggesting no heterogeneity of treatment effects.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Provider	Kolko, 2020[371] University of Pittsburgh, 2008[1134] ID: NCT00600470 Cluster RCT Multicenter N = 411 US Setting: Primary Care	**Target:** Children diagnosed with ADHD based on DSM-IV criteria **Other:** Parents **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist At intake, parents and children participated in a diagnostic/clinical interview based on the DSM-IV criteria to identify formal diagnoses. **Comorbidity:** N/A **Female:** 31 % **Age mean:** 8.0 (1.9) **Minimum age:** 5 **Maximum age:** 12 **Ethnicity:** % White : 70 N/A : No other race info reported outside of White	**Intervention:** Collaborative care, care manager delivered content modules which taught behavioral strategies to manage ADHD with caregivers and ADHD "survival skills" with participants in 3 to 4 1-hr sessions for 6 months **Control:** NA **Comparator:** ProviderEnhanced usual care; families received a referral to a mental health provider and could receive services for ADHD from their primary care provider and/or a community mental health provider **Follow-up:** 6 months	Vanderbilt ADHD Diagnostic Parent Rating Scale (VADPRS) change from baseline for intervention group compared to comparator group slope (−3.31) was significant (p 0.02). Collaborative care showed greater acute improvement in individualized ADHD treatment goals and follow-up improvements in quality of life and ADHD and oppositional defiant disorder goals.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Provider	Lavigne, 2011[386] Childrens Hospital of Chicago, 2005[661] ID: NCT00179894 Cluster RCT Multicenter N = 270 US Setting: Specialty care	**Target:** Participants must have a diagnosis of ADHD according to DSM-IV criteria, IQ >= 70; no comorbidity of ASD, Tourette, other major health conditions, not taken ADHD medications in the past 2 months, or taking medications incompatible with stimulants **Other:** Physicians from 24 Chicago-area pediatric practices **ADHD presentation:** inattentive : 41.2,hyperactive : 9.8,combined : 49.0 **Diagnosis:** Confirmation by specialist Diagnostic Interview Schedule for Children IV-Parent **Comorbidity:** N/A **Female:** 23.0 % **Age mean:** Specialized care SC: 8.25 (SD = 1.38, n = 138), treatment as usual TAU: 8.19 (SD = 1.62, n = 133) **Minimum age:** **Maximum age:** **Ethnicity:** % Hispanic or Latino : 12.2 % Black/African American : 2.5 % White : 81.5	**Intervention:** Derived medication management procedures: physicians received 2 hours of office-based training in using stimulant medications and atomoxetine, an ADHD specialist provided 1 hour of training to office staff in the use of software (Focus on ADHD Medication Management Program), and returned to the office/practice for the first 3 patients per physician to ensure that staff understood program use; follow treatments for up to 9 months **Control:** Other Pediatricians in treatment as usual group provided treatment per their usual procedure **Comparator:** NA **Follow-up:** 12 months	ADHD-RS total scale, parent report Children in both specialized care and treatment-as-usual groups improved on the ADHD Rating Scales and SNAP-IV, and there were no group differences in improvement rates. There were no differences on the Barkley adverse effects scale between groups at 4, 9, or 12 months.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Provider	Myers, 2015[451] Rockhill, 2016[1009]; Myers, 2013[947]; Vander Stoep, 2017[1141]; Rockhill, 2020[1008]; Seattle Children's Hospital, 2009[1031] ID: NCT00830700 RCT Multicenter N = 223 US Setting: Other	**Target:** Children with ADHD in rural underserved communities **Other:** Parents received behavior training; parents and teachers provided outcome data **ADHD presentation:** N/A : Percentages above do not add to 100 because they are not mutually exclusive (caregiver ratings, not clinician diagnosed) **Diagnosis:** Confirmation by specialist Children scoring >= 65 on the Child Behavior Checklist (CBCL) ADHD diagnostic subscale online were eligible. Clinician then confirmed in person via DSM-IV criteria **Comorbidity:** N/A **Female:** 26 % **Age mean:** 9.25 (2.0) **Minimum age:** 5 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 13.0 % Black/African American : 0.9 % American Indian or Alaska Native : 2.7 % Asian : 0.9 % Native Hawaiian or Pacific Islander : 1.8 % White : 80.7	**Intervention:** Telehealth intervention combining pharmacotherapy and caregiver behavior training; 6 sessions, 3-4 weeks apart over 22 weeks **Control:** NA **Comparator:** OtherChildren remained under care of their primary care providers and received a single consultation with a tele-psychiatrist, who shared treatment recommendations with the referring provider; providers were not restricted from referring to other resources **Follow-up:** 6 months	Vanderbilt ADHD Parent Rating Scale Number meeting parent-reported diagnostic criteria on Inattention subscale of the Vanderbilt Attention-Deficit/Hyperactivity Disorder (ADHD) Rating Scale, 25 weeks The percent of participants with at least 50% reduction in ADHD symptoms was significantly higher in the intervention group (p = 0.000). Lower proportions of children in the intervention arm met diagnostic criteria on the VADRS-Caregiver: inattention, hy Columbia Impairment Scale-Parent Version (CIS-P) Children assigned to the intervention improved significantly more than children in the comparator group (p<0.001).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Provider	Oppenheimer, 2019[466] Boston Childrens Hospital, 2014[691] ID: NCT02097355 Cluster RCT Multicenter N = 518 US Setting: Specialty care	**Target:** Children receiving ongoing treatment for ADHD, prescribed ADHD medication, parents and children proficient in English **Other:** Clinicians providing ADHD care **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Neurology department clinician **Comorbidity:** N/A **Female:** 24.3 % **Age mean:** Intervention 9.85 (3.21), control 11.09 (3.24) **Minimum age:** **Maximum age:** **Ethnicity:** % Hispanic or Latino : 5.8 % White : 78.4,Other : 406	**Intervention:** Trigger algorithm and alert resolution process, web-based platform that enables clinicians to administer online clinical questionnaires to parents and teachers to monitor patients remotely between visits, data collected for 13 months **Control:** No intervention Non-alert group **Comparator:** NA **Follow-up:** 15 months	CGI-S scores Alert group patients had lower scores than non-alert group patients indicating worse global functioning. Vanderbilt scores Alert group patients had higher Vanderbilt scores at time 2 than the non-alert group indicating a worse ADHD severity (p<0.001).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Abikoff, 2013[106] ID: N/A RCT Multicenter N = 158 US Setting: Other	**Target:** Children with ADHD and organizational deficits **Other:** Parents received training and provided some outcome data **ADHD presentation:** inattentive : 55.7,hyperactive : 0,combined : 44.3 **Diagnosis:** Confirmation by specialist DSM IV diagnosis confirmed by clinical evaluation required **Comorbidity:** Other : Organizational deficits **Female:** 35.4 % **Age mean:** 9.04 (0.82) **Minimum age:** 7 **Maximum age:** 11 **Ethnicity:** % Hispanic or Latino : 13.9 % Black/African American : 14.6 % White : 69.6	**Intervention:** Organizational skills training; session time is spent working with the child, with parents joining during the last 10 minutes; 20 hour long in-clinic sessions held twice-a-week after school over 10-12 weeks **Control:** Wait list Wait list **Comparator:** OtherPerformance-based intervention that precluded skills, training motivates children by training teachers and parents to establish specific, individualized goals for children on written charts completed daily and to prompt, monitor, and praise/reward childre **Follow-up:** 24 months	Clinical Global Impression-Improvement (CGI-I) Responder rates were significantly better for OST (85.3%) and PATHKO (86.9%) than waitlist (0%), overall p<0.0001). Children's Organizational Skills Scale, parent The intervention group performed better than the comparator group (p < 0.02). Teachers and parents were satisfied with treatments, with no significant differences by treatment tgroupype. p value not reported. Academic Performance Rating Scale (APRS) No significant difference in academic outcomes at 2 years (p value not reported). There were no significant group differences for any other event.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Antshel, 2003[123] ID: ID NA RCT Single center N = 120 US Setting: Specialty care	**Target:** Children with Inattentive type or Combined type ADHD taking a stimulant or SSRI **Other:** Parents **ADHD presentation:** inattentive : 49.2,combined : 50.8 **Diagnosis:** Confirmation by specialist DSM-IV per Diagnostic Interview for Children & Adolescents - Revised **Comorbidity:** N/A **Female:** 25 % **Age mean:** 9.95 (1.1) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino % Black/African American : 5.0 % Asian : 1.7 % Native Hawaiian or Pacific Islander % White : 93.3	**Intervention:** Social skills group training for children plus parent sessions; one 90 minute sessionper week, each week children were given a homework assignment to practice a skill, parents attended their own sessions on week 1, 4, and 8, for 8 weeks **Control:** Wait list Wait list **Comparator:** NA **Follow-up:** 3 months	No significant differences between groups on parent ratings for Cooperation, Responsibility, and Self-Control scores; no significant differences between groups on child ratings for Cooperation, Empathy, and Self-Control scores; intervention group improved significantly more on both parent and child Assertion scales (p = .001).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Boyer, 2016[160] Boyer, 2015[692] ID: NTR2142 RCT Multicenter N = 159 Netherlands Setting: Specialty care	**Target:** Adolescents with a prior DSM-IV-TR diagnosis of ADHD by a child psychiatrist or certified psychologist, a confirmed ADHD diagnosis on the ADHD sections of the diagnostic interview schedule for children for DSM-IV parent version; no alternative non-pharmacological treatment between pre- and post- participant assessment, alternative treatments stopped until post-test, no autism spectrum disorder, no predominant addiction, depression with suicidal ideations, acute familial crisis or conduct disorder, no pharmacological treatment with Atomoxetine **Other:** **ADHD presentation:** inattentive : 70,hyperactive : 5,combined : 25 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 26 % **Age mean:** Intervention 14.4(1.2), control 14.4(1.3) **Minimum age:** 12 **Maximum age:** 17 **Ethnicity:** N/A	**Intervention:** Cognitive behavioral treatment (Plan my life), 8 adolescent sessions and 2 parental sessions of 45–60 min, 1 session per week for 10 weeks **Control:** NA **Comparator:** BehavioralSolution-focused treatment, consisting of eight individual adolescent sessions and two parental sessions (between adolescent session 2 and 3, and between adolescent session 5 and 6) of 45–60 min. At every session the adolescent discussed a problem he/she **Follow-up:** 3 months	ADHD-RS (ADHD-Rating Scale), parent-rated Marginally significant differences were found in favor of the intervention. At 12 months there no significant differences. Overall impairment, parental report There was a significant time x treatment effect . Executive function, teacher rated, significantly improved over time. At 1 year, no differences between groups. Attendence Intervention group showed significantly higher attendance rates than comparator (p = .03). At 1 year, no differences in effect on depression, anxiety, parent-adolescent conflict, or neurological tasks.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Chu, 2021[199] Shanghai Children's Hospital, 2021[1038] ID: ChiCTR2100052803 RCT Single center N = 145 China Setting: Specialty care	**Target:** Children with ADHD, IQ at least 70, with parents or primary caregivers who did not want child to receive drug therapy; without autism spectrum disorder, schizophrenia, epilepsy, head injury, or verified neurological disorder, intellectual disability, sensory impairment (hearing/vision problems) or receiving other ADHD treatments **Other:** Parents & teachers provided outcomes; intervention group received parent training **ADHD presentation:** inattentive : 60,hyperactive : 14,combined : 26 **Diagnosis:** Confirmation by specialist DSM-V **Comorbidity:** N/A **Female:** 25 % **Age mean:** Intervention: 7.10 (0.47) Waitlist: 7.04 (0.61) **Minimum age:** 6 **Maximum age:** 8 **Ethnicity:** % Asian : 100 Other : Chinese	**Intervention:** Multimodal treatment for children and parents, TEAMS training (Training Executive, Attention, and Motor Skills), executive function training program hospital-based, 90 minute sessions, and online parent training program, each session 30 minutes long, for 8 weeks **Control:** Wait list Wait list **Comparator:** NA **Follow-up:** 2 months	SNAP- IV total score (Chinese version), parent Difference in parent score approached significance (p = 0.07); difference in teacher score was significant, favoring intervention group (p < 0.001). Weiss Functional Impairment Scale, parent The intervention had significantly greater improvement compared to control (p = 0.009). The intervention group had greater reduction in the scores of BRIEF behavioral regulation index (inhibition, emotional control) and metacognition index (working memory, planning/organization, monitoring) in executive function than those in the control group (p < 0.05).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Coles, 2020[204] ID: NA RCT Single center N = 127 US Setting: Mixed	**Target:** Unmedicated children with ADHD **Other:** Parents of the children **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV diagnosis required. A Ph.D.-level clinician conducted interview with parents and reviewed symptom rating and impairment scales (DBD-RS) **Comorbidity:** N/A **Female:** 16 % **Age mean:** 9.3 (2.0) **Minimum age:** 5 **Maximum age:** 13 **Ethnicity:** % Hispanic or Latino : Not reported % Black/African American : 13 % Asian : Not reported % White : 79	**Intervention:** Behavioral consultation with school and home components (high or low intensity); behavioral treatment summer block; 3 initial teacher visits to set up Daily Report Card with home-based rewards, bank of 3 additional consultation visits throughout year; 1 initial home visit to establish a homebased Daily Report Card, bank of 3 additional consultation visits throughout year, option to attend monthly group parent training booster sessions; total duration of 1 year **Control:** No intervention No behavioral consultation **Comparator:** NA **Follow-up:** 9 months	Inattention/Overactivity, Conners Score, parent report No difference in teacher or parent reported Conners Score, Oppositional/Defiant subscale or Inattention/ Overactivity subscale between children receiving or not receiving the behavioral consultation. Children who received the intervention were about half as likely those who did not to initiate medication use each week at school or home and used lower doses when medicated at school, 63% of the control group was medicated at home at endpoint compared to 26% of the intervention group (p < .01).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Fabiano, 2016[261] ID: NA RCT Unclear/Not reported N = 172 US Setting: Mixed	**Target:** Adolescents with ADHD-Combined Type **Other:** Parents and teachers **ADHD presentation:** combined : 100 **Diagnosis:** Confirmation by specialist DSM IV per Disruptive Behavior Disorder (DBD) rating scales of ADHD symptoms and DSM scale on the Child Behavior Checklist and Teacher Report Form **Comorbidity:** N/A **Female:** 27.4 % **Age mean:** 16.98 (0.70) and 16.88 (0.65) **Minimum age:** 16 **Maximum age:** 18 **Ethnicity:** % Black/African American : 11 % White : 85.5 % Multiracial : 1 Other : Other: 2%	**Intervention:** Supporting the Effective Entry to the Roadway (STEER), parent-teen intervention of weekly sessions divided into two 45-minute meetings with the first half including individual parent and teen meetings that occur in parallel and the second half including a joint activity, adjunct to drivers ed program which control group also received, for 8 weeks **Control:** Attention-matched control Driver education driver practice program, 10-week diver education co.urse with 30 hours of classroom instruction and 10 45-minute individual driving lessons **Comparator:** NA **Follow-up:** 12 months	Treatment satisfaction No difference between groups. Compared to the driver education practice program, the teens in the supporting the effective entry to the roadway group reported lower levels of risky driving behavior at the six-month (p=0.03) but not the 12-month follow-up (p= 0.07); there was also no significant differences for observed positive parenting.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Geissler, 2020[290] Jans, 2015[856]; Hage, 2018[812]; Jaite, 2019[854]; Hautmann, 2018[822] ID: CCT-ISRCTN73911400 RCT Multicenter N = 144 Germany Setting: Specialty care	**Target:** Children diagnosed with ADHD and their mothers also diagnosed with ADHD; not currently receiving psychopharmacotherapy, or their medication had been stable for at least 4 weeks prior to baseline assessment **Other:** **ADHD presentation:** combined : 52,combined_other : 52% children / 66% mothers **Diagnosis:** Confirmation by specialist DSM-IV specially trained expert clinicians at each study centre's Department of Child and Adolescent Psychiatry European Child & Adolescent Psychiatry (assessment and treatment of children; PCT) or Department of Psychiatry (assessment and treatment of **Comorbidity:** N/A **Female:** 26.5 % **Age mean:** Mean age 9.4 **Minimum age:** **Maximum age:** **Ethnicity:** N/A	**Intervention:** Parent-child training program comprised a structured and modular behavioral psychotherapy program with methylphenidate medication for mothers with ADHD (1 appointment/4 week), behavioral group psychotherapy for mothers who were also offered methylphenidate for 12 weeks, then 6 months of maintenance of all previous interventions; total duration 12 months **Control:** NA **Comparator:** Parent trainingIndividual non-specific counseling for mothers, seven 4-weekly sessions, 2 booster parent-child therapy sessions **Follow-up:** 12 months	Home Situations Questionnaire (HSQ), externalizing problem behavior in the family There were no differences between groups (p 0.62). ADHD symptoms, Schedule for Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL) No statistically significant difference between groups (p 0.35) Strength and Difficulties Questionnaire global score There was no significant difference between groups (p=0.54) No difference in Strengths and Difficulties Questionnaires rated by teachers (p=0.73).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Hiscock, 2019[329] Murdoch Childrens Research Institute, 2014[945] ID: ISRCTN50834814 RCT Multicenter N = 361 Australia Setting: Other	**Target:** Children who met full DSM-5 diagnostic criteria for ADHD; had a moderate to severe parent-rated sleep problem; met the International Classification of Sleep Disorders – 3rd edition criteria for chronic insomnia disorder or delayed sleep wake phase disorder, or had sleep-related anxiety **Other:** Parents **ADHD presentation:** **Diagnosis:** Confirmation by specialist DSM-5 diagnostic criteria for ADHD **Comorbidity:** Sleep **Female:** 25.1 % **Age mean:** 9.6 (1.7) **Minimum age:** 5 **Maximum age:** 13 **Ethnicity:**	**Intervention:** Sleep intervention, 2 face-to-face sessions with the parent and child approximately 2 weeks apart,each session 3.5 hours, parents completed a sleep diary, the second consultation and followup telephone call were used to review the sleep diary, reinforce suggested strategies, and troubleshoot any problems; clinician provided information about normal sleep, sleep cycles, and sleep hygiene strategies, and formulated a behavioral sleep management plan, follow up phone call a further 2 weeks later, min 4 weeks **Control:** TAU Families in the control group could access care as usual from their pediatrician, which does not typically include assessment and management of child sleep problems **Comparator:** NA **Follow-up:** 6 months	Children's Sleep Habits Questionnaire: proportion of children with moderate to severe sleep problems was lower in the intervention (28.0%, 35.8%) compared with usual care group (55.4%, 60.1%).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Hogue, 2020[330] National Center on Addiction and Substance Abuse at Columbia University, 2015[1115] ID: NCT02420990 Cluster RCT Multicenter N = 145 US Setting: Specialty care	**Target:** Adolescents with ADHD **Other:** Parents involved with intervention **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Yes, however only 77% of the sample met full diagnostic criteria for ADHD based on researcher administered interviews; per the study eligibility criteria, the remaining 23% were enrolled based on already being treated for ADHD **Comorbidity:** N/A **Female:** 28 % **Age mean:** 14.8 (1.95) **Minimum age:** 12 **Maximum age:** 18 **Ethnicity:** % Hispanic or Latino : 37 % Black/African American : 15 % White : 42 % Multiracial : 6	**Intervention:** Changing Academic Support in the Home for Adolescents with ADHD, a 3-module protocol that utilizes family and individual sessions to improve school performance, flexible protocol that do not prescribe a fixed number of sessions or intervention sequences, one year of observation **Control:** NA **Comparator:** Medication + behavioralMedication program is a family-based protocol designed to integrate medication services into behavioral treatment planning for adolescents with ADHD; contains 5 modular tasks: ADHD Assessment & Medication Consult, ADHD Psychoeducation & Client Acceptance, **Follow-up:** 12 months	National Youth Survey Self-Report Delinquency Scale, Delinquency Among adolescents who engaged in any delinquency, CASH-AA + MIP clients showed greater declines in delinquent acts than CASH-AA Only clients. Inattentive/Disorganized and Hyperactive/Impulsive subscale, Mini-International Neuropsychiatric Interview (MINI) There was a significant association between intervention group and fewer Inattentive symptoms (self report) in a quadratic equation controlling for age, race, sex, and baseline substance use. Effects on self-reported hyperactivity symptoms were not sign School functioning Association with grades, academic self-efficacy, problems with homework, and time spent on homework were not statistically significant in models controlling for age, sex, race, and baseline substance abuse.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Huang, 2015[335] ID: N/A Clinical trial Single center N = 97 Taiwan Setting: N/A	**Target:** Boys and girls with ADHD and without autism and mental retardation **Other:** Parents and teachers provided outcome data **ADHD presentation:** inattentive : 19.6,combined : 80.4 **Diagnosis:** Confirmation by specialist DSM-IV-TR **Comorbidity:** N/A **Female:** 17.5 % **Age mean:** 8.4 (0.9) **Minimum age:** 7 **Maximum age:** 10 **Ethnicity:** N/A	**Intervention:** Social skill training combined with parent training, 7 consecutive behavioral-basedgroup sessions, 80-minute group sessions during consecutive weeks teaching social skill modules using didactic instructions, modeling, role-play activities, behavior rehearsal, homework was assigned for each week for 8 weeks **Control:** No intervention Recruited from referral as a control group, motivated for group therapy but could not find a mutually available time **Comparator:** NA **Follow-up:** 4 months	Change in Delinquent Behavior, Child Behavior Check List (CBCL) No statistically significant group effect (p=0.38). Inattention scale SNAP-IV (Swanson, Nolan, and Pelham, version IV) change, parent There was no significant difference between groups on parent SNAP IV inattention (p=.41) or hyperactive/impulsivity (p = .13) scales. Significant effect of intervention on oppositional scale (p = .04). No significant effect of group on any teacher SNAP I Teacher version of modified social skill rating system (SSRS): intervention group improved more on Active Participation scale (p = .03) but not on Cooperative Behavior, Self Assertion, Self Control or Conflict Coping scales. For child report SSRS, difference in Self Control favored intervention (p = .03).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Psychological or behavioral	Huang, 2021[334] Fujian Maternity and Child Health Hospital, 2022[782] ID: ChiCTR2100049863 RCT Single center N = 201 China Setting: Other	**Target:** Treatment naive children with ADHD, IQ >=75, no history of seizures or psycho-morbidities **Other:** Parents provided some outcome information **ADHD presentation:** inattentive : 62.7,hyperactive : 13.9,combined : 23.4 **Diagnosis:** Confirmation by specialist 2 independent providers used DSM V **Comorbidity:** N/A **Female:** 29.4 % **Age mean:** 5.6 (0.65) Preschool **Minimum age:** **Maximum age:** **Ethnicity:** % Asian : 100	**Intervention:** Behavioral therapy, attention training (twice per day), relief therapy and game therapy, and parental training (1 hour weekly sessions) plus conventional therapy (biofeedback and a health education booklet), for 1 year **Control:** TAU Conventional treatment (biofeedback and a health education booklet) **Comparator:** NA **Follow-up:** 18 months	Impulsivity/ hyperactivity scale, Conners parent symptom questionnaire Significant effect of intervention (p < .001). Intervention effect on hyperactivity index was also significant (p < .001). Significant effect of intervention on full-scale attention quotient (FAQ; p < .001) and full-scale response control quotient (FRCQ, p = 0.014) from integrated visual and auditory comprehensive continuous performance tests.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Kareem, 2021[358] ID: ID NA RCT Single center N = 50 Egypt Setting: Specialty care	**Target:** Children recently diagnosed with ADHD **Other:** Parents provided outcome data **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-V **Comorbidity:** N/A **Female:** 24 % **Age mean:** Intervention: 10.44 (1.18) Control: 9.60 (2.08) **Minimum age:** 7 **Maximum age:** 13 **Ethnicity:** N/A	**Intervention:** Attention span training, time table activities and homework, 12 sessions, 30-45 min with 5 children and their parents, 1 session per week, for 12 weeks **Control:** No intervention No intervention **Comparator:** NA **Follow-up:** 2.5 months	Restless in the squirmy sense Intervention group improved significantly but not the control group,

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Li, 2022[392] ID: ID NA RCT Single center N = 180 China Setting: Specialty care	**Target:** Children with ADHD without co-morbid serious psychological disorders or medical conditions **Other:** Parents reported some outcomes **ADHD presentation:** inattentive : 38.3,hyperactive : 30.6,combined : 31.1 **Diagnosis:** Confirmation by specialist DSM IV **Comorbidity:** N/A **Female:** 47.8 % **Age mean:** 5.01 (0.36) **Minimum age:** 3 **Maximum age:** 7 **Ethnicity:** % Asian : 100	**Intervention:** Theme building block games to promote psychological and behavioral development, 2-3 children per group, once a week, interactive environment for children, research instructor gives specific instructions (e.g., we are going to build a castle today), for 8 weeks **Control:** Attention-matched control Attention matched control, children play with blocks with 2 to 3 children per group, once a week for 8 weeks **Comparator:** NA **Follow-up:** 2 months	Behavior, PHCSS (Piers-Harris Children's Self-concept Scale) Scores were significantly (p 0.05) higher in the intervention compared to the control group. Child Behavior Check List (CBLC) For boys, intervention group improved more than control group on CBCL Discipline violation, Hostility, Compulsion, Immaturity, Bad communication, Schizoid, and Physical complaint scales. For girls, intervention group improved more than control group on CB Swanson, Nolan, and Pelham, Version IV total score, parent Intervention showed significantly more improvement (p<.05).

