Draft Comparative Effectiveness Review

Number xx

Systematic Review – ADHD Diagnosis and Treatment in Children and Adolescents

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Contract No. [to be inserted in the final report]

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AHRQ Publication No. xx-EHCxxx
<Month Year>

This report is based on research conducted by the [to be inserted in the final report] Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. [to be inserted in the final report]). The Patient-Centered Outcomes Research Institute® (PCORI®) funded the report (PCORI® Publication No. 2023-SR-03). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ or PCORI®, its Board of Governors or Methodology Committee. Therefore, no statement in this report should be construed as an official position of PCORI®, AHRQ or of the U.S. Department of Health and Human Services.

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.

A representative from AHRQ served as a Contracting Officer's Representative and reviewed the contract deliverables for adherence to contract requirements and quality. AHRQ did not directly participate in the literature search, determination of study eligibility criteria, data analysis, interpretation of data, or preparation or drafting of this report.

AHRQ appreciates appropriate acknowledgment and citation of its work. Suggested language for acknowledgment: This work was based on an evidence report, Systematic Review – ADHD Diagnosis and Treatment in Children and Adolescents, by the Evidence-based Practice Center Program at the Agency for Healthcare Research and Quality (AHRQ).

Suggested citation: [to be inserted in the final report]. Systematic Review – ADHD Diagnosis and Treatment in Children and Adolescents. Effectiveness Review No. XXX. (Prepared by the [to be inserted in the final report] Evidence-based Practice Center under Contract No. [to be inserted in the final report].) AHRQ Publication No. [Insert Number]. PCORI Publication No. XXXX-SR-XX. Rockville, MD: Agency for Healthcare Research and Quality; [Insert Date]. DOI: [Insert DOI]
Posted final reports are located on the Effective Health Care Program search page.

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 EPC (to be added for the final version) (Contract Number: to be added for the final version).

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 (PCORI) was established to fund research that helps patients and caregivers make better informed health care 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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Acknowledgments

The authors gratefully acknowledge the following individuals for their contributions to this project: [to be inserted in the final report]

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.

The list of Key Informants who provided input to this report follows:

[to be inserted in the final report]

Technical Expert Panel

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.

Technical Experts 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 conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

The list of Technical Experts who provided input to this report follows:

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*Provided input on Draft Report

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 non-financial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential non-financial conflicts of interest identified.

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Systematic Review – 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, and clinicaltrials.gov and prior reviews for primary studies published since 1980. The draft report includes studies published to 2021, and an ongoing update search will capture 2022 and 2023 studies.

Review methods. The review followed a detailed protocol and was supported by a Technical Expert Panel (TEP). 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.

Results. Searches identified 22,091 citations, and 6,900 were obtained as full text. We included 533 studies reported in 1,058 publications (223 studies addressed diagnosis, 304 studies addressed treatment, and 9 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, biomarkers, activity monitoring, and observation. Multiple approaches showed promising diagnostic performance but estimates of performance varied considerably across studies and the SoE was generally low. Few studies report estimates for children under the age of 7 years. Treatment studies evaluated FDA-approved and newer, non-FDA-approved pharmacological agents, psychological/ behavioral approaches, combined pharmacological and behavior approaches, cognitive training, physical exercise, nutrition and supplements, integrative medicine, parent support, school interventions, and provider or model-of-care interventions. Pharmacological 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, neurofeedback, and school interventions showed improvement in ADHD symptoms (moderate SoE). Few studies have evaluated combinations of pharmacological and behavioral interventions and we did not find combination treatments superior to monotherapy. Monitoring approaches for ADHD were limited to nine evaluations of ADHD monitoring strategies, and the SoE is insufficient.

Conclusion. Many diagnostic tools are available to diagnose ADHD, but few monitoring strategies have been studied. Medication therapies remain important treatment options, even as other non-drug treatment approaches emerge.

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Executive Summary

Main Points

Diagnosis

- 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 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 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 7 years and more research is needed.
- The identified studies did not assess the adverse effects of being labeled correctly or incorrectly as having a diagnosis of ADHD.

Treatment

- We found moderate strength of evidence that several treatment modalities improve core ADHD symptoms with a moderate effect size compared to control groups (e.g., placebo). These include FDA-approved medications, psychosocial interventions, neurofeedback, and school interventions.
- FDA-approved stimulant (e.g., methylphenidate) and non-stimulant (e.g., atomoxetine) medications had the strongest evidence across interventions for significantly improving ADHD symptoms and additional outcomes, including broadband measures and functional impairment.
- Although indirect comparisons across studies suggest that the studies evaluating stimulants report larger effect sizes than studies evaluating non-stimulants for improving ADHD symptoms, head-to-head comparisons did not detect significant differences. Stimulant and non-stimulant medications yielded comparable effects on most effectiveness outcomes and adverse events, including appetite suppression.
- We did not find that combination therapies of medication plus psychococial 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 US 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 (TEP), a diverse panel of relevant stakeholders. The key questions (KQs) and the protocol were posted on the AHRQ Effective Health Care website (https://effectivehealthcare.ahrq.gov/) 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).

The draft report includes studies published Through 2021; an ongoing update search will capture 2022 and 2023 studies.

Results

The searches identified 22,091 citations. Of these, we obtained 6,900 as full text. In total, 533 studies reported in 1,058 publications met the eligibility criteria. This included 223 studies addressing diagnosis (KQ1), 304 studies addressing treatment (KQ2), and 9 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, biomarkers, activity measures, and observation. 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 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 7 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 pharmacological and new agents, psychological or behavioral approaches, combined pharmacological and behavior, cognitive training, 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 moderate to high strength of evidence that several treatment modalities improve core ADHD symptoms with a moderate effect size compared to control groups (e.g., placebo). These include FDA-approved medications (SMD -0.58; CI -0.67, -0.50; 46 studies, n=7237; RR 1.85, CI 1.38, 2.48; 11 studies, n=1751, high SoE), psychosocial interventions (SMD -0.34, CI -0.53, -0.14; 12 studies, n=1450; moderate SoE), neurofeedback (SMD -0.45; CI -0.83, -0.08; 8 studies, n=736; moderate SoE); and school interventions (SMD -0.50; CI -0.92, -0.07; 6 studies, n=898; moderate SoE).

FDA-approved medications had the strongest evidence for significantly improving additional outcomes, including measures describing child behavior more broadly (RR 0.53; CI 0.42, 0.64; 24 studies, n=4044; high SoE) and functional impairment (SMD 0.49; CI 0.12, 0.86; 12 studies, n=2152; moderate SoE). Effect sizes on ADHD symptoms in studies evaluating stimulants versus control (SMD -0.88; CI -1.13, -0.062; 12 studies, n=1471) were larger than those in studies evaluating non-stimulant medications versus control (SMD -0.50; CI -0.57, -0.43; 33 studies, n=5684), though head-to-head comparisons did not detect significant differences between these medication classes on ADHD symptoms (SMD 0.23; CI -0.03, 0.49; 7 studies, n=1611). Medication studies typically did not include children under 6 years of age. Identified combination therapies of medication plus psychosocial interventions did not produce better results than medication alone (e.g., ADHD symptoms SMD -0.02; CI -0.20, 0.15; 4 studies, n=630; moderate SoE), although existing research evaluated unique intervention component combinations, and the evidence base is limited.

Despite the large body of research, comparative effectiveness and safety information is limited. Stimulant and non-stimulant medications yielded comparable effects on most effectiveness outcomes and assessed adverse events. 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 few monitoring strategies have been studied. Medication therapy remains a central treatment modality even as evidence for other non-pharmacolocial therapies strengthen and as novel treatment approaches emerge.

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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 US children have received a clinical diagnosis of ADHD.[1] Clinical diagnoses have increased steadily over time,[2] though the higher rates seem 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. The increasing rates of diagnosis could in part 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 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] 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 reporters,[16] and likely overestimate the prevalence of ADHD.[17, 18] More objective diagnostic tools have been proposed, including activity monitors,[19] neuropsychological test measures,[20-23] biomarkers such as genotyping,[24] electrophysiological indices,[25, 26] and MRI measures,[27, 28] 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 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 children in elementary school are expected to have,[29] further obscuring the distinction between ADHD and neurotypical early childhood behaviors.

ADHD diagnosis is normally based on an assessment to determine whether the patient meets the criteria described in the DSM-5-TR.[30] 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[30] (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 is separating ADHD from other conditions that may appear similar (e.g., anxiety, conduct disorders, speech or language delay, other developmental disorders) and determining whether another condition may better explain ADHD symptoms or is present as a co-occurring diagnosis.

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.[29, 31] Prescription of stimulant medications across the US population has doubled in the last decade,[32] with a prevalence in 2019 of approximately 6 percent, and as high as 14 percent regionally.[33] These rates are higher than the 5.3 percent population prevalence of rigorously diagnosed ADHD,[34] suggesting that many youth may be receiving stimulants when they do not have ADHD.[34, 35] These trends have created alarm in the lay public, policy makers, and health care providers.[35, 36] Adding to their concern is that diversion and abuse of stimulants is common, particularly in college students.[37] 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 US children who receive a clinical diagnosis of ADHD are treated with stimulants,[38] suggesting a large number of children are not receiving medication when perhaps they should be. Additional important clinical consequences of an incorrect diagnosis include stigmatizing youth unnecessarily with a diagnosis of ADHD[29, 39] (i.e., "labeling harms," which can impair self-esteem or reduce future educational attainment or career opportunities).[40-42] 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, speech or language delay, complex trauma, difficult home environments, attachment problems or other medical disorders/diseases or developmental disorders).[43-46] 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.

1. Introduction

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.[47] 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).[48, 49] 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 (selective 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 therapies* (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 EEG activity), *nutritional or dietary supplements* (e.g., Omega-3, vitamins, herbs), *complementary, alternative, or integrative medicine* (acupuncture, homeopathy, physical therapy, and chiropractic treatment).
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.[50] 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.[51]

1. Introduction

Reported effect sizes on short-term outcomes for either class of stimulant medication (methylphenidate or amphetamine) have been large, whereas effect sizes for psychological and behavioral therapies on short-term outcomes generally have been small or moderate in magnitude.[50] Long-term outcomes for both medication and non-medication therapies have been less well studied,[50] 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. SMART (Sequential Multiple Assignment Randomized Trial) study designs have begun to emerge to help identify the best sequences of treatment and they have begun to call into question the dominant practice of beginning treatment with medication rather than behavioral therapy.[52] Emerging SMART designs also help identify which treatment sequences work best for which type of patient – young or old, in which ethnic group, with which co-occurring illnesses, and with which specific genotypes.[24, 53-56] 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 clinicians and stakeholders. These novel therapeutics include cognitive training,[57-60] game-based digital devices such as the FDA-approved EndeavorRx,[61] and neuromodulation techniques[62] such as repetitive Transcranial Magnetic Stimulation[63-65] and the FDA-approved external Trigeminal Nerve Stimulator.[66-68]

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?[69]

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.[70] 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 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 health care provider preferences. One-third to one-half of patients with ADHD will have clinically significant symptoms that persist into adulthood.

Co-occurring problems are the rule, as approximately half are diagnosed with an oppositional defiant or conduct disorder diagnosis, one-third have an anxiety disorder, and 20 percent have depression.[2] 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 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.[47] In addition, the long-term effectiveness of standard and novel interventions for ADHD, and their potential long-term adverse effects, are not well known[71-75] and are difficult to detect and document,[76-78] 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.[79]

1.2 Purpose and Scope of the Systematic Review

This review updates prior AHRQ reviews on ADHD.[11, 50, 80] 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.[16, 17, 23, 26, 81] 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).[82]

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.[52, 59, 67, 83-85] 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.

1. Introduction

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 *(available at https://effectivehealthcare.ahrq.gov/topics/cer-methods-guide/overview)*.

The topic of this report was developed by the Patient-Centered Outcomes Research Institute (PCORI) in consultation with AHRQ. KQs were posted on AHRQ's Effective Health Care (EHC) website for public comment in August 2021 for three weeks. PCORI conducted an online townhall meeting of stakeholder to discuss the comments in November 2021 (Appendix E). The protocol was refined following stakeholder input through public posting of the KQs, the townhall meeting, and input from key informants. The final protocol is posted on the EHC website at https://effectivehealthcare.ahrq.gov/products/attention-deficit-hyperactivity-disorder/protocol. A panel of technical experts provided high-level content and methodological expertise throughout development of the review protocol.

2.1.1 Key Questions (KQs)

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

We obtained input from eight key informants. Key informants included a parent of an underserved, ethnic minority youth with 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 elicit responses from stakeholders 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 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.[70]

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 stakeholder 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?

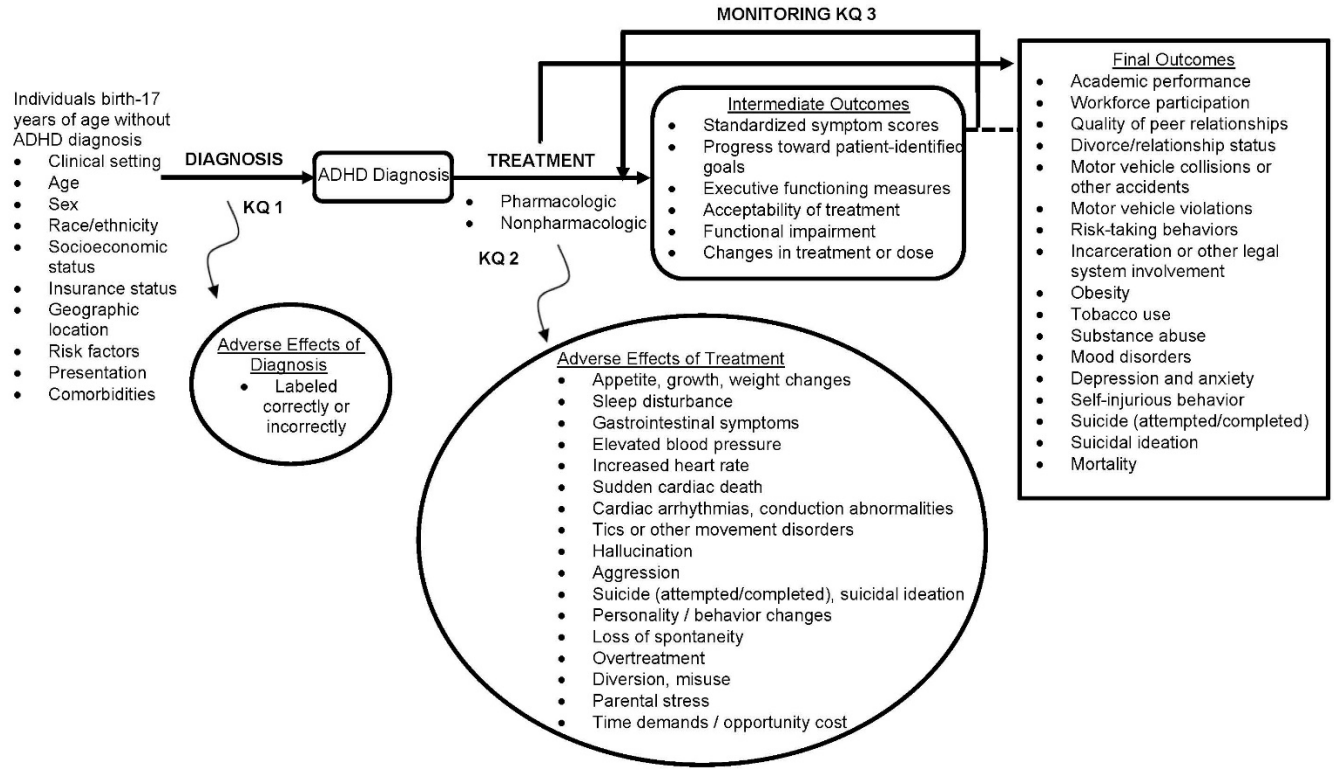
While the diagnosis and treatment KQs are unchanged from the 2018 AHRQ EPC report on the topic, the KQ regarding monitoring ADHD over time was rephrased for clarity. Of note, the restricted age range for sub-question 1b is based on recognition that most of these specialized technologies require the child 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



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 draft report includes studies published from 1980 to 2021, an ongoing update search will capture 2022 and 2023 studies.

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.[86-90] 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,[91] 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 is under peer review and open for public comment, we will update the search and include any eligible studies identified either during that search or through peer or public reviews 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

PICOTS 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 will be greater than 17, but these studies are 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)
Study Design	• Randomized controlled trials (RCTs)	• Randomized controlled trials (RCTs)	• Randomized controlled trials (RCTs)

2. Methods

PICOTS Element	KQ1 (Diagnosis)	KQ2 (Treatments)	KQ3 (Monitoring)
	• 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 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.	• 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 needs 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	• No study size restriction **Exclusion**: Editorials, nonsystematic reviews, letters, case series, case reports, pre-post studies. Systematic reviews are 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)

Note: FDA: Food and Drug Administration, KQ: Key Question

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.[92-95] 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 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.[96, 97]

QUADAS 2 evaluates four domains: *patient selection*, *index test* characteristics, *reference standard* quality, as well as *flow and timing*.[97]

- 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.

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.[98] 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 (CI) for all summary estimates. We tested for 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 or above. 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.[99] 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. For KQ3, we documented outcomes as reported by the original authors.

Pre-defined subgroups for KQ1 included children younger than 7 years of age and children and adolescents, 7 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 assessed the potential for publication bias for all key outcomes using the Begg and the Egger test.[100, 101] The trim and fill method provides alternative estimates where evidence of publication bias was detected.[102]

Applicability was assessed in accordance with the AHRQ's Methods Guide. Factors that may affect applicability, which we have identified a priori, include patient, intervention, comparisons, outcomes, settings, and study design features. 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.

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.[103] The initial assessment was then discussed in the team.

2.6.1 Key Outcomes

We prioritized outcomes with the help of the TEP 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
  - Inter-rater reliability
  - Internal consistency
  - Test-retest reliability
  - Misdiagnosis
- 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)[104] 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),[105, 106] 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.[107, 108] 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 number of patients reporting at least one adverse event; all other measures (including the number of adverse events across participants) 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 or magnitude of effect for a particular outcome; graded as consistent, inconsistent, or unknown (in the case of a single study).
- 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 reflects 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. Graded as precise or imprecise. When quantitative synthesis is not possible, sample size and assessment of variance within individual studies will be considered.
- 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. If sufficient numbers of RCTs are available, we reviewed Begg and Egger tests 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 limitations 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.[103] 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[109]

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. We will summarize updated evidence and describe what it adds to the previous review and highlight changes to the key findings.

2.7 Peer Review and Public Commentary

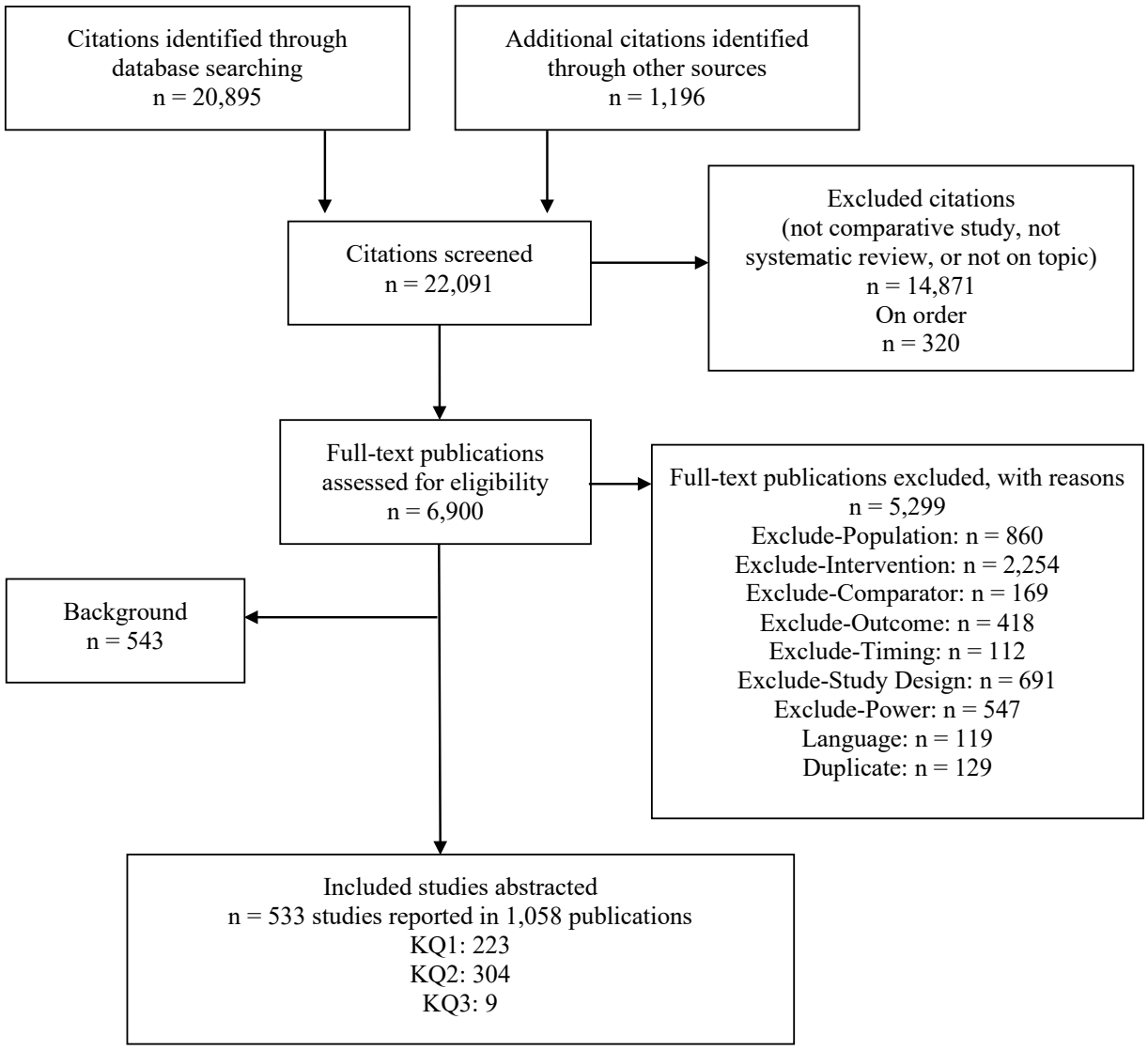
The report will be updated after having undergone peer review and public commentary.

3. Results: Description of Included Evidence

Below we provide the report results, including the Key Points for each 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 the Appendix.

The searches identified 22,091 citations. Of these, we obtained 6,900 as full text. The flow diagram (Figure 2) describes the study flow through the literature review.

Figure 2. Flow Diagram



In total, 533 studies reported in 1,058 publications met the eligibility criteria.[17, 20, 23, 26, 27, 52, 59, 83, 110-1159] This included 223 studies addressing KQ1, 304 studies addressing KQ2, and 9 studies addressing KQ3. 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 ADHD research that were then reference-mined to ensure that all eligible studies had been included in the report.

The median minimum age in included studies was six years old and the median number of girls included in the studies was 25 percent.

The following subchapters address each KQ.

4. Results: Diagnosis of ADHD

The 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 ADHD among individuals younger than 7 years of age?
- 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?
- 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, using a well-validated and reliable process of confirming the diagnosis of ADHD according to the DSM. Many identified studies included a broader age range rather than differentiating clearly between younger (KQ1a) or older (KQ1b) than 7 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 7 years of age regardless of the applied test. The KQ1b section describes teen/child self reports, EEG, imaging, and neuropsychological tests.

4.1 KQ1 ADHD Diagnosis Key Points

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

- Diagnostic test performance likely depend 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 unique 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 7 years and more research is needed.
- The identified 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 223 studies addressing the performance of tests aiming to diagnose ADHD.[17, 20, 23, 26, 27, 118, 119, 122, 124, 126-128, 131, 135, 140, 141, 147-151, 160, 161, 165, 167, 170, 175-178, 180, 185, 187-196, 201, 202, 215, 217, 218, 222, 227, 229, 235, 236, 238, 239, 241, 245, 246, 248-250, 254, 256, 263, 266, 270, 278, 279, 283-285, 287, 293, 297-300, 305, 307, 309, 311, 312, 315, 318, 319, 322, 326, 332, 334-336, 338, 340, 341, 345, 346, 349, 352, 355, 357, 359-362, 364, 373, 377, 380-382, 384-386, 388, 392-396, 398, 399, 402, 403, 405-407, 410-414, 417, 419, 423, 425, 426, 433-439, 450-453, 455-459, 461, 463, 465, 467, 471, 475, 476, 480-484, 486-490, 494, 502-504, 506, 507, 512, 515, 516, 524, 525, 529-532, 535-538, 542, 546, 547, 551, 553, 557, 558, 563, 567-571, 574, 579, 580, 586-588, 591, 592, 595, 597, 603, 604, 614, 618-621, 623, 626, 627, 629, 631, 634] Table 3 provides a very broad overview of the identified research. Results of the individual studies are shown in the evidence table in the appendix.

Table 3. 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	SoE*
KQ1a Diagnostic tests for under 7 year olds	Sensitivity	6 studies[170, 175, 193, 326, 406, 458]	Sensitivity ranged from 66% combining teacher and parent ratings (no corresponding specificity reported)[193] to 97% (corresponding specificity 84%) for an activity measure[406] differentiating ADHD and neurotypical development Sensitivity ranged from 64% (corresponding specificity 75%) for a neuropsychological test[170] to 76% (corresponding specificity 70%) for a different neuropsychological test[458] in clinical samples	Low
KQ1a Diagnostic tests for under 7 year olds	Specificity	6 studies[170, 175, 193, 326, 406, 458]	Specificity ranged from 38% (corresponding sensitivity 95) using EEG data[193] to 84% (corresponding sensitivity 97% and 87%)[193, 406] for an activity measure and an EEG algorithm differentiating ADHD and neurotypical development Specificity ranged from 70% (corresponding sensitivity 76%) for a neuropsychological test[458] to 91% (corresponding sensitivity 71%) for the *Child Behavior Checklist* for ages 1.5 to 5 Attention-Deficit/Hyperactivity Problems scale[326] in clinical samples	Low
KQ1a Diagnostic tests for under 7 year olds	Accuracy	5 studies[170, 193, 326, 406, 455]	Accuracy ranged from 64%[455] combining different executive function tasks to 93%[455] combining teacher and parent ratings, both in a model supported by machine learning differentiating ADHD and neurotypical development Accuracy ranged from 70%[170] for a neuropsychological test to 80%[326] for parent rating of the *Child Behavior Checklist* for ages 1.5 to 5 Attention-Deficit/Hyperactivity Problems scale in clinical samples	Low
KQ1a Diagnostic tests for under 7 year olds	AUC	6 studies[175, 193, 326, 402, 406, 455]	AUC ranged from 0.68[193] using EEG data to 0.98[455] for combined teacher and parent ratings differentiating ADHD and neurotypical development AUC was 0.83 in a clinical sample[326] using the *Child Behavior Checklist* for ages 1.5 to 5 Attention-Deficit/Hyperactivity Problems scale	Low

4. Results: Diagnosis of ADHD

Tests to diagnose ADHD	Outcome	Number of Studies; Study Design; IDs	Findings	SoE*
KQ1a Diagnostic tests for under 7 year olds	Inter-rater reliability	1 study[175]	ICC 0.92 between researchers administering the *Disruptive Behavior Diagnostic Observation Schedule*[175] differentiating ADHD and neurotypical development	Low
KQ1a Diagnostic tests for under 7 year olds	Internal consistency	2 studies[455, 504]	Neurotypical samples: Cronbach's alpha 0.92 for parent ratings on the *Diagnostic Infant and Preschool Assessment Likert version* (DIPA-L)[504] 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[455]	Low
KQ1a Diagnostic tests for under 7 year olds	Test-retest reliability	1 study[504]	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[504] differentiating ADHD and neurotypical development	Low
KQ1a Diagnostic tests for under 7 year olds	Misdiagnosis consequences	0 studies	No data	Insufficient
KQ1a Diagnostic tests for under 7 year olds	Costs	0 studies	No data	Insufficient
KQ1b Diagnostic tests for 7-18 year olds	Sensitivity	See test-specific results	See test-specific results	See test-specific results
KQ1b Diagnostic tests for 7-18 year olds	Specificity	See test-specific results	See test-specific results	See test-specific results
KQ1b Diagnostic tests for 7-18 year olds	Accuracy	See test-specific results	See test-specific results	See test-specific results
KQ1b Diagnostic tests for 7-18 year olds	AUC	See test-specific results	See test-specific results	See test-specific results
KQ1b Diagnostic tests for 7-18 year olds	Inter-rater reliability	See test-specific results	See test-specific results	See test-specific results
KQ1b Diagnostic tests for 7-18 year olds	Internal consistency	See test-specific results	See test-specific results	See test-specific results
KQ1b Diagnostic tests for 7-18 year olds	Test-retest reliability	See test-specific results	See test-specific results	See test-specific results
KQ1b Diagnostic tests for 7-18 year olds	Misdiagnosis consequences	See test-specific results	See test-specific results	See test-specific results

4. Results: Diagnosis of ADHD

Tests to diagnose ADHD	Outcome	Number of Studies; Study Design; IDs	Findings	SoE*
KQ1b Diagnostic tests for 7-18 year olds	Costs	See test-specific results	See test-specific results	See test-specific results
KQ1c (effect modifier) setting	Sensitivity	N/A	Indirect analyses indicated that the setting may be associated with reported results (p<0.001)	Low
KQ1c (effect modifier) setting	Specificity	N/A	Indirect analyses indicated that the setting may be associated with reported results (p<0.001)	Low
KQ1c (effect modifier) population	Sensitivity	N/A	Indirect analyses did not detect a systematic effect (p 0.21)	Low
KQ1c (effect modifier) population	Specificity	N/A	Indirect analyses indicated that the population may be associated with reported results (p 0.04)	Low
KQ1c (effect modifier) age	Sensitivity	N/A	Indirect analyses did not detect a systematic effect (p 0.90, p 0.58)	Low
KQ1c (effect modifier) age	Specificity	N/A	Indirect analyses did not detect a systematic effect (p 0.35, 0.45)	Low
KQ1c (effect modifier) gender	Sensitivity and specificity	N/A	Indirect analyses did not detect a systematic effect (p 0.80) but the number of female participants was small	Insufficient
KQ1d (labeling)	Any outcome	0 studies	No data	Insufficient

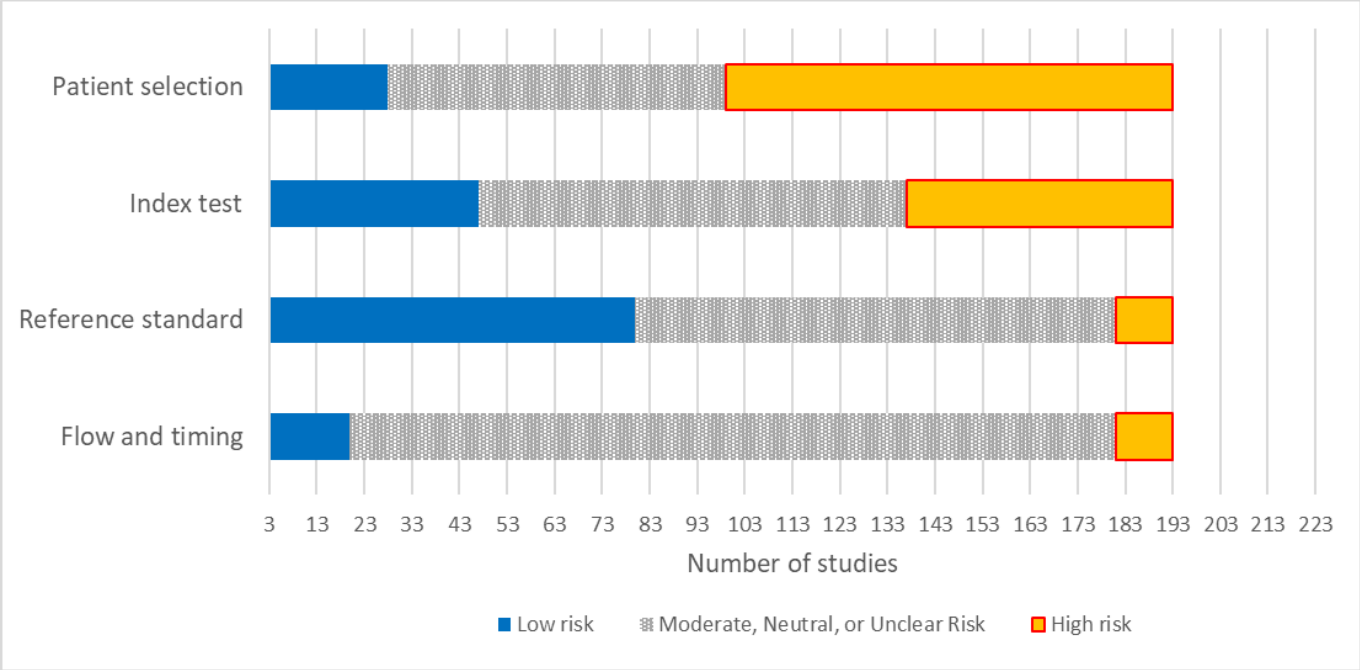
Notes: KQ key question, N/A not applicable, SoE strength of evidence

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. Few studies were available to diagnose ADHD in young children. Effect modifier analyses were hindered by the lack of reported detail, although indirect analyses indicated that the diagnostic setting (primary care or specialty care) may influence sensitivity and specificity estimates and population characteristics (comparison to neurotypical developing or clinical samples) may affect specificity estimates. Given that both aspects may be associated (e.g., clinical samples are seen in specialty care), we stratified the remainder of the 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.

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 and employed machine learning algorithm), 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).

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 3. The critical appraisal for the individual studies is in Appendix D.

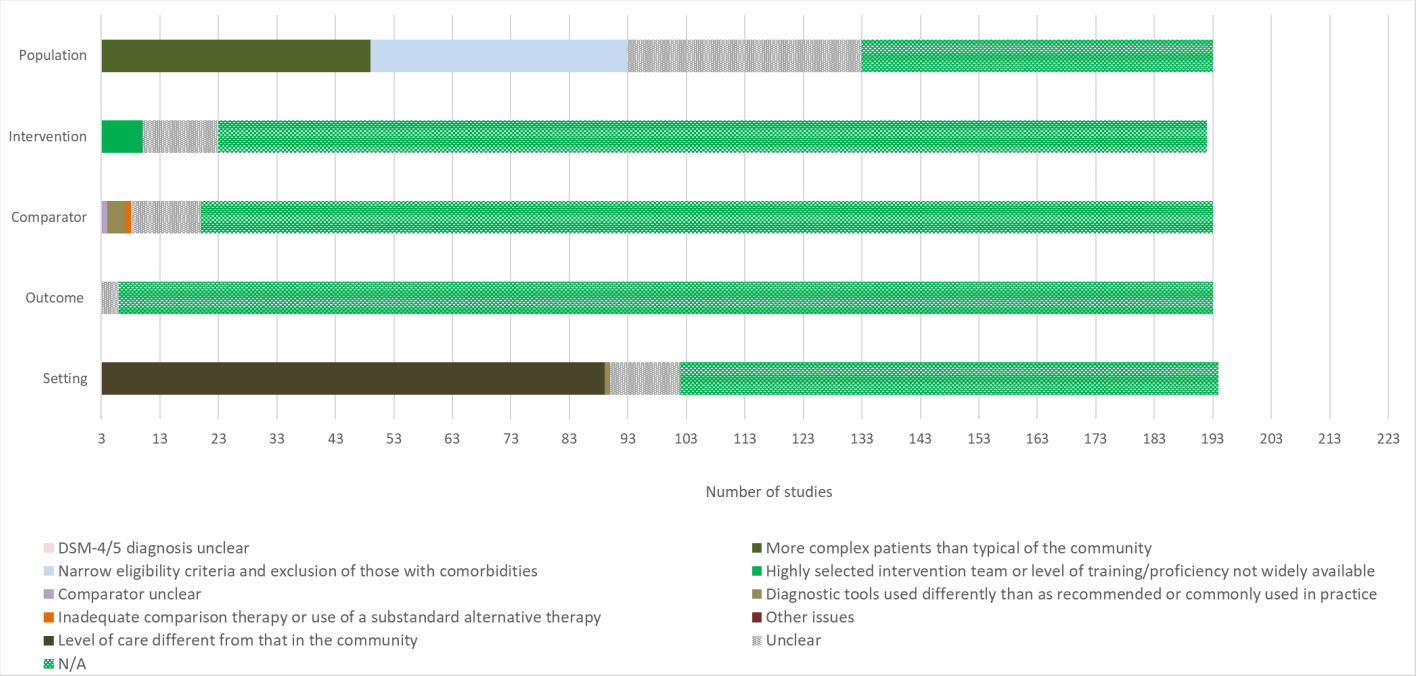
Figure 3. Risk of Bias in KQ1 Studies



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, in Robles et al., 2011,[487] a convenience sampling strategy was used. 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. [118, 149, 238, 338, 396, 402, 439, 504, 542, 569, 629] Flow and timing was rated as high risk of bias in several studies.[118, 128, 150, 170, 180, 309, 315, 345, 373, 489] 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 4 shows the summary of rated applicability. The applicability for the individual studies is in Appendix D.

Figure 4. KQ1 Applicability Rating



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., EKG indicators). This section describes diagnostic tools relevant to all age groups.

4.3.1 Parental Ratings

We identified 35 studies using Parental ratings to diagnose ADHD.[17, 124, 135, 176, 194, 222, 238, 239, 254, 266, 297, 299, 300, 311, 326, 335, 338, 352, 355, 382, 413, 414, 417, 435, 437, 452, 476, 480, 504, 507, 515, 516, 524, 542, 569, 629] The earliest study meeting inclusion criteria was published in 1994.[194, 437] Evaluations of parental rating tools came from five different English-language speaking countries, but most studies were from the US.[135, 238, 239, 266, 326, 335, 338, 352, 382, 413, 414, 437, 450, 452, 480, 504, 507, 515, 516, 524, 542, 629] The populations studied were predominately males between the ages of five and 18. Three studies exclusively included children younger than seven years old.[326, 504, 507] 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.[326] 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[326] or autism.[239, 435] 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 13 studies, White participants made up more than 70 percent of the sample.[124, 135, 266, 311, 338, 352, 355, 382, 437, 504, 507, 629] Two studies evaluated samples in which over 50 percent of participants were Black/African American,[450, 524] and one study was identified in which 85 percent of participants were Hispanic or Latino.[542]

Studies reported predominantly on sensitivity, specificity, and area under the curve (AUC). Table 4 shows the findings for the outcomes of interest together with the number of studies and study identifiers. We report findings from population samples that differentiated ADHD from neurotypical developing children separately from results obtained in clinical samples, given that the population was identified as one of the sources of heterogeneity in reported results (see KQ1c).

Table 4. KQ1 Summary of Findings and Strength of Evidence for Parental Ratings

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
KQ1 Parental Ratings	Sensitivity	13 studies[176, 300, 311, 326, 335, 352, 414, 437, 450, 515, 542, 569, 629]	Sensitivity ranged from 61% (corresponding specificity 73%)[417] to 94% (corresponding specificity 51%)[629] differentiating ADHD and neurotypical development Sensitivity showed more variation and ranged from 38% (corresponding specificity 96%)[335] to 87% (corresponding specificity 41%)[437] differentiating ADHD in clinical samples	Low
KQ1 Parental Ratings	Specificity	13 studies[176, 300, 311, 326, 335, 352, 414, 437, 450, 515, 542, 569, 629]	Specificity ranged from 50% (corresponding sensitivity 82%)[542] to 94% (corresponding sensitivity 73%)[515] differentiating ADHD and neurotypical development Specificity ranged from 22% (corresponding sensitivity 81%)[476] to 96% (corresponding sensitivity 38%)[335] differentiating ADHD in clinical samples	Low
KQ1 Parental Ratings	Accuracy	6 studies[326, 335, 417, 450, 524, 620]	Accuracy ranged from 67%[417] to 86% differentiating ADHD and neurotypical development Accuracy ranged from 60%[476] to 84%[524] differentiating ADHD in clinical samples	Low
KQ1 Parental Ratings	AUC	13 studies[176, 238, 239, 266, 300, 326, 335, 338, 352, 480, 542, 569]	AUC ranged from 0.70[542] to 0.91[569] differentiating ADHD and neurotypical development AUC ranged from 0.65[338] to 0.97[239] differentiating ADHD in clinical samples	Low
KQ1 Parental Ratings	Inter-rater reliability	1 study[413]	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*[413] in a sample of children with ADHD	Low
KQ1 Parental Ratings	Internal consistency	6 studies[176, 335, 338, 352, 413, 414, 515]	In neurotypical samples: Cronbach's alpha *Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Rating Scale* (SWAN) 0.95[176]; Cronbach's alpha *Behavior Assessment System for Children, Second Edition* (BASC-2), Executive Function Screener parent rating global sum score 0.91[352];	Low

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
			Cronbach's alpha *Parent Disruptive Behavior Disorder Ratings Scale* (DBDRS) Inattention 0.94, hyperactivity / impulsivity 0.91[515] In clinical samples: Cronbach's alpha *Child Behavior Checklist* (CBCL) Attention Problems 0.76[338]; Cronbach's alpha *Behavior Rating Inventory of Executive Function, Second Edition* (BRIEF2) global executive composite summary score 0.97[335]; Cronbach's alpha *DSM-ADHD-Symptom Rating Scale* total 0.90 for mother's rating, 0.91 for father's rating[413]; Cronbach's alpha *The Pediatric Symptom Checklist* (PSC) attention subscale 0.90[414]	
KQ1 Parental Ratings	Test-retest reliability	0 studies	N/A	Insufficient
KQ1 Parental Ratings	Misdiagnosis	0 studies	N/A	Insufficient
KQ1 Parental Ratings	Costs	0 studies	N/A	Insufficient

Notes: AUC area under the curve, KQ key question, N/A not applicable, SoE strength of evidence

Parental ratings reported mainly on the sensitivity, specificity, accuracy, and area under the curve. 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. 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). 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 13 studies using Teacher ratings to diagnose ADHD.[17, 222, 300, 311, 338, 352, 355, 382, 480, 507, 515, 516, 629] The earliest study meeting eligibility criteria was published 2008[222] from five different English-speaking countries, primarily the US.[338, 352, 382, 480, 507, 515, 516, 629] The populations studied were predominately males between the ages of five and 18. One study exclusively included children younger than seven years old[507] and one exclusively in children eight years or older.[352] 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 seven studies where White participants made up greater than 70 percent of the sample,[311, 338, 352, 355, 382, 507, 629] and one study where over 85 percent of the participants were Black/African American.[480]

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 included studies includes children where all had a dual diagnosis, such as ADHD and conduct disorder.

4. Results: Diagnosis of ADHD

Studies reported a variety of outcomes, with sensitivity, specificity, and area under the curve (AUC) being the most frequently reported outcomes. Table 5 shows the findings for the outcomes of interest together with the number of studies and study identifiers.

Table 5. KQ1 Summary of Findings and Strength of Evidence for Teacher Ratings

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
KQ1 Teacher Ratings	Sensitivity	6 studies[300, 311, 352, 515, 516, 629]	Sensitivity ranged from 48% in a long-term predictive validity study (corresponding specificity 70%)[515] to 82% (corresponding specificity 55%)[516] differentiating ADHD and neurotypical development Sensitivity ranged from 72% (corresponding specificity 75%)[300] to 97% (corresponding specificity 26%)[311] in clinical sample	Low
KQ1 Teacher Ratings	Specificity	6 studies[300, 311, 352, 515, 516, 629]	Specificity ranged from 55% (corresponding sensitivity 82%)[516] to 73% (corresponding sensitivity 70%)[629] differentiating ADHD and neurotypical development Specificity ranged from 26% (corresponding sensitivity 97%)[311] to 91% (corresponding sensitivity 48%)[300] in clinical samples	Low
KQ1 Teacher Ratings	Accuracy	0 studies	N/A	Insufficient
KQ1 Teacher Ratings	AUC	4 studies[300, 338, 352, 480]	AUC was 0.83[352] differentiating ADHD and neurotypical development AUC was 0.56[480] in a clinical sample	Low
KQ1 Teacher Ratings	Inter-rater reliability	2 studies[355, 382]	In clinical samples: Pearson correlations between teacher and parent ratings ranged from 0.17 to 0.41 over four subscales on the *Conduct-Hyperactive-Attention Problem- Oppositional Symptom* (CHAOS) scale[382]; Kappa 0.29 between teacher and parent ratings on the *Attention-Deficit/Hyperactivity Disorder Rating Scale, 4th edition*[355]	Low
KQ1 Teacher Ratings	Internal consistency	5 studies[338, 352, 382, 515, 516]	In neurotypical samples: Cronbach's alpha 0.94 for both teacher-rated inattention and hyperactivity symptom counts on the *Disruptive Behavior Disorder Rating Scale*[516] (DBDRS); Cronbach's alpha was 0.95 for the *Behavior Assessment System for Children, 2nd edition* (BASC-2), executive function screener[352] Cronbach's alpha was 0.94 for the *Teacher Disruptive Behavior Disorder Scale*[515] (DBDRS) In clinical samples: Cronbach's alpha 0.95 for the *Teacher Report Form* (TRF) Attention Problems[338]; Cronbach's alpha ranged from 0.64 to 0.91 over four subscales on the *Conduct-Hyperactive-Attention Problem- Oppositional Symptom* (CHAOS) scale[382]	Low
KQ1 Teacher Ratings	Test-retest reliability	1 study[382]	Pearson correlations ranged from 0.74 to 0.87 over four subscales on the *Conduct-Hyperactive-Attention Problem- Oppositional Symptom* (CHAOS) scale, retest between 1 and 829 days[382] in a clinical sample	Low

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
KQ1 Teacher Ratings	Misdiagnosis	0 studies	N/A	Insufficient
KQ1 Teacher Ratings	Costs	0 studies	N/A	Insufficient

Notes: AUC area under the curve, KQ key question, N/A not applicable, SoE strength of evidence

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.[311] 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 three studies using teen/child self-reports to diagnose ADHD.[176, 297, 480] The earliest study was published in 2017[480] and data came from two different countries, the US[297, 480] and Canada.[176] Self-reports were primarily completed by adolescents ages 12 to 18, 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, four percent hyperactive/impulsive presentation, and 25 percent combined presentation.[480] 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.[480]

Studies reported a limited number of outcomes, with area under the curve (AUC) being the most frequently reported outcome. Table 6 shows the findings for the outcomes of interest together with the number of studies and study identifiers.

Table 6. KQ1 Summary of Findings and Strength of Evidence for Self Reports

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
KQ1 Diagnostic Test	**Outcome**	**Number of Studies and IDs**	**Findings**	**SoE**
KQ1 Self Reports	Sensitivity	1 study[176]	Sensitivity 57% (corresponding specificity 81%) using the *Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Rating Scale* (SWAN) Self report,[176] differentiating ADHD and neurotypical development	Low
KQ1 Self Reports	Specificity	1 study[176]	Specificity 81% (corresponding sensitivity 57%) using the *Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Rating Scale* (SWAN) Self report,[176] differentiating ADHD and neurotypical development [176]	Low
KQ1 Self Reports	Accuracy	0 studies	N/A	Insufficient

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
KQ1 Self Reports	AUC	3 studies[176, 297, 480]	AUC was 0.71 for the *Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Rating Scale* (SWAN) Self report,[176] and the Kiddie-Computerized adaptive test (K-CAT)[297] differentiating ADHD and neurotypical development AUC was 0.56[480] for the *Youth Self Report of the Achenbach System of Empirically Based Assessment (ASEBA)* in a clinical sample	Low
KQ1 Self Reports	Inter-rater reliability	0 studies	N/A	Insufficient
KQ1 Self Reports	Internal consistency	1 study[176]	Cronbach's alpha was 0.88 for the *Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Rating Scale* (SWAN) Self Report[176] differentiating ADHD and neurotypical development	Low
KQ1 Self Reports	Test-retest reliability	0 studies	N/A	Insufficient
KQ1 Self Reports	Misdiagnosis	0 studies	N/A	Insufficient
KQ1 Self Reports	Costs	0 studies	N/A	Insufficient

Notes: AUC area under the curve, KQ key question, N/A not applicable, SoE strength of evidence

The reported diagnostic performance of teen self-reports was limited. We downgraded for 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.

4.3.4.1 Combined Ratings

We identified only four studies that assessed the diagnostic performance of ratings combined across informants.[17, 279, 297, 455] Only one of these studies compared performance when combining data from multiple informants vs 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] A second 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 83.5 percent and specificity of 35.7 percent for the combined rating when distinguishing ADHD from other clinically referred youth.[17] The study did not report diagnostic performance using either parent or teacher rating alone. A third 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.[279] A fourth study of 4 to 7 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.[455]

4.3.4 Clinicians Tools

We identified a small number of studies evaluating additional clinician tools (beyond neuropsychological tests; parent, teacher, or self report ratings; biomarkers; or imaging) to aid the diagnosis of ADHD.[26, 128, 175, 298, 355, 406, 487, 530] One study assessed an insurance claim-based algorithm[553] and another an electronic health record phenotype algorithm.[530] One study focused on the clinical utility of ICD-11 diagnostic guidelines[487] and a clinician diagnosis combined with an assessment aid that involved integrating EEG and theta/beta ratio data.[26] The earliest identified study was published in 2015.[26] Evaluations were published in three different countries, including one from the US.[26] Three studies measured child activity levels,[128, 298, 406] and two evaluated direct observation as a diagnostic tool.[175, 355]

The populations studied were predominately males between the ages of five and 17. None of the studies distinguished between ADHD presentations. Two studies mentioned race and ethnicity demographics; for both, the majority of participants were White (69%).[26]

Studies are difficult to compare since they assess different tools and approaches. Studies reported a variety of outcomes, with sensitivity, specificity, and inter-rater reliability being the most frequently reported outcomes. Table 7 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 7. KQ1 Summary of Findings and Strength of Evidence for Clinician Tools

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
KQ1 Clinician tool – activity measurement	Sensitivity	3 studies	Activity measures ranged from 80% (corresponding specificity 90%)[298] to 98% (corresponding specificity 100%)[128] differentiating ADHD and neurotypical development	Low
KQ1 Clinician tool – activity measurement	Specificity	3 studies	Activity measures ranged from 84% (corresponding sensitivity 97%)[406] to 100% (corresponding sensitivity 98%)[128] differentiating ADHD and neurotypical development	Low
KQ1 Clinician tool – activity measurement	Accuracy	2 studies	Activity measures ranged from 0.82[298] to 0.99[128] differentiating ADHD and neurotypical development	Low
KQ1 Clinician tool – activity measurement	AUC	2 studies	Activity measures ranged from 0.94[406] to 0.999[128] differentiating ADHD and neurotypical development	Low
KQ1 Clinician tools	Inter-rater reliability	2 studies[26, 487]	Kappa was 0.46[487] and ICC was 0.83[26] in clinical samples	Low
KQ1 Clinician tools	Internal consistency	0 studies	N/A	Insufficient
KQ1 Clinician tools	Test-retest reliability	0 studies	N/A	Insufficient

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
KQ1 Clinician tools	Misdiagnosis	0 studies	N/A	Insufficient
KQ1 Clinician tools	Costs	0 studies	N/A	Insufficient

Notes: AUC area under the curve, KQ key question, N/A not applicable, 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.

4.3.5 Biomarkers

We identified six studies using proposed biomarkers to diagnose ADHD that were not based on EEG or imaging.[218, 307, 489, 551, 592, 623] EEG and imaging approaches are reported in the next section. Four studies used blood measures, including membrane potential ratio,[551] miRNA,[592, 623] and erythropoietin/erythropoietin receptor.[307] The other two studies evaluated pupillometrics (pupil-size dynamics)[218] and urine tetrahydroisoquinoline levels.[489] The earliest identified study was published in 2007.[489] Evaluations were published in five different countries, including two from the US.[218, 551]

The populations studied were predominately males between the ages of six and 17. Most studies required participants to not be taking stimulant medication.[218, 307, 592, 623] For studies that distinguished between ADHD presentations, most of the participants were diagnosed with the combined presentation.[551, 623] Only two studies mentioned race and ethnicity demographics, one where 100 percent of the participants were Han Chinese[592] and the other where the majority of participants (71%) were Black/African American.[551] None of the studies used a clinical sample or children with a consistent co-morbidity.

Table 8 shows the 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 Biomarkers

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
KQ1 Biomarkers	Sensitivity	6 studies[218, 307, 489, 551, 592, 623]	Sensitivity ranged from 56% (corresponding specificity 95%)[489] to100% (corresponding specificity 100%)[307] differentiating ADHD and neurotypical development	Low
KQ1 Biomarkers	Specificity	6 studies[218, 307, 489, 551, 592, 623]	Specificity ranged from 25% (corresponding sensitivity 79%)[551] to 100% (corresponding sensitivity 100%)[307] differentiating ADHD and neurotypical development	Low
KQ1 Biomarkers	Accuracy	3 studies[218, 551, 592]	Accuracy ranged from 55%[551] to 85%[592] differentiating ADHD and neurotypical development	Low
KQ1 Biomarkers	AUC	4 studies[218, 307, 592, 623]	AUC ranged from 0.68[623] to 1.00[307] differentiating ADHD and neurotypical development	Low
KQ1 Biomarkers	Inter-rater reliability	0 studies	No data	Insufficient

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
KQ1 Biomarkers	Internal consistency	0 studies	No data	Insufficient
KQ1 Biomarkers	Test-retest reliability	0 studies	No data	Insufficient
KQ1 Biomarkers	Misdiagnosis	0 studies	No data	Insufficient
KQ1 Biomarkers	Costs	0 studies	No data	Insufficient
KQ1 Blood Biomarkers	Sensitivity	4 studies[307, 551, 592, 623]	Sensitivity ranged from 68% (corresponding specificity 71%)[623] to 100% (corresponding specificities 97% and 100%)[307] differentiating ADHD and neurotypical development	Low
KQ1 Blood Biomarkers	Specificity	4 studies[307, 551, 592, 623]	Specificity ranged from 25% (corresponding sensitivity 79%)[551] to 100% (corresponding sensitivity 100%)[307] differentiating ADHD and neurotypical development	Low
KQ1 Blood Biomarkers	Accuracy	4 studies[307, 551, 592, 623]	Accuracy ranged from 55%[551] to 85%[592] differentiating ADHD and neurotypical development	Low
KQ1 Blood Biomarkers	AUC	4 studies[307, 551, 592, 623]	AUC ranged from 0.68[623] to 1.00[307] differentiating ADHD and neurotypical development	Low

Notes: AUC area under the curve, KQ key question, N/A not applicable, SoE strength of evidence

Biomarker studies reported mainly on the sensitivity and specificity. Individual studies achieved very high sensitivity. 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. We identified four studies that reported on blood biomarkers specifically.

4.3.6 Diagnosis Supported by Machine Learning

We identified 44 studies in total using machine learning algorithms to diagnose ADHD using different measurement modalities.[27, 122, 127, 128, 150, 160, 165, 180, 187, 191, 192, 195, 215, 218, 238, 239, 256, 283, 318, 336, 359, 364, 385, 402, 426, 438, 439, 455, 456, 461, 482, 483, 506, 532, 558, 567, 580, 586, 592, 618-621, 1153] Studies were published since 2012[27] and came from 20 different countries, but primarily the US[27, 160, 238, 239, 402, 455, 483, 506, 1153] and China.[191, 192, 195, 385, 558, 567, 618, 620] A third of identified studies used electroencephalogram (EEG) markers as the data source[122, 127, 150, 165, 180, 187, 191, 192, 318, 336, 359, 364, 385, 402, 426, 438, 456, 461, 482, 580] with another third of the studies using functional magnetic resonance imaging (MRI)[195, 283, 483, 506, 567, 618] or multimodal MRI (using some combination of structural, functional, or diffusion tensor imaging).[558, 621, 1153] A wide variety of machine learning algorithms were used for classification, with the most popular being support vector machine followed by neural network classification. Studies reported a variety of outcomes, with sensitivity, specificity, and accuracy being the most frequently reported outcomes.

The majority of studies reported on sensitivity.[27, 127, 128, 150, 160, 165, 180, 187, 195, 215, 218, 256, 283, 364, 439, 461, 483, 506, 532, 558, 567, 580, 592, 618, 619, 621, 1153] Reported sensitivity ranged from 59 percent (corresponding specificity 83%)[319] to 100 percent (corresponding specificity 100%)[150, 160] Specificity estimates ranged from 55 percent (corresponding sensitivity 95%)[506] to 100 percent

(corresponding sensitivities 100, 97, 75, 98, and 100% respectively).[128, 150, 160, 364, 439] Accuracy was reported in 40 studies [122, 127, 128, 150, 160, 165, 180, 191, 192, 215, 218, 256, 283, 318, 336, 359, 364, 385, 426, 438, 439, 455, 456, 461, 482, 483, 506, 532, 558, 567, 580, 586, 592, 618-621, 1153] and ranged from 61 percent[283] to 100 percent.[150, 160, 456] Area under the curve estimates were reported in some of the included studies[127, 128, 187, 191, 215, 218, 238, 239 , 402, 455, 506, 567, 586, 592, 619, 621, 1153] and performance ranged from 0.698[1153] to 0.9993[128] Studies rarely reported on reliability measures, and the impact of misdiagnosis or costs were not mentioned.

In studies using EEG data only, sensitivity ranged from 80 percent (corresponding specificity 80%)[187] to 98 percent (corresponding specificity 92% and 99%).[165, 180] One study combining EEG data and demographics reported a sensitivity of 100% (corresponding specificity 100%).[150] In the studies using neuroimaging datasets, sensitivity ranged from 61 percent (corresponding specificity 68%)[1153] to 99 percent (corresponding specificity 99%).[567] Several studies combined neuroimaging data with demographic data; sensitivity ranged from 70 percent (corresponding specificity 65%)[506] to 89 percent (corresponding specificity 84%)[619] including two near-infrared spectroscopy studies that reported 73 percent sensitivity (corresponding specificity 87%)[215] and 89 percent sensitivity (corresponding specificity 84%).[619]

4.4.1 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 three studies that explicitly reported on diagnostic performance data collected in primary care.[170, 433, 595]The earliest identified study was published in 2004[595] with data from the US and Portugal. The percent female ranged from 24 to 39 percent, where reported. One study was restricted to young children,[170] whereas the others had a broader age range. One study reported on race and ethnicity and included 23 percent Hispanic and 10 percent African American children.[1160]

Studies evaluated parent ratings and neuropsychological tests. Sensitivity and specificity was reported in all three studies. Sensitivity ranged widely, with estimates from 28 percent (corresponding specificity 95%)[433] using a neuropsychological test battery, to 84 percent (corresponding specificity 84%) for the attention problems subscale of the Child Behavior Checklist.[595]

We identified 10 studies focused on the diagnosis of ADHD in children under seven years old.[170, 175, 193, 326, 402, 406, 455, 458, 504, 507] The earliest study was published in 2012[406] and data came from six different countries, primarily the US.[170, 326, 402, 455, 504, 507] The populations studied were predominately males between the ages of one and seven. Half of the studies mentioned race and ethnicity demographics with five studies where White participants made up over 50 percent of the sample,[170, 175, 326, 504, 507] and one study that was 83 percent Hispanic or Latino.[455] Several studies used clinic populations of children referred for diagnostic purposes and children often presented with multiple co-occurring disorders.

The most common tests used for diagnosis in these studies were parent rating, teacher rating, and neuropsychological testing. Two studies used electroencephalography (EEG),[193, 402] one study used imaging,[455] one used 24-hour long actigraphic registries,[406] and one used observation of behavior.[175]

Studies reported a variety of outcomes, with sensitivity, specificity, and area under the curve (AUC) being the most frequently reported outcomes. The KQ1a section of the Summary of Findings Table 3 shows the findings for the outcomes of interest together with the number of studies and study identifiers for children under seven years old. The table shows that six studies[170, 175, 193, 326, 406, 458] reported on sensitivity, with the results depending highly on the test used for diagnosis and the sample characteristic (e.g., clinical samples or general samples differentiating ADHD from neurotypical development).Sensitivity ranged from 66 percent combining teacher and parent ratings [193] to 97 percent for an activity measure[406] in samples differentiating ADHD and neurotypical development. Sensitivity ranged from 64 percent for a neuropsychological test[170] to 76 percent for a different neuropsychological test[458] in clinical samples. Specificity also varied substantially and ranged from 38 percent using EEG data in this age group[193] to 84 percent[193, 406] for an activity measure and an EEG algorithm differentiating ADHD and neurotypical development. Specificity ranged from 70 percent for a neuropsychological test[458] to 91 percent for a rating scale[326] in clinical samples. Similar variation was seen in other diagnostic measures.

Few of these diagnostic studies reported reliability measures. Most commonly reported was the internal consistency of rating scales. Cronbach's alpha was 0.92 for parent ratings on the Diagnostic Infant and Preschool Assessment Likert version (DIPA-L).[504] Cronbach's alpha for the *Behavior Rating Inventory of Executive Function* preschool version was 0.976 for teacher ratings and 0.970 for parent ratings and 0.724 for teacher ratings and 0.978 for parent ratings for the child version.[455]

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.

4.4.2 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?

This section documents the evidence for diagnostic approaches using EEG and various imaging technologies. In addition, the section summarizes the diagnostic utility of neuropsychological tests. The neuropsychological tests included multiple measures of executive function. Questionnaires assessing executive function through parent or teacher report are documented in the beginning of the chapter.