Psychological or behavioral	Lv, 2023 [410] ID: China research registry 8696 RCT Single center N = 90 China Setting: Specialty care	**Target:** Children with ADHD; patients with mental retardation, character disorder, mood disorder, tic disorder, childhood autism, and schizophrenia were excluded **Other:** Parents provided some outcomes; some underwent parent training **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM 5 **Comorbidity:** N/A **Female:** 18.9 % **Age mean:** pharma intervention 9.03 (1.78), non-pharma intervention 9.23 (1.65) **Minimum age:** 6 **Maximum age:** 18 **Ethnicity:** % Asian : 100	**Intervention:** Behavior modification, sensory integration therapy, sand tray therapy with parent training; parent training involved four sessions, including disease awareness, pros and cons of drugs, parent-child relationship, and methods to improve attention span; behavior modification involved two major courses covering the positive reinforcement method of behavior modification, temporary isolation method, fading method, demonstration method, cognitive behavior therapy, and applied behavior analysis; sensory integration therapy involved 45–60 min of training per session, including warm-up, vestibular sensory, proprioception, balance, hand-eye coordination, sedation, and fine motor; Sand tray therapy involved 10–12 sessions with a unified sand tray therapist, with each session lasting about 40–60 minutes, including instructional language, familiarization with the environment, feeling the sand, creating a sand tray, playing with the sand tray, dialogue and communication, dismantling the work, and discussion and analysis with parents; homeopathy Tiaoshen Yizhi Decoction powder dissolved in water taken every morning and evening, for 3-6 months **Control:** NA **Comparator:** MedicationMethylphenidate and atomoxetine, dosage not described; participants also received homeopathy Tiaoshen	Swanson, Nolan, and Pelham, Version IV (SNAP-IV) No significant difference in improvement. Weiss Functional Impairment Rating Scale (WFIRS), family subscore Non-pharma group improved more on family function, life skills, and self concept scores ($p < 0.05$); no difference between groups regarding learning/school, social activities, and risk-taking activities.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
			Yizhi Decoction powder dissolved in water taken every morning and evening for 6 months **Follow-up:** 6 months	
Psychological or behavioral	McGrath, 2011[426] ID: NA RCT Single center N = 72 Canada Setting: Other	**Target:** Children with ADHD, able to speak and understand English; no co-intervention (within 6 months) and disorder severity, involvement with child protection authorities, autism, schizophrenia, or other psychosis, complex comorbidity, and serious cognitive delay **Other:** Parents **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV, K-SADS-PL **Comorbidity:** N/A **Female:** 25 % **Age mean:** 8.89 (1.92) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Strongest Families intervention, skill-focused learning, anxiety program consisted of 11 sessions and the behavior programs had 12 sessions (Parenting the Active Child, positive parenting strategies), weekly coach session calls were on average 40 minutes, for 12 weeks **Control:** No intervention Control participants received one call from the coach to review the randomization placement results and to inform the parent that the next contact from study staff would be at the 120-day follow-up time point to collect assessment data only **Comparator:** NA **Follow-up:** 12 months	% recovered, Schedule for Affective Disorders - Present and Lifetime (K-SADS-PL) The percent successful rate (no diagnosis according to K-SADS-PL) was higher for the treatment group than for the control group for 8 months (p=0.05) and 12 months (p=0.04) .

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Meyer, 2021[430] Uppsala County Council, 2016[1136] ID: ISRCTN17366720 RCT Multicenter N = 184 Sweden Setting: Specialty care	**Target:** Adolescents with ADHD; without severe depression, suicidality, psychosis, or bipolar disorder without stable medication, mental retardation, autism, current substance abuse **Other:** Parents reported some outcomes. **ADHD presentation:** inattentive : 25.6,combined : 70.7,N/A : Unspecified: 3.7 **Diagnosis:** Confirmation by specialist DSM V per Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID) **Comorbidity:** N/A **Female:** 63.9 % **Age mean:** SSTG 16.46 (0.88), control 16.71 (0.94) **Minimum age:** 15 **Maximum age:** 18 **Ethnicity:** N/A	**Intervention:** Dialectical behavioral therapy, age-adapted structured skills training group program, manualized consisting of 14 weekly 2-hour sessions where each session focused on a specific theme; the program includes elements of DBT, psychoeducation and strategies for managing difficulties related to ADHD; total of 14 weeks **Control:** NA **Comparator:** OtherManual-based psychoeducational group program of three 2-hour sessions focusing on psychoeducation about ADHD, including information about ADHD symptomatology, strengths and challenges with ADHD, sleep and diet; the participants also received a book descri **Follow-up:** 6 months	ASRS-A (ADHD Self-Report Scale for Adolescents) - Self-rating No group effect on patient or parent reported symptoms. Child Sheehan Disability Scale (CSDS), adolescent report No difference in effect on patient or parent report. No significant group differences regarding acceptability. No difference in effect on Quality of Life or Impact of ADHD Symptoms (IAS) on well-being. No difference in effect on Hospital Anxiety and Depression Scale (HADS).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Psychological or behavioral	Pelham, 2016[471] ID: ID NA Crossover trial Single center N = 152 US Setting: Mixed	**Target:** Children clinically diagnosed ADHD; should not have (1) IQ<70; (b) history of seizures or other neurological problems; (c) history of other medical problems; (d) childhood history or concurrent diagnosis of pervasive developmental disorder, schizophrenia or other psychotic disorders, sexual disorder, organic mental disorder, or eating disorder; (e) lack of functional impairment; and (f) placement in special education classrooms **Other:** Parents, teachers **ADHD presentation:** inattentive_other : mean score: Medication First: 7.6 (1.9); Behavioral First: 8.1 (1.5),hyperactive_other : mean score Hyperactivity/Impulsivity: Medication First: 7.1 (2.2); Behavioral First: 6.8 (2.1) **Diagnosis:** Confirmation by specialist DSM-IV by clinicians **Comorbidity:** N/A **Female:** 24 % **Age mean:** Medication first 8.3 (2), behavioral first 8.5(1.8) **Minimum age:** 5 **Maximum age:** 12 **Ethnicity:** % Black/African American : 12.3 % White : 80.1	**Intervention:** Behavioral first intervention, social skills training sessions for children, parenttraining (8 group sessions), and brief teacher consultation to establish a daily report card, report cards were sent home each day and parents provided rewards for good performance, monthly parent-training booster session for 8 weeks, case manager communicated with teacher monthly for 1 school year **Control:** NA **Comparator:** MedicationMedication first intervention, extended-release methylphenidate (equivalent to .15 mg/kg/dose bid) **Follow-up:** 4 months	Classroom rule violations The behavior management intervention exhibited significantly fewer classroom rule violations per hour than the comparator of medication intervention (incidence rate ratio 0.66, p<0.01). ADHD, Disruptive Behavior Disorders Rating Scale No difference between groups (effect size -0.01). Social Skills Total Score SSRS, parent There was no significant difference between groups for the Social Skills Total Score. 67% of the children who began treatment with behavioral interventions required additional treatment by the end of the school year compared with 47% of the children who began the school year receiving a low dose of medication (OR 2.23). Survival analyses indicated a significant group difference (p < .01).

Psychological or behavioral	Pfiffner, 2014[476] Tran, 2018[1120]; Haack, 2017[808]; Rooney, 2018[1013]; Adalio, 2018[652] ID: N/A RCT Multicenter N = 199 US Setting: Specialty care	**Target:** Children with ADHD-inattentive type and IQ > 80, living with at least one parent for the past year, attending school full time in a regular classroom **Other:** Parents received training and provided some outcomes **ADHD presentation:** inattentive : 100 **Diagnosis:** Confirmation by specialist DSM-IV diagnosis confirmed by the KSADS-PL by clinician **Comorbidity:** N/A **Female:** 42 % **Age mean:** 8.6 (1.2) **Minimum age:** 7 **Maximum age:** 11 **Ethnicity:** % Hispanic or Latino : 17 % Black/African American : 5.0 % Asian : 8.0 % White : 54.0 % Multiracial : 17.0	**Intervention:** Child Life and Attention Skills (CLAS) program included three manualized coordinated components: (a) ten 90-minute parent group meetings, along with up to six 30-minute family meetings (parent, child, and therapist); (b) ten 90-minute child group meetings; and (c) teacher consultation, which included one 30-minute orientation meeting involving the teacher and therapist and up to five subsequent 30-minute meetings with the parent, child, teacher, and therapist and booster sessions, treatment occurred over a 10- to 13-week period **Control:** TAU Treatment as usual did not receive either study intervention; families received a written diagnostic report based on the assessment conducted at baseline, a list of community treatment providers, but no specific treatment recommendations; families were o **Comparator:** BehavioralParent-focused treatment included parent training teaching parent skills but did not receive specific training in how to work with teachers and were not informed about the child skills taught in the CLAS condition; families received the same number of par **Follow-up:** 7 months	Clinical Global Impression (CGI) - I, parent report Intervention and comparator performed better than control. No group differences on teacher reported CGI-I. Inattentive symptoms CSI (Child Symptom Inventory), parent rating Responders (mean parent rated CSI inattention symptom severity score fell within 1 SD of norms) At follow-up according to parents, 63.0% of CLAS, 52.7% of PFT, and 36.2% of control were positive responders (p=0.016); the difference between CLAS and control was significant (p=0.004), but not between CLAS and PFT (p>.05). At follow-up according to tea IRS (Impairment Rating Scale) Teachers did not report differences across groups regarding overall impairment. Parent and teacher satisfaction Parent and teacher satisfaction with CLAS was very high; >95% of parents rated the child and parent skills taught as useful or very useful, 94% of teacher rated the classroom challenge as helpful or very helpful. Parent satisfaction with the comparator in

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Power, 2012[480] ID: N/A RCT Single center N = 199 US Setting: Specialty care	**Target:** Children meeting criteria for ADHD, Combined Type or ADHD, Inattentive Type who are enrolled in school and scored at or above 0.75 of a standard deviation above the mean on the Homework Problem Checklist; children scoring at or above an estimated IQ of 75 on the 2-subtest version of the Wechsler Abbreviated Scale of Intelligence **Other:** Parents, teachers **ADHD presentation:** inattentive : 51.8,combined : 48.3 **Diagnosis:** Confirmation by specialist Parent-report on the Schedule for Affective Disorders and Schizophrenia for School Age Children - DSM IV by clinician **Comorbidity:** Learning disability : homework problems,N/A **Female:** 32 % **Age mean:** Grade level (M and SD) 3.5 (1.2) **Minimum age:** 7 **Maximum age:** 10 **Ethnicity:** % Hispanic or Latino : 7.1 % Black/African American : 22.2 % Asian : 2.0 % White : 72.4 % Multiracial : 3.5	**Intervention:** Family-School Success, which included 6 groupsessions (90 minutes each), 4 individualized family sessions (60 minutes each), and 2 school-based consultations (45 minutes each), over the course of 12 weekly sessions **Control:** NA **Comparator:** BehavioralCoping with ADHD through Relationships and Education (CARE) included 11 group sessions and 1 family-school meeting, which were held on consecutive weeks. The initial session was conducted on a Saturday for 3 hours and subsequent meetings were 75 minutes (**Follow-up:** 3 months	SNAP-P (Swanson, Nolan, and Pelham Questionnaire), parent-report There was no intervention effect on ADHD and ODD symptoms, as assessed by parent and teacher ratings on the SNAP-IV. parent-rated Treatment Acceptability Questionnaire (TAQ) Tx acceptance significantly higher for intervention (p = .006). Academic Performance Rating Scale (APRS) Group had no effect on improvement.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Qian, 2021[485] ZIli Fan, 2016[1191] ID: NCT02656758 Crossover trial Unclear/Not reported N = 70 China Setting: Specialty care	**Target:** Children with ADHD who received initial training approximately 14 ± 7 months before the current study; no history of head injury; no diagnosis of other congenital or acquired neurological conditions; estimated full-scale IQ>=80; no diagnosis of autism spectrum disorders, psychosis, or an emergent psychiatric condition that needed immediate medication **Other:** Parents **ADHD presentation:** inattentive : 51.43,hyperactive : 4.29,combined : 44.29 **Diagnosis:** Confirmation by specialist DSM-IV criteria based on parent ratings of the ADHD-rating scale-IV and was then confirmed by a semi-structured interview conducted by experienced pediatric psychiatrists using the clinical diagnostic interview scale. **Comorbidity:** N/A **Female:** 23 % **Age mean:** 9.24 (1.04) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:**	**Intervention:** Ecological executive skills training which includes child training program and parent self-help group, multiple-family role-play component, and behavior parent training group, each session lasting 120 minutes, consisted of 12 weekly sessions **Control:** Wait list 12-week waitlist, after which group received intervention **Comparator:** NA **Follow-up:** 3 months	ADHD-RS-IV (ADHD Rating Scale IV) scores Intervention group improved more (group x time p = 0.004). Same for inattention (p =0.007) and hyperactivity (p = 0.020) subscales. WEISS Function Impairment Scale-Parent report, total There was no significant difference between groups. Behavior Rating Scales of Executive Function (BRIEF) : no effect of group on any subscales.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Schramm, 2016[521] ID: NA RCT Single center N = 113 Germany Setting: Specialty care	**Target:** Participants with ADHD and not meeting the criteria for severe comorbid disorders **Other:** **ADHD presentation:** **Diagnosis:** Confirmation by specialist DSM-IV-TR by dministered by a clinical psychologist under supervision of a board-certified child and adolescent psychotherapist **Comorbidity:** N/A **Female:** 15 % **Age mean:** 13.99 (1.44) **Minimum age:** 12 **Maximum age:** 17 **Ethnicity:** N/A : Germans	**Intervention:** Learning Skills Training for Adolescents With ADHD, manualized, multimodal intervention combining an adolescent-direct training approach (maximum of 20 sessions of 60 mins each) with a behavioral training component in methods of contingency management for parents and teachers (3 sessions of 90 mins each) for average duration of 6 months **Control:** Wait list Waiting list controls were invited twice for data collection with an average interval of 5.76 (SD 1.65) months in between and expected to start intervention after post-measurement **Comparator:** OtherProgressive muscle relaxation training, adolescents met in groups of 4-5 twice-weekly for 12–15 sessions (60 mins) and were trained by 2 BA-level students followed by playtime; the students did not mention or talk about ADHD or related problems with the a **Follow-up:** 6 months	Inattention, FBB-HKS (Fremdbeurteilungsbogen für Hyperkinetische Störungen), parent report The training significantly reduced ADHS symptoms and parent- and teacher-rated internalizing problems and increased teacher rated academic enablers compared to waiting list controls. The training significantly reduced parent- and teacher-rated internalizing problems and increased teacher rated academic enablers compared to waiting list controls.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Schuck, 2018[522] Schuck, 2018[1027] ID: NA RCT Single center N = 88 US Setting: Community	**Target:** Children with ADHD Combined Type **Other:** Parents **ADHD presentation:** combined : 100 **Diagnosis:** Confirmation by specialist DSM-IV confirmed by Kaufman-Schedule for Affective Disorders and Schizophrenia for School-Age Children: Present and Lifetime Version (K-SADS-PL) **Comorbidity:** N/A **Female:** 28.5 % **Age mean:** 7.65 (0.75) **Minimum age:** 7 **Maximum age:** 9 **Ethnicity:** % Hispanic or Latino : 29.5 % Black/African American : 1.5 % Asian : 12.5 % Native Hawaiian or Pacific Islander : 1.5 % White : 62 % Multiracial : 20.5	**Intervention:** Canine assisted psychosocial intervention, weekly 2-hour sessions for 12 weeks **Control:** Wait list Wait list condition **Comparator:** BehavioralBehavioral parent training plus social skills training, parents participated in 12 weekly 2-hour sessions of group Behavioral Parent Training emphasizing positive reinforcement strategies and nonphysical discipline **Follow-up:** 3 months	Social Skills Improvement System (SSIS) Problem Behaviors scale A significant interaction of group by time (p 0.002) was found at treatment completion for problem behaviors. ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale, 4th Edition) total score, parent report Ratings were significantly lower in the intervention group than control group but the difference was borderline significant (p 0.06). Self esteem was measured by the Self-Perception Profile for Children and children's self-perceptions in the domains of behavioral conduct, social, and scholastic competence, were significantly increased from baseline to post-treatment in intervention group (p 0.021, p 0.008, and p 0.011) while the control group did not experience significant increases. Participants with adverse events There were no adverse events across seven cohorts of treatment.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Sciberras, 2020[523] Murdoch Childrens Research Institute (MCRI) (Australia), 2010[946]; Hiscock, 2015[834]; Sciberras, 2010[1029] ID: ISRCTN68819261 RCT Multicenter N = 244 Australia Setting: Mixed	**Target:** Children with ADHD and behavioral sleep disorder or experiencing significant bedtime anxiety leading to insomnia, parents needed to rate as moderate/severe sleep problem **Other:** Parents **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** Sleep **Female:** 14.7 % **Age mean:** 10.1 (2.0) **Minimum age:** 5 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Sleep intervention for family, 2 face to face, fortnightly consultations about sleep witha trained clinician; clinician assessed the child's sleep problem, elicited parent goals for sleep management, provided information about normal sleep, sleep cycles, and sleep hygiene strategies, and formulated a behavioral sleep management plan tailored to the child's sleep problem; parents were asked to complete a sleep diary; the second consultation and a follow-up telephone call were used to review the sleep diary, reinforce suggested strategies, and troubleshoot any problems; total duration of 4 weeks **Control:** TAU Families allocated to 'usual care' accessed care from their child's pediatrician, which does not usually involve the assessment and treatment of sleep problems **Comparator:** NA **Follow-up:** 12 months	Strengths & Difficulties Questionnaire (SDQ) conduct problems, teacher report No difference in improvement in conduct reported by parent (p 0 .17) or teacher (p 0 .11) adjusted for confounding variables. ADHD-RS-IV (ADHD rating scale IV), total score, parent Intervention group improved more on parent rating (p = .001) but not teacher rating (p = 0.91). Daily Parent Rating of Evening and Morning Behavior (DPREMB) The intervention group improved more than control group (p = .001). Child sleep habits questionnaire—total score: Intervention group improved more than control (p < .02).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Shuai, 2020[530] Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, 2018[1181] ID: NCT03515135 RCT Unclear/Not reported N = 96 China Setting: N/A	**Target:** Native Chinese speaking preschool children with DSM-V diagnosed ADHD, no major sensory-motor disorders, no history of brain damage, epilepsy, no diagnosis of autism spectrum disorder, no IQ score <80, and no pharmacological or nonpharmacological treatment **Other:** Parents **ADHD presentation:** inattentive : 8.3,hyperactive : 19.8,combined : 71.9 **Diagnosis:** Confirmation by specialist Parents of the children were interviewed by two independent psychiatrists to confirm DSM-V diagnosed ADHD **Comorbidity:** N/A **Female:** 18.75 % **Age mean:** Intervention group age mean in months (61.78) and SD (6.67). Waitlist group age mean in months (59.09) and SD (6.62). **Minimum age:** 4 **Maximum age:** 5 **Ethnicity:** Other : Presumably 100% Chinese	**Intervention:** Psychotherapy (Executive Function Training for Preschool), structured program, 90-min sessions (60-min for children, 30-min for parents), sessions contain 4 parts: tasks and games aiming to practice executive function (40min), paper-pencil tasks (15min), relaxation (5 min) for children; parents received session on guiding their child (30 min); sessions once a week for 8 weeks **Control:** Wait list Put on waitlist and received treatment as usual **Comparator:** NA **Follow-up:** 2 months	SNAP-IV (Swanson, Nolan, and Pelham Rating Scale Chinese version) The intervention group had significnatly reduced ODD symptoms compared to control group (p=.02), but differences in inattention scores were not significant (p=0.24). Differences in BRIEF-P scores between intervention group and control group were not significant (p=0.47).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Sibley, 2016[533] ID: NA RCT Multicenter N = 128 US Setting: School	**Target:** Children with ADHD with significant academic impairment and without autism spectrum disorder **Other:** Parents were involved in intervention and supplied some outcome data **ADHD presentation:** inattentive : 39.1,combined : 60.9 **Diagnosis:** Confirmation by specialist Phone screen containing the DSM-IV-TR ADHD symptoms and questions about impairment was administered to the primary caretaker. Then in person parent structured interview (Computerized-Diagnostic Interview Schedule for Children) and symptom assessment con **Comorbidity:** N/A **Female:** 35.2 % **Age mean:** 12.7 (0.86) **Minimum age:** 11 **Maximum age:** 15 **Ethnicity:** % Hispanic or Latino : 78.5 % Black/African American : 10.8 % White : 7.7	**Intervention:** Supporting Teens' Academic Needs Daily (STAND) consists of ten 50-minute manualized family therapy sessions attended by the parent and teen, uses motivational interviewing, for a total of 10 weeks **Control:** TAU Treatment as usual, without intervention **Comparator:** NA **Follow-up:** 6 months	Disruptive behavior, parent report Group by time effects were nonsignificant (p=0.343). ADHD Symptom Severity, Disruptive Behavior Disorder Rating Scale (DBD), parent report The intervention group improved compared to the control group (p < .001). Cumulative GPA There were no significant differences between intervention and comparator group (p=0.265).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Sibley, 2020[534] Sibley, 2016[1067] ID: NA RCT Unclear/Not reported N = 123 US Setting: School	**Target:** Adolescents with ADHD, without any history of autism, intellectual disability or IQ<70 **Other:** Parents provided outcome data **ADHD presentation:** inattentive_other : Dyadic, 49.2% / Parent-Teen Group, 58.3%,combined_other : Dyadic, Parent-Teen 50.8% / Group, 41.7% **Diagnosis:** Confirmation by specialist DSM 5 via Diagnostic Interview Schedule for Children **Comorbidity:** N/A **Female:** 19.6 % **Age mean:** Dydactic 13.63 (1.49), Parent-teen group 13.59 (1.78) **Minimum age:** 11 **Maximum age:** 17 **Ethnicity:** Other : Dyadic, 85.7% / Parent-Teen Group, 85% Other : Dyadic, 4.8% / Parent-Teen Group, 5% Other : Dyadic, 7.9% / Parent-Teen Group, 8.3%	**Intervention:** Supporting Teens' Autonomy Daily (STAND), manualized parent-teen dyadic, ten 60-minweekly sessions attended by the participant and a parent, skill instruction blended with motivational interviewing and parent-teen behavioral contracting, for total 10 weeks **Control:** NA **Comparator:** BehavioralGroup Supporting Teens' Autonomy Daily (STAND), manualized, eight 90-min weekly group sessions, teens and parents meet in separate groups for the first 75 minutes and meet for the final 15 minutes **Follow-up:** 6 months	ADHD symptoms inattention, parent rating No difference in parent reported inattention (p = 0.61) or hyperactivity (p=0.37) scores. No difference in teacher reported inattention (p = 0.07) or hyperactivity (p= 0.50) scores. Organization, time management, and planning impairment, skills applied to homework, school, and chores, parent report There was no difference across groups in either parent (p=0.84) or teacher (p=0.23) reported. Teen treatment satisfaction No significant differences in treatment satisfaction (p = 0.81) or percentage of treatment attended (p=0.16). Grade Point Average (GPA) No difference between groups (p = 0.50).