We identified 34 EEG, imaging, or executive function studies restricting to children between the ages of seven and 17.[118, 127, 147, 161, 180, 195, 218, 256, 283, 297-299, 309, 345, 346, 352, 359, 364, 373, 385, 388, 426, 434, 438, 452, 453, 455, 482, 506, 558, 567, 586, 597, 1153] However, we identified a large number of studies that included younger as well as older children, suggesting a broader applicability of the evaluated tests. Most of the identified samples did not include very young children, but the large majority included five and six year old children. In addition, meta-regressions (see KQ1) did not detect a systematic effect of the proportion of young children in the sample on the reported effect sizes. Hence, the following sections report on the results for the individual tests across all identified

diagnostic studies, and we did not restrict to studies that exclusively targeted individuals aged 7 and above.

presentationpresentationpresentation4.4.2.1 EEG

We identified 35 studies using EEG markers to diagnose ADHD.[26, 118, 122, 127, 150, 165, 180, 187, 191-193, 196, 201, 309, 318, 336, 345, 359, 361, 362, 364, 385, 386, 388, 402, 403, 405, 426, 438, 453, 456, 461, 476, 482, 580] The earliest identified study was published in 2005.[386] EEG evaluations were published in 17 different countries, primarily Iran,[122, 165, 359, 426, 482] China,[191, 192, 385, 386] and Taiwan.[187, 193, 201] 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.[165, 193, 336] One study included only female participants,[201] and seven studies included only males.[118, 187, 402, 403, 438, 456, 461] In several studies, participants were required to demonstrate an IQ of 80 or higher.[118, 187, 191, 192, 336, 385, 388] 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. Only two studies included individuals solely with the hyperactive/impulsive presentation.[318, 361] 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[364] or other behavioral disorders.[150] The large majority of studies had unselected samples, i.e., comparing children with ADHD to neurotypical developing children.

Two thirds of studies used machine learning algorithms for classification. Table 9 shows findings for the outcomes of interest together with the number of studies and study identifiers.

Table 9. KQ1 Summary of Findings and Strength of Evidence for EEG

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
KQ1 EEG	Sensitivity	18 studies[26, 118, 127, 150, 165, 180, 187, 193, 201, 336, 345, 364, 386, 388, 403, 461, 476, 580]	Sensitivity ranged from 46% (corresponding specificity 74%)[201] to 100% (corresponding specificities 71% or 100%)[150, 403] differentiating ADHD and neurotypical development Sensitivity ranged from 82% (corresponding specificity 94%)[26] to 94% (corresponding specificity 100%)[476] in clinical samples Sensitivity ranged from 67%[399] to 98%[180] restricting to children 7 or above	Low
KQ1 EEG	Sensitivity	18 studies[26, 118, 127, 150, 165, 180, 187, 193, 201, 336, 345, 364, 386, 388, 403, 461, 476, 580]	Sensitivity ranged from 46% (corresponding specificity 74%)[201] to 100% (corresponding specificities 71% or 100%)[150, 403] differentiating ADHD and neurotypical development Sensitivity ranged from 82% (corresponding specificity 94%)[26] to 94% (corresponding specificity 100%)[476] in clinical samples Sensitivity ranged from 67%[399] to 98%[180] restricting to children 7 or above	Low
KQ1 EEG	Accuracy	26 studies[26, 118, 122, 127, 148, 150, 165, 180, 191-193, 201, 318, 336, 345, 359, 362, 364, 385, 388, 426, 438, 456, 461, 482, 580]	Accuracy ranged from 58%[201] to 100%[150, 456] differentiating ADHD and neurotypical development Accuracy ranged from 61%[26] to 88%[26] in the same study using a different prediction model in a clinical sample	Low

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KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
			Accuracy ranged from 73%[388] to 99.8%[180] restricting to children 7 and above	
KQ1 EEG	AUC	9 studies[127, 187, 191, 193, 201, 336, 402, 403, 405]	AUC ranged from 0.63[201] to 0.92[191] differentiating ADHD from neurotypical development AUC was 0.91[127] in a study with children 7 and above	Low
KQ1 EEG	Inter-rater reliability	3 studies[118, 122, 127]	Kappa between the DSM and behavioral/psychological/neurophysiological data was 0.75[118] (all children were 7 and above) Kappa for classifiers ranged from 0.73[127] to 0.99[122] differentiating ADHD and neurotypical development Kappa was reported as 0.75[118] and 0.82[127] in children 7 and above	Low
KQ1 EEG	Internal consistency	0 studies	N/A	Insufficient
KQ1 EEG	Test-retest reliability	1 study[26]	ICC was 0.83 for Theta/Beta ratio; repeated measures collected on two different visits in a clinical sample[26] (all children were 7 and above)	Low
KQ1 EEG	Misdiagnosis	0 studies	N/A	Insufficient
KQ1 EEG	Costs	0 studies	N/A	Insufficient
KQ1 EEG plus ratings or demographics combined	Sensitivity	4 studies[26, 150, 193, 345]	Sensitivity ranged from 87% (corresponding specificity 84%)[193] to 100% (corresponding specificity100%)[150] differentiating ADHD and neurotypical development Sensitivity was 82% (corresponding specificity 94%)[26] in clinical samples	Low
KQ1 EEG plus ratings or demographics combined	Specificity	4 studies[26, 150, 193, 345]	Specificity ranged from 84% (corresponding sensitivity 87%)[193] to 100% (corresponding sensitivity 100%)[150] differentiating ADHD and neurotypical development Specificity was 82% (corresponding sensitivity 94%)[26] in a clinical sample	Low
KQ1 EEG plus ratings or demographics combined	Accuracy	5 studies[26, 150, 193, 318, 345]	Accuracy ranged from 76%[318] to 100%[150] differentiating ADHD and neurotypical development Accuracy was 88%[26] in a clinical sample	Low
KQ1 EEG plus ratings or demographics combined	AUC	1 study [193]	AUC was 0.926[193] differentiating ADHD and neurotypical development	Low

Notes: AUC area under the curve, KQ key question, N/A not applicable, SoE strength of evidence

EEG studies predominantly reported accuracy estimates. Sensitivity in individual studies ranged widely from 46 percent[201] to perfect sensitivity (corresponding specificities 71%);[150, 403] 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 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.[150] 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 outcomes, no study was identified, and it was not possible to determine the effects associated with the test.

4.4.2.2 Imaging

We identified 17 studies using neuroimaging, mainly magnetic resonance imaging (MRI), to diagnose ADHD.[27, 195, 215, 283, 315, 452, 455, 483, 506, 512, 538, 558, 567, 618, 619, 621, 1153] A publicly available dataset (ADHD-200) produced numerous analyses.[195, 283, 483, 567] The populations studied were predominately males between the ages of six and 17, with three studies including only male participants.[215, 483, 618] In several studies, participants were required to demonstrate an IQ of 80 or higher to be included in the sample.[215, 483, 538, 558, 618, 619] A quarter of the studies required participants not take stimulant medication or stop medication several days before testing.[215, 558, 618, 621] Approximately a third of the studies included only right-handed participants.[483, 558, 618, 1153] For studies that distinguished between ADHD presentations, most focused on the combined and inattentive presentations. Only three studies specified including individuals with the hyperactive/impulsive presentation.[215, 538, 621] 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.[512] One evaluated the diagnostic performance of an algorithm differentiating ADHD from autism.[283] 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).

Most imaging studies used a large number of imaging indicators and utilized machine learning algorithms to detect markers and to optimize the classifications. Reported diagnostic accuracy estimates varied widely. Table 10 shows the findings for the outcomes of interest, together with the number of studies and study identifiers.

Table 10. KQ1Summary of Findings and Strength of Evidence for Neuroimaging

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
KQ1 Imaging to diagnose ADHD	Sensitivity	13 studies[27, 215, 283, 315, 483, 506, 538, 558, 567, 618, 619, 621, 1153]	Sensitivity ranged from 61% (corresponding specificity 64%) combining structural and functional MRI[1153] to 100% (corresponding specificity 100%) utilizing resting state functional MRI in a complex machine learning procedure[195] differentiating ADHD and neurotypical development (both studies restricted to children 7 and above)	Low
KQ1 Imaging to diagnose ADHD	Specificity	13 studies[27, 215, 283, 315, 483, 506, 538, 558, 567, 618, 619, 621, 1153]	Specificity ranged from 55% (corresponding sensitivity 95%) in a model using resting state functional MRI[506] to 100% (corresponding sensitivity 100%) utilizing resting state functional MRI in a complex machine learning procedure[195] differentiating ADHD and neurotypical development (both studies restricted to children 7 and above)	Low

4. Results: Diagnosis of ADHD

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
KQ1 Imaging to diagnose ADHD	Accuracy	11 studies[215, 283, 315, 483, 506, 558, 567, 618, 619, 621, 1153]	Accuracy ranged from 64% combining functional and structural MRI[1153] to 99.6% in a model based on resting state functional MRI[195] differentiating ADHD and neurotypical development (both studies restricted to children 7 and above)	Low
KQ1 Imaging to diagnose ADHD	AUC	8 studies[215, 315, 506, 538, 567, 619, 621, 1153]	AUC ranged from 0.72[506] in a complex machine learning approach to 0.996 in a model based on resting state functional MRI[619] differentiating ADHD and neurotypical development (the same range was also seen in studies restricting to children 7 and above)	Low
KQ1 Imaging to diagnose ADHD	Inter-rater reliability	0 studies	N/A	Insufficient
KQ1 Imaging to diagnose ADHD	Internal consistency	0 studies	N/A	Insufficient
KQ1 Imaging to diagnose ADHD	Test-retest reliability	0 studies	N/A	Insufficient
KQ1 Imaging to diagnose ADHD	Misdiagnosis	0 studies	N/A	Insufficient
KQ1 Imaging to diagnose ADHD	Costs	0 studies	N/A	Insufficient
KQ1 Imaging and phenotypic or demographic variables	Sensitivity	5 studies[215, 283, 506, 619, 621]	Sensitivity ranged from 70% (corresponding specificity 65%)[506] to 89% (corresponding specificity 84%) in a complex machine learning approach to 0.996 in a model based on resting state functional MRI[619] differentiating ADHD and neurotypical development	Low
KQ1 Imaging and phenotypic or demographic variables	Specificity	5 studies[215, 283, 506, 619, 621]	Specificity ranged from 55% (corresponding sensitivity 95%) in a complex machine learning approach[506] to 100% (corresponding sensitivity 100%) in a model based on resting state functional MRI[195] differentiating ADHD and neurotypical development	Low
KQ1 Imaging and phenotypic or demographic variables	Accuracy	6 studies[215, 283, 483, 506, 619]	Accuracy ranged from 68% in a complex machine learning approach[506] to 86% in a model based on resting state functional MRI[619] differentiating ADHD and neurotypical development	Low
KQ1 Imaging and phenotypic or demographic variables	AUC	4 studies[215, 506, 619, 621]	AUC ranged from 0.70 using structural, functional, and diffusion-tensor MRI plus age, sex, and IQ[621] to 0.898 in a model based on resting state functional MRI[619] differentiating ADHD and neurotypical development	Low

Notes: AUC area under the curve, KQ key question, N/A not applicable, 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.

4.4.2.3 Neuropsychological Tests

We identified a large number of studies using neuropsychological tests, assessing executive function and/or encompassing a variety of cognitive assessments, including continuous performance tests, to diagnose ADHD.[20, 23, 147, 148, 160, 161, 170, 178, 194, 202, 250, 256, 266, 270, 298, 312, 341, 346, 373, 384, 412, 433, 434, 439, 450, 455, 457-459, 475, 488, 525, 532, 597, 603, 620, 627, 634] Rating scales of executive function are described in the parent and teacher rating section in the beginning of the chapter.

Studies evaluating neuropsychological tests were published between 2000[597] and 2021[193, 373, 455, 458, 525] from 18 different countries, primarily the US.[147, 160, 170, 178, 266, 338, 450, 455, 597] The populations studied were predominately males between the ages of six and 18. Four studies exclusively included children seven years old or younger.[170, 193, 455, 458] In several studies, participants were required to demonstrate an IQ of 70 or higher[23, 341, 346, 361, 453, 455, 457, 488] with some studies requiring IQ to be at least 80[20, 160, 256, 458, 634] or 85.[373, 434, 475] Almost 60 percent 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,[20, 170, 178, 266, 338, 450, 597] one study where all of the participants were Asian,[384] one study where over 50% were Black/African American,[450] and one study where 83 percent of the participants were Hispanic or Latino.[455]

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.[23, 161, 170, 266, 312, 338, 458] One study specifically looked at distinguishing between children with ADHD, developmental dyslexia, and those who had both disorders.[434] The remaining studies used samples of neurotypically developing children as controls rather than clinical samples.

Studies described a wide range of test batteries but 25 studies used continuous performance testing (CPT) to diagnose children and adolescents.[20, 23, 147, 148, 160, 161, 170, 194, 202, 256, 266, 298, 312, 341, 384, 439, 450, 457, 459, 488, 525, 532, 620, 627, 634] CPTs provide multiple behavioral outputs relevant to ADHD, including omission errors (reflecting inattention), commission errors (reflecting impulsivity), and reaction time standard deviation (RTSD; reflecting moment-to-moment response variability). Studies varied in their use of traditional visual CPTs, such as the TOVA, 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 often used idiosyncratic combinations of individual cognitive measures. 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 11 shows the findings for the outcomes of interest together with the number of studies and study identifiers for key outcomes that were assessed in more than one study.

Table 11. KQ1 Summary of Findings and Strength of Evidence for Neuropsychological Tests

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
KQ1 Neuropsychological tests	Sensitivity	26 studies[20, 23, 160, 161, 170, 178, 193, 202, 256, 270, 341, 346, 373, 384, 433, 434, 439, 450, 457-459, 475, 525, 532, 627, 634]	Sensitivity ranged from 28% (corresponding specificity 95%)[433] to 100% (corresponding specificity 100%)[160] differentiating ADHD and neurotypical development Sensitivity ranged from 59% (corresponding specificity 77%)[412] to 91% (corresponding specificity 22%)[627] in clinical samples Sensitivity ranged from 63%[161] to 83[256] in studies restricting to children 7 and above	Low
KQ1 Neuropsychological tests	Specificity	26 studies[20, 23, 160, 161, 170, 178, 193, 202, 256, 270, 341, 346, 373, 384, 433, 434, 439, 450, 457-459, 475, 525, 532, 627, 634]	Specificity ranged from 46% (corresponding sensitivity 85%)[457] to 100% (corresponding sensitivity 100% and 75% respectively)[160, 439] differentiating ADHD and neurotypical development Specificity ranged from 22% (corresponding sensitivity 91%)[627] to 85% (corresponding sensitivity 63%)[161] in clinical samples Specificity ranged from 70%[603] to 94%[603] in studies restricting to children 7 and above	Low
KQ1 Neuropsychological tests	Accuracy	18 studies[160, 170, 178, 193, 202, 256, 341, 439, 450, 453, 455, 457, 459, 488, 525, 532, 597, 620]	Accuracy ranged from 57%[488] to 100%[160] differentiating ADHD and neurotypical development Accuracy ranged from 64%[170] to 84%[597] in children with co-occurring oppositional defiance disorder Accuracy ranged from 70%[217] to 87[256] restricting to children 7 and above	Low
KQ1 Neuropsychological tests	AUC	14 studies[23, 147, 178, 193, 202, 266, 270, 341, 346, 433, 434, 455, 457, 475]	AUC ranged from 0.65[457] to 0.93 for individual Go/No-Go task measures[384] differentiating ADHD and neurotypical development AUC ranged from 0.62[23, 266] to 0.87[266] in clinical samples AUC ranged from 0.80[346] to 0.92[147] in studies restricting to children 7 and above	Low
KQ1 Neuropsychological tests	Inter-rater reliability	3 studies[178, 266, 627]	Neurotypical samples: Kappa was 0.55 between *Cognitive Assessment System* discriminant function analysis classifications and a priori diagnosis[178] Clinical samples: Kappa 0.15 between *Groundskeeper* game and *Conners* subscales, 0.18 between *Groundskeeper* game and *Conners Continuous Performance Test* (CPT), and 0.3 between *Conners* subscales and Conners CPT[266] Kappa 0.15 between *Test of Variables of Attention* and diagnosis by clinical assessment[627]	Low
KQ1 Neuropsychological tests	Internal consistency	1 study[202]	Cronbach's alpha ranged from 0.906 to 0.987 across 15 variables in the diagnosis-supported decision support system (DS-ADHD) across all children[202]	Low
KQ1 Neuropsychological tests	Test-retest reliability	1 study[457]	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[457]	Insufficient

4. Results: Diagnosis of ADHD

KQ1 Diagnostic Test	Outcome	Number of Studies and IDs	Findings	SoE
KQ1 Neuropsychological tests	Misdiagnosis	0 studies	N/A	Insufficient
KQ1 Neuropsychological tests	Costs	1 study[312]	£31 [~$42] for QbTest including 30-minute appointment, £108 a consultation within the UK Medway NHS Trust at the time of audit[312] in a clinical sample	Insufficient
KQ1 CPT	Sensitivity	19 studies[20, 23, 147, 160, 170, 202, 256, 266, 298, 312, 341, 439, 450, 457, 488, 525, 532, 620, 634]	Sensitivity ranged from 84% (corresponding specificity 94%) combining two commercial test software scores[20] to 100% (corresponding specificity 75%) for a virtual reality based test[634] differentiating ADHD from neurotypical development Sensitivity ranged from 47% (no corresponding specificity) using the QbTest[23] to 91% (corresponding specificity 22%) for the TOVA[411] in clinical samples	Low
KQ1 CPT	Specificity	10 studies[20, 161, 170, 341, 384, 450, 457, 459, 525, 627]	Specificity ranged from 46% (corresponding sensitivity 85%) using the Advanced Test of Attention[457] to 100% (corresponding sensitivity 89%) using the PANDAS[439] differentiating ADHD from neurotypical development Specificity ranged from 22% (corresponding sensitivity 91%) using TOVA[627] to 85% (corresponding sensitivity 63%) using TOVA[161] in clinical samples	Low
KQ1 CPT	Accuracy	8 studies[148, 341, 439, 457, 459, 488, 525, 620]	Accuracy ranged from 57% using a virtual reality CPT[488] to 95% using TOVA[148] differentiating ADHD from neurotypical development	Low
KQ1 CPT	AUC	5 studies[147, 266, 341, 384, 457]	AUC ranged from 0.65 using the Advanced Test of Attention[457] to 0.92 using the MOXO CPT [147] differentiating ADHD from neurotypical development AUC was 0.79 using a go/no go task with multimodal distractions[266] in a clinical sample	Low
KQ1 CPT Attention	Sensitivity	3 studies[20, 23, 170]	Sensitivity ranged from 48% (corresponding specificity 83%)[23] to 68% (corresponding specificity 76%,)[20]	Low
KQ1 CPT Attention	Specificity	3 studies[20, 23, 170]	Specificity ranged from 64% (corresponding sensitivity 55%)[170] to 83% (corresponding sensitivity 48%)[23]	Low
KQ1 CPT Impulsivity	Sensitivity	2 studies[23, 170]	Sensitivity ranged from 48% (corresponding specificity 83%)[23] to 55% (corresponding specificity 64%)[170]	Low
KQ1 CPT Impulsivity	Specificity	2 studies[23, 170]	Specificity ranged from 64% (corresponding sensitivity 55%)[170] to 83% (corresponding sensitivity 48%)[23]	Low

Notes: AUC area under the curve, KQ key question, N/A not applicable, SoE strength of evidence; CPT continuous performance test, TOVA test of variable attention

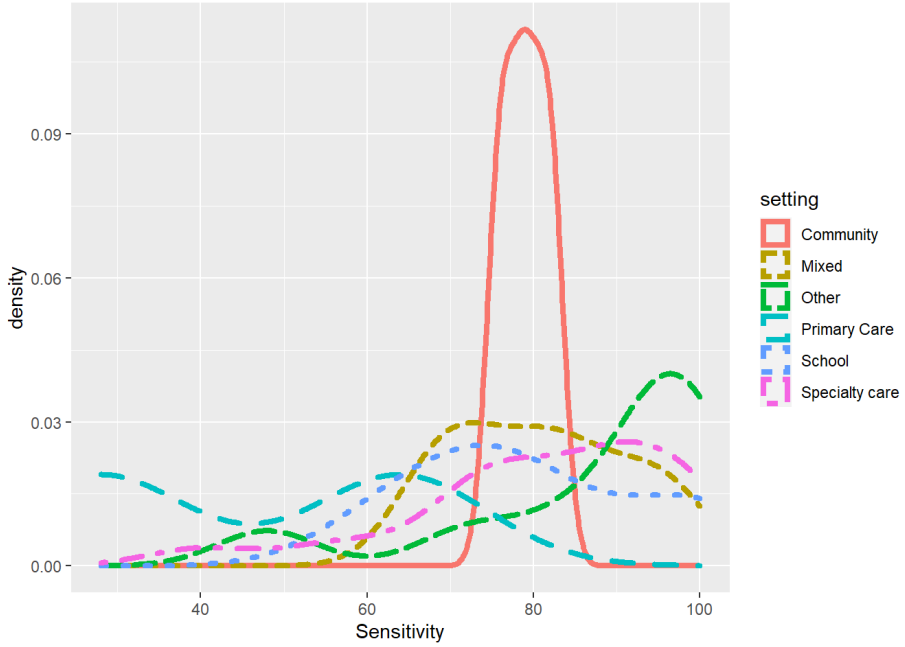
Studies evaluating neuropsychological tests reported predominantly on sensitivity and specificity. Selected studies reported perfect diagnostic performance for neuropsychological tests.[160] However, those studies reported the diagnostic performance for composite measures (unique combinations of individual cognitive measures), making it difficult to compare test performance across studies. The wide range in performance was narrower in studies restricting to children 7 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 outcomes, no study was identified, and it was not possible to determine the effects associated with the test.

4.4.3 KQ1c. For both populations, how does the comparative diagnostic accuracy of these approaches vary by clinical setting or patient subgroup, or other risk factors associated with ADHD?

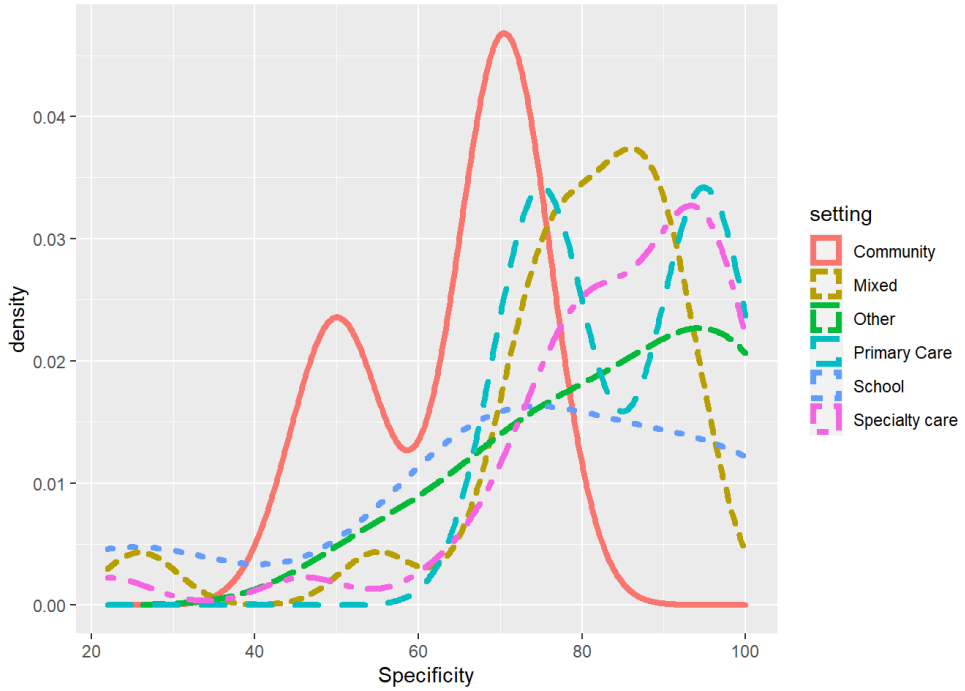
We did not identify studies comparing the accuracy in different settings in direct, head-to-head comparisons. Hence, we had to address this KQ in indirect analyses across studies. Our analyses were further limited by studies providing insufficient details on the accuracy of performance (e.g., reporting 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 of sensitivity and specificity as reported by the study authors to explore potential effect modifiers. The most common reported diagnostic performance measures were sensitivity and specificity. Figure 5 plots reported sensitivity by setting.

Figure 5. Sensitivity by Setting



The figure shows the large number of community settings that, when reporting on sensitivity, reported homogenous values around 80 percent. Studies specifying the context as healthcare settings primary care or specialty care reported a larger range of achieved sensitivity. Comparing the reported sensitivities, a simple regression analysis indicated that setting is associated with reported sensitivity ($p<0.001$). 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 6.

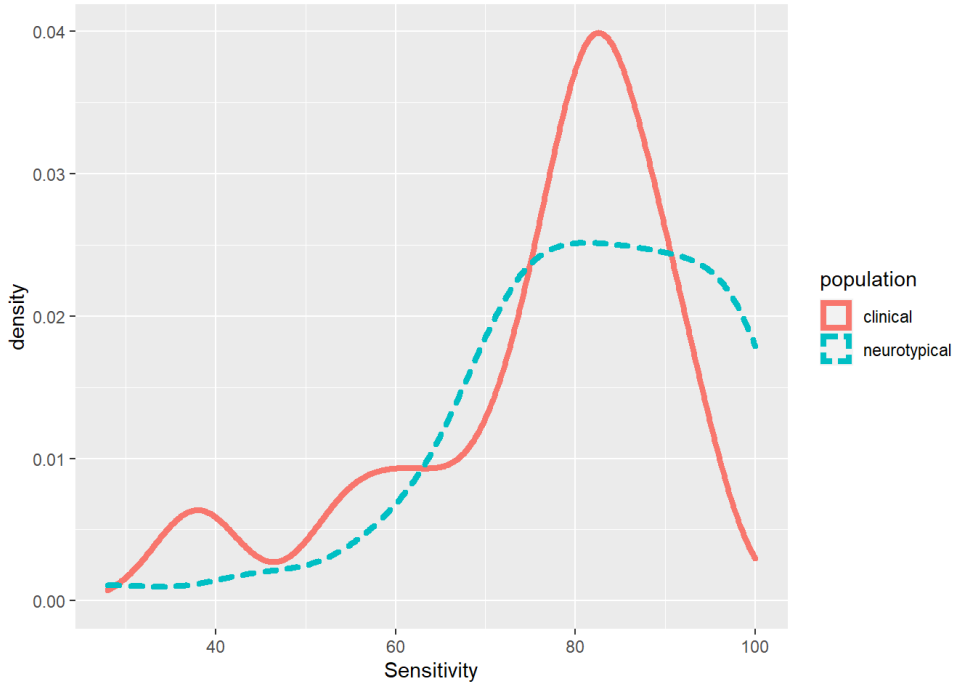
Figure 6. Specificity by Setting



Reported specificity values ranged considerably in all settings. Comparing the reported specificities, a simple regression analysis indicated that setting is associated with reported specificity ($p<0.001$). 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.

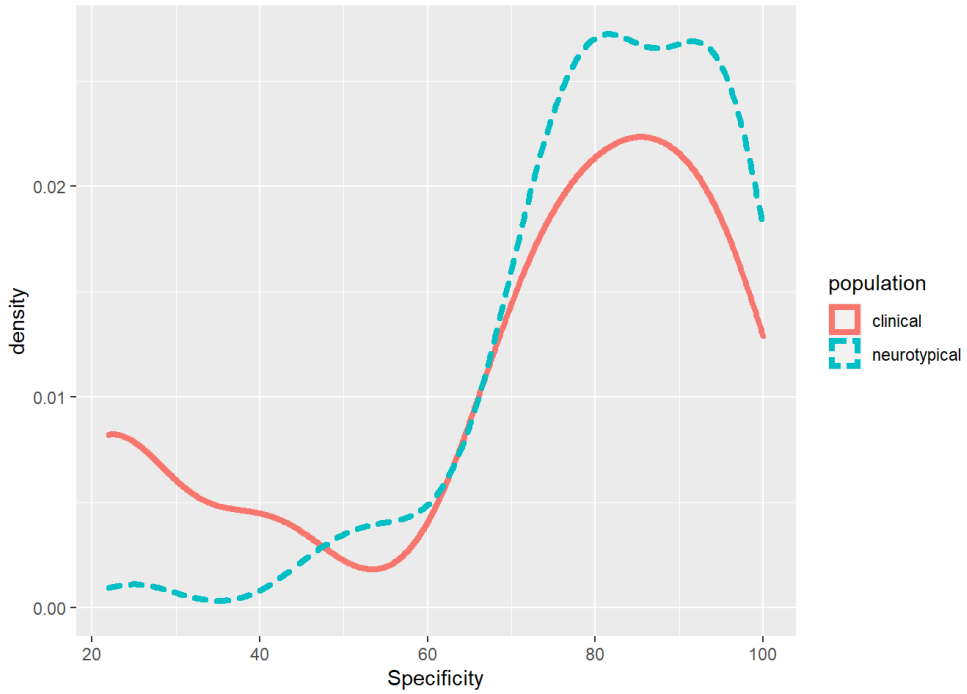
We also evaluated whether the studies in clinical samples (i.e., referred for a clinical diagnosis of ADHD, oppositional defiance disorder, or autism) and those with primarily neurotypical developing children reported different diagnostic performance values. The figure plots the sensitivity results for the two populations (Figure 7).

Figure 7. Sensitivity by Clinical Population



Across studies, we did not detect a statistically significant difference in reported sensitivity results (p 0.21). The next figure plots the specificity stratified by population (Figure 8).

Figure 8. Specificity by Clinical Population

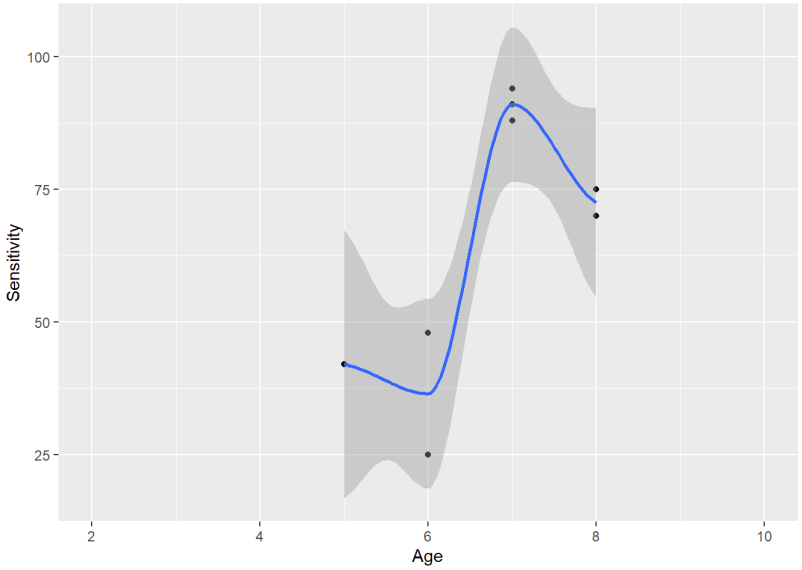


The analysis indicated that the reported specificity was associated with the population that was used to establish diagnostic accuracy (p 0.04). On average, clinical samples reported lower specificities than studies in neurotypical samples (mean 71.3, SD 26.4 vs mean 82.0, SD 14.4). The result suggests 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, but used the diagnostic performance data as reported by the original authors.