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Psychological or behavioral	Sibley, 2021[532] Bickman, 2021[1062]; Florida International University, 2016[777] ID: NCT02694939 RCT Multicenter N = 278 US Setting: Community	**Target:** Adolescents with ADHD; without diagnosis of autism spectrum disorder or intellectual disability **Other:** Parents involved in intervention. Parents & teachers provided some outcomes **ADHD presentation:** inattentive : 52.2,combined : 47.8 **Diagnosis:** Confirmation by specialist DSM-5 **Comorbidity:** N/A **Female:** 29.5 % STAND 29.7, usual care 29.3 **Age mean:** 13.97 (1.51) and 14.08 (1.50) **Minimum age:** 11 **Maximum age:** 17 **Ethnicity:** % Hispanic or Latino : 81.7 % Black/African American : 13.3 % White : 4.7 % Multiracial : 0.7	**Intervention:** Supporting Teens' Autonomy Daily (STAND) consisting of weekly 60-minute motivationalinterviewing-enhanced behavior therapy sessions attended by dyads of teens and parents for 10 weeks **Control:** No intervention No intervention, controls continued with any already existing treatment as usual **Comparator:** NA **Follow-up:** 9.8 months	Number of disciplinary incidents No difference in number of disciplinary incidents (p 0.063). Inattention, DSM score, parent report No difference in parent rated inattention score (p = .162), teacher rated inattention score (p = .6340, parent rated hyperactivity score (p = .272), or teacher rated hyperactivity score (p = .801). Satisfaction with treatment No group differences in adolescent satisfaction. Grade Point Average (GPA) No difference (p = .904).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Siebelink, 2021[535] Karakter Kinder en Jeugdpsychiatrie, 2017[873]; Siebelink, 2018[1071] ID: NCT03220308 RCT Single center N = 103 Netherlands Setting: Mixed	**Target:** Dutch-speaking children and adolescents with ADHD; could use ADHD medication if stable dose was reached two weeks prior to study; no current psychosis, bipolar illness, active suicidality, untreated post-traumatic stress disorder or substance use disorder; no IQ<80 **Other:** Parents **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-4 or DSM-5 confirmed with a structured interview conducted by trained researchers **Comorbidity:** N/A **Female:** 30 % **Age mean:** Intervention 11.0 (1.8), control 11.4 (1.8) **Minimum age:** 8 **Maximum age:** 16 **Ethnicity:** N/A	**Intervention:** Mindfulness-based intervention for family, weekly 90-minute group sessions, followedby a booster session 8 weeks later, homework of approximately 30–45 min/day for parents and 15 min/day for children, also received care-as-usual, for 8 weeks **Control:** TAU Care-as-usual only **Comparator:** NA **Follow-up:** 8 months	Oppositional behavior scale, Conners Parent Rating Scale (CPRS) No difference between groups. Hyperactivity-impulsivity, SWAN (Strengths and Weaknesses of ADHD symptoms and Normal behaviour) parent-rated Parent-rated hyperactivity-impulsivity group differences were larger and significant in favor of intervention group (p<.05). Difference in parent-rated inattentiveness not significant. No differences in teacher reported hyperactivity-impulsivity or inatte No difference in parent-rated self-control deficits measured using 75-item Behaviour Rating Inventory of Executive Function-Adult Version (BRIEF). No CAU- or MBI-related Serious Adverse Events were spontaneously reported by the participants or mindfulness teachers.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Storebo, 2012[565] Storebo, 2011[997]; Storebo, 2011[1089] ID: NCT00937469 RCT Single center N = 56 Netherlands Setting: Specialty care	**Target:** ADHD diagnosis according to DSM, without schizophrenia or autism, no violent and criminal children, IQ of 80 or above, without having previously taken medication for ADHD **Other:** **ADHD presentation:** inattentive : 29.1,hyperactive : 3.9,combined : 58 **Diagnosis:** Confirmation by specialist DSM-IV by psychologists from the Clinic **Comorbidity:** N/A **Female:** 30 % **Age mean:** 10.4 (1.31) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** N/A	**Intervention:** Social skills training offered weekly, 90 minute sessions, in additionto standard treatment that encompassed offer of medical treatment for the child following a medication protocol, treatment started with the first choice: methylphenidate; the second choice: dexamphetamine; and atomoxetine was considered in patients where there was a suspicion of abuse of dexamphetamine or a significant anxiety component change; standard treatment involved an educational parent group, where the parents met 3 times during the 8 week trial and received general information about ADHD, duration of 8 weeks **Control:** TAU Standard treatment encompassed family was offered medical treatment for the child following a medication protocol, treatment started with the first choice: methylphenidate; the second choice: dexamphetamine; and atomoxetine was considered in patients wher **Comparator:** NA **Follow-up:** 6 months	Hyperactivity-impulsivity subindex Conner's 3rd Edition Rating Scale Social skills training plus parental training did not show any significant benefit for children with attention deficit hyperactivity disorder when compared with standard treatment. Academic performance based on Conners-3 and CBRS No difference between groups. Participants with adverse events No adverse events were observed.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Psychological or behavioral	Valero, 2021[594] ID: NA RCT Unclear/Not reported N = 30 Spain Setting: Community	**Target:** Children with ADHD **Other:** Parents also received mindfulness training **ADHD presentation:** inattentive : 30,hyperactive : 13,combined : 57 **Diagnosis:** Confirmation by specialist Diagnosis had to be performed by a specialist—psychologist, neuro-pediatrician, or psychiatrist—at least 2years prior to participation. ADHD confirmed by parent version of Conners—3rd Edition **Comorbidity:** N/A **Female:** 23.3 % **Age mean:** 10.6 (1.69) **Minimum age:** 9 **Maximum age:** 14 **Ethnicity:** N/A	**Intervention:** Mindfulness training, children's sessions were1 hour long, parent sessions were1.5 hours, 8 sessions over 8 weeks **Control:** Wait list Wait list **Comparator:** NA **Follow-up:** 6 months	Conners—3rd Edition, aggressive behavior scale Intervention group had less aggression at follow-up (p = .045). Inattention score, Conner's Version 3, parent report At follow-up, intervention group showed less inattention compared to the wait-list group (p=.0324). There was no difference in hyperactivity/impulsivity score p = (.103). Conners Version 3, parent report, executive function, intervention group had better executive function (p=.002).

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Wilkes-Gillan, 2016[624] Barnes, 2017[676] ID: ACTRN12614000973617 Crossover trial Single center N = 31 Australia Setting: Mixed	**Target:** Children with ADHD with co-morbid difficulties; no other major developmental disorders **Other:** Parents, plus a "typical" friend of each child **ADHD presentation:** inattentive : 38,hyperactive : 3,combined : 59 **Diagnosis:** Confirmation by specialist DSM-IV by pediatrician or psychiatrist **Comorbidity:** Learning disability **Female:** 13 % **Age mean:** 8.4 (1.6) **Minimum age:** 5 **Maximum age:** 11 **Ethnicity:** N/A	**Intervention:** Play-based intervention, 1-hour sessions for 10 weeks **Control:** Wait list No treatment for 10 weeks, after which the group crossed over to the 10-week play-based intervention. Outcomes reported pre-crossover. **Comparator:** NA **Follow-up:** 2.5 months	The change in play scores for the intervention-first group was significantly greater than the change in the control-first group during their 10 week wait period (p < .001). One year follow up did not have adequate power.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Psychological or behavioral	Zhu, 2022[643] ID: ID NA RCT Single center N = 120 China Setting: N/A	**Target:** Children with ADHD, not on medication, without co-occurring psycological or medical problems **Other:** Parents provided some outcomes **ADHD presentation:** inattentive : 33.3,hyperactive : 27.5,combined : 37.5 **Diagnosis:** Confirmation by specialist DSM IV **Comorbidity:** N/A **Female:** 34.2 % **Age mean:** 4.28 (0.38) **Minimum age:** 2 **Maximum age:** 7 **Ethnicity:** % Asian : 100	**Intervention:** Musicotherapy combined with cognitive behavioral intervention: behavioral intervention provided basic attention training in the auditory and visual senses, 5 times every week, 60 minutes per session, while musicotherapy was provided once per weeks to groups of 5 children, for 16 weeks **Control:** Wait list Intervention provided after completion of the study **Comparator:** NA **Follow-up:** 4 months	ADHD RS IV, total score, parent report Intervention group improved more (p<0.05). Numerical cross-attention test: Intervention group improved more than control group (p<0.05).

Teacher, school environment	Breaux, 2018[163] Langberg, 2018[893]; Smith, 2020[1078]; Breaux, 2019[694] ID: ID NA RCT Multicenter N = 222 US Setting: School	**Target:** Children with ADHD; intelligence quotient of 80 or above; no pervasive developmental disorder, bipolar disorder, or psychosis **Other:** School mental health professionals, parents of children with ADHD, teachers of children with ADHD **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV-TR per psychologist **Comorbidity:** N/A **Female:** 28 % **Age mean:** 12.00 (1.02) **Minimum age:** **Maximum age:** **Ethnicity:** % Hispanic or Latino : 9 % Black/African American : 28 % White : 56 % Multiracial : 12 Other : 4% other/did not report	**Intervention:** Homework, Organization, and Planning Skills (HOPS) is skills-based treatment that focuses on teaching organization and planning skills that are important for homework completion; 2 parent/family meetings focused on promoting generalization; 16 sessions delivered during the school day; sessions conducted with individual students; first 10 sessions occurred twice weekly and final 6 sessions occurred once per week; also two 1-hour sessions with provider and family, families left first session with formal written monitoring and behavior rewarding plan, for 11 weeks **Control:** Wait list Wait list **Comparator:** Teacher, school environmentCompleting Homework by Improving Efficiency and Focus (CHIEF) is contingency management-based treatment, 16 sessions delivered during the school day, first 10 sessions occurred twice weekly and final 6 sessions occurred once per week, also included two 1- **Follow-up:** 6 months	Parent satisfaction, 5 point Likert scale No significant difference between groups. Grade Point Average (GPA) No difference among groups (p 0.236).
Teacher, school environment	Corkum, 2019[208] Dalhousie University, 2012[730] ID: NCT01547702 RCT Multicenter N = 58	**Target:** Children with ADHD; on a stable dose of medication for ADHD or was taking no medication, with no plan to start or change medications for the duration of the study; no Individualized Program Plan due to significant physical, behavioral, communication, or intellectual difficulties; no significant co-occurring mental health problems aside	**Intervention:** Teachers given weekly online sessions, session covered a different topicrelated to education, treatment, support and additional interventions, for total of 6 weeks **Control:** Wait list	ADHD Index Conners 3-T Significant improvements based on teacher (but not parent) reports of core ADHD symptoms. Impairment ratings score, teacher Significant improvement associated with the intervention.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
	Canada Setting: School	from ADHD; no moderate or severe intellectual impairment; no previous involvement with the Teacher Help for ADHD program **Other:** Teachers of students with ADHD **ADHD presentation:** N/A **Diagnosis:** No doesn't indicate confirmation, but does indicate that participants were previously diagnosed by a certified health care provider **Comorbidity:** N/A **Female:** 12 % **Age mean:** 8.83 (1.72) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % White : 90 Other : 10% non-caucasian	Waitlist group did not receive any intervention but were free to access usual care. Waitlist lasted 12 weeks **Comparator:** NA **Follow-up:** 6 months	Teacher intervention satisfaction (content presented was easy to understand) Rated 5.28 90.84) on a 6-point scale

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Teacher, school environment	DuPaul, 2021[238] Ohio University, 2020[970] ID: NCT04480346 RCT Multicenter N = 186 US Setting: School	**Target:** Adolescents with ADHD in school for at least half the day, an IQ of 75 for above, and not diagnosed with psychosis, bipolar, or obsessive compulsive disorder **Other:** Parents and teacher provided some outcome data **ADHD presentation:** inattentive,combined : 50 **Diagnosis:** Confirmation by specialist diagnostic criteria for at leastADHD based on the Parent-Children's Interview for Psychiatric Syndromes (P-ChIPS) **Comorbidity:** N/A **Female:** 20 % **Age mean:** 15 (0.8) Grades 9 through 11 **Minimum age:** **Maximum age:** **Ethnicity:** % Hispanic or Latino : 10.2 % Black/African American : 14.5 % Asian : 1.0 % White : 74 Other : Other 4.8%	**Intervention:** Multi-component training interventions: individual coaching sessions for 15–20 mintwice per week, at least monthly collaborative problem-solving between the teen and coach, ten 90-min evening group sessions at their school offered separately for adolescents and parents, duration of the academic year **Control:** TAU Community care, given a list of available resources in their community, including locally available providers of child and family psychosocial and pharmacological interventions. Participants in both groups were informed that they could continue with any s **Comparator:** NA **Follow-up:** 6 months	Tardiness frequency There was no statistically significant Group (p=0.75) or Time (p=0.96) effect for school tardiness. Adolescent Academic Problems Checklist Total The intervention group had significantly fewer academic problems compared to the comparator group (p<0.01). Children's Organization Skills Scale Task Planning showed steeper negative slopes (i.e., more improvement over time) for intervention participants than those in the community care condition.

Teacher, school environment	Evans, 2016[259] Langberg, 2016[894]; Schultz, 2017[1028] ID: ID NA RCT Multicenter N = 326 US Setting: School	**Target:** Children had to attend one of the participating schools, met full DSM–IV–TR diagnostic criteria for either ADHD–Predominantly Inattentive Type or ADHD–Combined Type ADHD based on the Parent Children's Interview for Psychiatric Syndromes or combined with teacher ratings on the Disruptive Behavior Disorders Rating Scale, demonstrated impairment based on parent or teacher report on the Impairment Rating Scale, IQ of 80 or above, did not meet diagnostic criteria for a pervasive developmental disorder or bipolar disorder, psychosis, or obsessive–compulsive disorder **Other:** Parents and teachers provided data **ADHD presentation:** combined : 49 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 29 % **Age mean:** 12.1 (1.0) 6th grade to 8th grade **Minimum age:** **Maximum age:** **Ethnicity:** % Hispanic or Latino : 3 % Black/African American : 12 % White : 70 % Multiracial : 8	**Intervention:** Challenging Horizons Program–after school version (CHP-AS): 2 days per week for 2 hr 15 min per day for 9 months **Control:** TAU Community care condition received a list of available resources in their community at the start of the school year; resource lists were developed in collaboration with school staff to include locally available child and family psychosocial and pharmacolog **Comparator:** Teacher, school environmentChallenging Horizons Program–mentoring version provided by a teacher or other staff member in their school (mentor); mentor participation was voluntary, and mentors received a small stipend ($100) for participation. Mentors agreed to meet weekly with thei **Follow-up:** 18 months	Inattention and hyperactivity/impulsivity scale, Disruptive Behavior Disorders (DBD) Rating Scale Challenging Horizons Program after school version is associated with moderate effect size improvements in ADHD symptoms of inattention but not hyperactive/impulsive symptoms. IRS (Impairment Rating Scale), relation with peers scale, teacher There were no significant differences between groups. Classroom Performance Survey (CPS), Academic factor, teacher There were no significant differences between groups. Intervention group performed better than mentoring group (p = .0011) and better than community care (p = 0007). Similar results for COSS materials management scale (p=.0430 vs mentoring, p=0 .0010 vs community care).
Teacher, school environment	Mikami, 2013[433] ID: ID NA RCT Single center N = 24 US Setting: School	**Target:** Children with ADHD who recently completed grade 1, 2, or 3, with "peer impairment" and fewer than 50% of peers rated as liking them **Other:** 113 neurotypical children participated in programs; teachers received intervention training and provided some outcomes	**Intervention:** Contingency Management (COMET) plus Making Socially-Accepting Inclusive Classrooms (MOSAIC), to reduce exclusionary and increase positive peer behavior, MOSAIC teachers set explicit classroom rules for social inclusion, while teachers modeled for peers that children	Problem behaviors, Teacher-Child Rating Scale No main effects for treatment condition on Teacher Rating Scale for internalizing behavior, hyperactivity, inattention, or oppositional behavior, nor on observations of off-task behavior or aggressive/noncompliant behavior.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
		ADHD presentation: inattentive : 25,hyperactive : 0,combined : 75 **Diagnosis:** Confirmation by specialist DSM IV via Kiddie Schedule for Affective Disorders and Schizophrenia **Comorbidity:** ODD : half had ODD **Female:** 45.8 % **Age mean:** 8.15 (0.79) **Minimum age:** 6.8 **Maximum age:** 9.8 **Ethnicity:** % Hispanic or Latino : 2 % Black/African American : 3 % Asian : 6 % White : 81 % Multiracial : 8	with ADHD were worthy of liking by developing positive relationships with children through warm, one-on-one interactions to discuss the child's personal interests; contingency management worked by providing children with specific expectations for desired behavior whereby children gained and lost points based on their compliance; to minimize social comparisons between children based on points, MOSAIC teachers provided corrections about behavior privately by calling the child aside when feasible; 4-week program (one component for 2 weeks only) **Control:** Other Contingency management (COMET) alone: teachers provided children with specific expectations for desired behavior whereby children gained and lost points based on their compliance, children needing extra assistance had specialized behavior plans where addi **Comparator:** NA **Follow-up:** 1 month	Children with ADHD displayed improved sociometric preference and more reciprocated friendships, and received more positive messages from peers, when they were in MOSAIC relative to in COMET

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Teacher, school environment	Shen, 2021[529] School of Public Health, 2018[1026] ID: ChiCTR1800014945 Cluster RCT Multicenter N = 232 China Setting: School	**Target:** Children with ADHD; without intellectual disability (IQ <70). autistic spectrum disorder, epilepsy, schizophrenia, cerebral palsy and other nervous system diseases and mental disorders, severe heart, brain, kidney, and other organ dysfunction **Other:** Teachers and parents received training **ADHD presentation:** inattentive : 40.2,hyperactive : 28.9,combined : 30.9 **Diagnosis:** Confirmation by specialist DSM 5 **Comorbidity:** N/A **Female:** 14.2 % **Age mean:** Intervention 7.71 (1.22) Control 8.39 (1.38) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Asian : 100	**Intervention:** Primary school-based multimodal treatment for teachers and parents; 2 teacher training meetings (1 2-hrsessionand 1 30-min session), 2 group parent trainings sessions (4.5-hrs) and 2 individualized family therapy sessions (2hrs), participants also received stimulant medication prescribed by their pediatricians, for 16 weeks **Control:** TAU Stimulant medication prescribed by pediatricians referring to the clinical practice guidelines for ADHD children published by the American Academy of Pediatrics **Comparator:** NA **Follow-up:** 4 months	SNAP-IV (Swanson Nolan and Pelham version 4) Intervention group had significantly greater improvement than control group ($p < 0.05$) Treatment Acceptability Questionnaire (TAQ) scale 64.8% of the parents in the intervention group indicated that this treatment would help their children. Academic Performance Questionnaire (APQ) change There was no significant time by group effect ($p > 0.05$). Parental stress measured with the PSI improved in both groups. "There were no serious adverse events and adverse events reported."

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Teacher, school environment	Sibley, 2018[531] Sibley, 2020[1065]; Sibley, 2019[1063] ID: NA RCT Single center N = 325 US Setting: School	**Target:** Children with ADHD that meets DSM IV criteria, displaying significant academic impairment (at least a 3 on a 0–6 teacher Impairment Rating Scale), without autism spectrum disorder **Other:** Parents and teachers provided data **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist ADHD diagnosis was confirmed through a combination of parent structured interview (Computerized-Diagnostic Interview Schedule for Children; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000) and parent and teacher symptom and impairment ratings. Clinic **Comorbidity:** N/A **Female:** 25.8 % **Age mean:** Rising 6th & 9th graders **Minimum age:** **Maximum age:** **Ethnicity:** % Hispanic or Latino : 72.7 % Black/African American : 17.4	**Intervention:** Summer program between transitions from middle to highschool, 8-week intensive summer program from 8-5 pm on weekdays (45 hrper week), alternated between 30- and 50-min small- and large-group modules, parent training once per week for 1.5 hours, for 8 weeks **Control:** No intervention No intervention **Comparator:** Teacher, school environmentSummer program, low intensity, organization skills group 1.5 hr per week; also parent training once per week for 1.5 hours, for 8 weeks **Follow-up:** 12 months	School Disciplinary Incidents There were no significant group by time interaction effects for school disciplinary incidents. Inattention severity, Disruptive Behavior Disorder Rating Scale, parent There were no significant Group by Time interaction effects between the groups. Satisfaction with treatment Both groups reported high overall satisfaction that did not significantly differ between groups. Grade Point Average (GPA), 9th Grade Ninth-grade intervention youth showed smaller reductions in GPA over time than ninth-grade control youth. There were no GPA effects for sixth graders.

Intervention	**Study:** Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-Up	**Outcome and Results**
Teacher, school environment	Tamm, 2017[577] ID: NA RCT Multicenter N = 216 US Setting: Mixed	**Target:** Children with ADHD and word reading/decoding deficits **Other:** Parents **ADHD presentation:** combined : 54.6,N/A : sample included also inattentive and hyperactive presentations **Diagnosis:** Confirmation by specialist **Comorbidity:** Learning disability : Word-level reading difficulties or disabilities **Female:** 38.9 % **Age mean:** 8.8 (1.3) Grades 2 through 5 **Minimum age:** **Maximum age:** **Ethnicity:** % Hispanic or Latino : 12.0 % Black/African American : 72.2 % Multiracial : 6.5	**Intervention:** Reading training by teachers plus medication plus parent training; 9 parent group sessions, each 1.5 hours, over 10 weeks, low dose extended release methylphenidate, atomoxetine or extended release guanfacine could be used if MPH not tolerated, reading treatment provided by teachers to one or two students at a time for 45 minutes, four days per week for 16 weeks **Control:** Other Parent training plus medication; parent training in behavior management, 9 group sessions conducted by clinical psychologists, each 1.5 hours, over 10 weeks; medication: open label, typically beginning with low dose extended release methylphenidate; at **Comparator:** NA **Follow-up:** 5 months	Inattention scale, SNAP-IV, parent rating The medication plus parent training group ($p<.012$) and combined ($p<.001$) treatment groups were rated as significantly less inattentive than the reading treatment alone group, but did not significantly differ from one another ($p=.058$). The medication plu Wechsler Individual Achievement Test, Word Reading score: the reading ($p<0.001$) and combined ($p<0.001$) treatment groups had higher phonemic decoding scores than the medication plus parent training group but did not differ from one another (p 0.65). There were not significant differences between groups on word reading at follow-up.

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Teacher, school environment	Volpe, 2009[602] Jitendra, 2007[866] ID: NA RCT Multicenter N = 167 US Setting: School	**Target:** Children with ADHD who were experiencing achievement problems in either math or reading **Other:** Teachers conducted intervention **ADHD presentation:** combined : 65.0,N/A : sample included inattentive and hyperactive presentations **Diagnosis:** Confirmation by specialist Parent and teacher ratings on the ADHD Rating Scale IV and NIMH diagnostic interview scale for children IV **Comorbidity:** Learning disability : Problems with either math or reading **Female:** 24.0 % **Age mean:** 8.7 (1.23) **Minimum age:** **Maximum age:** **Ethnicity:** % Hispanic or Latino : 26.9 % Black/African American : 11.4 % White : 58.0	**Intervention:** Intensive data-based academic intervention involves ongoing feedback to teachers from consultants, individual interventions are selected based on functional and academic assessment data for 15 months **Control:** NA **Comparator:** Teacher, school environmentTraditional data-based academic intervention, design of intervention based on teacher choice **Follow-up:** 12 months	Woodcock-Johnson III tests of achievement, standardized math fluency score No differences between groups on Woodcock-Johnson tests of achievement, Curriculum based measurement (CBM) scores, Academic Competency Evaluation Scale (ACES), or Report Card grades

Intervention	Study: Author, Year; Multiple Publications; Trial ID; Study Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Comorbidity; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-Up	Outcome and Results
Teacher, school environment	Zheng, 2020[640] ID: ID NA Cluster RCT Multicenter N = 219 China Setting: School	**Target:** Children with ADHD, IQ ≥70, and no prior ADHD medication use; no comorbidity with autism spectrum disorder, schizophrenia, epilepsy, head injury, verified neurological disorder, or sensory retardation (hearing/vision problems) **Other:** Parents, teachers **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-5 **Comorbidity:** N/A **Female:** 15.2 % **Age mean:** Intervention group mean age 7.93 (1.38); Control group mean age 7.21 (1.22) **Minimum age:** 6 **Maximum age:** 11 **Ethnicity:** % Asian : 100	**Intervention:** School-based teacher and parent training, teacher training was 4 weekly 2-hour sessions consisting of knowledge about ADHD, behavioral strategies to manage conduct problems, classroom behavior management, teaching how to use scaffolding to promote the development of self-regulation in children with ADHD, parent training 4 weekly 2-hour sessions addressing knowledge about ADHD, medication, behavioral strategies, how to combine procedures and behavior management techniques; medication given was either methylphenidate or atomoxetine; for 4 weeks **Control:** Other Methylphenidate or atomoxetine alone **Comparator:** NA **Follow-up:** 6 months	SNAP-IV (Chinese Version, Swanson Nolan and Pelham, Version IV) Difference in score change was statistically significant (p 0.009), favoring intervention Medication adherence was significantly higher ($p < 0.01$) in the intervention group.

Notes: ADHD = attention deficit hyperactivity disorder; N/A = not available

Table C.3. KQ3 evidence table

Study: Author, Year; Multiple Publications; Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Co-Occurring Disorders; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Intervention**	**Results**
Cedergren, 2021[173] Göteborg University, 2017[796] ID: NCT03250013 Pre-post study Single center N = 78 Sweden Setting: Specialty care	**Target:** Participants between the ages of 6-18; ADHD diagnosis meets DSM-V criteria; IQ > 70; excluded if participant physically/psychologically unable to complete monitoring test, has cardiovascular disease, seizures, other unstable medical conditions, bipolar disorder, conduct disorder, psychosis, severe autism, or other severe psychiatric conditions, taking psychoactive medications, or has substance use disorder **ADHD presentation:** inattentive: 31,combined: 68; 26% had an autism spectrum disorder (ASD), and another 19% had ASD traits. **Diagnosis:** Confirmation by specialist Pediatrician, child psychiatrist, psychologists **Comorbidity:** N/A **Female:** 37 % **Age mean:** 12.4 (3.6) **Minimum age:** 6 **Maximum age:** 18 **Ethnicity:** Other info on race or ethnicity: N/A	Open-label monitoring consisting of 5 follow-up visits in 12 months using a continuous performance test (QbTest) and investigator rating on the ADHD-RS. Qualitative comparison of change in ADHD-RS and QbTest scores over 12 months Naturalistic follow up, with medication administered according to clinician judgement of need.	Bonferroni-adjusted pairwise comparisons showed statistically significant reductions in QbTest and ADHD-RS scores over the 12-month study. Both measures appear to capture symptom change over time, but weak correlations between the measures suggest that their role in medical follow-up might be complementary rather than interchangeable.

Study: Author, Year; Multiple Publications; Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Co-Occurring Disorders; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Intervention**	**Results**
Cohen, 1989[203] ID: N/A RCT Single center N = 26 US Setting: N/A	**Target:** 21 children of active-duty and retired military service personnel, between ages 8-12, clinically diagnosed using DSM-III criteria, no history of stimulant treatment Parents and teachers **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Pediatrician **Comorbidity:** N/A **Female:** 14 % **Age mean:** **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A	Randomized, double-blind, placebo-controlled crossover study of the use of monitoring ADHD symptoms – before and during treatment with methylphenidate – using the ADD-H Comprehensive Teacher Rating Scale, Conners parent rating scale, and the Gordon Diagnostic System (a computerized continuous performance task assessing vigilance and impulse control). Group differences in change in symptom scores over time. Naturalistic follow up, before and during treatment with fixed-dose (5mg for children weighing less than 30kg, 10mg for children weighing 30kg or more), short-acting methylphenidate administered twice daily for 1 month, with measures collected at baseline, 1 month (the time of crossover), and 2 months (endpoint).	Both rating scales demonstrated significant change in symptoms (inattention and hyperactivity on the ADD-H scale; hyperactivity on the Conners scale) during treatment with methylphenidate compared with placebo, whereas the Gordon task did not demonstrate change. Rating scales, but not this continuous performance task, appear helpful in monitoring the short-term effects of stimulant treatment.

Epstein, 2007[256] ID: NA Cluster RCT Multicenter N = 377 US Setting: Primary Care	**Target:** 377 children from participating practices who met DSM-IV criteria for ADHD, stimulant-I, attending 1st – 5th grade 52 pediatricians (27 men, 25 women) from 12 practices; 146 randomly selected for follow-up assessments **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Conners Rating Scale **Comorbidity:** N/A **Female:** 36.3 % **Age mean:** 7.8 (1.5) **Minimum age:** 6 **Maximum age:** 10 **Ethnicity:** % Hispanic or Latino : .68 % Black/African American : 16.4 % White : 79.5 Other info on race or ethnicity:	12 pediatric practices were randomly assigned to receive access to collaborative consultative services or a control group. In the collaborative consultation services, pediatricians were encouraged and assisted to use rating scales for symptom monitoring and titration trials to determine optimal medication dosages. Physicians were taught to prescribe 4 different doses of methylphenidate during a titration trial (placebo, 18 mg, 36 mg, 54 mg); the order of week-long dosing was blinded but standardized across patients (week 1, 18 mg; week 2, placebo; week 3, 36 mg; week 4, 54 mg) to determine optimal dosing for each patient. Parents and teachers completed weekly behavioral ratings (Conners Global Index) & side effect rating scales. Data were returned to Duke Univ psychiatrist to determine the best starting medication dose; a report describing the titration results was faxed back to pediatricians. Patients in control group practices received treatment as usual, without access to consultative services. Assessed Conners Global Index & side effect rating scales. Monthly follow up with Conners and side effect rating scales for 12 months, sent to Duke U psychiatrists for interpretatin, with recommendations returned to the pediatrician	Use of symptom ratings did not differ significantly by group, nor did the change in symptoms over time. Pediatrician compliance with the collaborative consultation service was poor (pediatricians for 29 of 59 patients in the consultation group received a titration trial and 13/59 participated in monthly medication monitoring). Preliminary secondary analyses indicated that those children whose pediatricians complied with titration had significantly better outcomes compared with those who did not and TAU controls (group x time P<.01) Children in the collaborative consultation service–complier group had a 27% reduction in symptom scores compared with 18% reduction in the TAU controls and 13% reduction in consultation non-compliers.
Epstein, 2016[255] Childrens Hospital Medical Center, Cincinnati, 2010[710] ID: NCT01143701 Cluster RCT Multicenter	**Target:** 577 patients in grades 1 through 5, presenting for ADHD evaluation, and were ADHD medication naive 50 community-based pediatric primary care practices with ≥2 physicians (213 providers), uses an	Cluster randomized controlled trial of either a technology-assisted quality improvement (QI) intervention or TAU control. QI intervention consisted of 4 training sessions, office flow modification, guided QI, and an ADHD	Intent-to-treat analyses examining outcomes (parent ratings of ADHD severity) in all 577 children assessed for ADHD were not significant (b=-1.97, P=0.08), but among the 373 children prescribed ADHD medication, a significant intervention effect on reducing parent-rated symptom severity

Study: Author, Year; Multiple Publications; Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Co-Occurring Disorders; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Intervention	Results
N = 577 US Setting: Primary Care	electronic billing system, office has Internet access, must not have co-located mental health care **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV by research staff **Co-occurring disorders:** N/A **Female:** 29.5 % **Age mean:** 7.8 (1.4) **Minimum age:** **Maximum age:** **Ethnicity:** 79.5% White, 16% Black/African American	Internet portal to assist with treatment monitoring versus TAU control practices Assessed intervention effects on parent- and teacher-rated ADHD severity using on the Vanderbilt ADHD total symptom score. 12 months follow up	(b=-2.42, P=0.04) but not teacher-rated symptoms was observed. Prescriber compliance with treatment guidelines was poor, as only 373 of the 577 patients received medication at any time in the 1-year follow-up, and many who did receive it were prescribed sub-optimal doses. Compared with the usual care group, providers in the intervention group had 25% more patient contacts (d=.38, p=.0008) and collected 4.6 (d=.57, p<.0001) and 9.9 (d=.54, p<.0001) times more parent and teacher ratings, respectively. However, providers in the intervention group collected parent ratings in only half and teacher ratings in a quarter of their patients during the initial year of medication treatment.

Study: Author, Year; Multiple Publications; Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Co-Occurring Disorders; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Intervention**	**Results**
Fiks, 2017[268] Childrens Hospital of Philadelphia, 2014[711] ID: NCT02271386 Cluster RCT Multicenter N = 790 US Setting: Primary Care	**Target:** Children aged 5-12 years with ADHD diagnosis; children with autism spectrum disorder excluded. 105 clinicians practicing at 19 sites within a hospital-owned primary care research network **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Diagnosis made by clinicians **Co-occurring disorders:** N/A **Female:** 29.9 % **Age mean:** 9.3 (1.9) For intervention group; 9.2(2.0) for control group **Minimum age:** 2 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 16 (4.0),Other : 18 (6.4) for control % Black/African American : 104 (25.9),Other : Control group: 221 (57.0 % White : 248 (61.7),Other : Control Other info on race or ethnicity:	Cluster-randomized open label trial at the practice level (9 intervention, 10 control sites) for 3-component quality-improvement program that employs distance learning: (1) 3 15-minute web-based presentations on evidence-based practices for managing ADHD in primary care; (2) optional collaborative consultation with ADHD experts via a health system online networking site or private email/telephone conversation; (3) and performance feedback reports or calls every 2 months informing them of their rates of sending and receiving ADHD rating scales from parents and teachers and allowed them to compare their results to results of the entire group; feedback reports were discussed during four, 1-hour conference calls). Participation qualified for Maintenance of Certification credit from the American Board of Pediatrics. Collection of rating scales was facilitated via an electronic application linked to the electronic health record versus waitlist control Number of parent and teacher rating scales sent out and received back assessed	Differences between intervention arms were not statistically significant, though clinicians in both study arms were significantly more likely to administer and receive parent and teacher rating scales compared to an 8-month baseline period. Intervention clinicians who participated in at least one performance feedback call were more likely to send out parent rating scales than intervention clinicians who did not participate (relative difference of 14.2 percentage points, 95% CI: 0.6, 27.7. For all study outcomes, practices with the highest rates of clinician participation in the study (≥ 80%), were not superior to practices with lower rates of involvement (< 80%). Participation was low (105 of 166 invited); 42 of 53 in the intervention group completed all 3 education presentations; 30 (57%) participated in at least one feedback call, and 19 (36%) participated in all 3 components of the intervention.

Study: Author, Year; Multiple Publications; Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Co-Occurring Disorders; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Intervention	Results
Florida International University, 2010[274] ID: NCT01109849 RCT Single center N = 71 US Setting: Mixed	**Target:** 23 children with ADHD with no history of chronic stimulant use **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist **Comorbidity:** N/A **Female:** % **Age mean:** N/A **Minimum age:** **Maximum age:** **Ethnicity:** Other info on race or ethnicity: N/A	Randomized to receive either osmotic release oral system-methylphenidate alone (78%) or behavioral therapy alone (22%). After 6 months, children with a decline in body mass index >0.5 z-units were randomized to 1 of 3 weight recovery treatments: (1) monthly height/weight monitoring plus daily medication; (2) drug holidays on non-school days (with monthly monitoring); or (3) daily caloric supplements (with daily medication and monthly monitoring). Standardized body weight and height assessed 18 follow-up visits over 30 months	All groups significantly increased their weight gain. Drug holidays + monitoring, caloric supplementation + monitoring, and monitoring alone all led to increased weight velocity in children taking CNS stimulants, but with no differences between groups, and no intervention led to increased height velocity. When analyzed by what parents did (versus what they were assigned to), caloric supplementation ($p<0.01$) and drug holidays ($p<0.05$) increased weight velocity more than monitoring of height and weight. Over the entire study, participants declined in standardized weight (-0.44 z-units) and height (-0.20 z-units).

Study: Author, Year; Multiple Publications; Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Co-Occurring Disorders; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Intervention**	**Results**
Oppenheimer, 2019[466] Boston Childrens Hospital, 2014[691] ID: NCT02097355 Cluster RCT Multicenter N = 518 US Setting: Specialty care	**Target:** 98 children receiving ongoing treatment for ADHD, prescribed ADHD medication, parents and children proficient in English. 88 clinicians providing ADHD care **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Neurology department clinician at 1 of 5 locations **Comorbidity:** N/A **Female:** 24.3 % **Age mean:** 11 Intervention 9.85 (3.21), control 11.09 (3.24) **Minimum age:** **Maximum age:** **Ethnicity:** % Hispanic or Latino : 5.8 % White : 78.4,Other : 406 Other info on race or ethnicity:	Naturalistic study of a web-based platform enabling clinicians to administer online monthly clinical questionnaires to parents and teachers for monitoring of patients remotely between visits. Trigger algorithm alerts clinicians to clinically actionable events that are documented in the medical record versus non-alert group Patients were the unit of analysis. Parent and teacher reports of current medication, medication side effects inventory, Vanderbilt ADHD Parent Rating Scale, Clinical Global Impression-Severity (CGI-S) scale, and Clinical Global Impression-Improvement (CGI-I) scale 15 months follow up	Trigger algorithms produced alerts requiring immediate review in 8% of the parent reports. Clinicians perceived 74% of alerts to be significant enough to prompt urgent follow-up with parents, suggesting a low rate of false positive alerts. Patients who generated alerts compared to those who did not had more severe ADHD symptoms (beta = 5.8, 95% CI: 3.5–8.1 [p < 0.001] in the 90 days prior to an alert, further supporting validity of the alerts.

Study: Author, Year; Multiple Publications; Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Co-Occurring Disorders; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Intervention**	**Results**
Smith, 2000[545] ID: N/A Cohort study Single center N = 36 US Setting: Specialty care	**Target:** 36 adolescents who completed a summer treatment program; 12 years and older; diagnosis meets DSM-III criteria; verbal IQ higher than 80; no medical conditions that precluded stimulant medication or full participatio' in study's academic and physical activities **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Psychologist confirmed **Comorbidity:** N/A **Female:** 19 % **Age mean:** 13.4 (0.8) 1994 cohort; 14.1 (1.5) for 1995 cohort **Minimum age:** 12 **Maximum age:** **Ethnicity:** Other: 6 % White: 85 Other info on race or ethnicity:	**Intervention:** assessed the reliability, validity, and unique contributions of self-reports by adolescents receiving treatment for ADHD in a summer treatment program that included self-monitoring as a treatment component.. Self-reported IOWA Conners Inattention/Overactivity and Oppositional/Defiant subscales, ratings of interactions with peers and staff. Assessed changes in reliability during a placebo-controlled, cross-over study of 30 mg of methylphenidate. Observed frequencies of negative behavior, rating from parents and teachers	Average reliability for the adolescent self-report across all measures was .78 (range .74-.83), similar to the reliability of .82 for counselors (range .78-.85), and significantly better than the teacher reliability of .60 (range .51-.68). Teacher and counselor ratings on the Conners changed significantly during stimulant treatment whereas adolescent self-ratings did not. The findings suggest that adolescents can provide reliable information on their symptoms, but not beyond what parents can provide. Adolescents may also be poor sources of information about the change in ADHD symptoms, but a good source of information about improved interactions with others in response to treatment.

Study: Author, Year; Multiple Publications; Design; Sites; Study Size; Location Setting	Population: Setting; Study Target; ADHD Presentation; Diagnosis; Co-Occurring Disorders; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	Intervention	Results
Weisman, 2018[609] ID: N/A RCT Single center N = 39 Israel Setting: Specialty care	**Target:** Children with ADHD, medication naive or already treated for ADHD with stimulant medications Parents **ADHD presentation:** inattentive : 41.0,hyperactive : 10.3,combined : 46.2 **Diagnosis:** Confirmation by specialist DSM by psychiatrist **Comorbidity:** N/A **Female:** 30.8 % **Age mean:** 9.56 (2.41) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** Other info on race or ethnicity: Other : 100% Israeli	**Intervention:** ICON™ mobile app allows patients or their parents to report their clinical status following initiation of prescription or after changing medication dosage; purpose of the app is to facilitate communication with MD; app includes questions on severity of ADHD symptoms and potential side effects and can also function as a medication reminder **Control:** Treatment as usual, without app **Comparator:** **Follow-up:**	CGI-Severity No significant difference ADHD-RS, total No significant difference on ADHD-RS, possibly due to inadequate power, Significant difference (p= 0 .008) favoring intervention group on the Clinician Rating Scale (CRS). Intervention group had significantly better adherence, as measured by pill count (p < .015)

Study: Author, Year; Multiple Publications; Design; Sites; Study Size; Location Setting	**Population:** Setting; Study Target; ADHD Presentation; Diagnosis; Co-Occurring Disorders; % Female; Age Mean; Minimum Age; Maximum Age; Ethnicity	**Intervention**	**Results**
Yang, 2012[629] ID: N/A Crossover trial Single center N = 39 Korea Setting: Other	**Target:** 39 children ages between ages 7-13; diagnosis meets DSM-IV criteria; capacity to communicate with investigators; current use of fixed dose osmotic-controlled release oral delivery system methylphenidate medication; exclusion of children with developmental disorders, severe medical conditions, seizure disorder; children excluded if medication was adjusted during study period **ADHD presentation:** inattentive : 15.4,hyperactive : 2.6,combined : 76.9 **Diagnosis:** Confirmation by specialist Child-adolescent psychiatrists **Comorbidity:** N/A **Female:** 10.3 % **Age mean:** 10.44 (2.22) **Minimum age:** 7 **Maximum age:** 13 **Ethnicity:** Other info on race or ethnicity: N/A	Naturalistic study of medication adherence assessed using the Medication Event Monitoring System (MEMS), a bottle cap with a microprocessor that records all instances and times that the bottle is opened Patient self-report, clinician rating, pill count assessed; measure of adherence 8 weeks follow up	The rate of non-adherence measured by the MEMS was 46.2%, higher than patient self-report of 17.9%, clinician rating of 31.7%, and pill count of 12.8%. Pill count and MEMS concordance was 0.249 (95% CI: 0.102-0.386). Self-report and MEMS concordance was 0.237 (95% CI: -0.024-0.468). Non-adherent patients (based on the MEMS) had more severe symptoms at baseline and inferior improvement compared with adherent patients.

Notes: ADHD = attention deficit hyperactivity disorder; N/A = not available

Appendix D. Critical Appraisal and Applicability Tables

Table D.1. Critical appraisal for included studies, KQ1

Author, Year	Patient Selection	Index Test	Reference Standard	Flow Timing	Overall RoB
Abramov, 2019[111]	Unclear risk	Unclear risk	High risk	High risk	High risk
Adams, 2009[112]	High risk	High risk	Unclear risk	Unclear risk	High risk
Ahmadi, 2021[115]	High risk	Unclear risk	Low risk	Unclear risk	High risk
Algorta, 2016[117]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Alloway, 2009[119]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Altınkaynak, 2020[120]	High risk	High risk	Low risk	Unclear risk	High risk
Amado-Caballero, 2020[121]	High risk	Low risk	Low risk	High risk	High risk
Arjona, 2023[124]	High risk	High risk	Unclear risk	Unclear risk	High risk
Bansal, 2012[28]	High risk	Low risk	Low risk	Unclear risk	Moderate risk
Bard, 2013[134]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Barkley, 1994[135]	High risk	High risk	Unclear risk	Unclear risk	High risk
Berger, 2010[141]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Berger, 2017[140]	High risk	Low risk	Low risk	Unclear risk	High risk
Bergeron, 2017[142]	Unclear risk	High risk	High risk	Unclear risk	High risk
Beriha, 2018[143]	Unclear risk	High risk	Unclear risk	High risk	High risk
Bledsoe, 2020[152]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Bloch, 2012[153]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Boroujeni, 2019[157]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Boucugnani, 1989[159]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Breaux, 2016[162]	High risk	Low risk	Unclear risk	High risk	Moderate risk
Bunte, 2013[167]	High risk	Low risk	Low risk	Unclear risk	Moderate risk
Burton, 2019[168]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Bussing, 1998[169]	High risk	Low risk	Low risk	High risk	High risk
Canivez, 2016[170]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Catherine Joy, 2021[172]	High risk	Unclear risk	Low risk	High risk	High risk
Caudal, 2011[260]	High risk	High risk	Unclear risk	Unclear risk	Moderate risk
Chan, 2022[177]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Chang, 2019[179]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk

Author, Year	Patient Selection	Index Test	Reference Standard	Flow Timing	Overall RoB
Chang, 2022[182]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Chang, 2023[181]	High risk	High risk	Unclear risk	Unclear risk	High risk
Charach, 2009[183]	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk
Chelune, 1986[184]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Chen, 1994[190]	High risk	Low risk	Unclear risk	Unclear risk	Moderate risk
Chen, 2019[187]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Chen, 2019[188]	High risk	Low risk	Unclear risk	Unclear risk	Moderate risk
Chen, 2020[191]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Chen, 2021[189]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Chen, 2022[185]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Chen, 2023[186]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Chiarenza, 2018[192]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Chow, 2019[197]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Chu, 2017[198]	High risk	High risk	Unclear risk	Unclear risk	High risk
Cree, 2023[210]	Unclear risk	High risk	Unclear risk	Unclear risk	High risk
Crippa, 2017[211]	High risk	Unclear risk	Low risk	Unclear risk	High risk
Culbertson, 1998[213]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Das, 2021[214]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Deb, 2008[218]	High risk	High risk	Low risk	Unclear risk	High risk
Deserno, 2022[223]	Unclear risk	Low risk	Low risk	Unclear risk	Low risk
Doyle, 1997[230]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Doyle, 2007[231]	High risk	High risk	Low risk	Unclear risk	High risk
Duda, 2016[234]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Duda, 2017[233]	High risk	Low risk	High risk	Low risk	High risk
DuPaul, 1992[237]	Low risk	Unclear risk	Unclear risk	Unclear risk	High risk
Ebesutani, 2010[241]	Low risk	High risk	Unclear risk	Unclear risk	Moderate risk
Edwards, 2015[242]	Low risk	High risk	Unclear risk	Unclear risk	Moderate risk
Eiraldi, 2000[244]	Unclear risk	High risk	Low risk	Unclear risk	Moderate risk
Ekhlasi, 2022[245]	High risk	High risk	Unclear risk	Unclear risk	Moderate risk
Elkins, 2014[251]	High risk	High risk	Low risk	Unclear risk	Moderate risk
El-Sayed, 1999[246]	High risk	High risk	Low risk	Unclear risk	High risk
Emser, 2018[253]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Faraone, 2016[263]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Ferrin, 2012[267]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Forbes, 1998[276]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Francois-Sevigny, 2022[277]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Gao, 2020[282]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Garcia-Argibay, 2022[283]	Low risk	Unclear risk	High risk	Unclear risk	Moderate risk