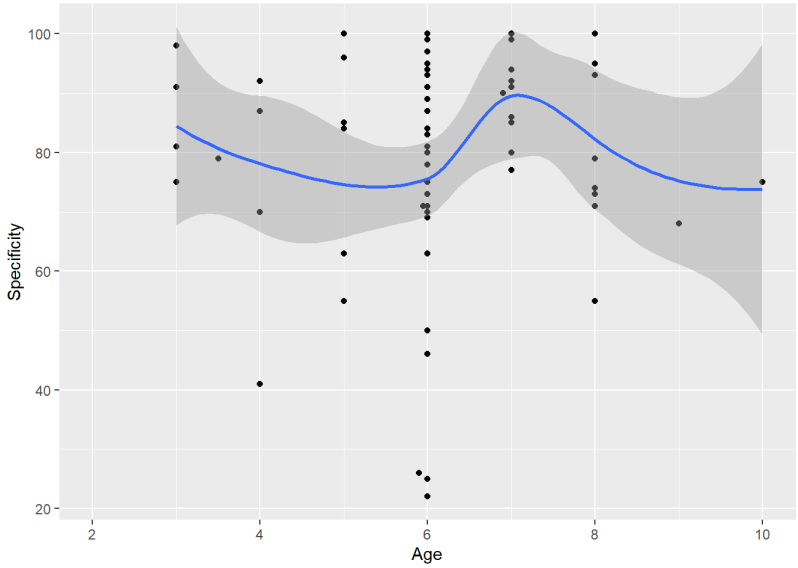
We further investigated whether age of the participants is associated with the achieved diagnostic performance. Figure 9 plots sensitivity by minimum age in the sample.

Figure 9. Sensitivity by Minimum Age



Across studies, we did not detect a statistically significant linear association between samples including younger children versus not on sensitivity (p 0.90). However, it should be noted that the number of studies that included smaller children was low and thus hindered statistical power to detect differences. The equivalent figure for the specificity is shown in Figure 10.

Figure 10. Specificity by Minimum Age

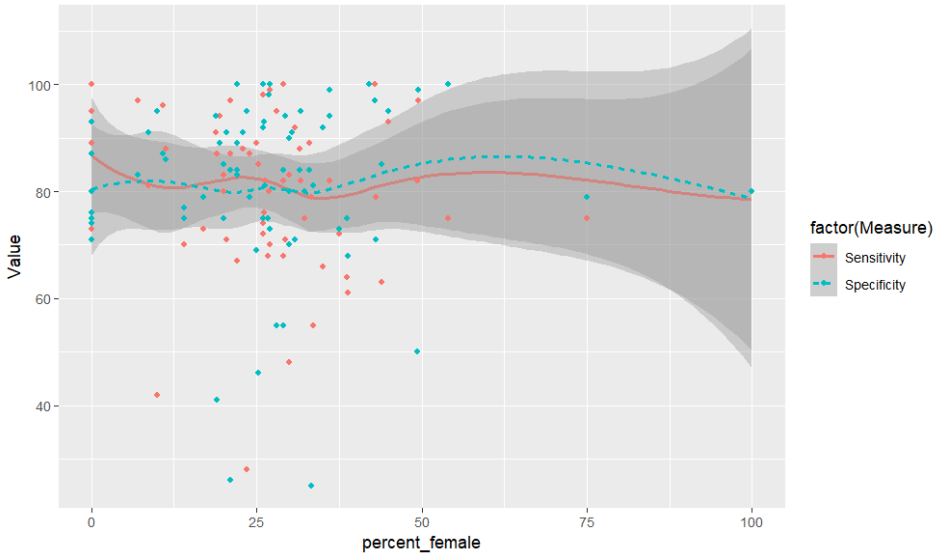


Across studies, there was no statistically significant linear association between samples including younger children or not on specificity (p 0.35). We also categorized studies as younger versus older children and results are shown in the next sample. Using a dichotomous indicator

differentiating between young (under 7) and older children (7 and over) also did not indicate a systematic effect for sensitivity (p 0.58) or specificity (p 0.45).

We also analyzed the gender distribution in the identified studies, as the accuracy of a diagnosis may be associated with the reported gender of the participants. Figure 11 plots the percent female participants and sensitivity.

Figure 11. Sensitivity and Specificity by Proportion of Female Participants



Across samples, the proportion of girls was not associated with reported sensitivity or specificity (p 0.80). 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.

4.4.4 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.[435] None of the included studies reported on stigma associated with being diagnosed or labeled with ADHD.

5. Results: Treatment of ADHD

This section describes studies reporting on a treatment of 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 moderate strength of evidence that several treatment modalities improve core ADHD symptoms with a moderate effect size compared to control groups (e.g., placebo). These include FDA-approved medications, psychosocial interventions, school interventions, and neurofeedback
- FDA-approved stimulant (e.g., methylphenidate) and non-stimulant (e.g., atomoxetine) medications had the strongest evidence for significantly improving ADHD symptoms and additional outcomes, including broadband measures and functional impairment.
- Although indirect comparisons across studies suggest that studies evaluating stimulants report larger effect sizes than studies evaluating non-stimulants for improving ADHD symptoms, head-to-head comparisons did not detect significant differences. Stimulant and non-stimulant medications yielded comparable effects on most effectiveness outcomes and adverse events, including appetite suppression.
- We did not find 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.

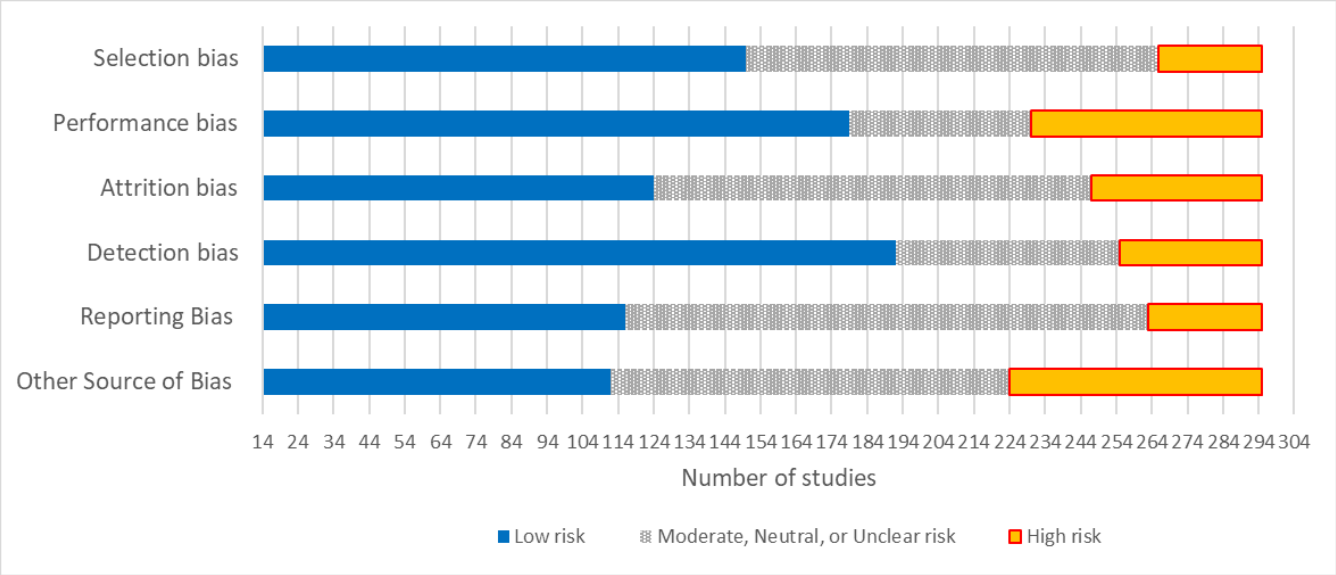
5.2 KQ2 ADHD Treatment Summary of Findings

We identified 304 studies evaluating a treatment for ADHD. Although studies from 1980 were eligible, the earliest treatment studies meeting inclusion criteria were published in 1995.[52, 59, 83, 110-117, 120, 121, 123, 125, 129, 130, 132-134, 136-139, 142-146, 152-159, 162-164, 166, 168, 169, 171-174, 179, 182-184, 186, 197-200, 203-206, 208-214, 216, 219-221, 223-226, 228, 230-234, 237, 240, 242-244, 247, 251-253, 255, 257-262, 264, 265, 267-269, 272-276, 280-282, 286, 288-292, 294-296, 301-304, 306, 308, 310, 313, 314, 316, 317, 320, 321, 323-325, 327-331, 333, 337, 339, 342-344, 347, 348, 350, 351, 353, 354, 356, 358, 363, 365-372, 374-376, 378, 379, 383, 387, 389-391, 397, 400, 401, 404, 408, 409, 415, 416, 418, 420-422, 424, 427-432, 440-449, 454, 460, 462, 464, 466, 468-470, 472-474, 477-479, 485, 491-493, 495-501, 505, 508-511, 513, 514, 517-523, 526-528, 533, 539-541, 543-545, 548-550, 552, 554-556, 559-562, 564-566, 572, 573, 575-578, 581-585, 589, 590, 593, 594, 596, 598-602, 605-613, 615, 616, 622, 624, 625, 628, 630, 632, 633] Studies were published in 30 different countries, although about 40 percent were US studies (contributing 120 included studies).

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

The potential for risk of bias in KQ2 studies is documented in Figure 12. The critical appraisal for the individual studies is in Appendix D.

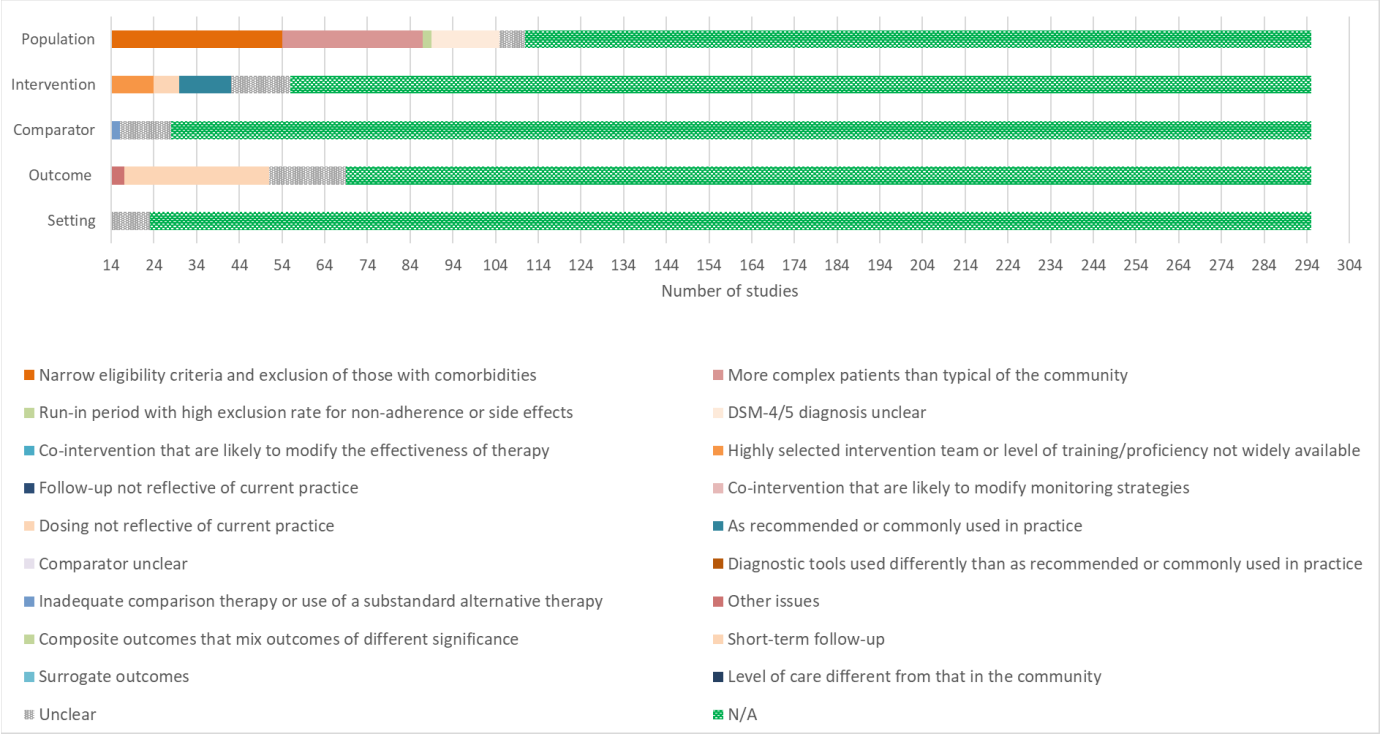
Figure 12. Risk of Bias in KQ2 ADHD Treatment Studies



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

Figure 13. KQ2 ADHD Treatment Applicability Rating



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.

The populations studied were predominately males, and some studies (2%) were restricted to boys; samples included on average a quarter 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. Additional information on study-specific primary outcomes are documented in the evidence table.

5.2.1 Effects of ADHD Treatment on Behavior

The results for any achieved changes in 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 (SMD 0.33; CI 0.10, 0.56; 27 studies, n=2989). There was evidence of heterogeneity (I-squared 87%). 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 0.78). There was evidence of publication bias (Begg p 0.04, Egger, p 0.03). However, the alternative effect estimate using the trim and fill method was unchanged. We also estimate in a sensitivity analysis whether the result was mainly driven by high risk-of-bias studies; after removing high risk-of-bias studies, the estimate was similar (SMD 0.30; CI 0.02, 0.58). 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 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 (Begg p 0.33, Egger p 0.58). 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 0.43, CI 0.33, 0.54; 52 studies, n=6997). There was some evidence of heterogeneity (I-squared 74%). We tested whether the intervention was the key source of heterogeneity to explain differences in effects and the analysis suggested that the type of intervention is systematically associated with the effect size seen in the study (p 0.03). There was no evidence of publication bias (Begg p 0.77, Egger p 0.45). We removed high risk-of-bias studies in a sensitivity analysis, but the effect estimate remained similar (SMD 0.48, CI 0.35, 0.61). 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 0.56; CI 0.48, 0.65; 36 studies, n=5515). There was evidence of heterogeneity (I-squared 77%). 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 0.71). There was evidence of publication bias (Begg 0.01, Egger 0.001) and an alternative estimate using the trim and fill method showed a somewhat smaller effect (RR 0.63; CI 0.54, 0.74). 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 0.56; CI 0.46, 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 -0.46, CI -0.55, -0.38; 126 studies, n=16743). There was evidence of heterogeneity (I-squared 85%). We tested whether the intervention was the key source of heterogeneity to explain differences in effects and found that the reported effect size is systematically associated with the type of intervention evaluated (p 0.04). There was no statistically significant evidence of publication bias (Begg p 0.28, Egger, p 0.06). Excluding 40 high-risk-of-bias studies in a sensitivity analysis resulted in a similar estimate (SMD -0.45, CI -0.55, -0.35) 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 1.58, CI 1.28, 1.95; 21 studies, n=3041). We detected heterogeneity (I-squared 76%) but a moderator analysis did not detect the intervention as a source of heterogeneity (p 0.46). There was evidence of publication bias (Begg p 0.04, Egger p<0.001). A more appropriate estimate of the true effect on symptom reduction may be somewhat smaller (RR 1.31, CI 1.02, 1.70). We also removed four high risk of bias studies in a sensitivity analysis which showed the treatment effect to be robust (RR 1.52, CI 1.23, 1.95) 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 0.39; CI 0.23, 0.54; 33 studies, n=4293). 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 0.86). There was no significant publication bias (Begg p 0.09, Egger p 0.08). When removing ten high risk of bias studies in a sensitivity analysis, the estimate remained similar (SMD 0.35; CI 0.16, 0.53) 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).[366]

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 0.22; CI -0.09, 0.53; 1 study, n=164).[264] 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).[211] 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 -0.26; CI -0.62, 0.09; 9 studies, n=1549). There was evidence of heterogeneity (I-squared 88%). We tested whether the intervention was the key source of heterogeneity to explain differences in effects and the intervention contributed to the heterogeneity of effects (p 0.04). Publication bias tests did not indicate potential bias (Begg p 0.12, Egger 0.62). Removing high risk-of-bias studies in a sensitivity analysis showed a smaller effect, and the difference between groups remained not statistically significant (-0.052; CI -0.23, 0.13). 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 significantly reducing appetite in studies reporting continuous outcomes (SMD 0.44; CI 0.04, 0.84; 12 studies, n=2016). Heterogeneity was high (I-squared 92%). The type of intervention was one source of heterogeneity, as indicated in a meta-regression (p 0.01). There was no evidence of publication bias (Begg p 1.00, Egger 0.34). Removing two high-risk-of-bias studies in a sensitivity analysis found a similar point estimate, but the effect was not statistically significant (SMD 0.48; CI -0.01, 0.97); heterogeneity was not reduced. Across all ADHD interventions, ADHD treatment was associated with decreased appetite compared to control group participants (RR 2.66; CI 2.10, 3.42; 56 studies, n=8070). 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 60%). We tested whether the intervention was the key source of heterogeneity to explain some of the heterogeneity, but we did not detect a systematic effect (p 0.61). 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 0.08, Begg p<0.04). The alternative estimate of the effect using the trim and fill method to account for unpublished studies was somewhat smaller (RR 2.22; CI 1.70, 2.90). We also conducted a sensitivity analysis removing high risk-of-bias studies; the resulting estimate suggested an even stronger effect (RR 2.88; CI 2.20, 3.77) 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 an adverse event. Across ADHD interventions, participants undergoing active ADHD treatment were more likely to report adverse events than control group participants (RR 1.25; CI 1.17, 1.32; 55 studies, n=8191). We did not detect noticeable heterogeneity in this analysis (I-squared 58%). An analysis of the intervention as a potential source of heterogeneity indicated borderline results (p 0.5). There was no evidence of publication bias (Begg p 0.84, Egger p 0.25). Removing 11 high risk-of-bias studies in a sensitivity analysis did result in a similar point estimate (RR 1.25; CI 1.17, 1.34) and heterogeneity estimates were unchanged.

5.3 Effects by Intervention

The identified interventions were highly 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 behavioral treatment
- FDA-approved pharmacological agents
- New pharmaceutical agents
- Psychosocial treatment
- Cognitive training
- Neurofeedback
- Physical exercise
- Nutrition and supplements
- Complementary, alternative, and integrative medicine (CAM)
- Parent support
- School interventions
- Provider intervention

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

augmentation, 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.

5.3.1 Combined Pharmacological and Behavioral Treatment

We identified nine eligible treatment studies that evaluated a combination of pharmacological intervention and nonpharmacological behavioral therapy.[114, 159, 205, 220, 339, 350, 462, 485, 548] The behavioral or psychological treatment had to be directed at the participating children in order to be included here. 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 NIMH Multimodal Treatment Study of Children with ADHD (MTA), which dates to 1999. For the current review, we used the Jensen et al. 3-year follow-up[339] as the key outcome data publication, but we reviewed information from the MTA that has been56ategoshed thus far in 73 articles, as shown in the evidence table. Half of the identified combined pharmacological and behavioral studies were conducted in the US.[159, 339, 485, 1127]

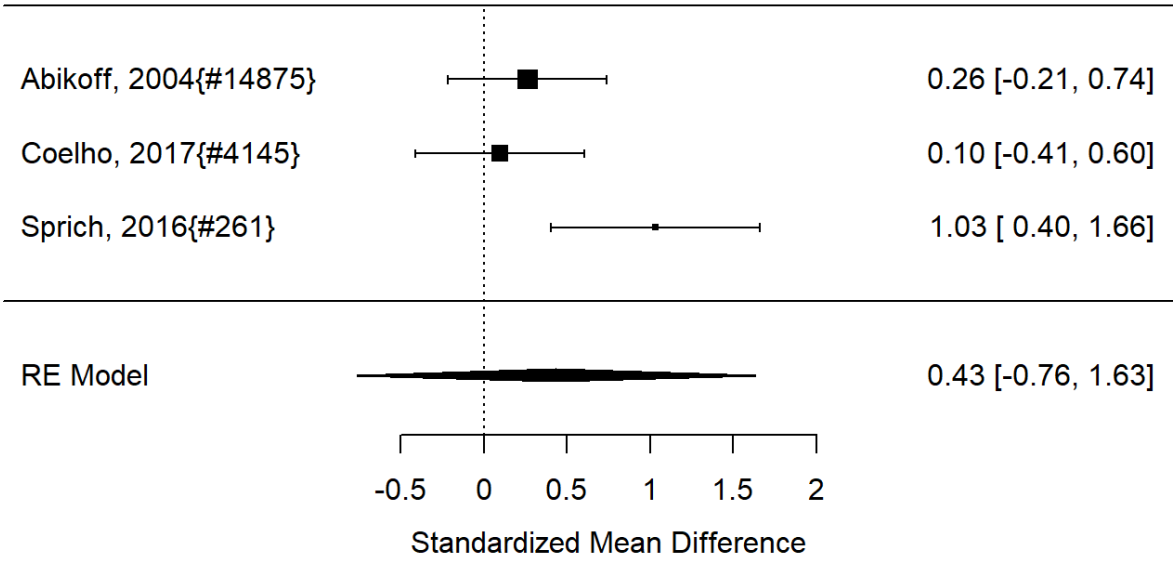
The populations studied were predominately males (girls/females comprised a quarter of the target ADHD cohorts across studies) between the ages of five and 18. Evidence of intellectual disability (i.e., full-scale IQ < 70) was exclusionary in all studies, and most studies required full-scale IQ scores 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%[205] to 88%[339] 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. One study[159] specifically required ADHD plus a co-occurring disruptive disorder and significant aggressive behavior, as it examined the usefulness of adjunctive risperidone and/or divalproex sodium in addition to optimal stimulant dosing and behavior therapy. 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 this area were predominantly short- or long-acting stimulants (such as methylphenidate and amphetamine)[159, 205, 260, 339, 485] or else the non-stimulant medication atomoxetine, which is an SNRI (Serotonin and Norepinephrine Reuptake Inhibitor).[220] Behavioral treatment components varied in approach and complexity and included cognitive behavioral therapy,[205, 220, 485, 548] multi-modal psychosocial treatment;[114, 339] a solution-focused approach,[350] behavioral therapy,[159] and a humanistic intervention.[462] Studies compared most frequently combinations of pharmacological and psychosocial treatment to pharmacology or psychosocial treatment alone rather than no treatment or placebo.

Studies reported a variety of often study-specific outcomes, such as improvement in core ADHD symptoms or co-occurring symptoms. In terms of pre-specified key outcomes, symptom scores were most frequently reported.

Three studies reported on changes in a specific behavior, but they used different metrics and reported different effect estimates and could not be combined; none detected statistically significant difference between the intervention and a control group (SMD -0.04; CI -2.26, 2.18; 2 studies, n=311; RR 0.47; CI 0.18, 1.25; 1 study, n=26).[114, 159, 339] Studies reporting on broadband measures are shown in Figure 14.

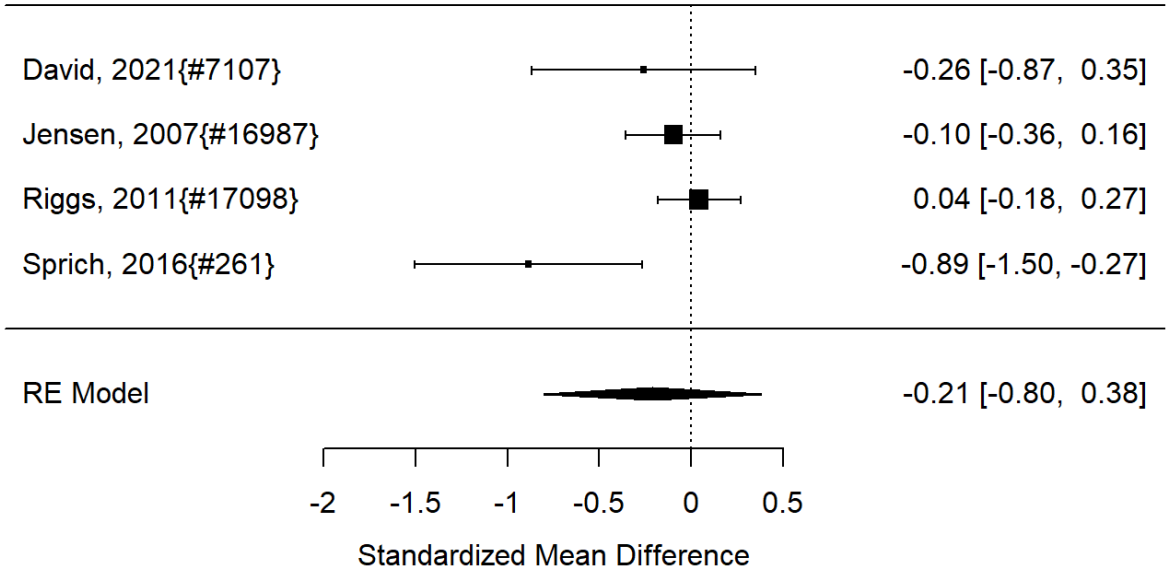
Figure 14. Effects of Combined Pharmacological and Psychological Treatment on Broadband Measures (SMD)



Across studies, we found no systematic difference between intervention and control groups (SMD 0.43; CI -0.76, 1.63; 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;[114] CBT plus methylphenidate;[205] and CBT plus FDA-approved medication[471]) and compared to medication alone.[114, 205, 548] The analysis detected some heterogeneity (I-squared 66%). 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).[485]

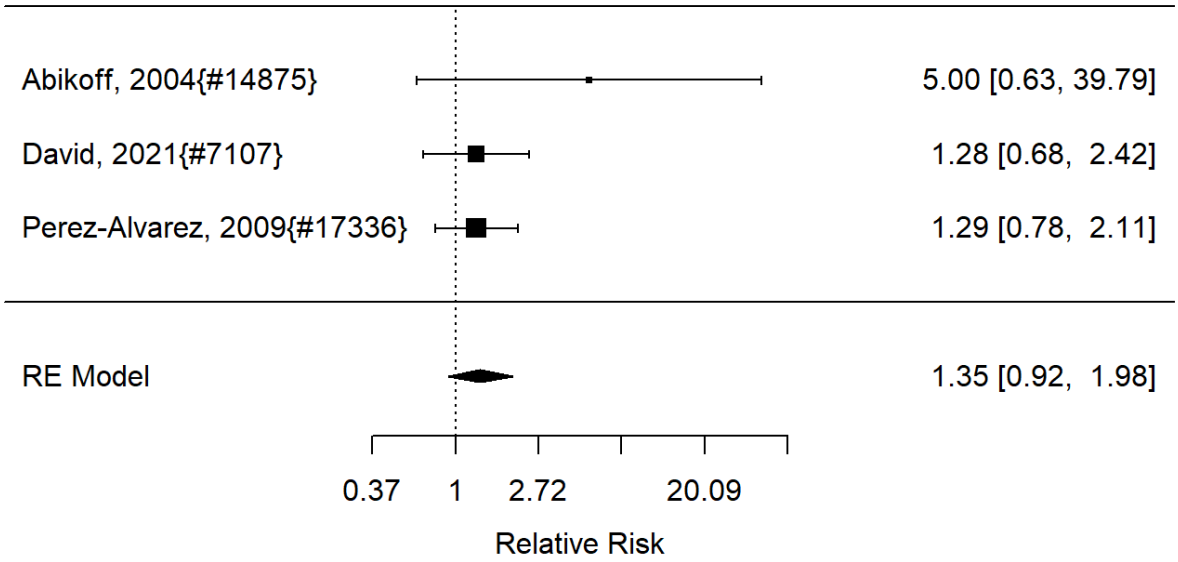
Studies reporting on ADHD symptom scales are shown in the next forest plot (Figure 15).

Figure 15. Effects of Combined Pharmacological and Psychological Treatment on Symptoms (SMD)



Studies did not identify a systematic treatment effect to indicate superiority of the combined pharmacological and psychological treatment versus control (SMD -0.21; CI -0.80, 0.38; 4 studies, n=630). However, the control groups consisted of groups that received the pharmacological intervention component alone rather than no intervention, i.e., the analysis was typically a comparative effectiveness analysis rather than a pure effectiveness analysis. There was some indication of statistical heterogeneity (I-squared 71%). The analysis did not detect publication bias. Removing two high risk of bias studies in a sensitivity analysis did not result in a different effect (SMD -0.02; CI -0.89, 0.85). The forest plot (Figure 16) shows studies reporting on a categorical symptom assessment.

Figure 16. Effects of Combined Pharmacological and Psychological Treatment on Symptoms (RR)



Studies did not identify a statistically significant treatment effect in the categorical outcome either (RR 1.35; CI 0.92, 1.98; 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.

The MTA follow up reporting on functional impairment (SMD 0.11; CI -0.15, 0.37; 1 study, n=243) and an academic performance measure (SMD -0.12; CI -0.37, 0.14; 1 study, n=243) also did not find statistically significant differences.[220] We did not identify studies reporting on treatment satisfaction. One study reporting on appetite suppression found no difference between groups (RR 0.93; CI 0.29, 3.03; 1 study, n=29). None of the identified studies reported on the number of participants experiencing adverse events.

5.3.1.1 Combined Pharmacological and Psychological Treatment Comparative Effectiveness

In addition to comparing combined pharmacologic and psychological interventions to pharmacologic treatments alone, one study also compared one pharmacologic and psychological intervention to an alternative pharmacologic and psychological intervention. The study compared combined behavioral therapy and stimulant treatment plus risperidone versus behavioral therapy and stimulants plus divalproex sodium in children with aggressive behavior and ADHD.[159] The study reported on aggressive behavior and concluded that both adjuvants were efficacious (RR 0.61; CI 0.31, 1.20; 1 study, n=175) but also noted that rigorous titration of stimulant medication and concurrent behavior therapy may avert the need for additional medication.

5.3.1.2 Combined Pharmacological and Psychological Treatment Summary of Findings

Table 12 shows the findings for all key outcomes of interest, together with the number of studies and study identifiers.

Table 12. KQ2 Summary of Findings and Strength of Combined Pharmacological and Psychological Treatment

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	SoE
KQ2 combined treatment vs control (individual component or usual care)	Behavior	3 RCTs[114, 159, 339]	No systematic difference (SMD -0.04; CI -2.26, 2.18; 2 studies, n=311; RR 0.47; CI 0.18, 1.25; 1 study, n=26)	Low for no difference
KQ2 combined treatment vs control (individual component, wait list)	Broadband measures	4 studies[114, 205, 485, 548]	Studies favored the combination intervention but there was no statistically significant difference and effect estimates varied (SMD 0.43; CI -0.76, 1.63; 3 studies, n=171; RR 0.85; CI 0.54, 1.36; 1 study, n=227)	Low for no difference
KQ2 combined treatment vs control (individual component, usual care, wait list)	ADHD symptoms	6 studies, 5 RCTs,[114, 220, 339, 462, 485] and one crossover trial[548]	Analyses did not detect a difference between groups across two analyses (SMD -0.02; CI -0.20, 0.15; 4 studies, n=630; RR 1.17; CI 0.91, 1.51; 3 studies, n=155)	Moderate for no difference
KQ2 combined treatment vs control (individual component, usual care)	Functional impairment	2 RCTs[114, 339]	No systematic differences between groups detected (SMD 0.11; CI -0.15, 0.37; 1 study, n=243)	Insufficient
KQ2 combined treatment vs control	Acceptability of treatment	0 studies	N/A	Insufficient
KQ2 combined treatment vs usual care	Academic performance	1 RCT[339]	No systematic differences between groups (SMD -0.12; CI -0.37, 0.14; 1 study, n=243)	Insufficient
KQ2 combined treatment vs control (individual component, usual care)	Appetite suppression	2 RCTs[220, 339]	No systematic differences (RR 0.93; CI 0.29, 3.03; 1 study, n=29)	Low for no difference

Notes: CI 95% confidence interval, KQ key question, N/A not applicable, RR relative risk, RCT randomized controlled trial, 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 behavior treatment as superior to control groups where control groups typically provided 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).