Author, Year	Patient Selection	Index Test	Reference Standard	Flow Timing	Overall RoB
Garcia-Sanchez, 1997[284]	High risk	High risk	Unclear risk	Unclear risk	High risk
Gardner, 2007[285]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Gargaro, 2014[287]	Unclear risk	High risk	Low risk	Low risk	Moderate risk
Geurts, 2004[293]	High risk	High risk	Unclear risk	Unclear risk	High risk
Gibbons, 2020[297]	High risk	High risk	Low risk	Unclear risk	High risk
Gilbert, 2016[298]	High risk	Unclear risk	Low risk	Unclear risk	Low risk
Goh, 2023[299]	High risk	High risk	Unclear risk	Unclear risk	Moderate risk
Gomez, 2018[300]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Gomez, 2021[301]	High risk	High risk	Unclear risk	Unclear risk	Moderate risk
Grazioli, 2023[303]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Grodzinsky, 1992[307]	High risk	High risk	Unclear risk	Unclear risk	High risk
Gungor, 2021[309]	High risk	High risk	Low risk	Low risk	High risk
Guttentag, 2022[311]	Unclear risk	Low risk	Low risk	Low risk	Moderate risk
Hager, 2021[312]	High risk	Low risk	Unclear risk	High risk	High risk
Hall, 2016[315]	Low risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Hall, 2020[314]	Low risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Hamadache, 2021[316]	Unclear risk	High risk	Low risk	Unclear risk	High risk
Hasaneen, 2017[319]	High risk	Low risk	Low risk	High risk	High risk
Helgadottir, 2015[322]	Unclear risk	Low risk	Low risk	Unclear risk	High risk
Heller, 2013[323]	Unclear risk	High risk	Low risk	Unclear risk	High risk
Hinshaw, 2002[327]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Hong, 2019[331]	Unclear risk	Low risk	Unclear risk	Unclear risk	Low risk
Hudziak, 2004[336]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Hult, 2018[24]	High risk	High risk	Low risk	Unclear risk	High risk
Ickowicz, 2006[338]	High risk	Low risk	Unclear risk	Unclear risk	Moderate risk
Jacobson, 2020[339]	Unclear risk	Low risk	Low risk	Unclear risk	Moderate risk
Jahanshahloo, 2017[340]	High risk	High risk	Low risk	Unclear risk	High risk
Jarrett, 2018[342]	Unclear risk	High risk	High risk	Unclear risk	High risk
Jensen-Doss, 2013[344]	Unclear risk	Unclear risk	High risk	Unclear risk	High risk
Jimenez-Figueroa, 2017[346]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Johansson, 2021[347]	High risk	Unclear risk	Low risk	Unclear risk	High risk
Johnstone, 2021[351]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk

Author, Year	Patient Selection	Index Test	Reference Standard	Flow Timing	Overall RoB
Juneja, 2019[352]	Low risk	Low risk	Low risk	Low risk	Low risk
Kam, 2010[355]	Low risk	Low risk	Low risk	Unclear risk	Low risk
Karabiber Cura, 2023[356]	High risk	High risk	High risk	Unclear risk	High risk
Karr, 2021[359]	Unclear risk	Low risk	Low risk	Unclear risk	Moderate risk
Kennerley, 2018[362]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Kim, 2015[366]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Kim, 2015[365]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Koh, 2021[369]	Low risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Koh, 2022[370]	Unclear risk	Low risk	Low risk	Unclear risk	Moderate risk
Krieger, 2021[379]	High risk	Low risk	Low risk	High risk	Moderate risk
Kurokami, 2022[382]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Lau, 2018[385]	Low risk	Unclear risk	Low risk	Unclear risk	Low risk
Lee, 2022[388]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Lefler, 2012[389]	High risk	High risk	Low risk	Unclear risk	High risk
Lesica, 2023[390]	High risk	Unclear risk	High risk	Unclear risk	High risk
Levy, 2017[391]	Low risk	Low risk	Low risk	Low risk	Low risk
Li, 2005[395]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Li, 2016[393]	High risk	High risk	Unclear risk	Unclear risk	Moderate risk
Li, 2018[394]	Unclear risk	High risk	Unclear risk	Unclear risk	High risk
Liechti, 2013[397]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Lin, 2022[402]	Low risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Lin, 2023[400]	Unclear risk	Low risk	Unclear risk	Unclear risk	Low risk
Lin, 2023[401]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Lindhiem, 2022[403]	High risk	High risk	Unclear risk	Unclear risk	High risk
Liu, 2022[404]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Longridge, 2019[405]	Unclear risk	Unclear risk	High risk	High risk	High risk
Luo, 2022[408]	High risk	High risk	Low risk	Unclear risk	Moderate risk
Luo, 2022[407]	High risk	High risk	Unclear risk	Unclear risk	Moderate risk
Marcano, 2018[412]	High risk	Unclear risk	High risk	Unclear risk	High risk
Markovska-Simoska, 2017[413]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Martín-Brufau, 2017[415]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Martin-Martinez, 2012[416]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Matier-Sharma, 1995[417]	Low risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Maya-Piedrahita, 2022[420]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Mayes, 2002[421]	Unclear risk	High risk	Low risk	Unclear risk	Moderate risk
Mayes, 2004[422]	High risk	High risk	Low risk	Unclear risk	Moderate risk

Author, Year	Patient Selection	Index Test	Reference Standard	Flow Timing	Overall RoB
Mayfield, 2018[423]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
McCarthy, 2016[424]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
McIntosh, 1995[427]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Merzon, 2022[429]	High risk	High risk	Unclear risk	Unclear risk	Moderate risk
Mikolas, 2022[434]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Mitchell, 1990[436]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Miyahara, 2014[437]	High risk	High risk	Unclear risk	Unclear risk	High risk
Moghaddari, 2020[438]	Unclear risk	Low risk	Low risk	Unclear risk	High risk
Moura, 2017[446]	High risk	Low risk	Low risk	Low risk	Moderate risk
Moura, 2019[445]	Low risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Mouti, 2019[447]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Mulhern, 1994[448]	High risk	High risk	Low risk	Unclear risk	Moderate risk
Muthuraman, 2019[449]	High risk	Low risk	Low risk	Low risk	High risk
Mwamba, 2019[450]	High risk	Low risk	High risk	Low risk	Moderate risk
Newman, 2017[462]	Low risk	Low risk	Low risk	Low risk	Moderate risk
Nolan,1999[463]	Low risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Ogrim, 2012[465]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
O'Neill, 2021[464]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Oztekin, 2021[467]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Oztoprak, 2017[468]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	High risk
Park, 2019[469]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Parker, 2016[18]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Peijnenborgh, 2016[470]	Unclear risk	Low risk	Low risk	Unclear risk	Low risk
Pereda, 2018[473]	Unclear risk	Unclear risk	Low risk	Low risk	High risk
Perugini, 2000[475]	High risk	High risk	Unclear risk	Unclear risk	High risk
Pineda, 2011[477]	High risk	High risk	Unclear risk	Unclear risk	High risk
Power, 1998[479]	Low risk	High risk	Low risk	Unclear risk	Moderate risk
Preston, 2005[482]	Low risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Qin , 2018[486]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Quintana, 2007[487]	High risk	High risk	Low risk	Unclear risk	High risk
Raiker, 2017[491]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Reddy, 2021[493]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Rezaeezadeh, 2020[494]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Riaz, 2020[495]	Low risk	Low risk	Low risk	Low risk	Moderate risk

Author, Year	Patient Selection	Index Test	Reference Standard	Flow Timing	Overall RoB
Rielly, 1999[496]	Low risk	High risk	High risk	Unclear risk	High risk
Rishel, 2005[498]	Low risk	Low risk	Low risk	Low risk	Low risk
Robles, 2021[499]	High risk	Low risk	Unclear risk	Unclear risk	Moderate risk
Rodríguez, 2018[500]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Roessner, 2007[501]	Unclear risk	Low risk	Low risk	High risk	High risk
Rogers, 2022[502]	Low risk	High risk	Unclear risk	Unclear risk	Moderate risk
Rucklidge, 2002[506]	Unclear risk	High risk	Low risk	Unclear risk	Moderate risk
Satin, 1985[514]	Unclear risk	High risk	Unclear risk	Unclear risk	High risk
Schatz, 2001[515]	High risk	High risk	Low risk	Unclear risk	High risk
Scheeringa, 2020[516]	Low risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Schirmer, 2021[518]	High risk	High risk	Unclear risk	Unclear risk	Moderate risk
Schneider, 2020[519]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Serrallach, 2016[524]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Shemmassian, 2016[527]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Shemmassian, 2017[528]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Silverstein, 2016[536]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Simões, 2021[537]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Skogli, 2013[541]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Slaby, 2022[542]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	High risk
Slobodin, 2020[543]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Smith, 2000[547]	High risk	High risk	Unclear risk	Unclear risk	High risk
Smith, 2003[546]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Snyder, 2008[548]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Snyder, 2015[27]	Low risk	Low risk	Low risk	Unclear risk	Low risk
Soliva, 2010[549]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Spencer, 2018[553]	Low risk	High risk	Unclear risk	Unclear risk	Moderate risk
Sprafkin, 2002[559]	Low risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Sprafkin, 2007[558]	Low risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Stepanova, 2021[563]	Low risk	Low risk	Low risk	Low risk	Low risk
Stevanovic, 2023[564]	Unclear risk	High risk	High risk	Unclear risk	High risk
Straub, 2021[566]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Sullivan, 2007[570]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Sun, 2018[571]	High risk	Low risk	Unclear risk	Unclear risk	Moderate risk
Tallberg, 2019[576]	Unclear risk	Unclear risk	High risk	High risk	N/A

Author, Year	Patient Selection	Index Test	Reference Standard	Flow Timing	Overall RoB
Tang, 2022[581]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Tang, 2023[580]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Ter-Minassian, 2022[582]	Low risk	Low risk	Unclear risk	Unclear risk	Moderate risk
Tian, 2022[583]	Unclear risk	Low risk	Low risk	Unclear risk	Low risk
Tillman, 2005[584]	High risk	High risk	Low risk	Unclear risk	High risk
Tripp, 2006[587]	Low risk	Low risk	Low risk	Low risk	Moderate risk
Uyulan, 2023[591]	High risk	High risk	Unclear risk	Unclear risk	High risk
Vahid, 2019[592]	High risk	Low risk	Low risk	Unclear risk	Moderate risk
Varela Casal, 2019[599]	High risk	Low risk	Unclear risk	Unclear risk	Moderate risk
Vogt, 2011[600]	Low risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Wang, 2018[603]	Unclear risk	Low risk	Unclear risk	Unclear risk	High risk
Wassenberg, 2004[605]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Webster, 2000[607]	Low risk	Low risk	Low risk	Low risk	Low risk
Westerberg, 2004[614]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Weyandt, 1994[615]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Williams, 2010[21]	Unclear risk	High risk	Low risk	Unclear risk	Moderate risk
Wodka, 2008[625]	Low risk	High risk	Low risk	Unclear risk	Moderate risk
Wood, 2009[627]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Yao, 2018[630]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Yasumura, 2020[631]	Low risk	Low risk	Low risk	Low risk	Low risk
Yeh, 2020[632]	High risk	Unclear risk	Low risk	Low risk	Low risk
Yoo, 2020[633]	Unclear risk	Low risk	Low risk	Unclear risk	Moderate risk
Zadehbagheri, 2019[635]	Low risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Zelko, 1991[638]	Unclear risk	Low risk	Low risk	Low risk	Moderate risk
Zelnik, 2012[639]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Zhou, 2018[642]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Zhou, 2022[641]	Unclear risk	Unclear risk	Low risk	Unclear risk	High risk
Zhu, 2022[644]	Low risk	Low risk	Low risk	Unclear risk	Moderate risk
Zulueta, 2019[647]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk

Table D.2. Applicability for included studies, KQ1

Author, year	Population	Intervention	Comparator	Outcome	Setting
Abramov, 2019[111]	Narrow eligibility criteria	N/A	Unclear	N/A	N/A
Adams, 2009[112]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Ahmadi, 2021[115]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Algorta, 2016[117]	N/A	N/A	N/A	N/A	N/A
Alloway, 2009[119]	Unclear	N/A	N/A	N/A	N/A
Altınkaynak, 2020[120]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Amado-Caballero, 2020[121]	Unclear	N/A	N/A	Unclear	Unclear
Arjona, 2023[124]	Unclear	N/A	N/A	N/A	N/A
Bansal, 2012[28]	Unclear	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	Level of care different from that in the community
Bard, 2013[134]	N/A	N/A	N/A	N/A	N/A
Barkley, 1994[135]	Unclear	N/A	Unclear	N/A	N/A
Berger, 2010[141]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Berger, 2017[140]	Narrow eligibility criteria	N/A	Comparator unclear	N/A	N/A
Bergeron, 2017[142]	Unclear	N/A	N/A	N/A	N/A
Beriha, 2018[143]	Unclear	N/A	N/A	N/A	Unclear
Bledsoe, 2020[152]	Narrow eligibility criteria	Unclear	N/A	N/A	N/A
Bloch, 2012[153]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Boroujeni, 2019[157]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Boucugnani, 1989[159]	Unclear	N/A	N/A	N/A	Unclear

Author, year	Population	Intervention	Comparator	Outcome	Setting
Breaux, 2016[162]	Narrow eligibility criteria	As recommended or commonly used in practice	Diagnostic tools used differently than as recommended or commonly used in practice	Other issues	N/A
Bunte, 2013[167]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Burton, 2019[168]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Bussing, 1998[169]	More complex patients than typical of the community	Unclear	N/A	N/A	N/A
Canivez, 2016[170]	Unclear	N/A	N/A	N/A	N/A
Catherine Joy, 2021[172]	Unclear	N/A	N/A	N/A	N/A
Caudal, 2011[260]	N/A	N/A	N/A	N/A	N/A
Chan, 2022[177]	N/A	N/A	N/A	N/A	N/A
Chang, 2019[179]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Chang, 2022[182]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Chang, 2023[181]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Charach, 2009[183]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Chelune, 1986[184]	Unclear	N/A	N/A	N/A	N/A
Chen, 1994[190]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Chen, 2019[187]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Chen, 2019[188]	N/A	Highly selected intervention team or level of training/proficiency not widely available	N/A	Unclear	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Chen, 2020[191]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Chen, 2021[189]	Narrow eligibility criteria	N/A	N/A	N/A	Unclear
Chen, 2022[185]	Unclear	N/A	N/A	N/A	N/A
Chen, 2023[186]	Unclear	N/A	Unclear	N/A	N/A
Chiarenza, 2018[192]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Chow, 2019[197]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Chu, 2017[198]	Unclear	Unclear	N/A	N/A	Level of care different from that in the community
Cree, 2023[210]	N/A	N/A	N/A	N/A	N/A
Crippa, 2017[211]	Unclear	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	Level of care different from that in the community
Culbertson, 1998[213]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Das, 2021[214]	Unclear	N/A	Unclear	N/A	N/A
Deb, 2008[218]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Deserno, 2022[223]	Unclear	N/A	N/A	N/A	Unclear
Doyle, 1997[230]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Doyle, 2007[231]	Unclear	N/A	N/A	N/A	N/A
Duda, 2016[234]	More complex patients than typical of the community	Unclear	N/A	N/A	Level of care different from that in the community
Duda, 2017[233]	More complex patients than typical of the community	N/A	Diagnostic tools used differently than as recommended or commonly used in practice	N/A	Unclear

Author, year	Population	Intervention	Comparator	Outcome	Setting
DuPaul, 1992[237]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Ebesutani, 2010[241]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Edwards, 2015[242]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Eiraldi, 2000[244]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Ekhlasi, 2022[245]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Elkins, 2014[251]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
El-Sayed, 1999[246]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Emser, 2018[253]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Faraone, 2016[263]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Ferrin, 2012[267]	N/A	Unclear	N/A	N/A	Level of care different from that in the community
Forbes, 1998[276]	More complex patients than typical of the community	N/A	Unclear	N/A	Level of care different from that in the community
Francois-Sevigny, 2022[277]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community

Author, year	Population	Intervention	Comparator	Outcome	Setting
Gao, 2020[282]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Garcia-Argibay, 2022[283]	N/A	N/A	N/A	N/A	N/A
Garcia-Sanchez, 1997[284]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Gardner, 2007[285]	Unclear	N/A	N/A	N/A	N/A
Gargaro, 2014[287]	More complex patients than typical of the community	N/A	N/A	N/A	Unclear
Geurts, 2004[293]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Gibbons, 2020[297]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Gilbert, 2016[298]	Narrow eligibility criteria	Unclear	N/A	N/A	Level of care different from that in the community
Goh, 2023[299]	N/A	N/A	N/A	N/A	N/A
Gomez, 2018[300]	N/A	Unclear	N/A	N/A	N/A
Gomez, 2021[301]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Grazioli, 2023[303]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Grodzinsky, 1992[307]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Gungor, 2021[309]	Narrow eligibility criteria	Unclear	N/A	N/A	Unclear
Guttentag, 2022[311]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Hager, 2021[312]	N/A	N/A	N/A	N/A	Level of care different from that in the community

Author, year	Population	Intervention	Comparator	Outcome	Setting
Hall, 2016[315]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Hall, 2020[314]	More complex patients than typical of the community	N/A	Unclear	N/A	Level of care different from that in the community
Hamadache, 2021[316]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Hasaneen, 2017[319]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Helgadottir, 2015[322]	N/A	N/A	N/A	N/A	N/A
Heller, 2013[323]	More complex patients than typical of the community	Unclear	N/A	N/A	Level of care different from that in the community
Hinshaw, 2002[327]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Hong, 2019[331]	More complex patients than typical of the community	N/A	Inadequate comparison therapy or use of a substandard alternative therapy	N/A	N/A
Hudziak, 2004[336]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Hult, 2018[24]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Ickowicz, 2006[338]	Unclear	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	Level of care different from that in the community
Jacobson, 2020[339]	N/A	N/A	N/A	N/A	N/A
Jahanshahloo, 2017[340]	Unclear	N/A	N/A	N/A	Unclear

Author, year	Population	Intervention	Comparator	Outcome	Setting
Jarrett, 2018[342]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Jensen-Doss, 2013[344]	DSM-4/5 diagnosis unclear	N/A	Unclear	Unclear	N/A
Jimenez-Figueroa, 2017[346]	N/A	N/A	N/A	N/A	N/A
Johansson, 2021[347]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Johnstone, 2021[351]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Juneja, 2019[352]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Kam, 2010[355]	N/A	N/A	N/A	Unclear	N/A
Karabiber Cura, 2023[356]	Unclear	N/A	Unclear	N/A	N/A
Karr, 2021[359]	N/A	N/A	N/A	N/A	Unclear
Kennerley, 2018[362]	N/A	N/A	N/A	N/A	N/A
Kim, 2015[366]	Narrow eligibility criteria	Unclear	N/A	N/A	Level of care different from that in the community
Kim, 2015[365]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Koh, 2021[369]	More complex patients than typical of the community	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	N/A
Koh, 2022[370]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Krieger, 2021[379]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Kurokami, 2022[382]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Lau, 2018[385]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Lee, 2022[388]	Unclear	N/A	N/A	N/A	N/A
Lefler, 2012[389]	Unclear	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Lesica, 2023[390]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Levy, 2017[391]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Li, 2005[395]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Li, 2016[393]	Narrow eligibility criteria	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	N/A
Li, 2018[394]	N/A	N/A	N/A	N/A	N/A
Liechti, 2013[397]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Lin, 2022[402]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Lin, 2023[400]	N/A	N/A	N/A	N/A	N/A
Lin, 2023[401]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Lindhiem, 2022[403]	Unclear	N/A	N/A	N/A	N/A
Liu, 2022[404]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Longridge, 2019[405]	N/A	N/A	N/A	N/A	N/A
Luo, 2022[408]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Luo, 2022[407]	Unclear	N/A	N/A	N/A	N/A
Marcano, 2018[412]	Narrow eligibility criteria	Highly selected intervention team or level of training/proficiency not widely available	Unclear	N/A	Level of care different from that in the community
Markovska-Simoska, 2017[413]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Martín-Brufau, 2017[415]	Unclear	N/A	Unclear	Other issues	N/A
Martin-Martinez, 2012[416]	N/A	N/A	N/A	N/A	N/A
Matier-Sharma, 1995[417]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Maya-Piedrahita, 2022[420]	N/A	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Mayes, 2002[421]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Mayes, 2004[422]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Mayfield, 2018[423]	N/A	N/A	N/A	N/A	N/A
McCarthy, 2016[424]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
McIntosh, 1995[427]	N/A	N/A	N/A	N/A	N/A
Merzon, 2022[429]	N/A	N/A	Unclear	N/A	N/A
Mikolas, 2022[434]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Mitchell, 1990[436]	Unclear	N/A	N/A	N/A	N/A
Miyahara, 2014[437]	N/A	N/A	N/A	N/A	N/A
Moghaddari, 2020[438]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Moura, 2017[446]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Moura, 2019[445]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Mouti, 2019[447]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Mulhern, 1994[448]	More complex patients than typical of the community	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Muthuraman, 2019[449]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Mwamba, 2019[450]	N/A	N/A	N/A	N/A	N/A
Newman, 2017[462]	N/A	N/A	N/A	N/A	N/A
Nolan,1999[463]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Ogrim, 2012[465]	N/A	N/A	N/A	N/A	Level of care different from that in the community
O'Neill, 2021[464]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Oztekin, 2021[467]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Oztoprak, 2017[468]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Park, 2019[469]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Parker, 2016[18]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Peijnenborgh, 2016[470]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Pereda, 2018[473]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Perugini, 2000[475]	Unclear	N/A	N/A	N/A	N/A
Pineda, 2011[477]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Power, 1998[479]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Preston, 2005[482]	More complex patients than typical of the community	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Qin , 2018[486]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Quintana, 2007[487]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Raiker, 2017[491]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Reddy, 2021[493]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Rezaeezadeh, 2020[494]	Unclear	N/A	Comparator unclear	N/A	Level of care different from that in the community
Riaz, 2020[495]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Rielly, 1999[496]	More complex patients than typical of the community	N/A	Unclear	N/A	Level of care different from that in the community
Rishel, 2005[498]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Robles, 2021[499]	More complex patients than typical of the community	N/A	Unclear	N/A	Level of care different from that in the community
Rodríguez, 2018[500]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Roessner, 2007[501]	N/A	N/A	N/A	N/A	N/A
Rogers, 2022[502]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Rucklidge, 2002[506]	N/A	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Satin, 1985[514]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Schatz, 2001[515]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Scheeringa, 2020[516]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Schirmer, 2021[518]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Schneider, 2020[519]	N/A	N/A	N/A	N/A	N/A
Serrallach, 2016[524]	More complex patients than typical of the community	Unclear	Unclear	N/A	N/A
Shemmassian, 2016[527]	N/A	N/A	N/A	N/A	N/A
Shemmassian, 2017[528]	N/A	N/A	N/A	N/A	N/A
Silverstein, 2016[536]	N/A	N/A	N/A	N/A	N/A
Simões, 2021[537]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Skogli, 2013[541]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Slaby, 2022[542]	Unclear	N/A	Unclear	N/A	N/A
Slobodin, 2020[543]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Smith, 2000[547]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Smith, 2003[546]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Snyder, 2008[548]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Snyder, 2015[27]	N/A	N/A	Diagnostic tools used differently than as recommended or commonly used in practice	N/A	N/A
Soliva, 2010[549]	Unclear	N/A	N/A	N/A	Level of care different from that in the community

Author, year	Population	Intervention	Comparator	Outcome	Setting
Spencer, 2018[553]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Sprafkin, 2002[559]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Sprafkin, 2007[558]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Stepanova, 2021[563]	N/A	N/A	N/A	N/A	N/A
Stevanovic, 2023[564]	More complex patients than typical of the community	N/A	Unclear	N/A	N/A
Straub, 2021[566]	More complex patients than typical of the community	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	Level of care different from that in the community
Sullivan, 2007[570]	N/A	N/A	N/A	N/A	N/A
Sun, 2018[571]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Tallberg, 2019[576]	N/A	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	N/A
Tang, 2022[581]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Tang, 2023[580]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Ter-Minassian, 2022[582]	N/A	N/A	N/A	N/A	N/A
Tian, 2022[583]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Tillman, 2005[584]	Unclear	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Tripp, 2006[587]	More complex patients than typical of the community	N/A	N/A	N/A	Unclear
Uyulan, 2023[591]	Unclear	N/A	N/A	N/A	N/A
Vahid, 2019[592]	N/A	N/A	N/A	Unclear	N/A
Varela Casal, 2019[599]	N/A	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	Level of care different from that in the community
Vogt, 2011[600]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Wang, 2018[603]	Narrow eligibility criteria	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	Level of care different from that in the community
Wassenberg, 2004[605]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Webster, 2000[607]	DSM-4/5 diagnosis unclear	N/A	N/A	N/A	N/A
Westerberg, 2004[614]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Weyandt, 1994[615]	Unclear	N/A	N/A	N/A	N/A
Williams, 2010[21]	N/A	Unclear	N/A	N/A	N/A
Wodka, 2008[625]	N/A	N/A	N/A	N/A	N/A
Wood, 2009[627]	N/A	N/A	N/A	N/A	N/A
Yao, 2018[630]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Yasumura, 2020[631]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Yeh, 2020[632]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Yoo, 2020[633]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Zadehbagheri, 2019[635]	N/A	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Zelko, 1991[638]	N/A	N/A	N/A	N/A	N/A
Zelnik, 2012[639]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Zhou, 2018[642]	N/A	N/A	Comparator unclear	N/A	N/A
Zhou, 2022[641]	Unclear	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	N/A
Zhu, 2022[644]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Zulueta, 2019[647]	N/A	N/A	N/A	N/A	N/A