5.3.2 FDA-approved Pharmacological Treatment

We identified 103 studies evaluating an FDA-approved pharmacological intervention.[115, 116, 125, 133, 137, 138, 144, 153, 162, 166, 169, 172, 182, 183, 197, 198, 200, 206, 209, 211, 212, 221, 224, 230, 231, 251-253, 273-276, 282, 288, 289, 292, 303, 304, 317, 321, 333, 337, 342, 367, 368, 370, 372, 374, 375, 379, 404, 408, 409, 415, 421, 422, 430, 432, 441-444, 447-449, 470, 492, 499, 500, 513, 514, 526-528, 544, 545, 549, 555, 562, 575, 578, 585, 593, 598-601, 605-608, 610-612, 615, 622, 632, 892, 1088, 1161]

Although studies from 1980 were eligible, the earliest studies meeting inclusion criteria were published in 1995.[142, 528] Evaluations were published in 15 different countries, but 60 percent

was US-based. Although the percent of female participants ranged from seven to 56 percent, samples were predominantly male. The age minimum varied, but across all identified studies, only five studies included children three to five years old.[116, 198, 237, 274, 372] 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.[111, 114, 260, 367, 462, 477, 585, 611]

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,[182, 211, 224, 231, 260, 422, 612] Tourette syndrome or tic disorder,[125, 374, 528, 544] or learning disabilities.[514, 526] Demographics were often not reported, but where studies reported a breakdown by race or ethnicity, on average, 75 percent of children were white.

Of the identified studies, the majority reported on the comparison to a control group not receiving pharmacological treatment, most frequently placebo. Half of identified studies reported alternatively or in addition on the effects of an alternative intervention, for example a different dose of the same medication or a different medication.

Studies most frequently reported on 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 17.

Figure 17. Effects of FDA-Approved Pharmacological ADHD Treatment on Behavior (SMD)

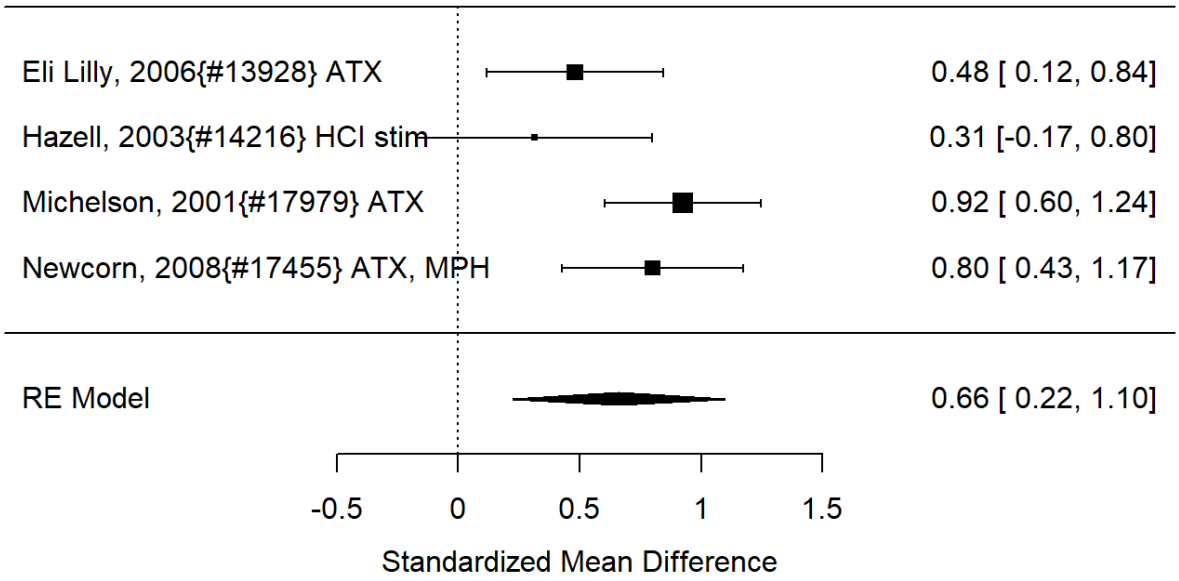


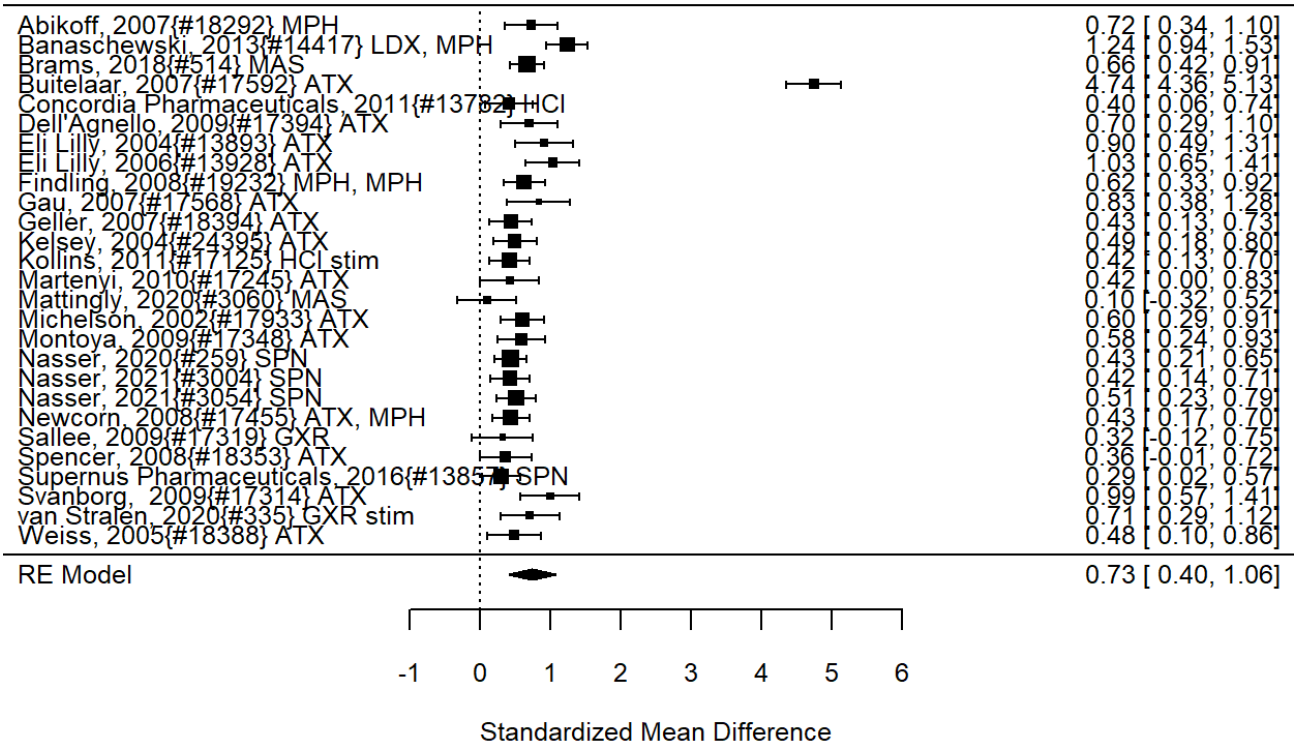
Figure notes: ATX atomoxetine, HCI clonidine hydrochloride, MPH methylphenidate, stim stimulants (not further defined)

Across studies, pharmacological intervention (all non-stimulants) were associated with significant improvements in individual problem behaviors (SMD 0.66; CI 0.22, 1.10; 4 studies, n=523). The minimum age in the included studies was six years old. There was little evidence of heterogeneity (49%). There was no indication of publication bias. Excluding a high risk of bias

study in a sensitivity analysis increased the CI and the effect was not statistically significant (SMD 0.64; CI -0.22, 1.51), but did not reduce heterogeneity. Stratifying the non-stimulants further, the norepinephrine reuptake inhibitor (SNRI) atomoxetine showed improved problem behaviors (SMD 0.74; CI 0.17, 1.32; 3 studies), while alpha agonist study detected no difference (SMD 0.31; CI -0.17, 0.80; 1 study). 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[317]); the study did not detect a statistically significant difference between arms (RR 0.31; CI -0.17, 0.80; 1 study, n=66).

Multiple studies reported on a broadband measure as shown in Figure 18.

Figure 18. Effects of FDA-Approved Pharmacological ADHD Treatment on Broadband Measures (SMD)



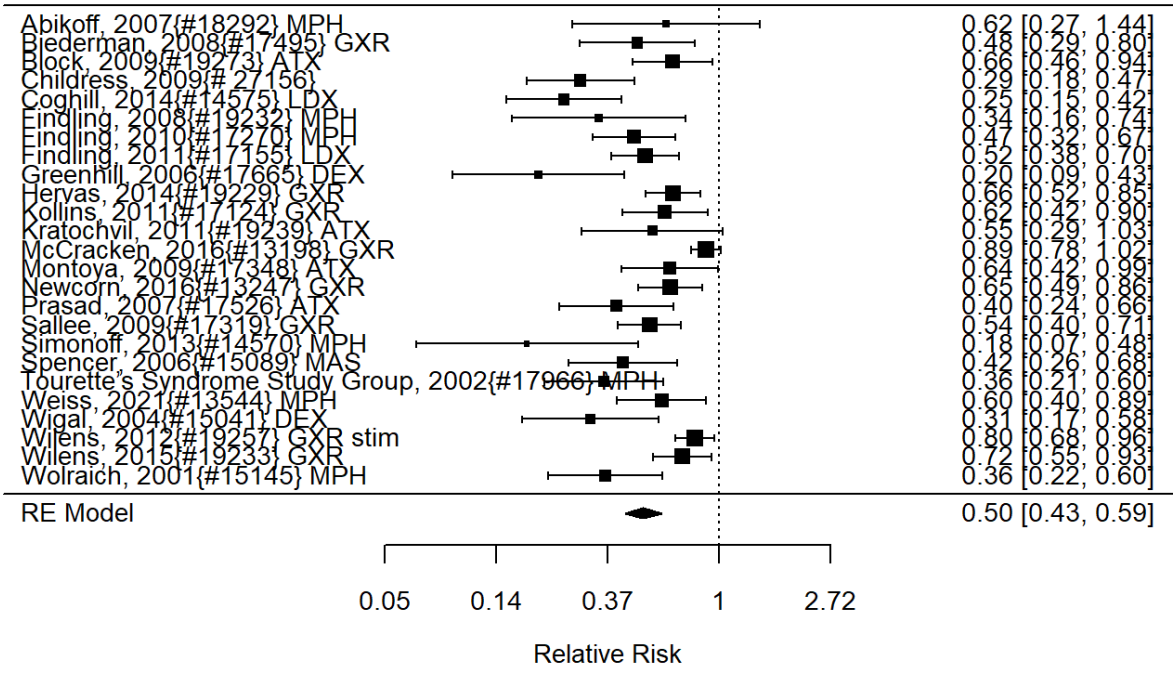
Notes: ATX atomoxetine, GXR guanfacine, LDX lisdexamfetamine dimesylate, MPH methylphenidate, SPN SPN-812, stim stimulants (not further defined)

Across studies, pharmacological treatment was associated with a systematic benefit on broadband scale assessments compared to control (SMD 0.73; CI 0.40, 1.06; 27 studies, n=4618). Only one study included children younger than six years old.[116] Studies assessed different medication regimes but analyses detected little heterogeneity (I-squared 58%). Largest effects were reported in studies evaluating lisdexamfetamine dimesylate,[137] atomoxetine,[251] methylphenidate,[116] and extended-release guanfacine added to usual care stimulant therapy,[585] respectively. There was no evidence of publication bias. Removing six high-risk-of-bias studies 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.

Several studies included in the pharmacological analysis assessed stimulants and when restricting to stimulants alone, we also found statistically significantly improved broadband scale scores, but heterogeneity in this intervention subgroup was not reduced but increased (SMD 0.67; CI 0.16, 1.18; 6 studies; I-squared 87%). Stratifying the stimulants into methylphenidate and amphetamine medication, we found that methylphenidate studies showed a similar point estimate, but the result was not statistically significant in this small subset and heterogeneity was negligible (SMD 0.58; CI -0.03, 1.19; 3 studies; I-squared 25%). Similarly, results across amphetamine versus placebo were not statistically significant in this equally small subset and heterogeneity was high and not reduced (SMD 0.76; CI -0.96, 2.46; 3 studies; I-squared 94%). A large intervention subgroup included in the pharmacological medications reporting on broadband measures were non-stimulants. Across studies, non-stimulants improved broadband scale scores with reduced, negligible heterogeneity (SMD 0.52; CI 0.41, 0.64; 18 studies; I-squared 32%). Results restricting to SNRIs only were similar to the combined non-stimulant analysis and indicated a clear effect on broadband measure scores, with heterogeneity reduced further (SMD 0.54; CI 0.42, 0.65; 15 studies; I-squared 25%). Most of the non-stimulant studies evaluated atomoxetine and excluding three viloxazine studies did not change the estimate (SMD 0.58; 0.43, 0.73; 12 studies; I-squared 38%). The alpha agonist studies that contributed to the non-stimulant estimate reported a similar effect to the main analysis and there was no heterogeneity in this subset (SMD 0.47; CI 0.10, 0.85; 3 studies; I-squared 0).

Multiple studies reported on broadband scale as a categorial outcome (e.g., criteria for improvement met or not) as shown in Figure 19.

Figure 19. Effects of FDA-Approved Pharmacological ADHD Treatment on Broadband Measures (RR)

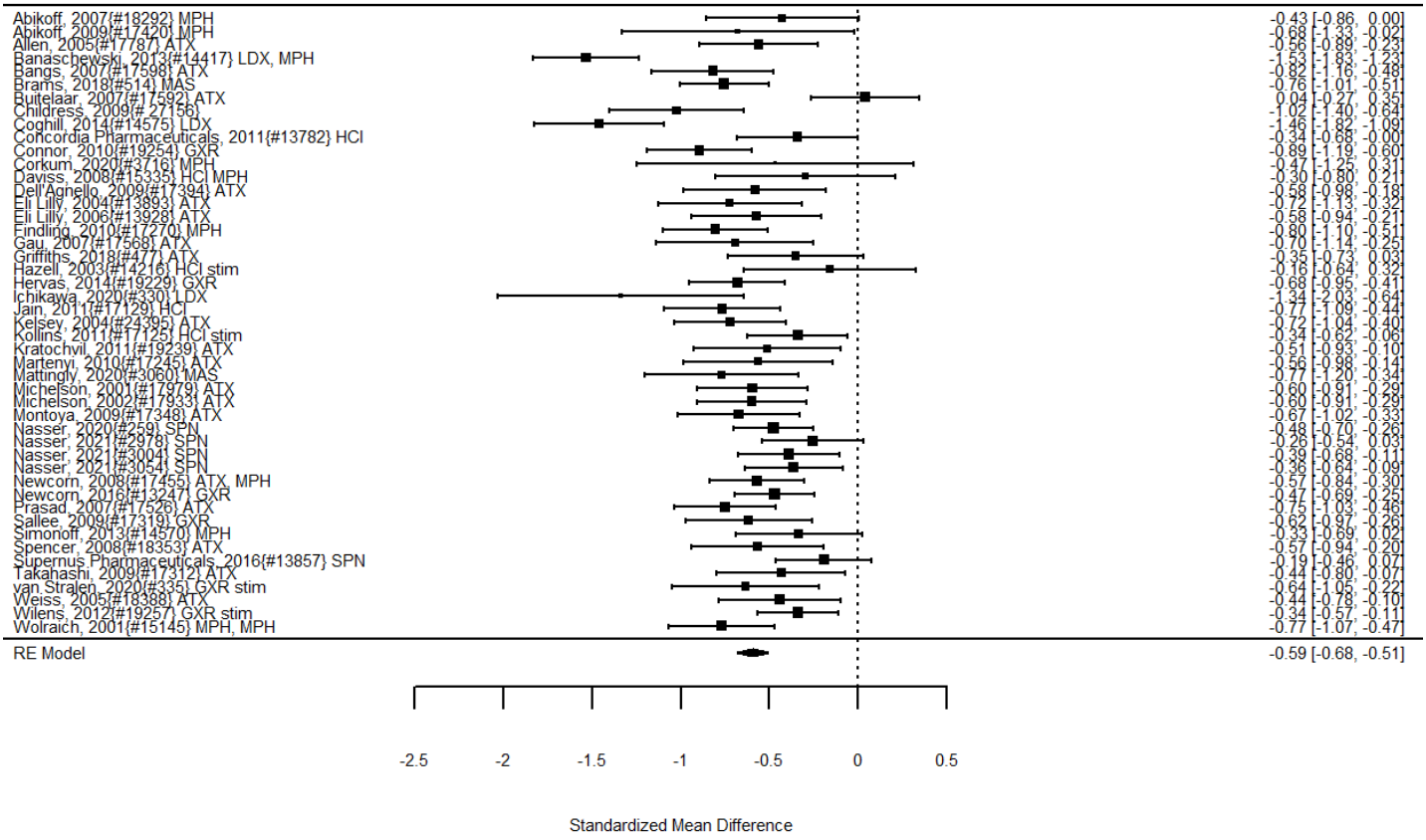


Notes: DEX dexmethylphenidate, GXR guanfacine, LDX lisdexamfetamine dimesylate, MPH methylphenidate, stim stimulants (not further defined)

Across studies, results also indicated that pharmacological ADHD treatment was associated with a systematic benefit compared to control (RR 0.50; CI 0.43, 0.59; 25 studies, n=3959). Only two studies included children younger than six years old.[116, 372] Analyses detected some heterogeneity (I-squared 74%). There was evidence of publication bias (Begg p 0.003, Egger p<0.001) and an alternative estimate using the trim and fill method suggested a somewhat smaller effect (RR 0.60; CI 0.50, 0.72). When excluding six high-risk-of-bias studies in a sensitivity analysis, effect estimates were similar to the original effect (RR 0.53; CI 0.42, 0.69) and heterogeneity was not reduced. This analysis included a substantial number of studies evaluating different stimulants and restricting to stimulants alone, we also found improved broadband scale scores with reduced heterogeneity (RR 0.39; CI 0.31, 0.49; 13 studies; I-squared 46%). Restricting to methylphenidate alone reduced heterogeneity further and the effect was also statistically significant in this smaller subset (RR 0.39; CI 0.30, 0.49; 9 studies; I-squared 33%). In the subset of amphetamine, results were similar but there was evidence of heterogeneity (RR 0.39; CI 0.26, 0.60; 3 studies; I-squared 65%). Across studies, non-stimulants compared to placebo improved broadband scale score evaluations and heterogeneity was low (RR 0.66; CI 0.57, 0.76; 11 studies; I-squared 36%). Results of restricting analyses to SNRIs to identify sources of heterogeneity also showed an improvement in broadband scale scores (RR 0.58; CI 0.46, 0.73; 4 studies),[162, 372, 430, 470] and the analysis did not detect any heterogeneity. The equivalent analysis for alpha agonists versus placebo was also statistically significant with little heterogeneity (RR 0.69; CI 0.58, 0.82; 7 studies; I-squared 49%).[153, 321, 368, 447, 499, 612]

A large number of studies reported on symptom Improvements. Standardized mean differences are shown in Figure 20.

Figure 200. Effects of FDA-Approved Pharmacological ADHD Treatment on ADHD Symptoms (SMD)



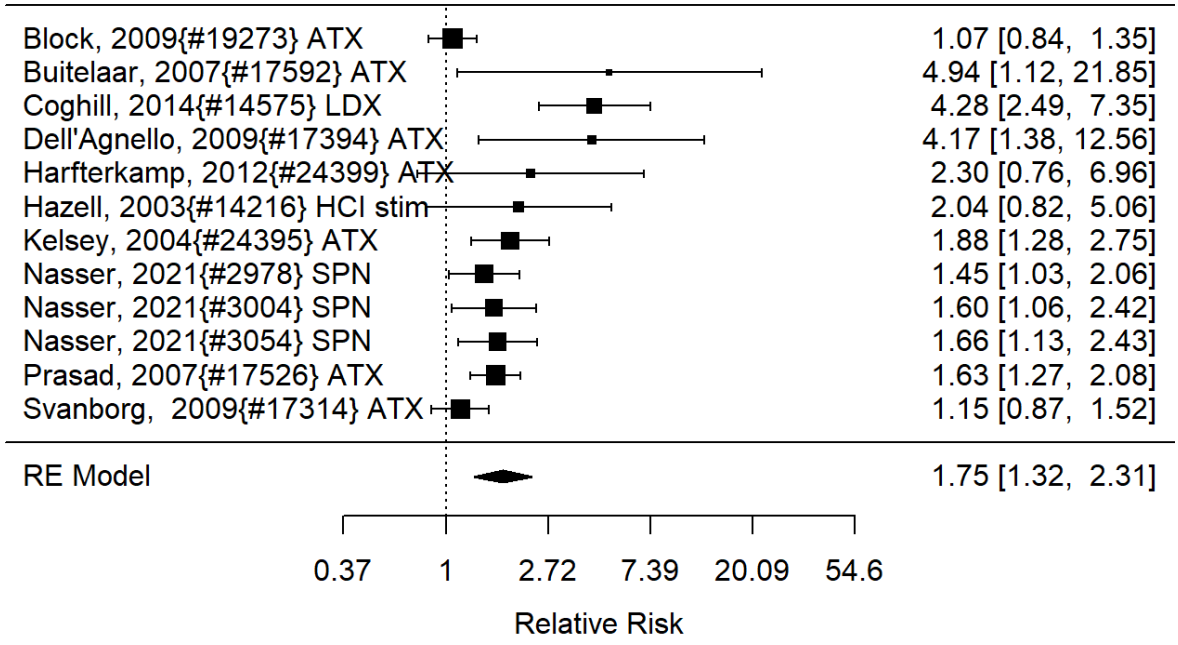
Notes: ATX atomoxetine, HCl clonidine hydrochloride, GXR guanfacine, LDX lisdexamfetamine dimesylate, MPH methylphenidate, SPN SPN-812, stim stimulants (not further defined)

Across studies, pharmacological interventions for ADHD were associated with a systematic reduction in symptom scale scores compared to control (SMD -0.59; CI -0.68, -0.51; 47 studies, n=7358). Only two studies included children younger than six years old.[116, 372] There was some evidence of heterogeneity (I-squared 67%). Tests for publication bias were not statistically significant. Excluding nine high-risk-of-bias studies 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). Restricting medications to stimulants also showed improved ADHD symptoms but heterogeneity remained (SMD -0.88; CI 1.13, -0.06; 12 studies; I-squared 77%). When restricting to methylphenidate evaluations only to explore heterogeneity, we found that methylphenidate showed improvement in ADHD symptom scores and heterogeneity was considerably reduced (SMD -0.61; CI -0.84, -0.39; 6 studies; I-squared 29%). The equivalent analysis for amphetamine studies also showed improvement in symptom scores but heterogeneity was not reduced (SMD -1.13; CI -1.62, -0.64; 5 studies; I-squared 79%).[137, 169, 206, 333, 409] Non-stimulants also improved ADHD symptom scores and heterogeneity was not remarkable (SMD -0.51; CI -0.58, -0.44; 35 studies; I-squared 47%). Results of restricting to SNRIs were similar to the overall non-stimulant analysis with heterogeneity further reduced (SMD -0.52; -0.60, -0.43; 24 studies; I-squared 34%). Most of these studies evaluated

atomoxetine specifically, and excluding other studies (assessing guanfacine or viloxanzine) found a similar treatment effect (SMD -0.57; CI -0.68, -0.46; 18 studies; I-squared 40%). Effects for alpha agonists versus placebo were also statistically significant (SMD -0.49; CI -0.64, -0.34; 11 studies).

Results for symptom measures used as categorical data are shown in Figure 21.

Figure 211. Effects of FDA-Approved Pharmacological ADHD Treatment on ADHD Symptoms (RR)



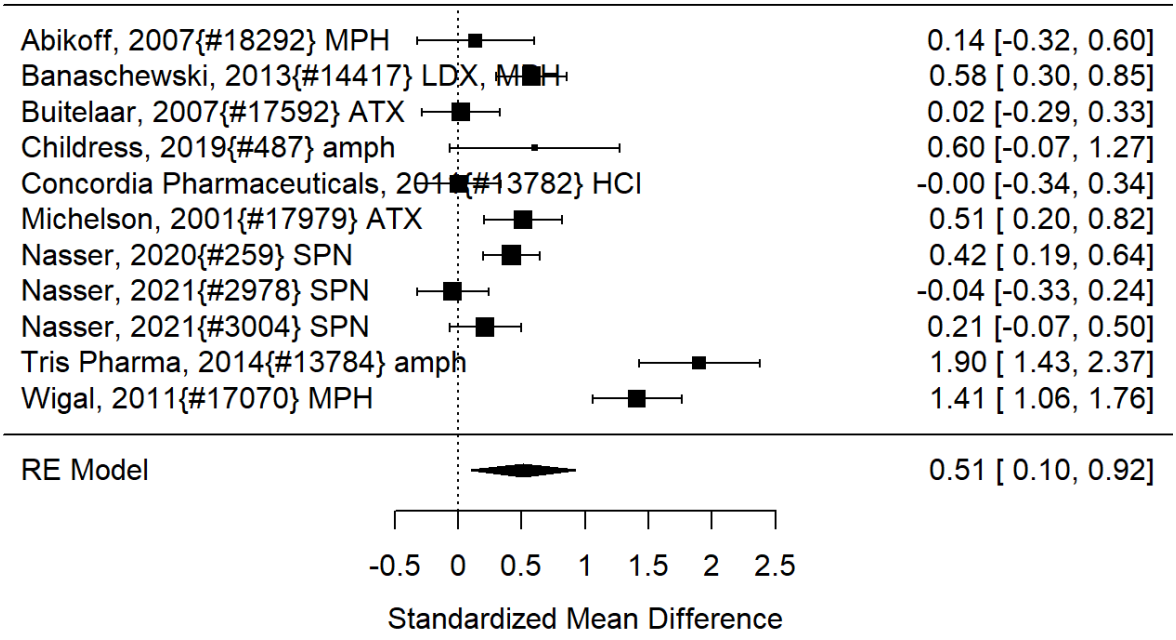
Notes: ATX atomoxetine, HCI clonidine hydrochloride, LDX lisdexamfetamine dimesylate, SPN SPN-812, stim stimulants (not further defined)

Results across studies also indicated a significant benefit (RR 1.75, CI 1.32, 2.31; 12 studies, n=1850). None of the studies included children under six years of age. There was some evidence of heterogeneity (I-squared 71%). There was also some evidence of publication bias (Begg p 0.07, Egger p 0.02). Applying the trim and fill method for an alternative estimate, results were similar (RR 1.76; CI 1.36, 2.27). When removing high risk of bias studies in a sensitivity analysis, the treatment effect was even higher than the main analysis (RR 1.92, CI 1.42, 2.59) and heterogeneity was further reduced, indicating that methodological rigor of the studies was one source of heterogeneity. Stratifying studies further found that stimulants improved ADHD symptoms (RR 2.61; CI 1.00, 6.77; 3 studies) and the small subset did not detect heterogeneity. Results for methylphenidate alone showed the same point estimate but results were not statistically significant due to wide confidence intervals (RR 1.72; CI 0.52, 5.12; 2 studies).[114, 462] The only amphetamine study reported a statistically significant effect (RR 4.28; CI 2.49, 7.35; 1 study).[206] Across studies, non-stimulants improved ADHD symptoms with negligible heterogeneity (RR 1.49; CI 1.21, 1.83; 10 studies; I-squared 46%). Most of the non-stimulant studies evaluated atomoxetine and excluding all other studies showed a very similar effect estimate (RR 1.49; CI 1.13, 1.95; 6 studies; I-squared 69%). One study assessing an alpha agonist did not find a systematic difference between groups due to wide confidence intervals (RR 2.04; CI 0.82, 5.06; 1 study).

5. Results: Treatment of ADHD

Some of the identified studies reported on functional outcomes as shown in Figure 22.

Figure 222. Effects of FDA-Approved Pharmacological ADHD Treatment on Functional Impairment (SMD)



Notes: amph amphetamines (not further defined), ATX atomoxetine, LDX lisdexamfetamine dimesylate, MPH methylphenidate, SPN SPN-812, stim stimulants (not further defined)

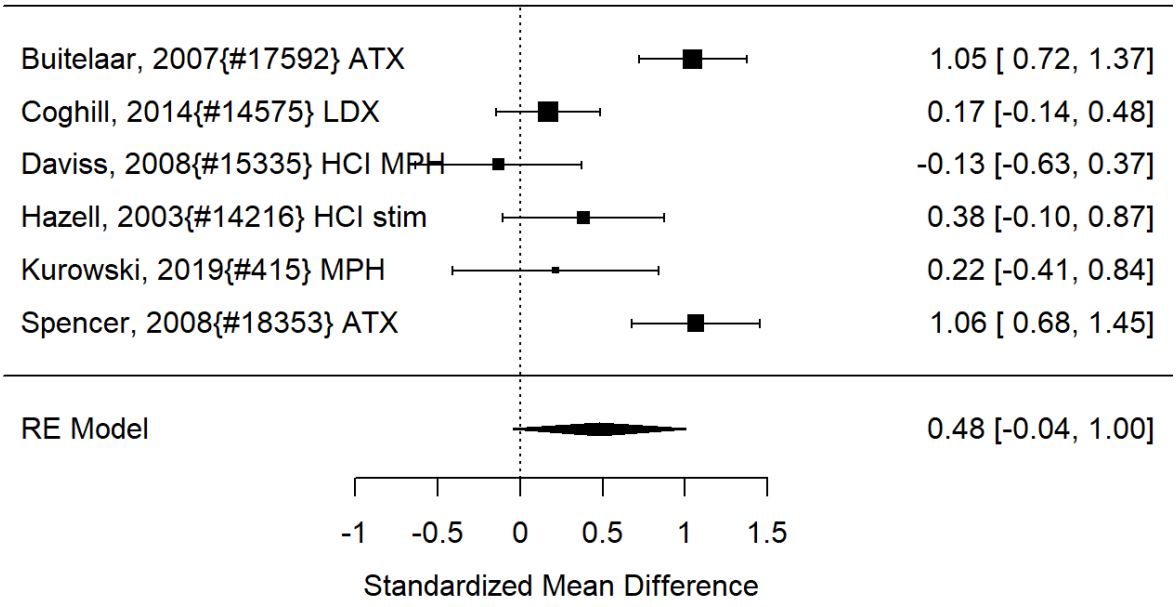
Across studies, treatment was associated with a decrease in functional impairment (SMD 0.51; CI 0.10, 0.92; 11 studies, n=1739). Only one study included children younger than six years old.[116] There was evidence of substantial heterogeneity (I-squared 92%). There was no evidence of publication bias. Excluding three high-risk-of-bias studies in a sensitivity analysis did not change the treatment estimate (SMD 0.50; CI 0.08, 0.92) and heterogeneity was not reduced. Across studies, stimulants specifically improved functional impairment; however, estimates varied substantially, and heterogeneity was high (SMD 0.93; CI 0.05, 1.81; 5 studies; I-squared 91%). Restricting to methylphenidate to explore the source of heterogeneity left two studies reporting different effect estimates for functional impairment that could not be meaningfully combined and the effect was not statistically significant (SMD 0.78; CI -7.36, 8.92; 2 studies, I-squared 94%). The results of the equivalent analysis for amphetamines showed a significant effect but there remained heterogeneity (SMD -1.16; CI -1.20, -0.67; 5 studies; I-squared 79%).[137, 197, 575] Across studies, non-stimulants also improved functional impairment but there remained evidence of heterogeneity (SMD 0.22; CI 0.02, 0.41; 7 studies; I-squared 56%). Removing the one alpha agonist study (SMD 0.00; CI -0.34, 0.34; 1 study)[209] and restricting to SNRIs alone did not change the effect estimate substantially and heterogeneity was not reduced (SMD 0.27; CI 0.00, 0.55; 6 studies; I-squared 71%). Restricting to atomoxetine studies, evaluated in three of the included studies, did not detect a systematic effect between intervention versus control and also did not reduce heterogeneity (SMD 0.34; CI -0.48, 1.17; 3 studies; I-squared 80%).

We only identified one study formally assessing treatment satisfaction for all study arms; the study reported significant satisfaction with the alpha agonist treatment compared to placebo

treatment (RR 0.47; CI 0.32, 0.68; 1 study, n=198).[211] 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 (PERMP).[607]

All studies reporting in sufficient detail on a continuous measure for appetite, weight or growth suppression are shown in the Figure 23.

Figure 233. Effects of FDA-Approved Pharmacological ADHD Treatment on Appetite Suppression (SMD)

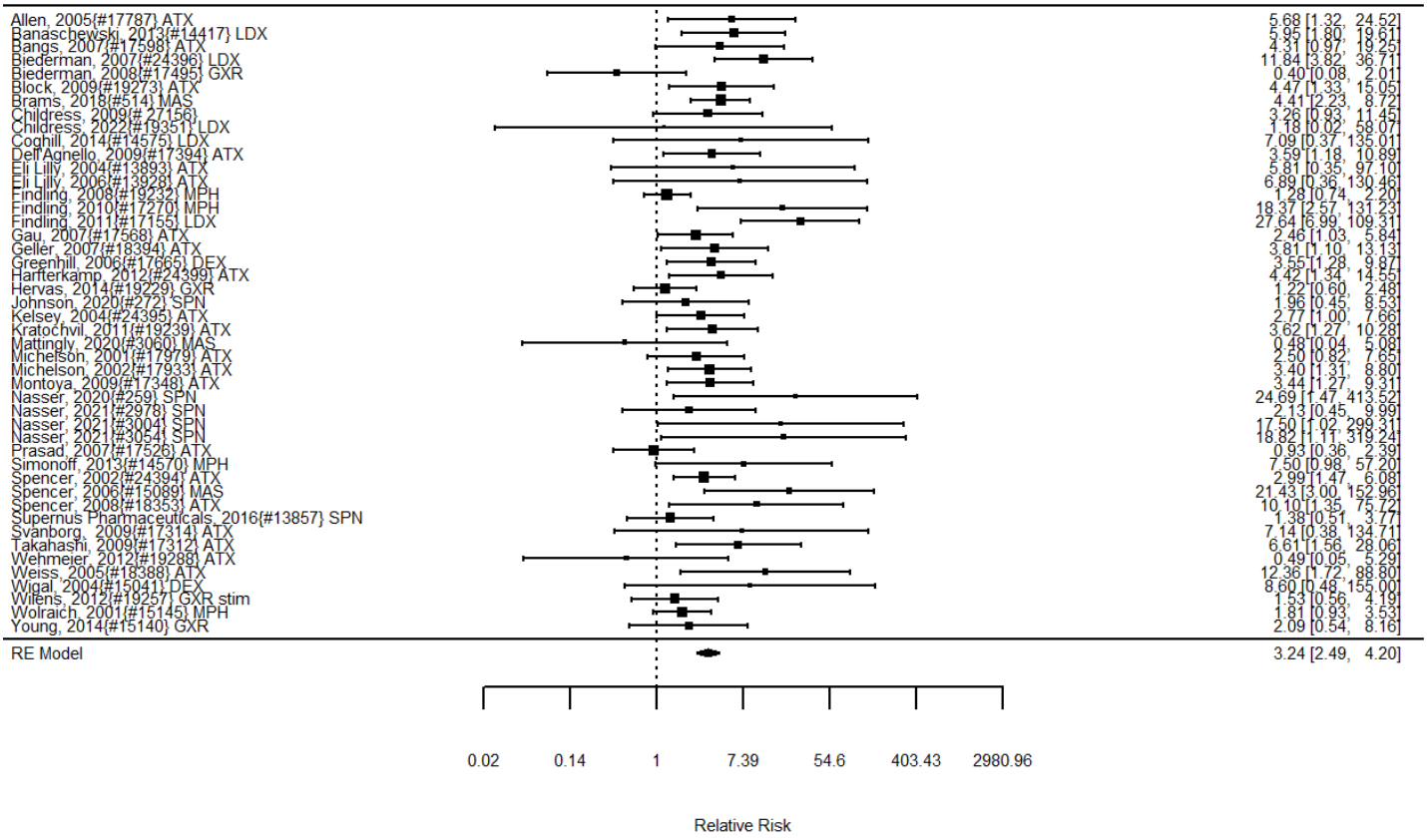


Notes: ATX atomoxetine, HCI clonidine hydrochloride, LDX lisdexamfetamine dimesylate, MPH methylphenidate, stim stimulants (not further defined)

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%). We did not detect publication bias. Removing one high-risk-of-bias study in a sensitivity analysis did not change the effect (SMD 0.46; CI 0.08, 0.83) and heterogeneity was not reduced. Across studies in this analysis, we found no statistically significant effect of stimulants on appetite suppression (SMD 0.12; CI -0.30, 0.54; 3 studies; I-squared 0) and no heterogeneity was detected in this subset of studies. A study evaluating methylphenidate found a smaller and not significant effect (SMD 0.22; CI -0.41, 0.84; 1 study). The single amphetamine study also did not show a statistically significant effect (SMD 0.18; CI -0.13, 0.50; 1 study).[206] Across non-stimulant studies, we found a statistically significant effect of non-stimulants on increasing appetite suppression but heterogeneity remained high (SMD 0.64; CI 0.04, 1.25; 4 studies; I-squared 84%). The alpha agonist studies reported conflicting results and did not detect a systematic effect across studies (SMD 0.13; CI -3.12, 3.39; 2 studies; I-squared 51%).

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 24.

Figure 244. Effects of FDA-Approved Pharmacological ADHD Treatment on Appetite Suppression (RR)



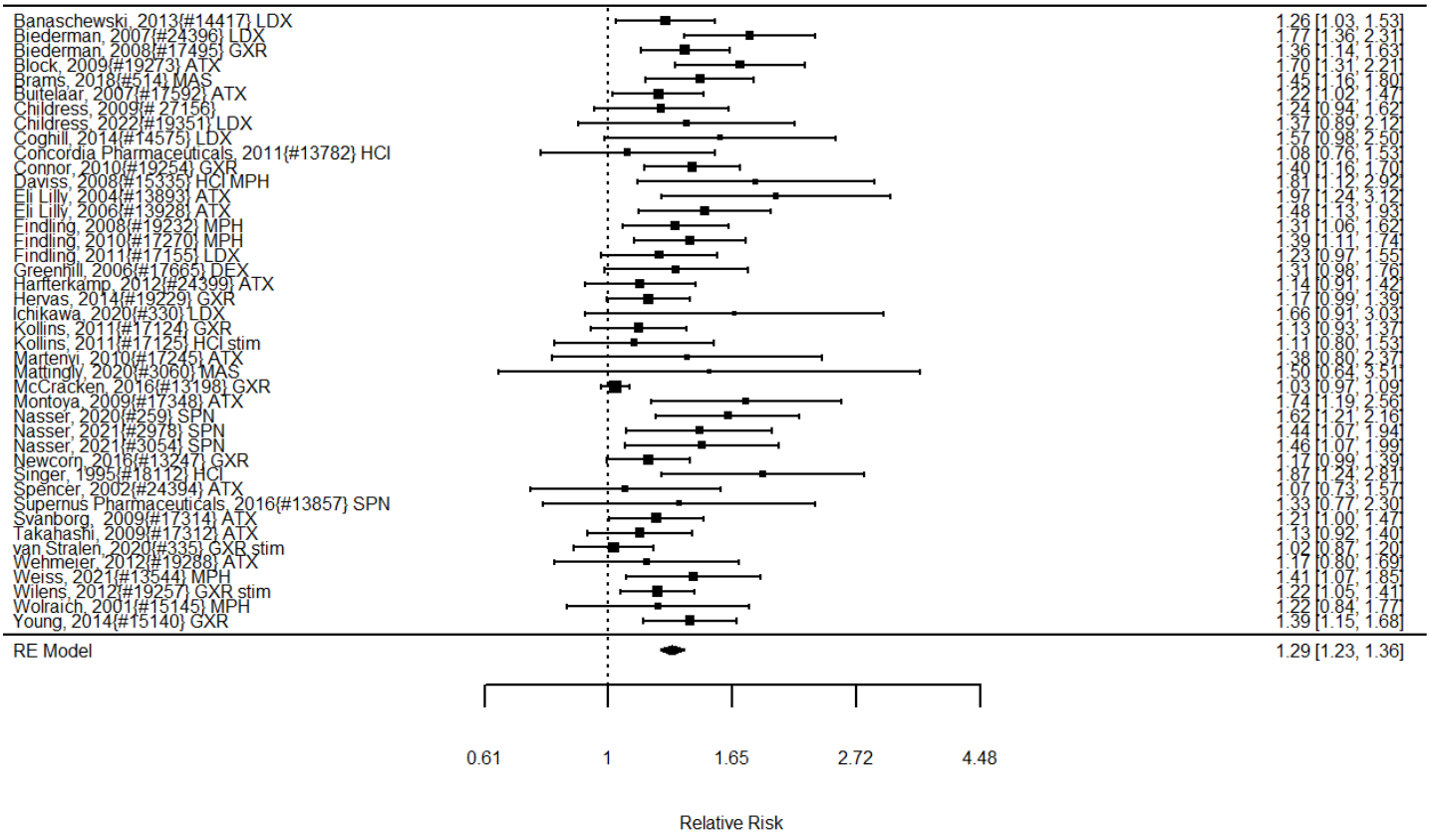
Notes: ATX atomoxetine, GXR guanfacine, LDX lisdexamfetamine dimesylate, MPH methylphenidate, SPN SPN-812, stim stimulants (not further defined)

Across studies, pharmacological treatment was associated with a suppression in appetite compared to control groups (RR 3.24; CI 2.49, 4.20; 46 studies, n=7389). Only two studies included children under the age of six.[198, 372] Heterogeneity was negligible (I-squared 45%). There was evidence of publication bias (Begg p 0.03, Egger p<0.005). An alternative treatment estimate using the trim and fill method suggested a somewhat smaller effect on appetite suppression (RR 2.41; CI 1.79; 3.25). When removing six high-risk-of-bias studies in a sensitivity analysis, effect estimates were similar to the main effect (RR 3.18; CI 2.35, 4.32). Across studies, stimulants specifically were associated with suppressed appetite compared to placebo, but there was some heterogeneity (RR 3.85; CI 2.33, 6.36; 19 studies; I-squared 64%). Restricting to methylphenidate only to explore heterogeneity found a somewhat reduced, but still clear and statistically significant effect (RR 3.02; CI 1.11, 8.25; 6 studies; I-squared 64%) and heterogeneity was not reduced when restricting to this subset. Amphetamine were also associated with appetite suppression compared to placebo and heterogeneity was not remarkable (RR 6.23; CI 2.48, 15.66; 7 studies; I-squared 55%).[137, 169, 198, 206, 273, 409, 545] The non-stimulants were also associated with suppressed appetite compared to placebo with negligible heterogeneity (RR 2.86; CI 2.09, 3.91; 25 studies; I-squared 24%). Results restricting to SNRIs also showed an association with suppressed appetite compared to placebo with no heterogeneity (RR 3.29; CI

2.42, 4.47; 22 studies; I-squared 2%). Most studies evaluated atomoxetine and excluding all other studies did not change the estimate substantially and heterogeneity was essentially nonexistent (RR 3.21; CI 2.34, 4.39; 17 studies; I-squared 4%). Although the small set did also not detect heterogeneity, the alpha agonist studies reported conflicting results and did not indicate a systematic effect (RR 1.25; CI 0.58, 2.70; 4 studies; I-squared).

The number of participants experiencing any adverse event is documented in Figure 25.

Figure 255. Effects of FDA-Approved Pharmacological ADHD Treatment on Number of Participants with Adverse Events (RR)



Notes: ATX atomoxetine, HCl clonidine hydrochloride, GXR guanfacine, LDX lisdexamfetamine dimesylate, MPH methylphenidate, stim stimulants (not further defined)

Pharmacological interventions were associated with a higher risk of experiencing adverse events compared to control groups (RR 1.29; CI 1.23, 1.36; 42 studies, n=7130). None of the studies included children under the age of six. We detected only negligible heterogeneity (I-squared 45%). There was evidence of publication bias (Begg p 0.12, Egger p<0.001) and an alternative effect estimate using the trim and fill method suggested a smaller effect (RR 1.23; CI 1.16, 1.30). We also assessed in a sensitivity analysis whether results were mainly driven by high-risk-of-bias studies; estimates remained stable (RR 1.28; CI 1.22, 1.35) after excluding eight high-risk of bias studies and heterogeneity was reduced further. Across studies, we found that stimulants were associated with an increased reporting of adverse events compared to control and heterogeneity remained the same as in the main analysis (RR 1.29; CI 1.14, 1.46; 14

studies; I-squared 51%). Stratifying medications further, we did not find a statistically significant effect of methylphenidate on the number of participants reporting on adverse events but heterogeneity estimates were higher than in the overall stimulant analysis (RR 1.22; CI 0.95, 1.55; 7 studies) (I-squared 72%). [221, 275, 276, 303, 601, 608, 615] Amphetamine treatment was associated with an increased risk of experiencing adverse events compared to placebo and the analysis detected no heterogeneity in this stimulant medication subset (RR 1.34; CI 1.20, 1.50; 7 studies). Non-stimulants were equally associated with increased reported adverse events (RR 1.29; CI 1.20, 1.38; 21 studies; I-squared 40%). Results restricting to SNRIs also showed increased reporting of adverse events in this subgroup and heterogeneity was further reduced (RR 1.36; CI 1.24, 1.50; 11 studies; I-squared 28%). Most of these studies evaluated atomoxetine and excluding all other studies found a similar effect estimate (RR 1.32; CI 1.18, 1.49; 8 studies; I-squared 34%). Similarly, alpha agonists were associated with the number of participants experiencing adverse events compared to placebo with some heterogeneity (RR 1.21; CI 1.10, 1.32; 13 studies; I-squared 61%).

5.3.2 FDA-Approved ADHD Pharmacological Treatment Comparative Effects

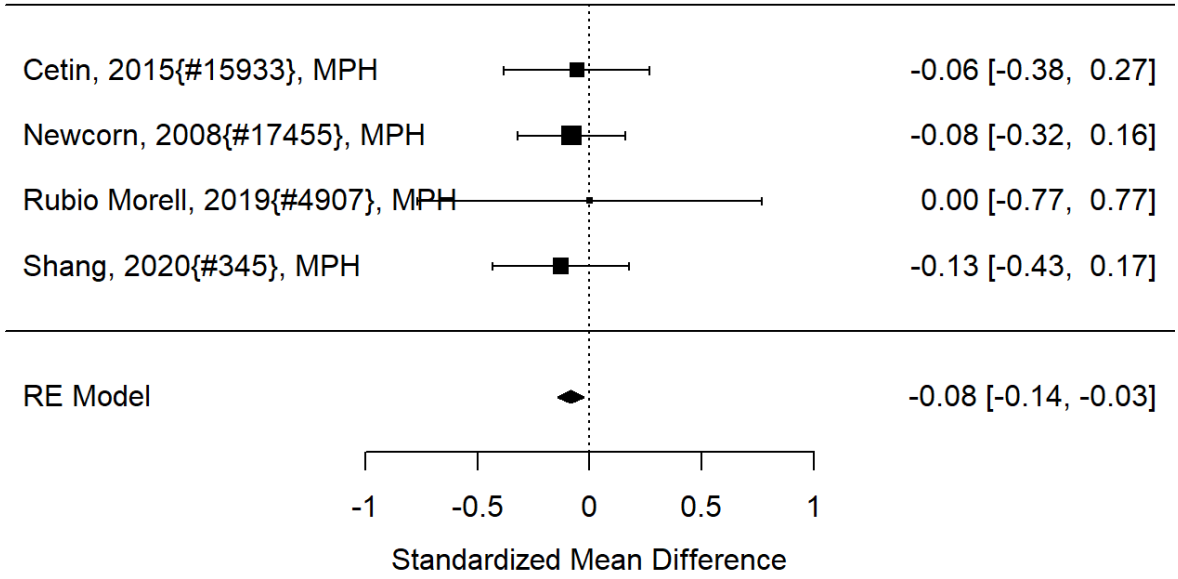
We identified over 60 studies comparing pharmacological agents to an alternative treatment; however, comparators varied. Comparators were often different doses of the same medication and some found a dose-response effect. For example, one study compared 200mg with 100mg of SPN-812 (extended release viloxazine, an SNRI) and reported improvement in both symptoms and functional impairment in both dosage groups, while the rate of children reporting decreased appetite was 7.5 in the 200mg group compared to 4.5 in the 100mg group.[442] 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 Non-Stimulants versus Stimulants

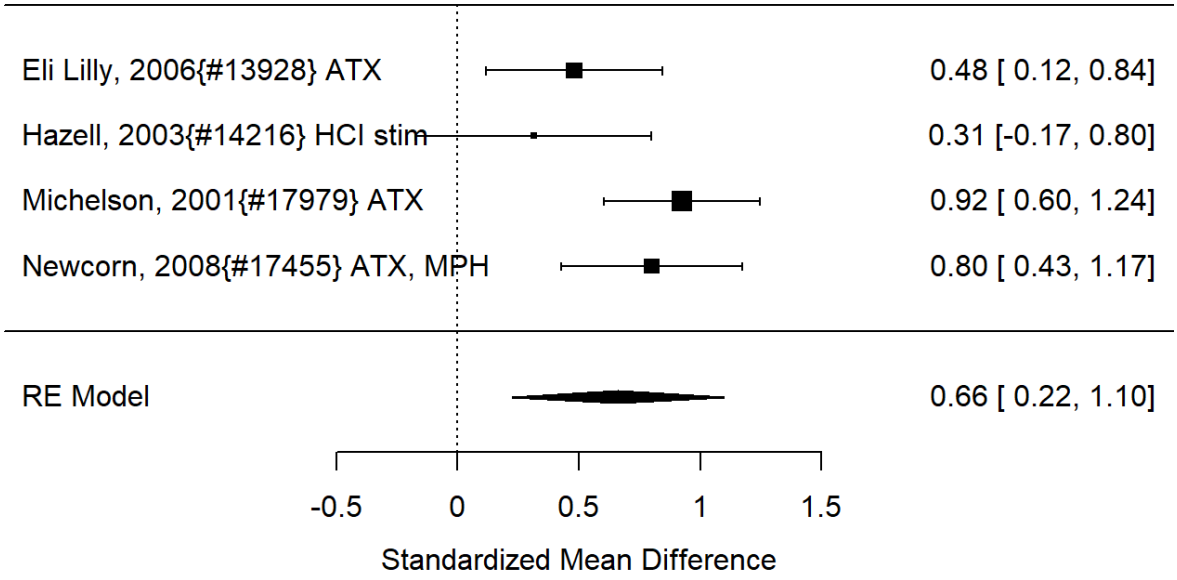
Non-stimulants versus stimulants in direct, head-to-head comparisons within identified studies for individual problem behaviors are shown in Figure 26.

Figure 26. Comparison Non-stimulant (All SNR, All Atomoxetine) versus Stimulant (All Methylphenidate) on Problem Behaviors (SMD)



Across studies, non-stimulants (all **SNRI**s) 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**. None of the studies included children under the age of 6. The analysis did not detect heterogeneity or evidence of publication bias. However, removing all high risk of bias studies left only one study, which individually did not detect a difference between atomoxetine versus methylphenidate (SMD -0.13; CI -0.43, 0.17). There were insufficient studies reporting on the outcome for indirect comparisons between non-stimulant and stimulant studies. Given the difference between medications, the next figure (Figure 27) reports a subgroup analysis for non-stimulants on problem behavior.

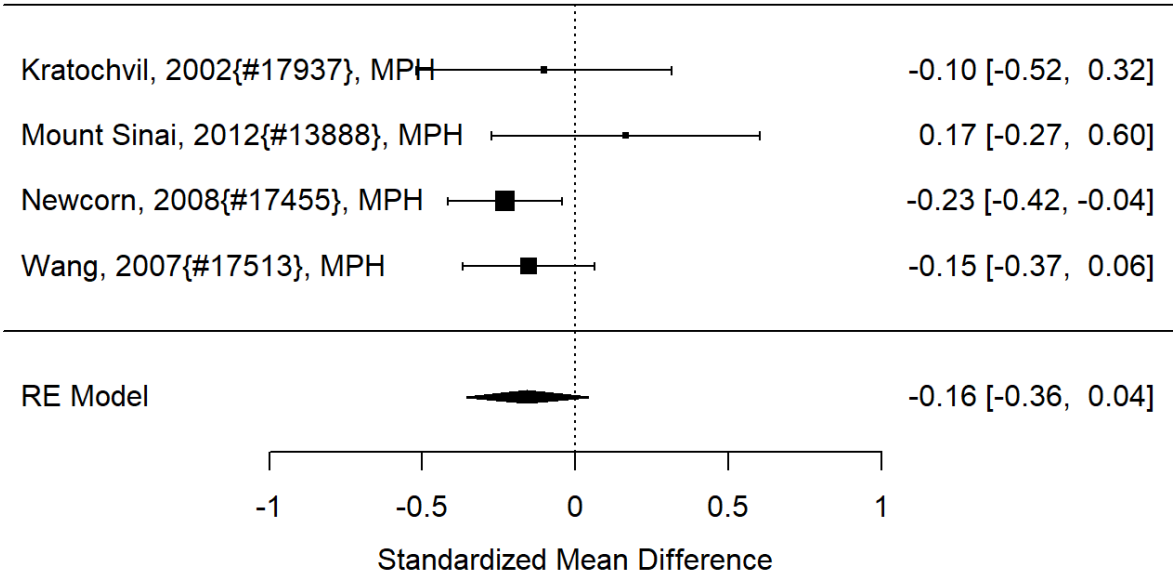
Figure 277. Subgroup Analysis: Non-Stimulants versus Control on Problem Behavior (SMD)



In the subgroup of **non-stimulant studies**, treatment was associated with a reduction in problem behavior compared to placebo (SMD 0.66; CI 0.22, 1.10; 4 studies, n=523). We identified only one study that compared **stimulants** alone to a control group, the study did not detect a systematic difference between methylphenidate and placebo (SMD 0.31; CI -0.33, 0.95; n=91).[228]

Results for broadband measures are shown in Figure 28; all studies compared atomoxetine with methylphenidate.

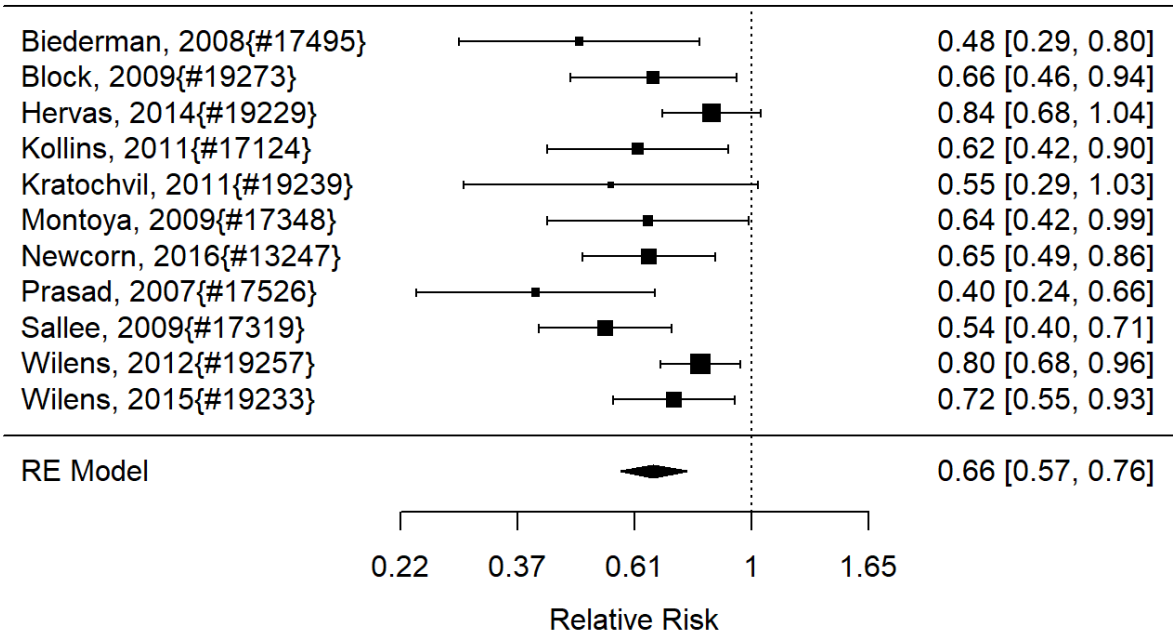
Figure 28. Comparison Non-stimulants (All SNRIs, all Atomoxetine) versus Stimulants (All Methylphenidate) on Broadband Measures (SMD)



Across studies, we did not detect a systematic difference between stimulants and non-stimulants for continuous broadband measure outcomes (SMD -0.16; CI -0.36, 0.04; 4 studies, n=1080); all studies compared the SNRI **atomoxetine versus methylphenidate**.[370, 448, 527, 593] We did not detect heterogeneity or evidence of publication bias. 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).[593] 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 0.17).

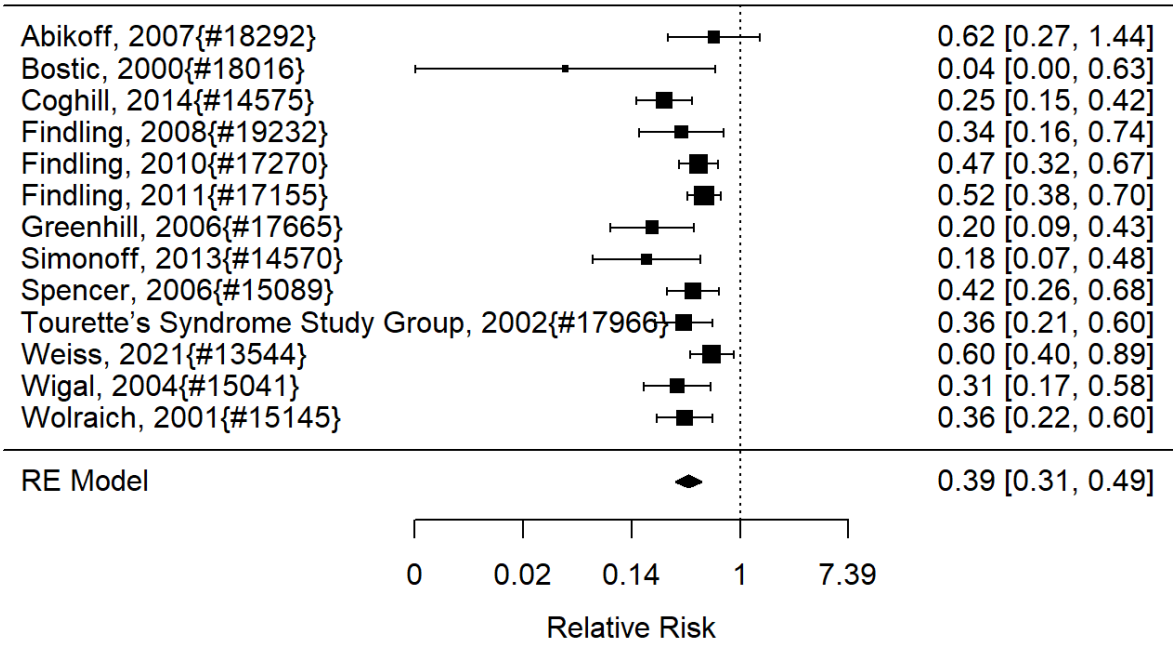
We identified only one study that reported on a categorical assessment of a broadband impression; the study found no difference between non-stimulants and stimulants (RR 1.01; CI 0.75, 1.37; 1 study, n=237); the study compared the **SNRI atomoxetine versus methylphenidate** specifically.[555] However, a meta-regression for categorical broadband measures indicated a statistically significant difference between results reported in **non-stimulant versus stimulant studies** (p 0.0004). The next figure (Figure 29) shows the subgroup analysis results.

Figure 29. Subgroup Analysis: Non-Stimulants versus Control on Broadband Measures (RR)



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 0.57, 0.76; 11 studies, n=2174). Only one of the studies included children under the age of six.[372] The subgroup analysis of stimulant studies is shown in Figure 30.