Table D.3. Critical appraisal for included studies, KQ2

Author, Year	Selection Bias	Performance Bias	Attrition Bias	Detection Bias	Reporting Bias	Other Source of Bias	Overall RoB
Abbasi, 2011[104]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Abikoff, 2004[107]	Low risk	High risk	High risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Abikoff, 2007[109]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Abikoff, 2009[108]	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	High risk
Abikoff, 2013[106]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate risk
Abikoff, 2015[110]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Aevi Genomic Medicine, 2016[113]	Moderate/Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Aevi Genomic Medicine, 2018[114]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Akhondzadeh, 2004[116]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Allen, 2005[118]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Amiri, 2008[122]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Antshel, 2003[123]	Low risk	High risk	Low risk	High risk	Moderate/ Unclear risk	Low risk	High risk
Arnold, 2022[126]	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Arnold, 2007[125]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	Moderate risk
Ashkenasi, 2011[127]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	High risk
Aviv, 2021[128]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	High risk	High risk
Azami, 2023[129]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Bakhshayesh, 2011[130]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	High risk
Banaschewski, 2013[131]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk
Bangs, 2007[132]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Bangs, 2008[133]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Baziar, 2019[136]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	High risk	High risk	High risk
Bedard, 2015[137]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Behdani, 2013[138]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	High risk	Moderate/ Unclear risk	High risk
Benzing, 2019[139]	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk

Author, Year	Selection Bias	Performance Bias	Attrition Bias	Detection Bias	Reporting Bias	Other Source of Bias	Overall RoB
Biederman, 2005[147]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Biederman, 2006[146]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Biederman, 2007[144]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk
Biederman, 2008[145]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Bigorra, 2016[148]	Low risk	Low risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate risk
Bikic, 2018[56]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Low risk	Moderate risk
Bilici, 2004[149]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Moderate risk
Binesh, 2020[150]	High risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Blader, 2021[151]	Low risk	Low risk	High risk	Low risk	High risk	Low risk	Moderate risk
Block, 2009[154]	Moderate/ Unclear risk	Low risk	High risk	Low risk	High risk	Moderate/ Unclear risk	High risk
Blumer, 2009[155]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Bluschke, 2022[156]	High risk	High risk	High risk	High risk	Low risk	High risk	High risk
Bostic, 2000[158]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Boyer, 2016[160]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk
Brams, 2018[161]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Breaux, 2018[163]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Buitelaar, 1996[165]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Buitelaar, 2007[164]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Bul, 2016[166]	Moderate/ Unclear risk	High risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Carucci, 2022[171]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Ceresoli-Borroni, 2021[174]	Low risk	Low risk	High risk	Low risk	Low risk	High risk	Moderate risk
Cetin, 2015[175]	High risk	High risk	High risk	High risk	High risk	High risk	High risk
Chacko, 2009[176]	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Chang, 2019[178]	Moderate/ Unclear risk	Low risk	Moderate/Unclear risk	Low risk	Low risk	Low risk	Moderate risk
Chang, 2022[180]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk
Childress, 2009[195]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Childress, 2022[194]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk
Cho, 2011[196]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	High risk

Author, Year	Selection Bias	Performance Bias	Attrition Bias	Detection Bias	Reporting Bias	Other Source of Bias	Overall RoB
Chu, 2021[199]	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Moderate risk
Churchill, 2018[200]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Low risk	High risk
Coelho, 2017[201]	High risk	Low risk	High risk	High risk	Moderate/ Unclear risk	High risk	High risk
Coghill, 2014[202]	Low risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Coles, 2020[204]	High risk	High risk	Low risk	High risk	Low risk	High risk	High risk
Concordia Pharm., 2011[205]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	High risk	High risk	High risk
Conners, 1996[206]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk
Connor, 2010[207]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Corkum, 2019[208]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk
Cornu, 2018[209]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	High risk	Moderate risk
Crippa, 2019[212]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Dashbozorgi, 2021[215]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
David, 2021[216]	Low risk	High risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Daviss, 2008[217]	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Dehbozorghi, 2019[219]	Moderate/ Unclear risk	Low risk	Moderate/Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Dell'Agnello, 2009[220]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Denton, 2020[221]	High risk	High risk	High risk	High risk	Moderate/ Unclear risk	High risk	High risk
Dentz, 2020[222]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	High risk
Diamond, 1999[224]	High risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk
Dittmann, 2011[226]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Dittmann, 2013[225]	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk
Dong, 2022[227]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Moderate risk
Dose, 2017[228]	Low risk	Moderate/ Unclear risk	Low risk	High risk	Low risk	Low risk	High risk
Dovis, 2015[229]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Dreakhshanpour, 2022[232]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Moderate risk
Duke University, 2009[235]	High risk	High risk	Moderate/ Unclear risk	High risk	High risk	Moderate/ Unclear risk	High risk
Duke University, 2009b[236]	High risk	High risk	Moderate/ Unclear risk	High risk	High risk	Moderate/Unclear risk	High risk

Author, Year	Selection Bias	Performance Bias	Attrition Bias	Detection Bias	Reporting Bias	Other Source of Bias	Overall RoB
DuPaul, 2021[238]	Low risk	High risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	High risk
Durgut, 2020[239]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate risk
Duric, 2017[240]	Moderate/ Unclear risk	High risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Egeland, 2013[243]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Eli Lilly, 2004[247]	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk
Eli Lilly, 2006[248]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Eli Lilly[249]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate risk
Elmaadawi, 2022[252]	High risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Enns, 2017 [254]	High risk	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	High risk
Epstein, 2007[256]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate risk
Epstein, 2016[255]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate risk
Ercan, 2014[257]	High risk	High risk	High risk	High risk	Moderate/ Unclear risk	High risk	High risk
Estrada-Plana, 2019[258]	Moderate/ Unclear risk	High risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Evans, 2016[259]	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Fabiano, 2016[261]	Low risk	High risk	Low risk	High risk	Moderate/ Unclear risk	Low risk	High risk
Fallah, 2018[262]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Moderate risk
Farmer, 2017[264]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Ferrin, 2014[265]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Ferrin, 2020[266]	Low risk	High risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Findling, 2001[271]	High risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Findling, 2008[273]	Moderate/ Unclear risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Findling, 2010[272]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk
Findling, 2011[270]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Findling, 2019[269]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Florida International University, 2015[275]	High risk	High risk	High risk	High risk	Moderate/ Unclear risk	High risk	High risk
Frei, 2001[279]	High risk	High risk	Low risk	High risk	High risk	High risk	High risk
Frei, 2005[278]	Low risk	Low risk	Low risk	Low risk	High risk	High risk	High risk

Author, Year	Selection Bias	Performance Bias	Attrition Bias	Detection Bias	Reporting Bias	Other Source of Bias	Overall RoB
Fuchs, 2003[280]	High risk	High risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	High risk
Fuentes, 2013[281]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	High risk	High risk
Gard, 2014[286]	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Gau, 2006[289]	Moderate/ Unclear risk	High risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Gau, 2007[288]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Geissler, 2020[290]	Low risk	High risk	High risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Gelade, 2017[291]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk
Geller, 2007[292]	Low risk	Moderate/Un clear risk	Low risk	Low risk	High risk	High risk	Moderate risk
Gevensleb en, 2010[294]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	High risk
Ghajar, 2018[295]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Ghanizade h, 2015[296]	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Gonzalez-Castro, 2016[302]	High risk	High risk	Low risk	High risk	Moderate/ Unclear risk	Low risk	High risk
Greenhill, 2006[305]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Greenhill, 2006[304]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Griffiths, 2018[306]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Guevara, 2021[308]	Low risk	High risk	Low risk	High risk	Moderate/ Unclear risk	High risk	Moderate risk
Gustafsson , 2010[310]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Hahn-Markowitz, 2020[313]	Low risk	High risk	Low risk	High risk	Low risk	High risk	High risk
Harfterkam p, 2012[317]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Hariri, 2012[318]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Hasslinger, 2021[320]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Hazell, 2003[321]	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Hemamy, 2021[324]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Herbert, 2013[325]	Low risk	High risk	Low risk	High risk	Low risk	Low risk	High risk
Hervas, 2014[326]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Hirayama, 2014[328]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk
Hiscock, 2019[329]	Low risk	High risk	Low risk	High risk	High risk	Moderate/ Unclear risk	Moderate risk
Hogue, 2020[330]	High risk	Moderate/Un clear risk	Low risk	Moderate/U nclear risk	High risk	High risk	High risk

Author, Year	Selection Bias	Performance Bias	Attrition Bias	Detection Bias	Reporting Bias	Other Source of Bias	Overall RoB
Hong, 2016[332]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	High risk	High risk
Hosainzadeh Maleki, 2014[333]	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk
Huang, 2015[335]	High risk	High risk	Low risk	High risk	Low risk	Low risk	High risk
Huang, 2021[334]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Ichikawa, 2020[337]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Jain, 2011[341]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Jensen, 2007[343]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Low risk	Moderate risk
Ji, 2023[345]	Moderate/ Unclear risk	Low risk	High risk	Low risk	Low risk	Low risk	High risk
Johnson, 2009[349]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Johnson, 2020[348]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Johnstone, 2022[350]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Kadri, 2019[353]	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Kahbazi, 2009[354]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Karakaya, 2019[357]	Low risk	High risk	Low risk	High risk	Moderate/ Unclear risk	Low risk	High risk
Kareem, 2021[358]	High risk	High risk	Moderate/ Unclear risk	High risk	High risk	High risk	High risk
Katz, 2010[360]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate risk
Kelsey, 2004[361]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Khaksarian, 2021[363]	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Khoshbakht, 2021[364]	Low risk	High risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Kim, 2022[367]	Moderate/Unclear risk	High risk	Low risk	Moderate/ Unclear risk	Low risk	High risk	High risk
Kofler, 2020[368]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Kolko, 2020[371]	Low risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Kollins, 2011[374]	Moderate/Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	High risk	Moderate/ Unclear risk	Moderate risk
Kollins, 2011[373]	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	High risk
Kollins, 2020[372]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate risk
Korfmacher, 2022[375]	Low risk	High risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk
Kratochvil, 2002[376]	High risk	High risk	High risk	High risk	Moderate/Unclear risk	High risk	High risk
Kratochvil, 2005[377]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

Author, Year	Selection Bias	Performance Bias	Attrition Bias	Detection Bias	Reporting Bias	Other Source of Bias	Overall RoB
Kratochvil, 2011[378]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Kurowski, 2019[383]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Lange, 2018[384]	Low risk	High risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	High risk
Lavigne, 2011[386]	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Law, 1999[387]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Li, 2022[392]	Low risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Liang, 2022[396]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Lilly, 2008[250]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate risk
Lim, 2019[398]	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Lin, 2014[399]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Ludyga, 2022[406]	Low risk	High risk	High risk	Moderate/ Unclear risk	Low risk	Low risk	High risk
Luo, 2022[409]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	High risk
Lv, 2023 [410]	Low risk	High risk	High risk	High risk	Low risk	High risk	High risk
Manor, 2012[411]	Low risk	Low risk	High risk	Low risk	Low risk	Moderate/Unclear risk	High risk
Martenyi, 2010[414]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk
Matthijssen, 2019[418]	Moderate/ Unclear risk	Low risk	Moderate/Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Mattingly, 2020[419]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	Moderate risk
McCracken, 2016[425]	Low risk	Low risk	High risk	Low risk	High risk	Moderate/ Unclear risk	Moderate risk
McGrath, 2011[426]	Low risk	Moderate/ Unclear risk	Low risk	Low risk	High risk	Low risk	High risk
Mehri, 2020[428]	Low risk	High risk	Low risk	High risk	Moderate/ Unclear risk	Low risk	High risk
Meyer, 2021[430]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate risk
Michelson, 2001[432]	Moderate/Unclear risk	Low risk	Low risk	Low risk	Low risk	High risk	Moderate risk
Michelson, 2002[431]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Mikami, 2013[433]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Minder, 2018[435]	Low risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	Low risk	High risk
Mohammadi, 2010[439]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk
Mohammadi, 2012[440]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Mohammadzadeh, 2019[441]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Montoya, 2009[442]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

Author, Year	Selection Bias	Performance Bias	Attrition Bias	Detection Bias	Reporting Bias	Other Source of Bias	Overall RoB
Morell, 2019[504]	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Mostajeran, 2020[443]	Low risk	High risk	High risk	Moderate/ Unclear risk	Low risk	Low risk	High risk
Motaharifard, 2019[444]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Mount Sinai, 2012[539]	Low risk	Low risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	High risk
Myers, 2015[451]	Low risk	Moderate/ Unclear risk	Low risk	Low risk	High risk	Low risk	Moderate risk
Nasser, 2020[453]	Moderate/Unclear risk	Low risk	Moderate/Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk
Nasser, 2021[454]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Nasser, 2021[455]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Nasser, 2021[452]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/Unclear risk	Moderate/ Unclear risk	Moderate risk
Nejati, 2021[456]	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Moderate risk
Nejati, 2022[457]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Moderate risk
Newcorn, 2005[461]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Newcorn, 2008[460]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Newcorn, 2016[459]	Low risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	High risk	High risk
NF Coll. Group, 2021[458]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate risk
Oppenheimer, 2019[466]	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Low risk	Moderate/ Unclear risk	High risk
Pelham, 2016[471]	Moderate/Unclear risk	High risk	Moderate/Unclear risk	High risk	Moderate/ Unclear risk	High risk	High risk
Pelsser, 2011[472]	Low risk	High risk	Low risk	High risk	Low risk	High risk	High risk
Perez-Alvarez, 2009[474]	High risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	High risk	High risk
Pfiffner, 2014[476]	Low risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Pongpitakdamrong, 2021[478]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk
Power, 2012[480]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Prasad, 2007[481]	Low risk	Low risk	Moderate/Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Purper-Ouakil, 2021[483]	Low risk	Low risk	Low risk	High risk	Moderate/ Unclear risk	Low risk	High risk
Qian, 2018[484]	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Qian, 2021[485]	Low risk	High risk	Moderate/ Unclear risk	High risk	Low risk	High risk	High risk

Author, Year	Selection Bias	Performance Bias	Attrition Bias	Detection Bias	Reporting Bias	Other Source of Bias	Overall RoB
Rafeiy-Torghabeh, 2021[488]	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	Moderate risk
Raghuveer, 2020[489]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Rahmani, 2022[490]	High risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Rajabi, 2020[492]	Moderate/ Unclear risk	High risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Riggs, 2011[497]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Rothe, 2023[503]	High risk	High risk	Low risk	Low risk	Moderate/Unclear risk	Low risk	High risk
Rucklidge, 2018[505]	Moderate/Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Saito, 2020[507]	Moderate/ Unclear risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Salardini, 2016[508]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	High risk	High risk	High risk
Salehi, 2010[509]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Salehi, 2016[510]	High risk	Low risk	Moderate/ Unclear risk	Low risk	High risk	High risk	High risk
Sallee, 2009[511]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Sangal, 2006[512]	Moderate/ Unclear risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Sangal, 2014[513]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Schertz, 2022[517]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	High risk
Schorr-Sapir, 2021[520]	Low risk	High risk	Moderate/ Unclear risk	High risk	Low risk	Low risk	High risk
Schramm, 2016[521]	Low risk	High risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	Moderate risk
Schuck, 2018[522]	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Sciberras, 2020[523]	Low risk	High risk	High risk	Moderate/ Unclear risk	Low risk	Low risk	High risk
Seattle Children's Hospital, 2015[193]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	High risk
Shang, 2020[525]	Low risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Shaywitz, 2017[526]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk
Shen, 2021[529]	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Moderate risk
Shuai, 2020[530]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	High risk	Low risk	High risk
Sibley, 2016[533]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Sibley, 2018[531]	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Moderate risk
Sibley, 2020[534]	Low risk	Moderate /Unclear risk	Moderate/Unclear risk	High risk	Low risk	Low risk	Moderate risk

Author, Year	Selection Bias	Performance Bias	Attrition Bias	Detection Bias	Reporting Bias	Other Source of Bias	Overall RoB
Sibley, 2021[532]	Low risk	High risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Siebelink, 2021[535]	Low risk	High risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	High risk
Simonoff, 2013[538]	Low risk	Low risk	Low risk	Low risk	High risk	Moderate/ Unclear risk	Moderate risk
Singer, 1995[540]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Smit, 2021[544]	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Sonuga-Barke, 2001[550]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	Low risk	Moderate risk
Sonuga-Barke, 2004[551]	High risk	High risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	High risk
Sonuga-Barke, 2018[552]	Low risk	High risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Spencer, 2002[554]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	High risk	Moderate/ Unclear risk	Moderate risk
Spencer, 2002[555]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	High risk	Moderate/ Unclear risk	Moderate risk
Spencer, 2006[557]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Spencer, 2008[556]	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate risk
Sprich, 2016[560]	Low risk	High risk	Low risk	Low risk	Low risk	High risk	High risk
Steele, 2006[561]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Steiner, 2014[562]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	High risk
Storebo, 2012[565]	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate risk
Strehl, 2017[567]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Su, 2016[568]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Sugaya 2022[569]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Supernus Pharmaceuticals, 2016[572]	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk
Svanborg, 2009[573]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Swanson, 2006[574]	Low risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	High risk	Moderate risk
Takahashi, 2009[575]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk
Tamm, 2013[578]	Low risk	High risk	Moderate/ Unclear risk	High risk	Low risk	Low risk	High risk
Tamm, 2017[577]	High risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	High risk
Tan, 2016[579]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

Author, Year	Selection Bias	Performance Bias	Attrition Bias	Detection Bias	Reporting Bias	Other Source of Bias	Overall RoB
Tiwawatpakorn, 2021[585]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Trebaticka, 2006[586]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Tris Pharma, 2014[588]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
TS Study Group, 2002[380]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
TS Study Group, 2002b[381]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Tutty, 2003[589]	Low risk	High risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Tzang, 2016[590]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk
Vaidyanathan, 2023[593]	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Valero, 2021[594]	Moderate/ Unclear risk	High risk	Low risk	High risk	Low risk	Low risk	High risk
van der Donk, 2015[595]	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk
Van der Heijden, 2007[596]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk
van der Oord, 2007[597]	Low risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Low risk	Low risk	High risk
van Stralen, 2020[598]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Voigt, 2001[601]	Low risk	Low risk	High risk	Low risk	High risk	Moderate/ Unclear risk	High risk
Volpe, 2009[602]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Wang, 2007[604]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Weber, 2008[606]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Wehmeier, 2012[608]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate risk
Weiss, 2005[611]	High risk	Moderate/ Unclear risk	Low risk	Low risk	High risk	High risk	High risk
Weiss, 2007[610]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Weiss, 2021[612]	Low risk	Low risk	High risk	Low risk	High risk	High risk	High risk
Wennberg, 2018[613]	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate risk
Wietecha, 2009[616]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Wigal, 2004[617]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Wigal, 2011[618]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	Moderate risk

Author, Year	Selection Bias	Performance Bias	Attrition Bias	Detection Bias	Reporting Bias	Other Source of Bias	Overall RoB
Wilens, 2005[621]	Low risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Wilens, 2008[619]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Wilens, 2011[105]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	High risk	Moderate risk
Wilens, 2012[622]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Wilens, 2015[623]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Wilkes-Gillan, 2016[624]	Low risk	High risk	Low risk	Moderate/ Unclear risk	High risk	High risk	High risk
Willens, 2011[620]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Wolraich, 2001[626]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk
Wu, 2023[628]	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	High risk
Young, 2014[634]	Low risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Zarinara, 2010[636]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Zavadenko, 2019[637]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Zheng, 2020[640]	Low risk	High risk	Low risk	High risk	High risk	Low risk	High risk
Zhu, 2017[645]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk
Zhu, 2022[643]	Low risk	High risk	High risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Zhuo, 2022[646]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

Table D.4. Applicability for included studies, KQ2

Author, Year	Population	Intervention	Comparator	Outcome	Setting
Abbasi, 2011[104]	N/A	Co-intervention that are likely to modify the effectiveness of therapy	N/A	N/A	N/A
Abikoff, 2004[107]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Abikoff, 2007[109]	Narrow eligibility criteria	Dosing not reflective of current practice	N/A	Short-term follow-up	N/A
Abikoff, 2009[108]	More complex patients than typical of the community	N/A	N/A	Other issues	N/A
Abikoff, 2013[106]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Abikoff, 2015[110]	N/A	N/A	N/A	N/A	N/A
Aevi Genomic Medicine, 2016[113]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Aevi Genomic Medicine, 2018[114]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Akhondzadeh, 2004[116]	N/A	As recommended or commonly used in practice	N/A	N/A	N/A
Allen, 2005[118]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Amiri, 2008[122]	N/A	N/A	N/A	N/A	N/A
Antshel, 2003[123]	N/A	N/A	N/A	N/A	N/A
Arnold, 2022[126]	N/A	Unclear	N/A	N/A	N/A
Arnold, 2007[125]	N/A	N/A	N/A	N/A	N/A
Ashkenasi, 2011[127]	N/A	N/A	N/A	N/A	N/A
Aviv, 2021[128]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Azami, 2023[129]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Bakhshayesh, 2011[130]	N/A	N/A	N/A	N/A	N/A
Banaschewski, 2013[131]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Bangs, 2007[132]	N/A	N/A	N/A	N/A	N/A
Bangs, 2008[133]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Baziar, 2019[136]	N/A	N/A	N/A	N/A	N/A
Bedard, 2015[137]	N/A	N/A	N/A	N/A	N/A

Author, Year	Population	Intervention	Comparator	Outcome	Setting
Behdani, 2013[138]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Benzing, 2019[139]	N/A	N/A	N/A	N/A	N/A
Biederman, 2005[147]	N/A	N/A	N/A	N/A	N/A
Biederman, 2006[146]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Biederman, 2007[144]	N/A	N/A	N/A	N/A	N/A
Biederman, 2008[145]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Bigorra, 2016[148]	N/A	N/A	N/A	N/A	N/A
Bikic, 2018[56]	N/A	N/A	N/A	N/A	N/A
Bilici, 2004[149]	N/A	N/A	N/A	N/A	N/A
Binesh, 2020[150]	N/A	N/A	N/A	Unclear	N/A
Blader, 2021[151]	Narrow eligibility criteria	Co-intervention that are likely to modify the effectiveness of therapy	Comparator unclear	Short-term follow-up	Unclear
Block, 2009[154]	N/A	N/A	N/A	N/A	N/A
Blumer, 2009[155]	N/A	N/A	N/A	N/A	N/A
Bluschke, 2022[156]	DSM-4/5 diagnosis unclear	Co-intervention that are likely to modify the effectiveness of therapy	Unclear	N/A	N/A
Bostic, 2000[158]	N/A	N/A	N/A	Short-term follow-up	N/A
Boyer, 2016[160]	N/A	N/A	N/A	N/A	N/A
Brams, 2018[161]	N/A	N/A	N/A	Short-term follow-up	N/A
Breaux, 2018[163]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Buitelaar, 1996[165]	N/A	N/A	N/A	N/A	N/A
Buitelaar, 2007[164]	N/A	N/A	N/A	N/A	N/A
Bul, 2016[166]	N/A	N/A	N/A	N/A	Unclear
Carucci, 2022[171]	N/A	N/A	N/A	N/A	N/A
Ceresoli-Borroni, 2021[174]	N/A	N/A	N/A	N/A	N/A
Cetin, 2015[175]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Chacko, 2009[176]	N/A	N/A	N/A	N/A	N/A
Chang, 2019[178]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Chang, 2022[180]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Childress, 2009[195]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Childress, 2022[194]	N/A	N/A	N/A	N/A	N/A

Author, Year	Population	Intervention	Comparator	Outcome	Setting
Cho, 2011[196]	N/A	Unclear	N/A	Short-term follow-up	N/A
Chu, 2021[199]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Churchill, 2018[200]	N/A	Highly selected intervention team or level of training/proficiency not widely available	Comparator unclear	N/A	N/A
Coelho, 2017[201]	N/A	N/A	N/A	N/A	N/A
Coghill, 2014[202]	N/A	N/A	N/A	N/A	N/A
Coles, 2020[204]	N/A	N/A	N/A	N/A	N/A
Concordia Pharm., 2011[205]	N/A	Unclear	N/A	N/A	N/A
Conners, 1996[206]	N/A	Unclear	N/A	Other issues	N/A
Connor, 2010[207]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Corkum, 2019[208]	DSM-4/5 diagnosis unclear	Co-intervention that are likely to modify the effectiveness of therapy	Unclear	Short-term follow-up	N/A
Cornu, 2018[209]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Crippa, 2019[212]	N/A	N/A	N/A	N/A	N/A
Dashbozorgi, 2021[215]	Narrow eligibility criteria	N/A	N/A	Short-term follow-up	N/A
David, 2021[216]	N/A	N/A	N/A	N/A	N/A
Daviss, 2008[217]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Dehbozorghi, 2019[219]	Narrow eligibility criteria	Co-intervention that are likely to modify the effectiveness of therapy	N/A	Short-term follow-up	N/A
Dell'Agnello, 2009[220]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Denton, 2020[221]	More complex patients than typical of the community	Co-intervention that are likely to modify the effectiveness of therapy	Unclear	Unclear	N/A
Dentz, 2020[222]	More complex patients than typical of the community	Co-intervention that are likely to modify the effectiveness of therapy	N/A	N/A	N/A

Author, Year	Population	Intervention	Comparator	Outcome	Setting
Diamond, 1999[224]	DSM-4/5 diagnosis unclear	As recommended or commonly used in practice	N/A	Other issues	N/A
Dittmann, 2011[226]	N/A	N/A	N/A	N/A	N/A
Dittmann, 2013[225]	N/A	N/A	Comparator unclear	N/A	N/A
Dong, 2022[227]	N/A	Unclear	N/A	N/A	N/A
Dose, 2017[228]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Dovis, 2015[229]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Dreakhshanpour, 2022[232]	N/A	N/A	N/A	N/A	N/A
Duke University, 2009[235]	N/A	Dosing not reflective of current practice	N/A	Other issues	N/A
Duke University, 2009b[236]	N/A	Dosing not reflective of current practice	N/A	Other issues	N/A
DuPaul, 2021[238]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Durgut, 2020[239]	N/A	Unclear	N/A	Unclear	N/A
Duric, 2017[240]	DSM-4/5 diagnosis unclear	Co-intervention that are likely to modify the effectiveness of therapy	N/A	Short-term follow-up	N/A
Egeland, 2013[243]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Eli Lilly, 2004[247]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Eli Lilly, 2006[248]	N/A	N/A	N/A	N/A	N/A
Eli Lilly[249]	N/A	N/A	N/A	N/A	N/A
Elmaadawi, 2022[252]	N/A	Highly selected intervention team or level of training/proficiency not widely available	N/A	Other issues	N/A
Enns, 2017 [254]	N/A	Unclear	Unclear	Other issues	N/A
Epstein, 2007[256]	N/A	Unclear	N/A	N/A	N/A
Epstein, 2016[255]	N/A	N/A	N/A	N/A	N/A
Ercan, 2014[257]	More complex patients than typical of the community	Co-intervention that are likely to modify the effectiveness of therapy	N/A	N/A	N/A
Estrada-Plana, 2019[258]	N/A	N/A	N/A	Short-term follow-up	Level of care different from that in the community
Evans, 2016[259]	N/A	N/A	N/A	N/A	N/A

Author, Year	Population	Intervention	Comparator	Outcome	Setting
Fabiano, 2016[261]	N/A	N/A	N/A	Other issues	N/A
Fallah, 2018[262]	More complex patients than typical of the community	N/A	N/A	Unclear	N/A
Farmer, 2017[264]	N/A	N/A	N/A	N/A	N/A
Ferrin, 2014[265]	N/A	N/A	N/A	N/A	N/A
Ferrin, 2020[266]	N/A	N/A	N/A	N/A	N/A
Findling, 2001[271]	N/A	Dosing not reflective of current practice	N/A	N/A	N/A
Findling, 2008[273]	N/A	N/A	N/A	N/A	N/A
Findling, 2010[272]	Narrow eligibility criteria	As recommended or commonly used in practice	N/A	N/A	N/A
Findling, 2011[270]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Findling, 2019[269]	N/A	N/A	N/A	N/A	N/A
Florida International University, 2015[275]	More complex patients than typical of the community	N/A	N/A	Other issues	N/A
Frei, 2001[279]	N/A	Highly selected intervention team or level of training/proficiency not widely available	Inadequate comparison therapy or use of a substandard alternative therapy	Other issues	N/A
Frei, 2005[278]	Run-in period with high exclusion rate	N/A	N/A	N/A	N/A
Fuchs, 2003[280]	N/A	N/A	N/A	N/A	N/A
Fuentes, 2013[281]	N/A	Co-intervention that are likely to modify the effectiveness of therapy	N/A	N/A	N/A
Gard, 2014[286]	N/A	As recommended or commonly used in practice	N/A	N/A	N/A
Gau, 2006[289]	Narrow eligibility criteria	N/A	Unclear	N/A	N/A
Gau, 2007[288]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Geissler, 2020[290]	N/A	N/A	N/A	N/A	N/A
Gelade, 2017[291]	N/A	N/A	N/A	N/A	N/A
Geller, 2007[292]	N/A	N/A	N/A	Short-term follow-up	Level of care different from that in the community
Gevensleben, 2010[294]	N/A	N/A	N/A	N/A	N/A
Ghajar, 2018[295]	Narrow eligibility criteria	N/A	N/A	Short-term follow-up	N/A

Author, Year	Population	Intervention	Comparator	Outcome	Setting
Ghanizadeh, 2015[296]	N/A	Dosing not reflective of current practice	N/A	N/A	N/A
Gonzalez-Castro, 2016[302]	N/A	N/A	N/A	Other issues	N/A
Greenhill, 2006[305]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Greenhill, 2006[304]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Griffiths, 2018[306]	N/A	N/A	N/A	N/A	N/A
Guevara, 2021[308]	DSM-4/5 diagnosis unclear	N/A	N/A	N/A	N/A
Gustafsson, 2010[310]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Hahn-Markowitz, 2020[313]	N/A	N/A	N/A	N/A	N/A
Harfterkamp, 2012[317]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Hariri, 2012[318]	DSM-4/5 diagnosis unclear	Co-intervention that are likely to modify the effectiveness of therapy	N/A	Unclear	N/A
Hasslinger, 2021[320]	N/A	N/A	N/A	N/A	N/A
Hazell, 2003[321]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Hemamy, 2021[324]	N/A	Dosing not reflective of current practice	N/A	Short-term follow-up	N/A
Herbert, 2013[325]	Unclear	Unclear	Unclear	N/A	N/A
Hervas, 2014[326]	DSM-4/5 diagnosis unclear	Dosing not reflective of current practice	Inadequate comparison therapy or use of a substandard alternative therapy	Short-term follow-up	N/A
Hirayama, 2014[328]	N/A	N/A	N/A	N/A	N/A
Hiscock, 2019[329]	N/A	N/A	N/A	N/A	N/A
Hogue, 2020[330]	DSM-4/5 diagnosis unclear	Highly selected intervention team or level of training/proficiency not widely available	N/A	Other issues	N/A
Hong, 2016[332]	N/A	Unclear	Unclear	Unclear	N/A
Hosainzadeh Maleki, 2014[333]	N/A	N/A	N/A	N/A	N/A
Huang, 2015[335]	N/A	N/A	N/A	N/A	N/A
Huang, 2021[334]	N/A	N/A	Comparator unclear	N/A	N/A
Ichikawa, 2020[337]	N/A	N/A	N/A	N/A	N/A

Author, Year	Population	Intervention	Comparator	Outcome	Setting
Jain, 2011[341]	N/A	N/A	N/A	N/A	N/A
Jensen, 2007[343]	Unclear	N/A	N/A	N/A	N/A
Ji, 2023[345]	Narrow eligibility criteria	N/A	N/A	Other issues	N/A
Johnson, 2009[349]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Johnson, 2020[348]	N/A	N/A	N/A	N/A	N/A
Johnstone, 2022[350]	N/A	N/A	N/A	N/A	N/A
Kadri, 2019[353]	DSM-4/5 diagnosis unclear	N/A	N/A	N/A	N/A
Kahbazi, 2009[354]	N/A	N/A	N/A	N/A	N/A
Karakaya, 2019[357]	N/A	N/A	N/A	N/A	N/A
Kareem, 2021[358]	DSM-4/5 diagnosis unclear	N/A	N/A	Other issues	N/A
Katz, 2010[360]	N/A	N/A	N/A	Unclear	N/A
Kelsey, 2004[361]	N/A	N/A	N/A	N/A	N/A
Khaksarian, 2021[363]	N/A	N/A	N/A	N/A	N/A
Khoshbakht, 2021[364]	N/A	N/A	N/A	N/A	N/A
Kim, 2022[367]	Narrow eligibility criteria	N/A	Comparator unclear	N/A	N/A
Kofler, 2020[368]	N/A	N/A	N/A	N/A	N/A
Kolko, 2020[371]	Unclear	N/A	Comparator unclear	N/A	N/A
Kollins, 2011[374]	N/A	N/A	N/A	N/A	N/A
Kollins, 2011[373]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Kollins, 2020[372]	Narrow eligibility criteria	N/A	N/A	Short-term follow-up	N/A
Korfmacher, 2022[375]	Narrow eligibility criteria	Co-intervention that are likely to modify the effectiveness of therapy	N/A	N/A	N/A
Kratochvil, 2002[376]	N/A	N/A	N/A	N/A	N/A
Kratochvil, 2005[377]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Kratochvil, 2011[378]	N/A	N/A	N/A	N/A	N/A
Kurowski, 2019[383]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Lange, 2018[384]	Narrow eligibility criteria	Highly selected intervention team or level of training/proficiency not widely available	Inadequate comparison therapy or use of a substandard alternative therapy	Short-term follow-up	Unclear
Lavigne, 2011[386]	N/A	N/A	N/A	N/A	N/A
Law, 1999[387]	Unclear	As recommended or commonly used in practice	N/A	Other issues	N/A

Author, Year	Population	Intervention	Comparator	Outcome	Setting
Li, 2022[392]	Narrow eligibility criteria	Unclear	N/A	N/A	N/A
Liang, 2022[396]	N/A	N/A	N/A	N/A	N/A
Lilly, 2008[250]	N/A	N/A	Unclear	N/A	N/A
Lim, 2019[398]	N/A	N/A	N/A	N/A	N/A
Lin, 2014[399]	N/A	N/A	N/A	Short-term follow-up	N/A
Ludyga, 2022[406]	N/A	Highly selected intervention team or level of training/proficiency not widely available	N/A	Other issues	N/A
Luo, 2022[409]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Lv, 2023 [410]	Narrow eligibility criteria	Co-intervention that are likely to modify the effectiveness of therapy	Comparator unclear	N/A	N/A
Manor, 2012[411]	Narrow eligibility criteria	N/A	N/A	Unclear	N/A
Martenyi, 2010[414]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Matthijssen, 2019[418]	N/A	N/A	N/A	N/A	N/A
Mattingly, 2020[419]	N/A	N/A	N/A	Short-term follow-up	N/A
McCracken, 2016[425]	N/A	N/A	Comparator unclear	Short-term follow-up	N/A
McGrath, 2011[426]	N/A	N/A	N/A	Unclear	N/A
Mehri, 2020[428]	More complex patients than typical of the community	N/A	N/A	Unclear	N/A
Meyer, 2021[430]	N/A	N/A	N/A	N/A	N/A
Michelson, 2001[432]	N/A	N/A	N/A	N/A	N/A
Michelson, 2002[431]	N/A	N/A	N/A	N/A	N/A
Mikami, 2013[433]	More complex patients than typical of the community	Highly selected intervention team or level of training/proficiency not widely available	N/A	Other issues	N/A
Minder, 2018[435]	N/A	N/A	N/A	N/A	N/A
Mohammadi, 2010[439]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Mohammadi, 2012[440]	N/A	N/A	N/A	N/A	N/A
Mohammadzadeh, 2019[441]	N/A	N/A	N/A	N/A	N/A
Montoya, 2009[442]	N/A	N/A	N/A	N/A	N/A
Morell, 2019[504]	N/A	N/A	N/A	N/A	N/A
Mostajeran, 2020[443]	N/A	N/A	N/A	N/A	N/A

Author, Year	Population	Intervention	Comparator	Outcome	Setting
Motaharifard, 2019[444]	Narrow eligibility criteria	As recommended or commonly used in practice	Comparator unclear	Short-term follow-up	Unclear
Mount Sinai, 2012[539]	DSM-4/5 diagnosis unclear	N/A	N/A	Short-term follow-up	N/A
Myers, 2015[451]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Nasser, 2020[453]	N/A	N/A	N/A	N/A	N/A
Nasser, 2021[454]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Nasser, 2021[455]	N/A	N/A	N/A	N/A	N/A
Nasser, 2021[452]	N/A	N/A	N/A	N/A	N/A
Nejati, 2021[456]	N/A	Unclear	N/A	N/A	N/A
Nejati, 2022[457]	N/A	N/A	N/A	N/A	N/A
Newcorn, 2005[461]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Newcorn, 2008[460]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Newcorn, 2016[459]	N/A	N/A	N/A	N/A	N/A
NF Coll. Group, 2021[458]	N/A	N/A	N/A	N/A	N/A
Oppenheimer, 2019[466]	N/A	N/A	Comparator unclear	Short-term follow-up	N/A
Pelham, 2016[471]	N/A	Co-intervention that are likely to modify the effectiveness of therapy	N/A	N/A	N/A
Pelsser, 2011[472]	Run-in period with high exclusion rate	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	N/A
Perez-Alvarez, 2009[474]	Narrow eligibility criteria	N/A	N/A	Other issues	N/A
Pfiffner, 2014[476]	N/A	N/A	N/A	N/A	N/A
Pongpitakdamrong, 2021[478]	N/A	N/A	N/A	N/A	N/A
Power, 2012[480]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Prasad, 2007[481]	N/A	N/A	N/A	N/A	N/A
Purper-Ouakil, 2021[483]	N/A	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	N/A
Qian, 2018[484]	N/A	N/A	N/A	N/A	N/A

Author, Year	Population	Intervention	Comparator	Outcome	Setting
Qian, 2021[485]	Narrow eligibility criteria	Highly selected intervention team or level of training/proficiency not widely available	Unclear	N/A	Level of care different from that in the community
Rafeiy-Torghabeh, 2021[488]	N/A	N/A	N/A	N/A	Unclear
Raghuveer, 2020[489]	N/A	Unclear	N/A	N/A	N/A
Rahmani, 2022[490]	N/A	N/A	N/A	N/A	N/A
Rajabi, 2020[492]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Riggs, 2011[497]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Rothe, 2023[503]	More complex patients than typical of the community	Co-intervention that are likely to modify monitoring strategies	N/A	Other issues	N/A
Rucklidge, 2018[505]	N/A	N/A	N/A	N/A	N/A
Saito, 2020[507]	N/A	N/A	N/A	N/A	N/A
Salardini, 2016[508]	N/A	N/A	N/A	Short-term follow-up	N/A
Salehi, 2010[509]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Salehi, 2016[510]	Narrow eligibility criteria	N/A	N/A	Other issues	N/A
Sallee, 2009[511]	N/A	N/A	N/A	N/A	N/A
Sangal, 2006[512]	N/A	N/A	N/A	N/A	N/A
Sangal, 2014[513]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Schertz, 2022[517]	N/A	Unclear	N/A	N/A	N/A
Schorr-Sapir, 2021[520]	N/A	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	N/A
Schramm, 2016[521]	N/A	N/A	N/A	N/A	N/A
Schuck, 2018[522]	N/A	N/A	N/A	N/A	N/A
Sciberras, 2020[523]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Seattle Children's Hospital, 2015[193]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Shang, 2020[525]	N/A	N/A	N/A	Unclear	N/A
Shaywitz, 2017[526]	More complex patients than typical of the community	As recommended or commonly used in practice	N/A	N/A	Unclear

Author, Year	Population	Intervention	Comparator	Outcome	Setting
Shen, 2021[529]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Shuai, 2020[530]	Narrow eligibility criteria	N/A	N/A	Short-term follow-up	N/A
Sibley, 2016[533]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Sibley, 2018[531]	N/A	N/A	N/A	N/A	N/A
Sibley, 2020[534]	N/A	N/A	Comparator unclear	N/A	N/A
Sibley, 2021[532]	N/A	N/A	N/A	N/A	N/A
Siebelink, 2021[535]	N/A	N/A	N/A	N/A	N/A
Simonoff, 2013[538]	DSM-4/5 diagnosis unclear	N/A	N/A	Short-term follow-up	N/A
Singer, 1995[540]	N/A	N/A	N/A	N/A	N/A
Smit, 2021[544]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Sonuga-Barke, 2001[550]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Sonuga-Barke, 2004[551]	DSM-4/5 diagnosis unclear	N/A	N/A	Unclear	N/A
Sonuga-Barke, 2018[552]	N/A	N/A	N/A	N/A	N/A
Spencer, 2002[554]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Spencer, 2002[555]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Spencer, 2006[557]	N/A	N/A	N/A	N/A	N/A
Spencer, 2008[556]	N/A	N/A	Comparator unclear	Short-term follow-up	N/A
Sprich, 2016[560]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Steele, 2006[561]	Narrow eligibility criteria	As recommended or commonly used in practice	N/A	N/A	N/A
Steiner, 2014[562]	N/A	N/A	N/A	N/A	N/A
Storebo, 2012[565]	N/A	N/A	N/A	N/A	N/A
Strehl, 2017[567]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Su, 2016[568]	N/A	N/A	N/A	N/A	N/A
Sugaya 2022[569]	N/A	N/A	N/A	N/A	N/A
Supernus Pharmaceuticals, 2016[572]	More complex patients than typical of the community	Unclear	N/A	N/A	N/A
Svanborg, 2009[573]	N/A	N/A	Comparator unclear	N/A	N/A

Author, Year	Population	Intervention	Comparator	Outcome	Setting
Swanson, 2006[574]	N/A	N/A	N/A	N/A	N/A
Takahashi, 2009[575]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Tamm, 2013[578]	N/A	N/A	N/A	N/A	N/A
Tamm, 2017[577]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Tan, 2016[579]	N/A	N/A	N/A	N/A	N/A
Tiwawatpakorn, 2021[585]	DSM-4/5 diagnosis unclear	N/A	N/A	N/A	N/A
Trebaticka, 2006[586]	Unclear	N/A	N/A	Other issues	N/A
Tris Pharma, 2014[588]	Unclear	Unclear	Unclear	Unclear	Unclear
TS Study Group, 2002[380]	N/A	N/A	N/A	N/A	N/A
TS Study Group, 2002b[381]	N/A	N/A	N/A	N/A	N/A
Tutty, 2003[589]	N/A	N/A	N/A	N/A	N/A
Tzang, 2016[590]	Narrow eligibility criteria	As recommended or commonly used in practice	N/A	Short-term follow-up	N/A
Vaidyanathan, 2023[593]	N/A	Co-intervention that are likely to modify the effectiveness of therapy	N/A	N/A	N/A
Valero, 2021[594]	N/A	N/A	N/A	N/A	N/A
van der Donk, 2015[595]	More complex patients than typical of the community	N/A	N/A	N/A	Unclear
Van der Heijden, 2007[596]	More complex patients than typical of the community	As recommended or commonly used in practice	N/A	N/A	N/A
van der Oord, 2007[597]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
van Stralen, 2020[598]	N/A	N/A	N/A	N/A	N/A
Voigt, 2001[601]	Narrow eligibility criteria	N/A	N/A	Other issues	N/A
Volpe, 2009[602]	More complex patients than typical of the community	N/A	N/A	Unclear	N/A
Wang, 2007[604]	N/A	Dosing not reflective of current practice	N/A	N/A	N/A
Weber, 2008[606]	N/A	N/A	N/A	N/A	N/A
Wehmeier, 2012[608]	N/A	N/A	N/A	N/A	N/A
Weiss, 2005[611]	N/A	N/A	N/A	Short-term follow-up	Unclear
Weiss, 2007[610]	N/A	N/A	N/A	N/A	N/A

Author, Year	Population	Intervention	Comparator	Outcome	Setting
Weiss, 2021[612]	N/A	N/A	N/A	Short-term follow-up	N/A
Wennberg, 2018[613]	Unclear	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	Unclear
Wietecha, 2009[616]	Narrow eligibility criteria	N/A	Unclear	N/A	N/A
Wigal, 2004[617]	N/A	N/A	N/A	N/A	N/A
Wigal, 2011[618]	N/A	N/A	N/A	N/A	N/A
Wilens, 2005[621]	N/A	N/A	N/A	Short-term follow-up	N/A
Wilens, 2008[619]	N/A	N/A	N/A	N/A	N/A
Wilens, 2011[105]	N/A	N/A	N/A	N/A	Unclear
Wilens, 2012[622]	N/A	N/A	N/A	N/A	N/A
Wilens, 2015[623]	Narrow eligibility criteria	As recommended or commonly used in practice	N/A	N/A	N/A
Wilkes-Gillan, 2016[624]	More complex patients than typical of the community	N/A	N/A	Unclear	N/A
Willens, 2011[620]	Narrow eligibility criteria	As recommended or commonly used in practice	N/A	Unclear	Level of care different from that in the community
Wolraich, 2001[626]	N/A	N/A	N/A	N/A	N/A
Wu, 2023[628]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Young, 2014[634]	Narrow eligibility criteria	Dosing not reflective of current practice	Inadequate comparison therapy or use of a substandard alternative therapy	N/A	Unclear
Zarinara, 2010[636]	N/A	N/A	N/A	N/A	N/A
Zavadenko, 2019[637]	N/A	N/A	Unclear	Unclear	Unclear
Zheng, 2020[640]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Zhu, 2017[645]	N/A	N/A	N/A	N/A	Unclear
Zhu, 2022[643]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Zhuo, 2022[646]	Narrow eligibility criteria	Unclear	N/A	N/A	N/A

Table D.5. Critical appraisal for included studies, KQ3

Author, Year	Selection Bias	Performance Bias	Attrition Bias	Detection Bias	Reporting Bias	Other Source of Bias	Overall RoB
Cedergren, 2021[173]	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	High risk	Low risk	Moderate/ Unclear risk	Moderate risk
Cohen, 1989[203]	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Epstein, 2007[256]	Moderate /Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate risk
Epstein, 2016[255]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate risk
Fiks, 2017[268]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate risk
Florida International University, 2010[274]	High risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Oppenheimer, 2019[466]	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Low risk	Moderate/ Unclear risk	High risk
Smith, 2000[545]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	High risk	Moderate/ Unclear risk	Moderate risk
Weisman, 2018[609]	Low risk	High risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Yang, 2012[629]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	High risk

Appendix E. List of Included Studies

This appendix shows the list of included studies for the review. We have indicated which Key Question it is included for at the end of the citation with the record ID.