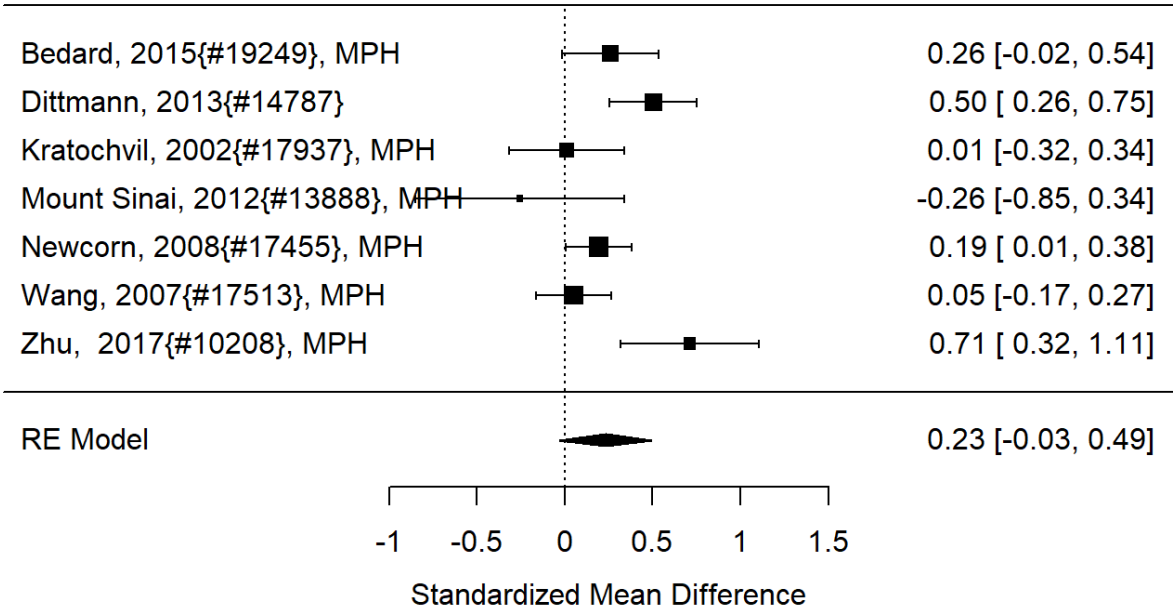
Figure 30. Subgroup Analysis: Stimulants versus Control on Broadband Measures (RR)



As already indicated in the prior section, the effect estimate for **stimulant studies** showed a clear effect for individual studies and across studies in this medication subgroup (RR 0.39; CI 0.31, 0.49; 13 studies, n=1569). Only one study included children younger than six years old.[116]

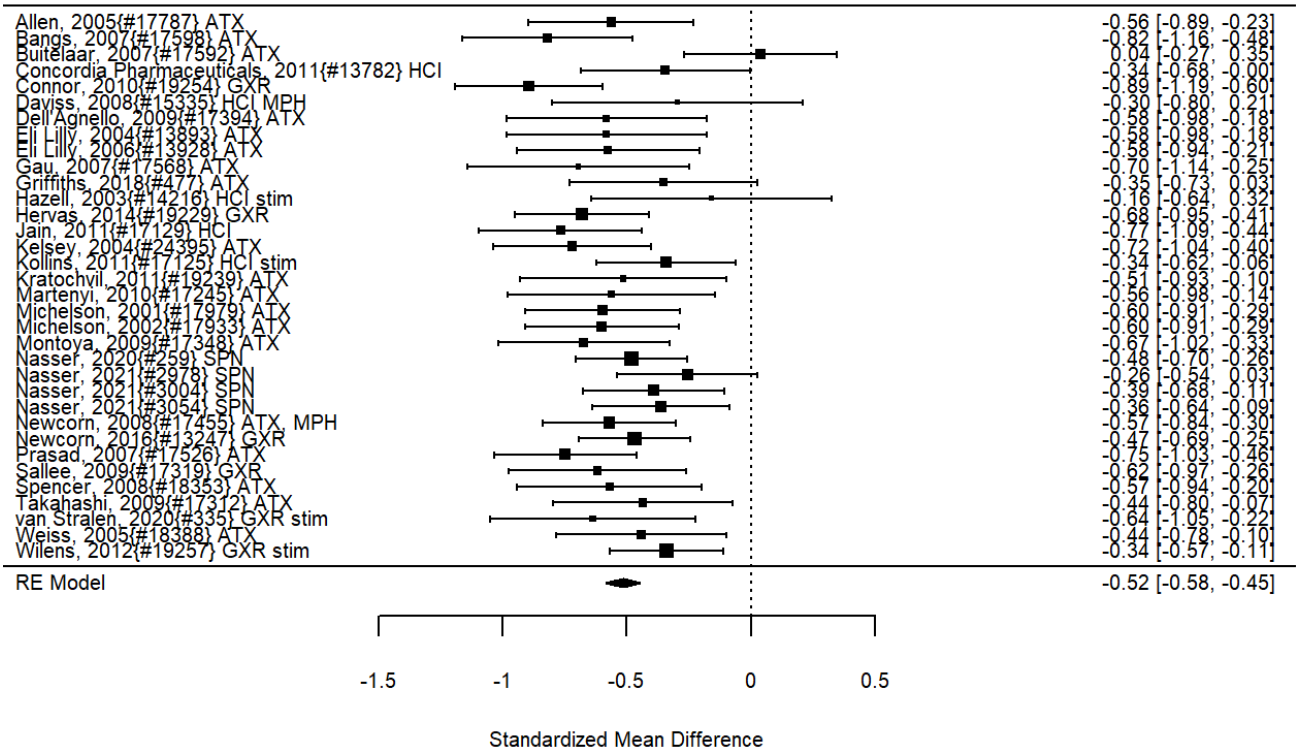
A large number of studies reported on ADHD symptoms, and we identified a number of head-to-head comparisons. The analysis comparing **non-stimulants versus stimulants** for ADHD symptoms is shown in Figure 31.

Figure 31. Comparison Non-stimulant (All SNRI) versus Stimulant on ADHD Symptoms (SMD)



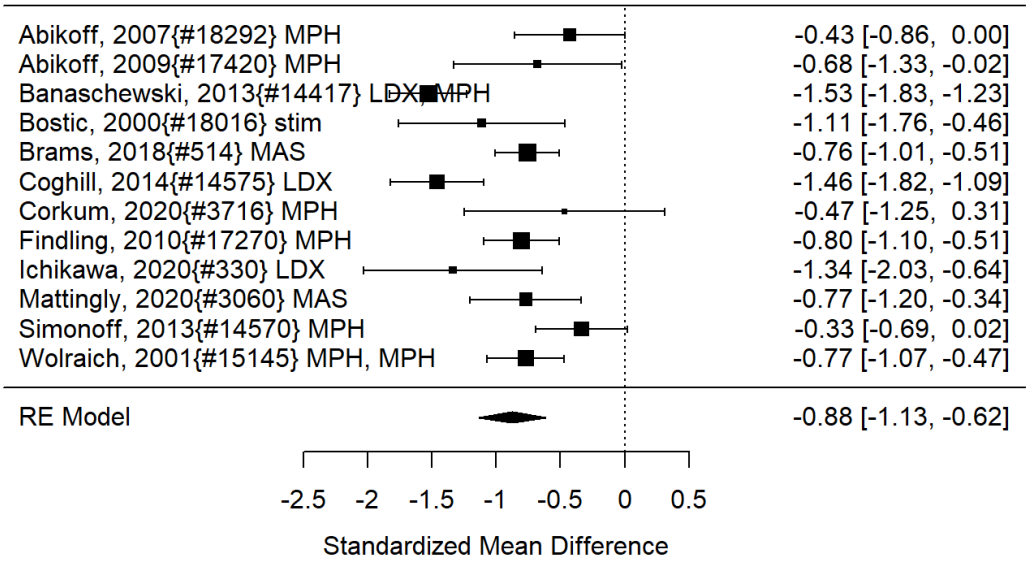
Although more studies favored stimulants, across studies, we did not detect a systematic difference between non-stimulants (all **SNRI**) versus stimulants (methylphenidate in all but one case) in direct comparisons (SMD 0.23; CI -0.03, 0.49; 7 studies, n=1611). We detected some heterogeneity (I-squared 69%) in this analysis. There was no evidence of publication bias. Removing all high risk of bias studies left only two studies that also found no systematic difference between interventions (SMD 0.33; CI -3.53, 4.20). When restricting to the comparator methylphenidate, the difference between stimulants and non-stimulants was not statistically significant either (SMD 0.18; CI -0.18, 0.44; 6 studies); all the studies compared **atomoxetine versus methylphenidate** in this comparison. Across studies, more evaluations favored methylphenidate, but overall, there was no systematic or statistically significant difference between atomoxetine versus methylphenidate in direct comparisons.[144, 370, 448, 527, 593, 632] There was little heterogeneity (I-squared 49%) in this analysis, although the direction of effects varied by study. There was no indication of publication bias. Removing high-risk-of-bias studies did not identify a statistically significant difference between atomoxetine versus methylphenidate for ADHD symptoms either (SMD 0.33; CI -3.53, 4.20) and heterogeneity was not reduced. However, we also analyzed whether indirect comparisons between **non-stimulant versus stimulant studies** indicate systematic differences, and we found a statistically significant difference (p 0.0001). The effect estimates for the subgroups are documented in the following section. Figure 32 shows the subgroup analysis for non-stimulants reporting on ADHD symptoms.

Figure 322. Subgroup Analysis: Non-Stimulants versus Control on ADHD Symptoms (SMD)



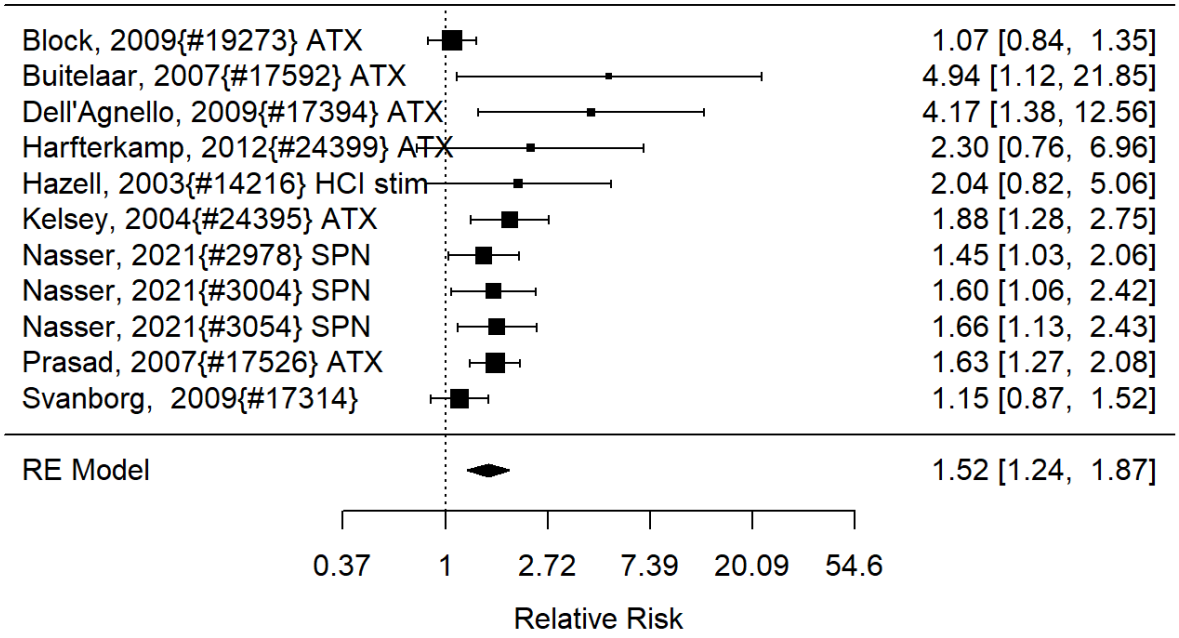
In the subgroup of **non-stimulant studies**, results were associated with a reduction in ADHD symptoms measured as a continuous variable (SMD -0.52; CI -0.58, -0.45; 34 studies, n=5593). Only one study included children younger than six years old.[372] Results for the subgroup of stimulant studies on ADHD symptoms are shown in Figure 33.

Figure 333. Subgroup Analysis: Stimulants versus Control on ADHD Symptoms (SMD)



In the subgroup of **stimulant studies**, treatment was associated with a substantial reduction in ADHD symptoms (SMD -0.88; CI -1.13, -0.62; 12 studies, n=1471). Only one study included children younger than six years old.[116] 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 (p= 0.02). The subgroups are shown separately in Figures 34 and 35.

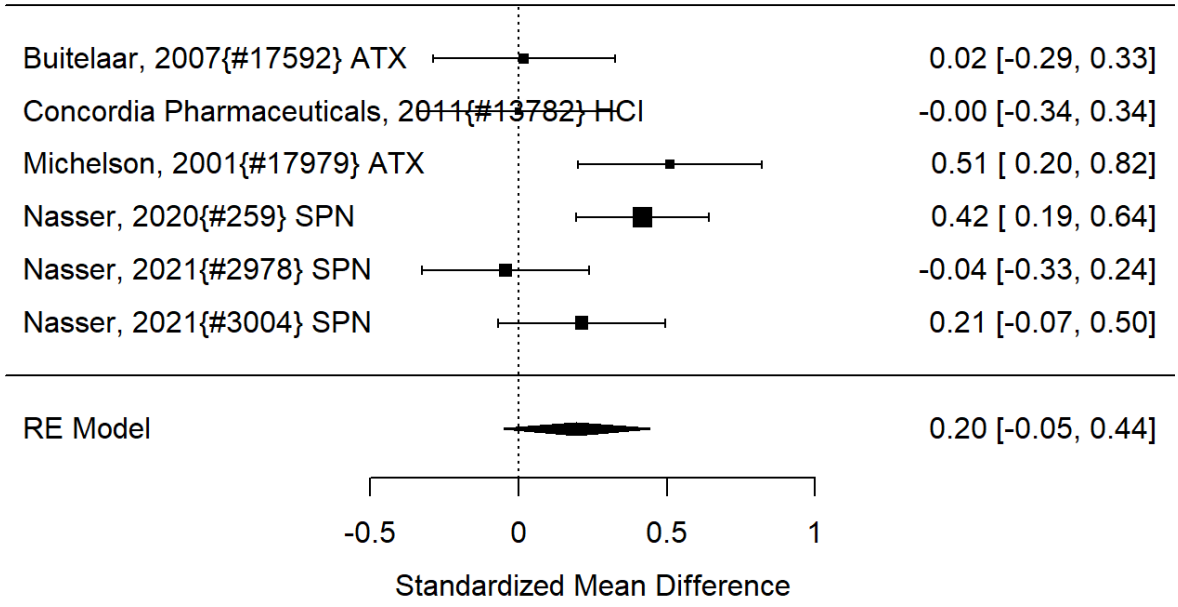
Figure 34. Subgroup Analysis: Non-Stimulants versus Control on ADHD Symptoms (RR)



In the subgroup of non-stimulant studies, we found a clear treatment effect on ADHD symptoms (RR 1.52; CI 1.24, 1.87; 11 studies, n=1697). 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 (RR 4.28; CI 2.49, 7.35; 1 study, n=153).[206]

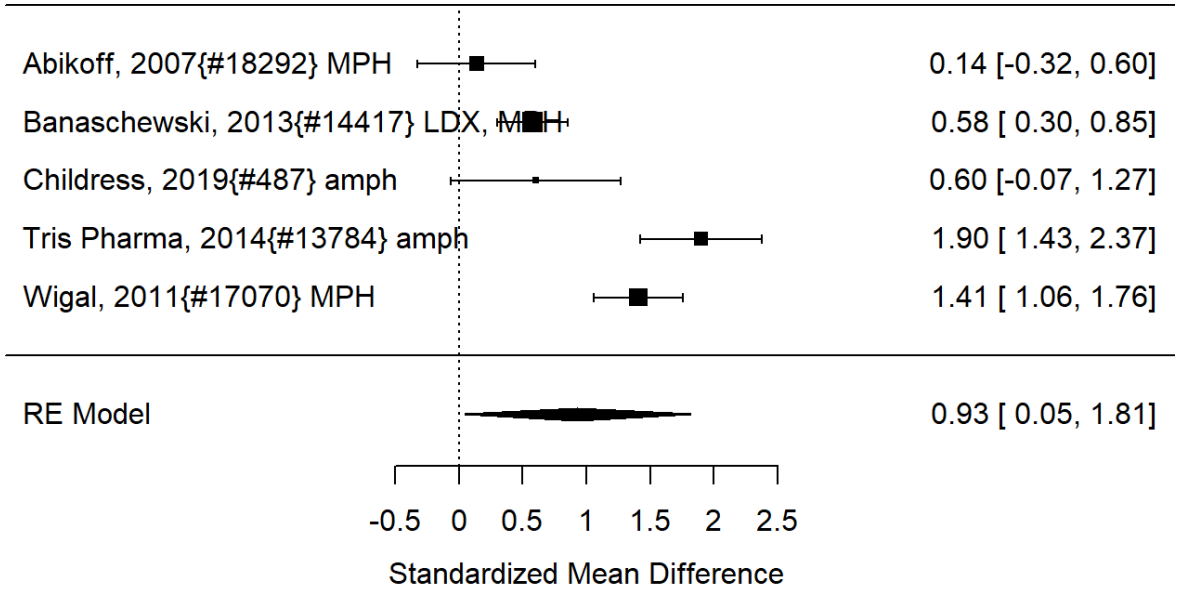
We did not identify studies reporting on functional impairment in a head-to-head comparison. Indirect analysis comparing non-stimulant versus stimulant studies showed a statistically significant result (p 0.02). Subgroup analyses are shown in Figure 35.

Figure 355. Subgroup Analysis: Non-Stimulants versus Control on Functional Impairment (SMD)



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). None of the studies included children under the age of six. The equivalent analysis for stimulant studies is shown in Figure 36.

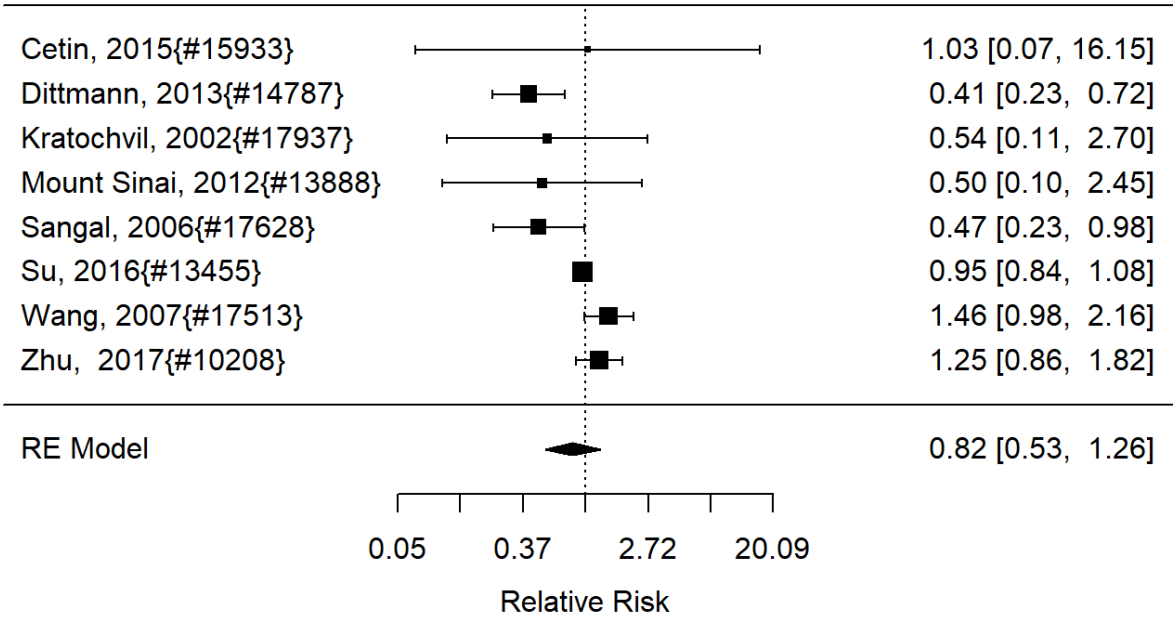
Figure 366. Subgroup Analysis: Stimulants versus Control on Functional Impairment (SMD)



In the subgroup of **stimulant studies**, treatment was associated with large improvement in functional impairment (SMD 0.93; CI 0.05, 1.81; 5 studies, n=576). Only one study included children younger than six years old.[116]

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 appetite suppression are shown in Figure 37.

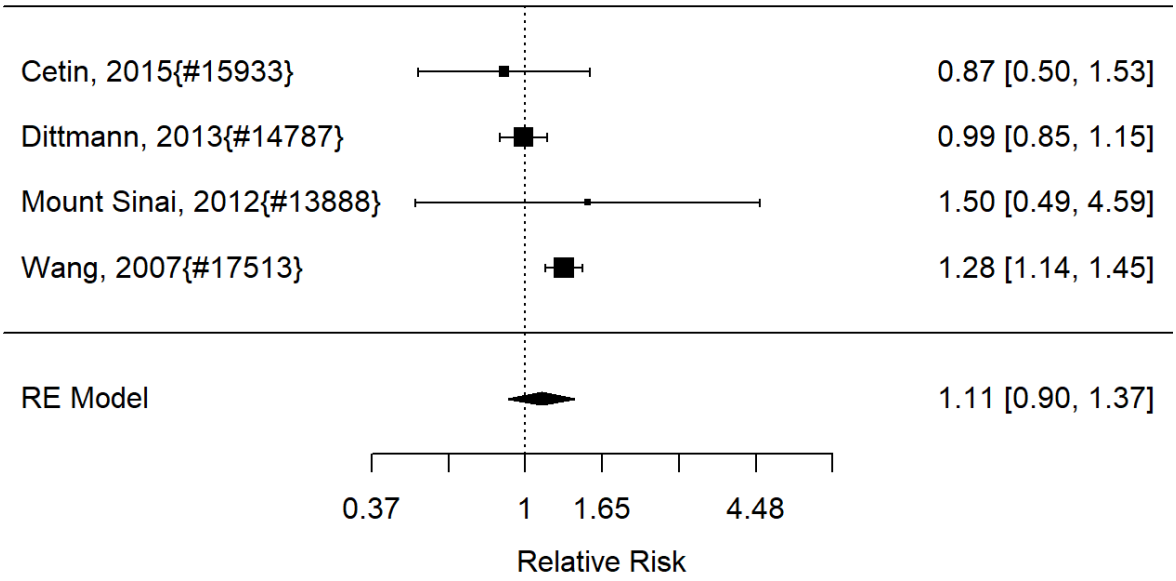
Figure 377. Comparison Non-stimulant (all SNRIs) versus Stimulant on Appetite Suppression (RR)



Across studies, we found no systematic difference between non-stimulant (all identified studies evaluated **SNRIs**) **versus stimulants** (RR 0.82; CI 0.53, 1.26; 8 studies, n=1463). 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, we found no systematic difference between SNRI and methylphenidate interventions either and heterogeneity was reduced, but in this subset, all studies compared **atomoxetine versus methylphenidate** (RR 0.98; CI 0.67, 1.44; 7 studies; I-squared 58%). Results varied, sometimes favoring atomoxetine, sometimes methylphenidate 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 0.34).

The comparative studies reporting sufficient detail to compute effect sizes for the number of participants with adverse events is shown in Figure 38.

Figure 388. Comparison Non-Stimulant (all SNRIs) versus Stimulant on Participants with Adverse Events (RR)



Across studies, we found no systematic difference between non-stimulant (all identified studies were **SNRIs) versus stimulant** interventions (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; the study favored stimulants (RR 1.28; CI 1.14, 1.45).[593] When restricting to methylphenidate as the stimulant comparator, there was a trend towards favoring methylphenidate, but the comparison between interventions was not statistically significant (RR 1.23; CI 0.99, 1.52; 3 studies); studies in this analysis all compared **atomoxetine versus methylphenidate**.[183, 527, 593] In this small set of studies, no heterogeneity was detected and there were insufficient studies for further analyses. 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 0.94).

Stimulant Comparisons: Amphetamine versus Methylphenidate

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

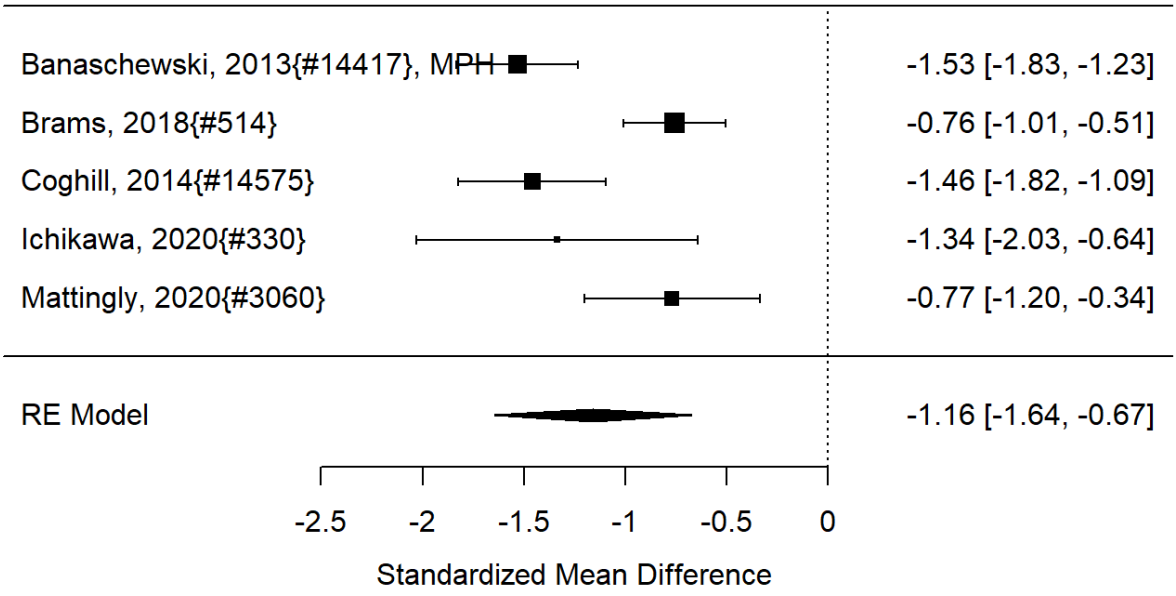
We did not identify any studies reporting on individual behaviors for a direct comparison of amphetamine and methylphenidate and indirect comparisons across studies also had insufficient number of studies for comparisons.

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).[137] Indirect comparisons across studies did not detect a systematic difference between amphetamine and methylphenidate studies (continuous outcomes p 0.97, categorical outcomes 0.89).

The single study also reported better symptom control with the amphetamine lisdexamfetamine dimesylate versus osmotic-release oral system methylphenidate (SMD -0.46; CI -0.73, -0.19; 1 study, n=221). Indirect comparisons detected a statistically significant

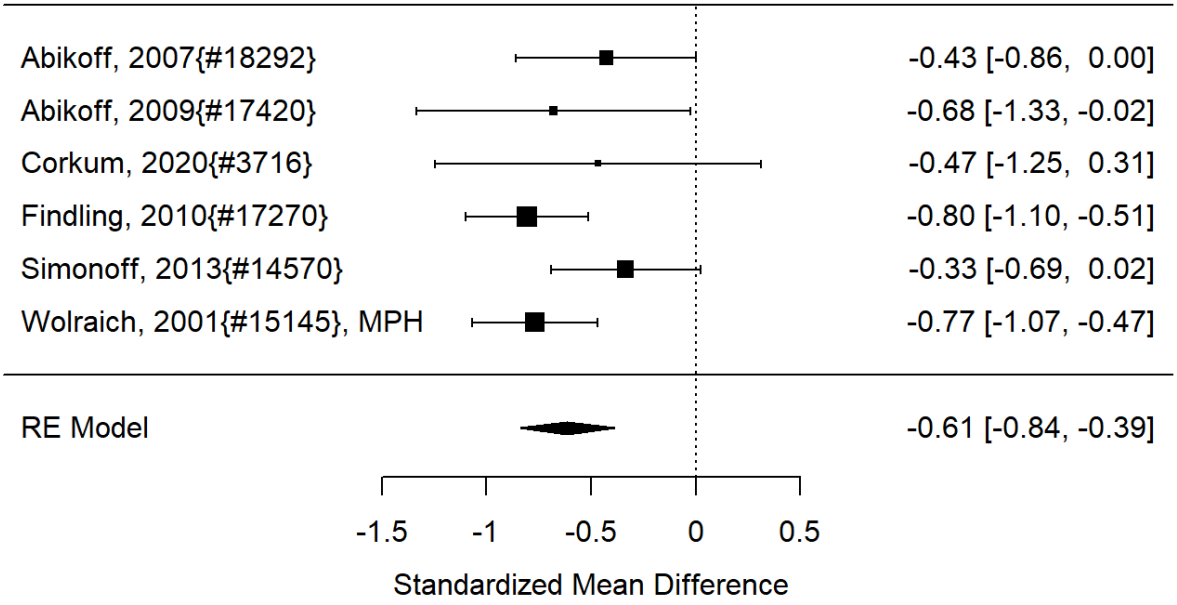
difference across studies for the continuous outcome analysis (p 0.02). The figure shows the results separately for the stimulant subgroups (see Figure 39 below).

Figure 399. Subgroup Analysis: Amphetamine versus Control on ADHD Symptoms (SMD)



In the subgroup of **amphetamine studies**, we found a significant effect of treatment (SMD -1.16; CI -1.20, -0.67; 5 studies, n=757). None of the studies included children under the age of six. The subgroup analysis results for methylphenidate studies are shown in Figure 40.

Figure 40. Subgroup Analysis: Methylphenidate versus Control on ADHD Symptoms (SMD)



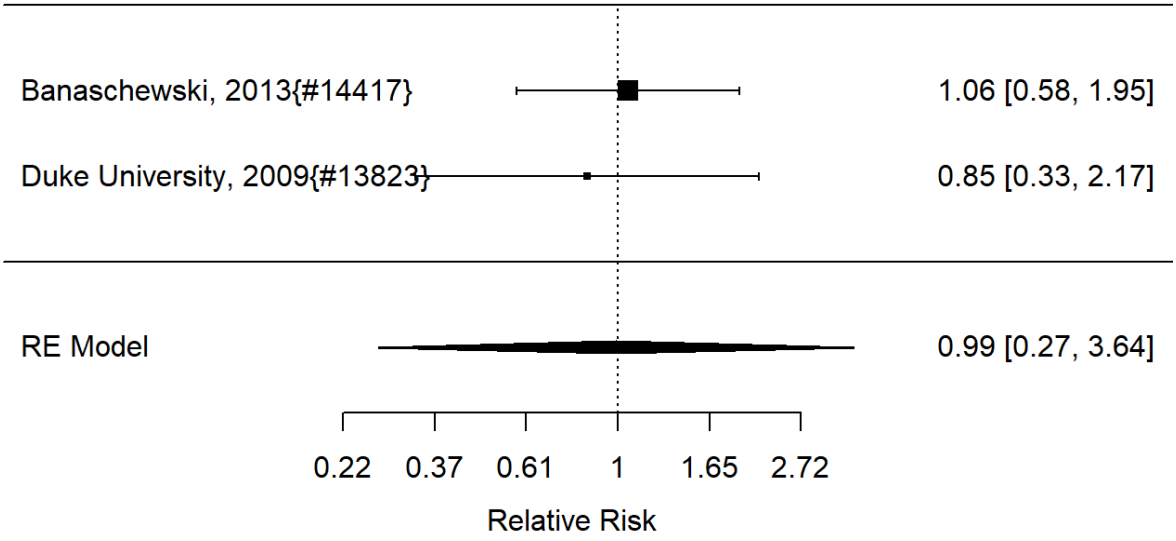
In the subgroup of **methylphenidate studies**, we found a significant treatment effect but effect estimates were smaller (SMD -0.61; CI -0.84, -0.39; 5 studies, n=757). Only one study

included children younger than six years old.[116] Indirect comparisons between amphetamine and methylphenidate using categorical data were not statistically significant (p 0.58).

There was no statistically significant differences in functional impairment in a head-to-had comparison (SMD 0.16; CI -0.11, 0.43; 1 study, n=211). The indirect comparison across studies did also not detect a systematic difference (p 0.76). We identified no studies report on treatment satisfaction or academic performance in direct head-to-head comparisons and there were insufficient data for indirect analyses.

Results for direct comparisons on the outcome appetite suppression are shown in Figure 41.

Figure 41. Comparison Amphetamine versus Methylphenidate on Participants with Adverse Events (RR)



The two studies reporting on appetite suppression did not find a systematic difference between the amphetamine lisdexamfetamine dimesylate versus osmotic-release oral system methylphenidate (RR 0.99; CI 0.27, 3.64; 2 studies, n=294).[137, 578] Similarly, indirect comparisons across studies did also not detect a significant difference between the two stimulant classes (p 0.29).