1. Abbasi SH, Heidari S, Mohammadi MR, et al. Acetyl-L-carnitine as an adjunctive therapy in the treatment of attention-deficit/hyperactivity disorder in children and adolescents: a placebo-controlled trial. Child Psychiatry Hum Dev. 2011 Jun;42(3):367-75. doi: 10.1007/s10578-011-0220-y. PMID: 21336630. *IncludeDE_KQ2* Record ID 17191

2. AbbVie, AbbVie. Safety and Tolerability Study of ABT-089 in Children With Attention-Deficit/Hyperactivity Disorder (ADHD). 2008. *IncludeDE_KQ2* Record ID 13767

3. Abikoff H, Gallagher R, Wells KC, et al. Remediating organizational functioning in children with ADHD: immediate and long-term effects from a randomized controlled trial. J Consult Clin Psychol. 2013 Feb;81(1):113-28. doi: 10.1037/a0029648. PMID: 22889336. *IncludeDE_KQ2* Record ID 14654

4. Abikoff H, Hechtman L, Klein RG, et al. Symptomatic improvement in children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. J Am Acad Child Adolesc Psychiatry. 2004 Jul;43(7):802-11. doi: 10.1097/01.chi.0000128791.10014.ac. PMID: 15213581. *IncludeDE_KQ2* Record ID 14875

5. Abikoff H, Nissley-Tsiopinis J, Gallagher R, et al. Effects of MPH-OROS on the organizational, time management, and planning behaviors of children with ADHD. J Am Acad Child Adolesc Psychiatry. 2009 Feb;48(2):166-75. doi: 10.1097/CHI.0b013e3181930626. PMID: 19127171. *IncludeDE_KQ2* Record ID 17420

6. Abikoff H, Vitiello B, Riddle M, et al. Methylphenidate effects on functional outcomes in the Preschoolers with Attention-Deficit/Hyperactivity Disorder Treatment Study (PATS). J Child Adolesc Psychopharmacol. 2007;17(5):581-92. PMID: 17979579. *IncludeDE_KQ2* Record ID 18292

7. Abikoff HB, Thompson M, Laver-Bradbury C, et al. Parent training for preschool ADHD: a randomized controlled trial of specialized and generic programs. J Child Psychol Psychiatry. 2015 Jun;56(6):618-31. doi: 10.1111/jcpp.12346. PMID: 25318650. *IncludeDE_KQ2* Record ID 15312

8. Abramov DM, Lazarev VV, Gomes SC, et al. Estimating biological accuracy of DSM for attention deficit/hyperactivity disorder based on multivariate analysis for small samples. PeerJ. 2019;2019(6). doi: 10.7717/peerj.7074. *IncludeDE_KQ1* Record ID 6307

9. Adams R, Finn P, Moes E, et al. Distractibility in Attention/Deficit/ Hyperactivity Disorder (ADHD): the virtual reality classroom. Child Neuropsychol. 2009 Mar;15(2):120-35. doi: 10.1080/09297040802169077. PMID: 18608217. *IncludeDE_KQ1* Record ID 24382

10. Aevi Genomic Medicine L, a Cerecor company, Inc C. Efficacy and Safety of NFC-1 in Adolescents With Genetic Disorders Impacting mGluR and ADHD. 2016. *IncludeDE_KQ2* Record ID 13819

11. Aevi Genomic Medicine L, a Cerecor company, Inc C. PART B: Efficacy and Safety of AEVI-001 in Children and Adolescents With ADHD and Without mGluR Mutations. 2018. *IncludeDE_KQ2* Record ID 13863

12. Ahmadi A, Kashefi M, Shahrokhi H, et al. Computer aided diagnosis system using deep convolutional neural networks for ADHD subtypes. Biomedical Signal Processing and Control. 2021;63. doi: 10.1016/j.bspc.2020.102227. *IncludeDE_KQ1* Record ID 6333

13. Akhondzadeh S, Mohammadi MR, Khademi M. Zinc sulfate as an adjunct to methylphenidate for the treatment of attention deficit hyperactivity disorder in children: a double blind and randomized trial [ISRCTN64132371]. BMC Psychiatry. 2004 Apr 8;4:9. doi: 10.1186/1471-244x-4-9. PMID: 15070418. *IncludeDE_KQ2* Record ID 24386

14. Algorta GP, Dodd AL, Stringaris A, et al. Diagnostic efficiency of the SDQ for parents to identify ADHD in the UK: a ROC analysis. Eur Child Adolesc Psychiatry. 2016 Sep;25(9):949-57. doi: 10.1007/s00787-015-0815-0. PMID: 26762184. *IncludeDE_KQ1* Record ID 12707

15. Allen AJ, Kurlan RM, Gilbert DL, et al. Atomoxetine treatment in children and adolescents with ADHD and comorbid tic disorders. Neurology. 2005 Dec 27;65(12):1941-9. doi: 10.1212/01.wnl.0000188869.58300.a7. PMID: 16380617. *IncludeDE_KQ2* Record ID 17787

16. Alloway TP, Gathercole SE, Holmes J, et al. The diagnostic utility of behavioral checklists in identifying children with ADHD and children with

working memory deficits. Child Psychiatry Hum Dev. 2009 Sep;40(3):353-66. doi: 10.1007/s10578-009-0131-3. PMID: 19280339. *IncludeDE_KQ1* Record ID 24671

17. Altınkaynak M, Dolu N, Güven A, et al. Diagnosis of Attention Deficit Hyperactivity Disorder with combined time and frequency features. Biocybernetics and Biomedical Engineering. 2020;40(3):927-37. doi: 10.1016/j.bbe.2020.04.006. *IncludeDE_KQ1* Record ID 6402

18. Amado-Caballero P, Casaseca-de-la-Higuera P, Alberola-Lopez S, et al. Objective ADHD Diagnosis Using Convolutional Neural Networks Over Daily-Life Activity Records. IEEE J Biomed Health Inform. 2020 Sep;24(9):2690-700. doi: 10.1109/jbhi.2020.2964072. PMID: 31905156. *IncludeDE_KQ1* Record ID 3394

19. Amiri S, Mohammadi MR, Mohammadi M, et al. Modafinil as a treatment for Attention-Deficit/Hyperactivity Disorder in children and adolescents: a double blind, randomized clinical trial. Prog Neuropsychopharmacol Biol Psychiatry. 2008 Jan 1;32(1):145-9. doi: 10.1016/j.pnpbp.2007.07.025. PMID: 17765380. *IncludeDE_KQ2* Record ID 17500

20. Antshel KM, Remer R. Social skills training in children with attention deficit hyperactivity disorder: a randomized-controlled clinical trial. J Clin Child Adolesc Psychol. 2003 Mar;32(1):153-65. doi: 10.1207/S15374424JCCP3201_14. PMID: 12611031. *IncludeDE_KQ2* Record ID 24627

21. Arjona A, Angulo-Ruiz BY, Rodríguez-Martínez EI, et al. Time-frequency neural dynamics of ADHD children and adolescents during a Working Memory task. Neurosci Lett. 2023 Feb 28;798:137100. doi: 10.1016/j.neulet.2023.137100. PMID: 36720344. *IncludeDE_KQ1* Record ID 25630

22. Arnold LE, Amato A, Bozzolo H, et al. Acetyl-L-carnitine (ALC) in attention-deficit/hyperactivity disorder: a multi-site, placebo-controlled pilot trial. J Child Adolesc Psychopharmacol. 2007 Dec;17(6):791-802. doi: 10.1089/cap.2007.018. PMID: 18315451. *IncludeDE_KQ2* Record ID 28665

23. Arnold LE, Arns M, Barterian JA, et al. Neurofeedback for Attention-Deficit/Hyperactivity Disorder: 25-Month Follow-up of Double-Blind Randomized Controlled Trial. J Am Acad Child Adolesc Psychiatry. 2022 Dec 8;62(4):435-46. doi: 10.1016/j.jaac.2022.07.862. PMID: 36521694. *IncludeDE_KQ2* Record ID 23948

24. Ashkenasi A. Effect of transdermal methylphenidate wear times on sleep in children with attention deficit hyperactivity disorder. Pediatr Neurol. 2011 Dec;45(6):381-6. doi: 10.1016/j.pediatrneurol.2011.09.003. PMID: 22115000. *IncludeDE_KQ2* Record ID 17185

25. Aviv TM, Katz YJ, Berant E. The Contribution of Therapeutic Horseback Riding to the Improvement of Executive Functions and Self-Esteem Among Children With ADHD. J Atten Disord. 2021 Oct;25(12):1743-53. doi: 10.1177/1087054720925898. PMID: 32508191. *IncludeDE_KQ2* Record ID 27246

26. Azami S, Alimadadi Z, Ahmadi A, et al. The efficacy of cognitive-motor rehabilitation on cognitive functions and behavioral symptoms of attention deficit/hyperactivity disorder (ADHD) children: Specification of near-transfer and far-transfer effects in comparison to medication. J Educ Health Promot. 2023;12:64. doi: 10.4103/jehp.jehp_189_22. PMID: 37113411. *IncludeDE_KQ2* Record ID 28210

27. Bakhshayesh AR, Hänsch S, Wyschkon A, et al. Neurofeedback in ADHD: a single-blind randomized controlled trial. Eur Child Adolesc Psychiatry. 2011 Sep;20(9):481-91. doi: 10.1007/s00787-011-0208-y. PMID: 21842168. *IncludeDE_KQ2* Record ID 17184

28. Banaschewski T, Soutullo C, Lecendreux M, et al. Health-related quality of life and functional outcomes from a randomized, controlled study of lisdexamfetamine dimesylate in children and adolescents with attention deficit hyperactivity disorder. CNS Drugs. 2013 Oct;27(10):829-40. doi: 10.1007/s40263-013-0095-5. PMID: 23893527. *IncludeDE_KQ2* Record ID 14417

29. Bangs ME, Emslie GJ, Spencer TJ, et al. Efficacy and safety of atomoxetine in adolescents with attention-deficit/hyperactivity disorder and major depression. J Child Adolesc Psychopharmacol. 2007 Aug;17(4):407-20. doi: 10.1089/cap.2007.0066. PMID: 17822337. *IncludeDE_KQ2* Record ID 17598

30. Bangs ME, Hazell P, Danckaerts M, et al. Atomoxetine for the treatment of attention-deficit/hyperactivity disorder and oppositional defiant disorder. Pediatrics. 2008 Feb;121(2):e314-20. doi: 10.1542/peds.2006-1880. PMID: 18245404. *IncludeDE_KQ2* Record ID 24404

31. Bansal R, Staib LH, Laine AF, et al. Anatomical brain images alone can accurately diagnose chronic neuropsychiatric illnesses. PLoS One. 2012;7(12):e50698. doi: 10.1371/journal.pone.0050698. PMID: 23236384. *IncludeDE_KQ1* Record ID 18

32. Bard DE, Wolraich ML, Neas B, et al. The psychometric properties of the Vanderbilt attention-

deficit hyperactivity disorder diagnostic parent rating scale in a community population. J Dev Behav Pediatr. 2013 Feb;34(2):72-82. doi: 10.1097/DBP.0b013e31827a3a22. PMID: 23363972. *IncludeDE_KQ1* Record ID 27337

33. Barkley RA, Grodzinsky GM. Are tests of frontal lobe functions useful in the diagnosis of attention deficit disorders? Clinical Neuropsychologist. 1994;8(2):121-39. doi: 10.1080/13854049408401552. *IncludeDE_KQ1* Record ID 27282

34. Baziar S, Aqamolaei A, Khadem E, et al. Crocus sativus L. Versus Methylphenidate in Treatment of Children with Attention-Deficit/Hyperactivity Disorder: A Randomized, Double-Blind Pilot Study. J Child Adolesc Psychopharmacol. 2019 Apr;29(3):205-12. doi: 10.1089/cap.2018.0146. PMID: 30741567. *IncludeDE_KQ2* Record ID 287

35. Bédard AC SM, Halperin JM, Krone B, Rajwan E, Newcorn JH. Differential impact of methylphenidate and atomoxetine on sustained attention in youth with attention-deficit/hyperactivity disorder. J Child Psychol Psychiatry. 2015 Jan;56(1):40-8. doi: 10.1111/jcpp.12272. PMID: 24942409. *IncludeDE_KQ2* Record ID 19249

36. Behdani F, Hebrani P, Naseraee A, et al. Does omega-3 supplement enhance the therapeutic results of methylphenidate in attention deficit hyperactivity disorder patients? J Res Med Sci. 2013 Aug;18(8):653-8. PMID: 24379840. *IncludeDE_KQ2* Record ID 27189

37. Benzing V, Schmidt M. The effect of exergaming on executive functions in children with ADHD: A randomized clinical trial. Scand J Med Sci Sports. 2019 Aug;29(8):1243-53. doi: 10.1111/sms.13446. PMID: 31050851. *IncludeDE_KQ2* Record ID 258

38. Berger I, Slobodin O, Cassuto H. Usefulness and Validity of Continuous Performance Tests in the Diagnosis of Attention-Deficit Hyperactivity Disorder Children. Arch Clin Neuropsychol. 2017 Feb;32(1):81-93. doi: 10.1093/arclin/acw101. PMID: 28122767. *IncludeDE_KQ1* Record ID 859

39. Berger I GG. Objective measures of attention-deficit/hyperactivity disorder: a pilot study. Isr Med Assoc J. 2010 Sep;12(9):531-5. PMID: 21287795. *IncludeDE_KQ1* Record ID 17002

40. Bergeron L, Smolla N, Berthiaume C, et al. Reliability, Validity, and Clinical Utility of the Dominic Interactive for Adolescents-Revised(A DSM-5-Based Self-Report Screen for Mental Disorders, Borderline Personality Traits, and Suicidality). Can J Psychiatry. 2017 Mar;62(3):211-22. doi: 10.1177/0706743716670129. PMID: 27638424. *IncludeDE_KQ1* Record ID 27340

41. Beriha SS. Computer aided diagnosis system to distinguish adhd from similar behavioral disorders. Biomedical and Pharmacology Journal. 2018;11(2):1135-41. doi: 10.13005/bpj/1474. *IncludeDE_KQ1* Record ID 6627

42. Biederman J, Krishnan S, Zhang Y, et al. Efficacy and tolerability of lisdexamfetamine dimesylate (NRP-104) in children with attention-deficit/hyperactivity disorder: a phase III, multicenter, randomized, double-blind, forced-dose, parallel-group study. Clin Ther. 2007 Mar;29(3):450-63. doi: 10.1016/s0149-2918(07)80083-x. PMID: 17577466. *IncludeDE_KQ2* Record ID 24396

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Appendix F. Expert Guidance and Review

Input in Formulating the Research Protocol

A virtual workshop facilitated by PCORI in November 2021 discussed the draft KQs and PICOTs. Details on the virtual workshop, including a list of participants, can be found at https://www.pcori.org/events/2021/pcori-stakeholder-webinar-adhd-children-and-adolescents.

Participants in the workshop represented different viewpoints which included patients, patient advocates, clinicians, guideline developers and researchers.

During the virtual workshop, participants provided input and guidance on the KQs and PICOTs. Based upon the from the workshop, the protocol was developed by the EPC and the KQs were modified with guidance from PCORI and AHRQ.

The participants did not do analysis of any kind or contribute to the writing of this draft report. They will be given the opportunity to review the report through the peer or public review mechanisms.

Appendix G. PCORI Checklist

This systematic review adheres to the PCORI Methodology Standards enumerated below.

PCORI Methodology Standards Checklist

Follow the instructions provided below. Upload the completed template as an Excel file into PCORI Online. Detailed instructions are included in the Submission Instructions for this PCORI Funding Announcement (PFA). Refer to the PCORI Methodology Report for explanations about the standards.

In the checklist below, you will see a complete list of the PCORI Methodology Standards. In column D, using the drop-down menu options, indicate whether or not each methodology standard applies to your research. If the standard applies, in column E, provide the page number of your research plan where the text illustrates how you addressed the standard. Lastly, in column F, indicate whether your study may deviate from the standard and provide a rationale. Repeat the sequence for each standard. **Note: Do not add or delete columns or rows in this template.**

Application ID	**Contract No. 75Q80120D00009**
PI Name	**Susanne Hempel**
Application Title	**Systematic Review – ADHD Diagnosis and Treatment in Children and Adolescents**

Standard Category	Abbrev.	Standard	Have you addressed how you plan to adhere to the standard in your application?	List page numbers	Notes
Cross-Cutting Standards for PCOR					
Standards for Formulating Research Questions	RQ-1	Identify gaps in evidence	Yes	1	Introduction
	RQ-2	Develop a formal study protocol	Yes	See notes	Available on the AHRQ website and registered in PROSPERO
	RQ-3	Identify specific populations and health decision(s) affected by the research	Yes	7	Methods
	RQ-4	Identify and assess participant subgroups	Yes	8 and 9	KQs1c
	RQ-5	Select appropriate interventions and comparators	Yes	9 and 11	Methods
	RQ-6	Measure outcomes that people representing the population of interest notice and care about	Yes	9 and 11	Methods
Standards Associated with Patient-Centeredness	PC-1	Engage people representing the population of interest and other relevant stakeholders in ways that are appropriate and necessary in a given research context	Yes	vi and vii	Frontmatter (KI and TEP)
	PC-2	Identify, select, recruit, and retain study participants representative of the spectrum of the population of interest and ensure that data are collected thoroughly and systematically from all study participants	Yes	7	Methods
	PC-3	Use patient-reported outcomes when patients or people at risk of a condition are the best source of information for outcomes of interest	Yes	See notes	Results
	PC-4	Support dissemination and implementation of study results	Yes	See notes	Accompanying manuscipt(s)
Standards for Data Integrity and Rigorous Analyses	IR-1	A priori, specify plans for data analysis that correspond to major aims	Yes	See notes	Published protocol
	IR-2	Assess data source adequacy	Yes	13	Risk of bias assessment
	IR-3	Describe data linkage plans, if applicable	Yes	See notes	Data will be published in SRDRPlus
	IR-4	Document validated scales and tests	Yes	See notes	Evidence tables in the appendix
	IR-5	Provide sufficient information in reports to allow for assessments of the study's internal and external validity	Yes	14, 15, 16	Methods
	IR-6	Masking should be used when feasible	N/A	N/A	Standard does not apply
	IR-7	In the study protocol, specify a data management plan that addresses, at a minimum, the following elements: collecting data, organizing data, handling data, describing data, preserving data, and sharing data.	Yes	See notes	Published protocol
	MD-1	Describe methods to prevent and monitor missing data	Yes	18 and 19	Methods

Standard Category	Abbrev.	Standard	Have you addressed how you plan to adhere to the standard in your application?	List page numbers	Notes
Standards for Preventing and Handling Missing Data	MD-2	Use valid statistical methods to deal with missing data that properly account for statistical uncertainty due to missingness	Yes	18 and reported in the Results chapter by each KQ	SoE assessment, result section
	MD-3	Record and report all reasons for dropout and missing data, and account for all patients in reports	Yes	Reported in the Results chapter by each KQ	Results
	MD-4	Examine sensitivity of inferences to missing data methods and assumptions, and incorporate into interpretation	Yes	Reported in the Results chapter by each KQ	Results
Standards for Heterogeneity of Treatment Effect (HTE)	HT-1	State the goals of HTE analyses, including hypotheses and the supporting evidence base	Yes	Reported in the Results chapter by each KQ	Results
	HT-2	For all HTE analyses, provide an analysis plan, including the use of appropriate statistical methods	Yes	14, 15	Methods
	HT-3	Report all prespecified HTE analyses and, at minimum, the number of post-hoc HTE analyses, including all subgroups and outcomes analyzed	Yes	Reported in the Results chapter by each KQ	Results
Standards for Specific Study Designs and Methods					
Standards for Data Registries	DR-1	Requirements for the design of registries	N/A		Standard does not apply
	DR-2	Documentation and reporting requirements of registry materials, characteristics, and bias	N/A		Standard does not apply
	DR-3	Adapting established registries for PCOR	N/A		Standard does not apply
	DR-4	Documentation requirements when using registry data	N/A		Standard does not apply
Standards for Data Networks as Research-Facilitating Structures	DN-1	Requirements for the design and features of data networks	N/A		Standard does not apply
	DN-2	Selection and use of data networks	N/A		Standard does not apply
Causal Inference Standards	CI-1	CI-I: Specify the causal model underlying the research question ***CROSS-CUTTING STANDARD***	N/A		Standard does not apply
	CI-2	Define and appropriately characterize the analysis population used to generate effect estimates	Yes	Reported in the Results chapter by each KQ and in Appendix C	Results and evicence table
	CI-3	Define with the appropriate precision the timing of the outcome assessment relative to the initiation and duration of exposure	Yes	Appendix C	Evidence tables
	CI-4	Measure potential confounders before start of exposure and report data on potential confounders with study results	Yes	Reported in the Results chapter by each KQ	Results and meta-regressions
	CI-5	Report the assumptions underlying the construction of propensity scores and the comparability of the resulting groups in terms of the balance of covariates and overlap	N/A	See notes	Standard does not apply

Standard Category	Abbrev.	Standard	Have you addressed how you plan to adhere to the standard in your application?	List page numbers	Notes
	CI-6	Assess the validity of the instrumental variable (i.e. how the assumptions are met) and report the balance of covariates in the groups created by the instrumental variable	N/A	See notes	Standard does not apply
Standards for Adaptive and Bayesian Trial Designs	AT-1	Specify planned adaptations, decisional thresholds, and statistical properties of those adaptations	N/A	See notes	Standard does not apply
	AT-2	Specify the structure and analysis plan for Bayesian adaptive randomized clinical trial designs	N/A	See notes	Standard does not apply
	AT-3	Ensure that clinical trial infrastructure is adequate to support planned adaptation(s) and independent interim analyses	N/A	See notes	Standard does not apply
	AT-4	When reporting adaptive randomized clinical trials, use the CONSORT statement, with modifications	N/A	See notes	Standard does not apply
Standards for Studies of Medical Tests	MT-1	Specify the clinical context and key elements of the medical test	N/A	See notes	Standard does not apply
	MT-2	Assess the effect of factors known to affect performance and outcomes	N/A	See notes	Standard does not apply
	MT-3	Focus studies of medical tests on patient-centered outcomes, using rigorous study designs with a preference for randomized controlled trials	N/A	See notes	Standard does not apply
Standards for Systematic Reviews	SR-1	Adhere to National Academy of Medicine (NAM) standards for systematic reviews of comparative effectiveness research, as appropriate	Yes	See notes	Published protocol and report
Standards on Research Designs Using Clusters	RC-1	Specify whether the study objectives, the interventions, and the primary outcomes pertain to the cluster level or the individual level	N/A	See notes	Standard does not apply
	RC-2	Justify the choice of cluster randomization	N/A	See notes	Standard does not apply
	RC-3	Power and sample size estimates must use appropriate methods to account for the dependence of observations within clusters and the degrees of freedom available at the cluster level	N/A	See notes	Standard does not apply
	RC-4	Data analyses must account for the dependence of observations within clusters regardless of its magnitude	N/A	See notes	Standard does not apply
	RC-5	Stratified randomization should be used when feasible	N/A	See notes	Standard does not apply
Standards for Studies of Complex Interventions	SCI-1	Fully describe the intervention and comparator and define their core functions	N/A	See notes	Standard does not apply
	SCI-2	Specify the hypothesized causal pathways and their theoretical basis.	N/A	See notes	Standard does not apply
	SCI-3	Specify how adaptations to the form of the intervention and comparator will be allowed and recorded	N/A	See notes	Standard does not apply
	SCI-4	Plan and describe a process evaluation	N/A	See notes	Standard does not apply
	SCI-5	Select patient outcomes informed by the causal pathway	N/A	See notes	Standard does not apply
	QM-1	State the qualitative approach to research inquiry, design, and conduct	Yes	13	Methods
	QM-2	Select and justify appropriate qualitative methods sampling strategy	Yes	13	Methods

Standard Category	Abbrev.	Standard	Have you addressed how you plan to adhere to the standard in your application?	List page numbers	Notes
Standards for Qualitative Methods	QM-3	Link the qualitative data analysis, interpretations, and conclusions to the study question	Yes	Reported in the Results chapter by each KQ	Results
	QM-4	Establish trustworthiness and credibility of qualitative research	Yes	Reported in the Results chapter by each KQ	Results
Standards for Mixed Methods Research	MM-1	Specify how mixed methods are integrated across design, data sources, and/or data collection phases	N/A	See notes	Standard does not apply
	MM-2	Select and justify appropriate mixed methods sampling strategy	N/A	See notes	Standard does not apply
	MM-3	Integrate data analysis, data interpretation, and conclusions	N/A	See notes	Standard does not apply
Standards for Individual Participant-Level Data Meta-Analysis (IPD-MA)	IPD-1	Specify the research question(s) that will be addressed through the IPD-MA and describe the specific information it will provide that other approaches would not	N/A	See notes	Standard does not apply
	IPD-2	Describe the proposed governance structure for the IPD-MA in the protocol and study reports	N/A	See notes	Standard does not apply
	IPD-3	Use systematic, reproducible methods to identify studies for inclusion in the IPD-MA	N/A	See notes	Standard does not apply
	IPD-4	Specify the design and planned analyses of the IPD-MA in a protocol, document any changes, and report significant amendments and modifications	N/A	See notes	Standard does not apply