One study reporting on a number of participants reporting adverse event found no statistically significant difference between intervention (RR 1.11; CI 0.93, 1.33).[137] Similarly, indirect comparisons did also not detect a difference between amphetamines and methylphenidate regarding the number of participants reporting adverse events (p 0.18).

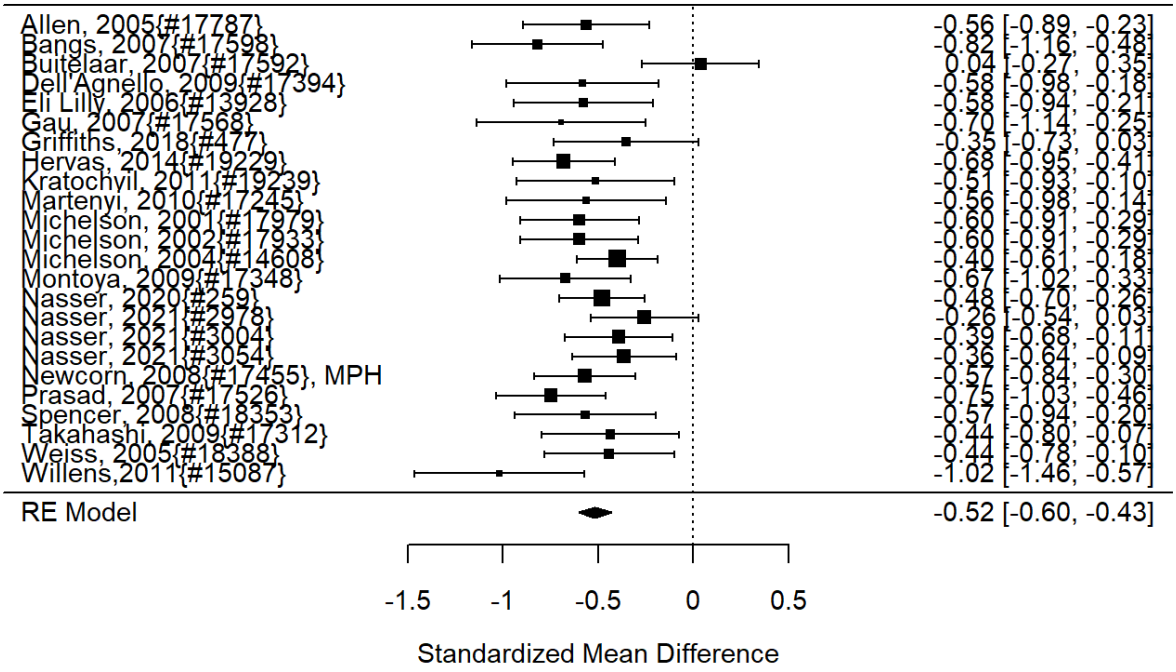
Non-Stimulant Comparisons: SNRIs versus Alpha Agonists

We identified one study comparing an alpha agonist (guanfacine) with an SNRI (atomoxetine) directly.[321] The study detected no difference for a broadband measure (number of improved patients per CGI). However, ADHD symptom improvement (ADHD-RS-IV) favored guanfacine over atomoxetine (SMD -0.47; CI -0.73, -0.2; 1 study). The study did not report on other effectiveness measures but found fewer instances of decreased appetite for guanfacine versus atomoxetine (RR 0.48; CI 0.27, 0.83; 1 study). There were no differences in the number of patients experiencing adverse events (RR 1.14; CI 0.97, 1.34) between the interventions.

In indirect comparisons, there were no differences for problem behaviors (p 0.31), broadband measures (p 0.75), ADHD symptoms (p 0.94), or functional impairment (p 0.38).

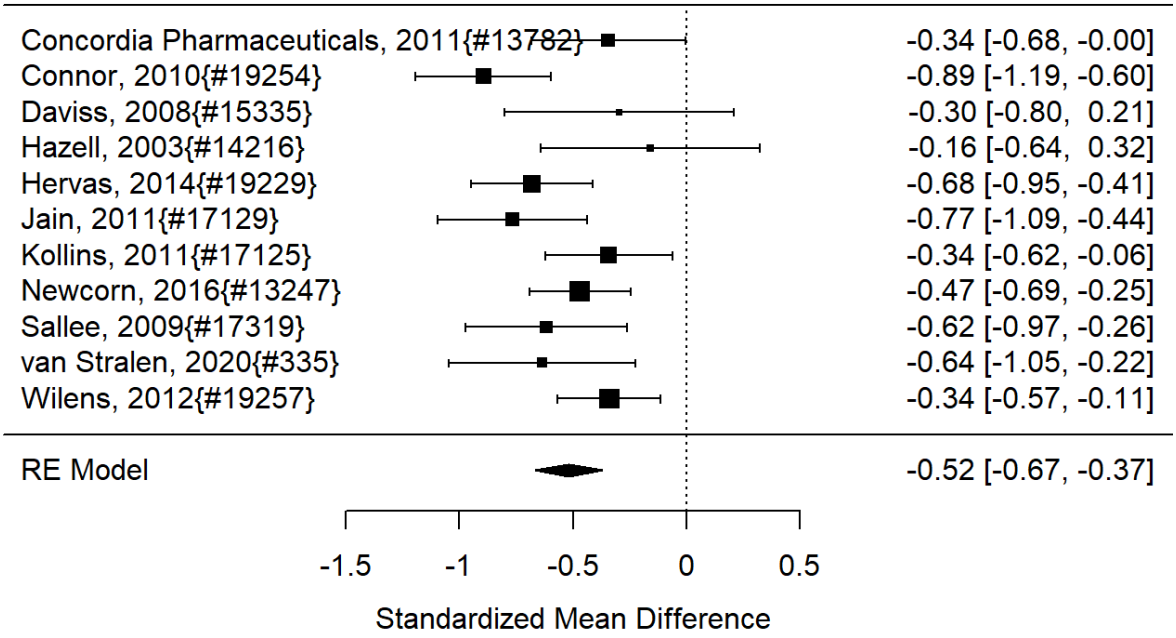
Effects for treatment satisfaction and academic performance could not be evaluated. However, indirect comparisons for the outcome appetite suppression indicated a significant difference between SNRIs and alpha agonists (p 0.003). The following shows the subgroup results for SNRI studies versus control separately for ADHD symptoms (Figure 42).

Figure 422. Subgroup Analysis: SNRIs versus Control on ADHD Symptoms (SMD)



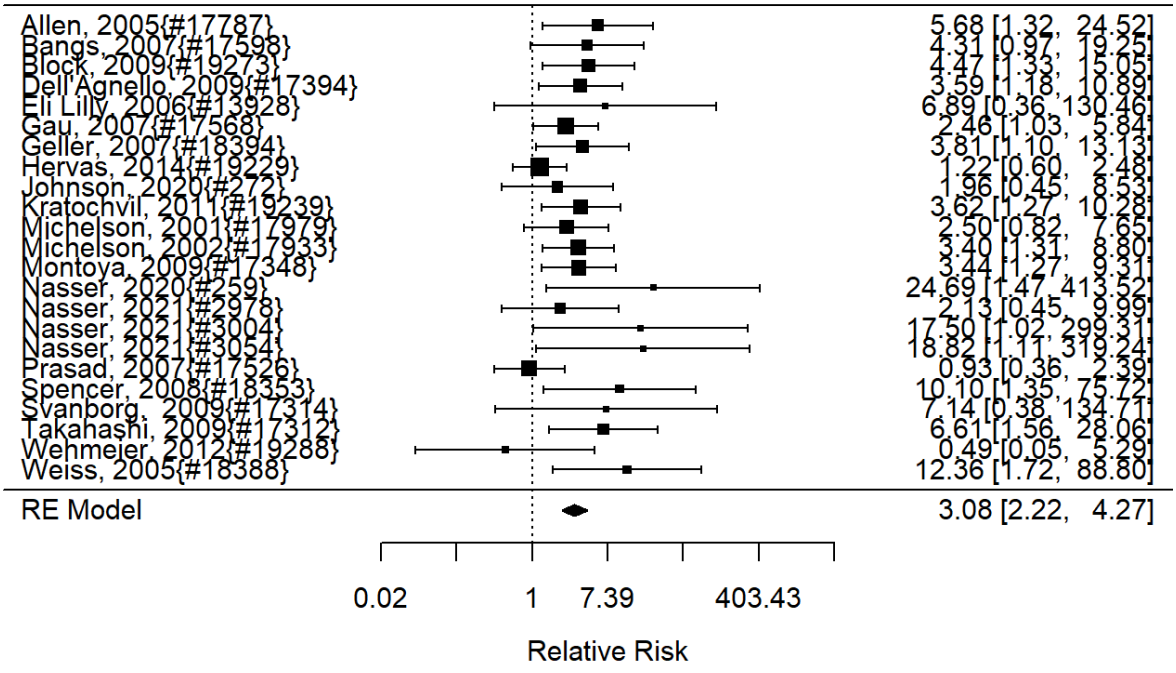
In the subgroup of **SNRI studies**, we found a clear effect on ADHD symptoms (SMD -0.52; CI -0.60, -0.43; 24 studies, n=4111). Only one study included children younger than six years old.[372] The equivalent analysis for the subgroup of alpha agonist studies is shown in Figure 43.

Figure 433. Subgroup Analysis: Alpha Agonists versus Control on ADHD Symptoms (SMD)



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). None of the studies reported on children younger than six years of age. Results for appetite suppression are shown in Figure 44.

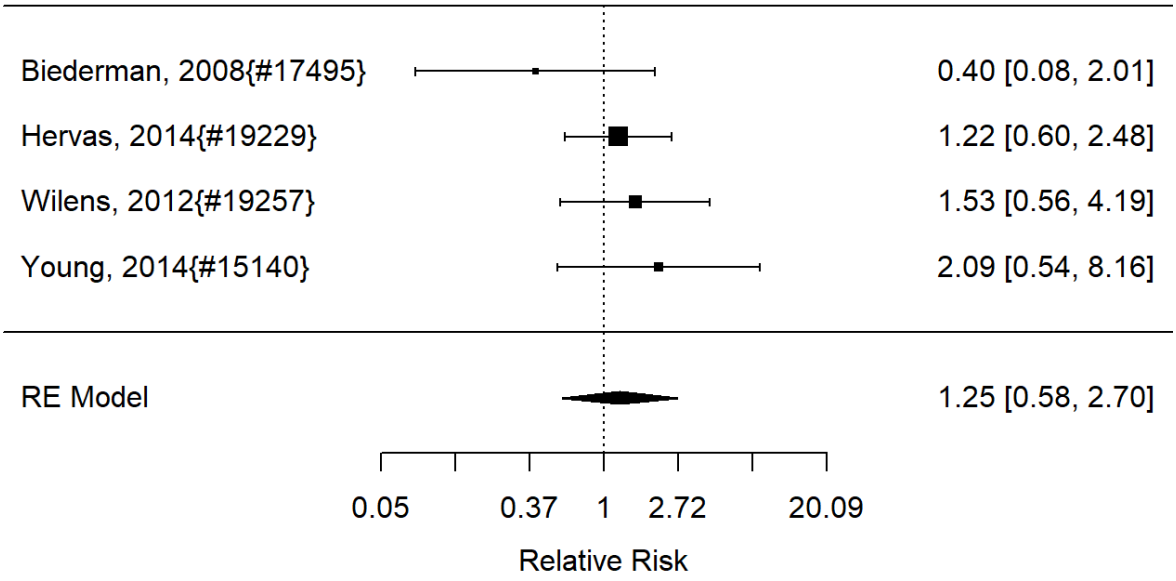
Figure 444. Subgroup Analysis: SNRIs versus Control on Appetite Suppression (SMD)



In the subgroup of **SNRI studies**, we found a substantially increased risk of appetite suppression (RR 3.08; CI 2.22, 4.47; 23 studies, n=3520). Only one study included children

younger than six years old.[1162] The equivalent analysis for the subgroup of alpha agonist studies is shown in Figure 45.

Figure 45. Subgroup Analysis: Alpha Agonists versus Control on Appetite Suppression (SMD)



Unlike in the SNRI studies, in the subgroup of **alpha agonist studies**, no systematic effect of appetite suppression was detected (RR 1.25; CI 0.58, 2.70; 4 studies; n=919). Potential differential effects for the number of participants reporting adverse events could not be evaluated.

5.3.3 FDA-Approved Medication Summary of Findings

Table 13 shows the findings for the outcomes of interest together with the number of studies and study identifiers. The table only shows unique comparison for the individual outcome, i.e., for some outcomes, we did not identify non-stimulant versus stimulant studies that were not atomoxetine versus methylphenidate.

Table 13. KQ2 Summary of Findings and Strength of Evidence for Pharmacological Interventions

Intervention and Comparison	Outcome	Number of Studies and Study Design	Findings	SoE
KQ2 pharmacological vs control	Behavior	9 RCTs[162, 231, 251, 317, 374, 422, 448, 598, 599]	Results favored intervention (SMD 0.66; CI -0.22, 1.10; 4 studies, n=523); RR 0.45; CI 0.25, 0.81; 2 studies, n=128)	Low for benefit
KQ2 pharmacological vs control	Broadband measures	57 RCTs[116, 137, 153, 162, 166, 169, 198, 206, 209, 211, 221, 224, 231, 251, 273, 275, 276, 288, 292, 303, 321, 337, 342, 367, 368, 372, 374, 404, 409, 415, 421, 422, 430, 441-444, 447-449, 470, 499, 526, 544, 545, 585, 598-601, 606, 608, 611, 612, 615, 622, 892	Results favored intervention (SMD 0.73; CI 0.40, 1.06; 27 studies, n=4618; RR 0.50; CI 0.43, 0.59; 25 studies, n=3959)	High for benefit
KQ2 pharmacological vs control	ADHD symptoms	69[115, 116, 125, 137, 138, 153, 162, 166, 169, 172, 198, 206, 209, 211, 212, 221, 224, 231, 251, 273-276, 288, 292, 303, 304, 317, 321, 333,	Results favor intervention (SMD -0.58; CI -0.67, -0.50; 46 studies, n=7237; RR 1.85, CI 1.38, 2.48; 11 studies, n=1751)	High for benefit

5. Results: Treatment of ADHD

Intervention and Comparison	Outcome	Number of Studies and Study Design	Findings	SoE
		337, 342, 367, 368, 372, 375, 404, 409, 415, 421, 422, 430, 441-444, 447-449, 470, 499, 514, 526, 528, 544, 545, 562, 585, 598-601, 606, 608, 611, 612, 615, 622, 892		
KQ2 non-stimulants vs control	ADHD symptoms	34 studies[125, 138, 172, 209, 211, 221, 224, 251, 288, 304, 317, 321, 337, 354, 367, 372, 389, 404, 421, 422, 430, 441-444, 447, 448, 470, 499, 544, 562, 585, 600, 611	Results favor intervention (SMD -0.52; CI -0.58, -0.45; 34 studies, n=5593; RR 1.52; CI 1.24, 1.87; 11 studies, n=1697)	High for benefit
KQ2 stimulants vs control	ADHD symptoms	12 studies[115, 116, 137, 166, 169, 206, 212, 275, 333, 409, 526, 615	Results favor intervention (SMD -0.88; CI -1.13, -0.62; 12 studies, n=1471; RR 4.28; CI 2.49, 7.35; 1 study, n=153)	High for benefit
KQ2 pharmacological vs control	Functional impairment	19 RCTs[116, 137, 172, 197, 206, 209, 374, 422, 441-444, 447, 449, 575, 607, 611, 612, 892	Results favor intervention (SMD 0.51; CI 0.10, 0.92; 11 studies, n=1739)	Moderate for benefit
KQ2 non-stimulants vs control	Functional impairment	6 RCTs[172, 209, 422, 442-444	No systematic effect (SMD 0.20; CI -0.05, 0.44; 6 studies, n=1163)	Low for no benefit
KQ2 stimulants vs control	Functional impairment	5 RCTs[116, 137, 197, 575, 607	Results favor intervention (SMD 0.93; CI 0.05, 1.81; 5 studies, n=576)	Moderate for benefit
KQ2 pharmacological vs control	Acceptability of treatment	2 RCTs[211, 599	Results favor alpha agonist intervention (RR 0.47; CI 0.32, 0.68; 1 study, n=198)	Insufficient
KQ2 pharmacological vs control	Academic performances	4 RCTs[514, 575, 607, 608	Results favor intervention (SMD -1.37; -1.72, -1.03; 1 study, n=156)	Low for benefit
KQ2 pharmacological vs control	Appetite suppression	52 RCTs[116, 125, 137, 138, 153, 162, 166, 169, 172, 198, 206, 221, 224, 251, 273, 275, 276, 288, 292, 303, 317, 321, 342, 372, 375, 404, 409, 421, 422, 430, 441-444, 448, 470, 499, 526, 544, 545, 562, 598-601, 606, 607, 611, 615, 622, 892, 1088	Intervention is associated with appetite suppression (SMD 0.48; CI -0.04, 1.00; 6 studies, n=605; RR 3.24; CI 2.49, 4.20; 46 studies, n=7389)	High for increased risk
KQ2 pharmacological vs control	Participants with adverse events	37 RCTs[**137, 153, 162, 169, 198, 206, 209, 211, 221, 251, 273, 275, 276, 303, 321, 333, 337, 367, 368, 404, 409, 415, 430, 441-443, 447, 528, 562, 585, 598, 601, 608, 611, 615, 622, 892**]	Pharmacological treatment is associated with a higher risk of reported adverse events (RR 1.30; CI 1.23, 1.36; 41 studies, n=6972)	High for increased risk
KQ2 Atomoxetine vs Methylphenidate	Behavior	4 studies[183, 448, 492, 513	SNRIs showed more improvement than stimulants (SMD -0.08; CI -0.14, -0.03; 4 studies, n=608)	Low for larger effects in SNRI
KQ2 Non-Stimulants vs Stimulants	Broadband measures	N/A (indirect comparison)	Non-stimulant studies reported smaller effects than stimulant studies (RR 0.66; CI 0.57, 0.76; 11 studies, n=2174 vs RR 0.39; CI 0.31, 0.49; 13 studies, n=1569; p 0.0004)	Low for larger effects in stimulants
KQ2 Atomoxetine vs Methylphenidate	Broadband measures	4 studies[183, 448, 492, 513	No difference detected (SMD -0.16; CI -0.36, 0.04; 4 studies, n=1080)	Low for no difference
KQ2 Non-stimulants vs stimulants	ADHD symptoms	N/A (indirect comparison)	Non-stimulant studies reported smaller effects than stimulant studies (SMD -0.49; CI -0.56, -0.42; 33 studies, n=5861 vs SMD -0.88; CI	Low for larger effects in stimulants

Intervention and Comparison	Outcome	Number of Studies and Study Design	Findings	SoE
			1.13, -0.062; 12 studies, n=1471; p 0.0001)	
KQ2 SNRIs vs stimulants	ADHD symptoms	7 studies[144, 230, 370, 448, 527, 593, 632]	No difference detected (SMD 0.24; CI -0.02, 0.50; 7 studies)	Low for no difference
KQ2 Atomoxetine vs Methylphenidate	ADHD symptoms	6 studies[144, 370, 448, 527, 593, 632]	No difference detected (SMD -0.16; CI -0.36, 0.04)	Low for no difference
KQ2 Non-stimulants vs stimulants	Functional impairment	N/A (indirect comparison)	Non-stimulant studies reported small effects than stimulant studies (SMD 0.22; CI 0.02, 0.41; 7 studies, n=1576 vs SMD 0.93; CI 0.05, 1.81; 5 studies, n=576; p 0.02)	Low for larger effects in stimulants
KQ2 Non-stimulants vs stimulants	Appetite suppression	8 studies[183, 230, 370, 500, 527, 555, 632]	No difference detected (RR 0.82; CI 0.53, 1.26; 8 studies, n=1463)	Low for no difference
KQ2 Atomoxetine vs Methylphenidate	Appetite suppression	7 studies[183, 230, 370, 500, 527, 555, 632]	No difference detected (RR 0.89; CI 0.71, 1.35; 7 studies, n=1201)	Low for no difference
KQ2 SNRIs vs stimulants	Participants with adverse events	4 studies[183, 230, 527, 593]	No difference detected (RR 1.11; CI 0.90, 1.37; 4 studies, n=756)	Low for no difference
KQ2 Atomoxetine vs Methylphenidate	Participants with adverse events	3 studies[183, 527, 593]	No difference detected (RR 1.23; CI 0.99, 1.52; 3 studies, n=494)	Low for no difference
KQ2 Amphetamine vs Methylphenidate	ADHD symptoms	N/A (indirect comparison)	Amphetamine studies reported larger effects than methylphenidate studies for continuous outcomes (SMD -1.16; CI -1.64, -0.67; n=757; SMD -0.61; CI -0.84, -0.39; 6 studies, n=672; p 0.02) but there was no systematic difference for categorical outcomes (p 0.58)	Insufficient for determining differences
KQ2 Amphetamine vs Methylphenidate	Appetite suppression	2 studies[137, 578]	No difference detected (RR 0.99; CI 0.27, 3.64; 2 studies, n=294)	Low for no difference
KQ2 SNRI vs Alpha agonists	Appetite suppression	N/A (indirect comparison)	SNRI studies reported larger effects than alpha agonist studies (RR 3.29; CI 2.42, 4.47; 22 studies, n=3295 vs RR 1.25; CI 0.58, 2.70; 4 studies; n=919; p 0.003)	Low for favoring alpha agonist studies

Notes: CI 95% confidence interval, KQ key question, N/A not applicable, RR relative risk, RCT randomized controlled trial, 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. Results were consistent when excluding high risk of bias studies or using an alternative estimate to account for possible publication bias. However, it should be noted that only few studies included children under six years of age in the evaluated interventions. We also found moderate strength of evidence that pharmacological treatment reduces impairment but we downgraded the strength of evidence due to 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.

The analyses comparing two alternative interventions and the corresponding strength of evidence were more limited. While SNRIs 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, though alpha agonist studies did not reduce appetite significantly. Comparing atomoxetine versus methylphenidate did not identify systematic differences for any of the key outcomes, but strength of evidence was low or insufficient. The comparison between amphetamine versus methylphenidate was downgraded to low due to imprecision in the small number of identified studies. All indirect comparisons were downgraded to low due to indirectness and insufficient where there were conflicting results between continuous and categorical variables.

5.3.3 New Pharmaceutical Agents

We also identified a small number of studies evaluating a pharmaceutical agent not FDA-approved for ADHD.[112, 120, 121, 129, 142, 154, 155, 163, 173, 210, 223, 267, 272, 302, 348, 371, 391, 427, 495, 496, 501, 561, 609, 624, 625] This included new formulations, off-label use of existing medication approved for other conditions such as modafinil,[129, 154, 155, 302, 348, 561] amantadine,[527] or venlafaxine,[624] and agents no longer available in the US such as agomelatine.[496] Identified studies were published between 2005 and 2020, 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[272, 371] and Iran.[223, 348, 427, 496] 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[495, 625] required only a preliminary clinical diagnosis. The populations were predominantly males between the ages of six and eighteen. Female population proportions ranged from 15 percent[495] to 29 percent[391] 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%[495] to 100%[348]) wa the combined presentation. Approximately half of studies did not report data regarding ADHD presentation type.[120, 267, 272, 317] The only study that addressed co-occurring disorders in the form of a dual diagnosis evaluated children with ADHD and mood disorders.[371] Race and ethnicity demographics were described only in a portion of studies.[120, 272, 371, 391]

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.[129, 154, 155, 302, 348, 561] 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.[112, 121] Two studies tested an inhibitor of G protein-coupled inward-rectifying potassium channels (GIRKs, tipepidine).[223, 495] All of the studies of new pharmaceutical agents reported on a control group, typically placebo.[223, 272, 348, 371, 391, 495, 625] 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.[272, 371, 391, 495]

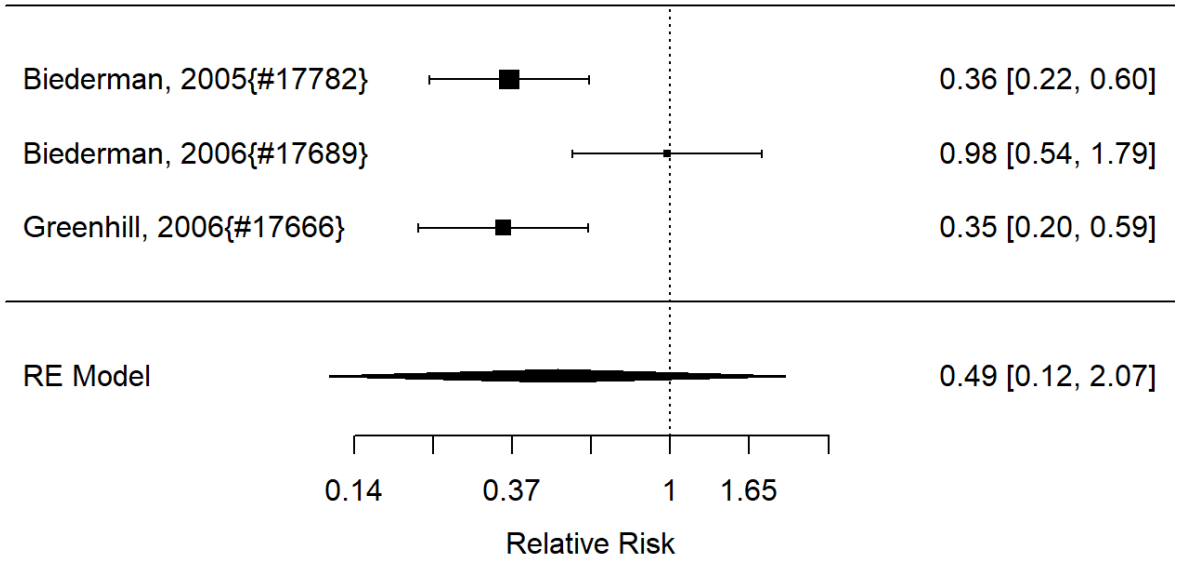
Studies reported a variety of study-specific outcomes, such as treatment-related adverse effects. In terms of pre-specified outcomes, broadband scale scores, standardized symptom scores, and appetite changes were the most frequently reported outcomes.

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

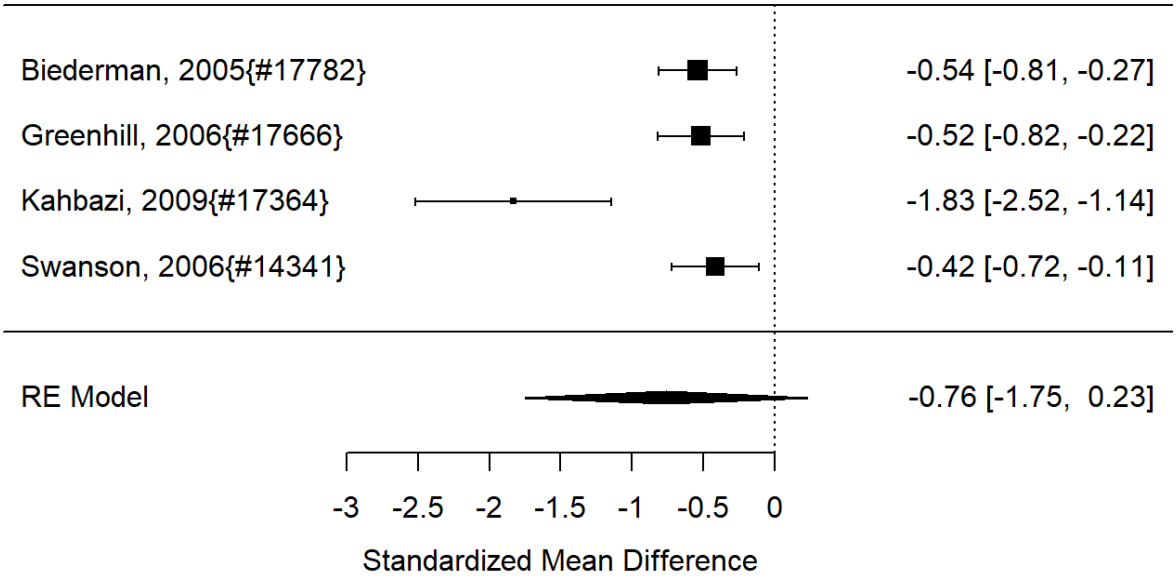
The identified studies that reported on a broadband measure are shown in Figure 46.

Figure 46. Effects of Modafinil on Broadband Measures (RR)



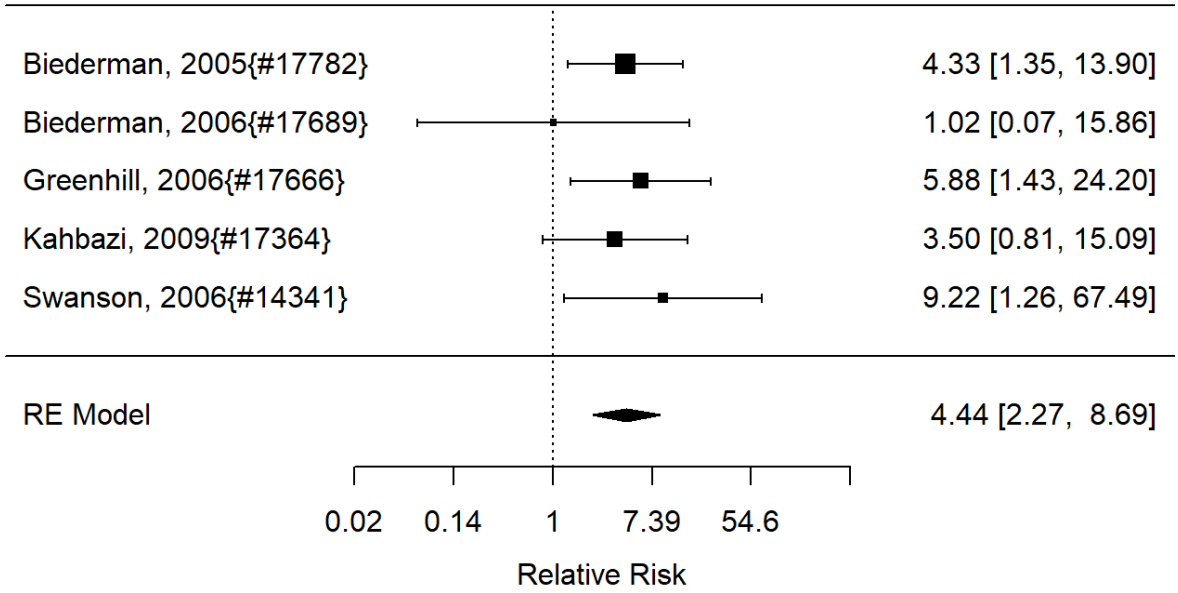
Across studies, we did not detect a systematic effect of modafinil on broadband scores (RR 0.49; CI -.12, 2.07; 3 studies, n=539). Two out of three studies were positive and there was heterogeneity (I-squared 76%). There was no indication of publication bias. None of the studies was considered high risk of bias, hence methodological rigor was not a likely source of the heterogeneity. Studies reporting on symptoms are shown in Figure 47.

Figure 47. Effects of Modafinil on ADHD Symptoms (SMD)



Although all studies reported a positive effect, estimates varied and we did not find a statistically significant effect 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).[348] Studies did not report on other outcomes other than appetite suppression (see Figure 48).

Figure 48. Effects of Modafinil on Appetite Suppression (RR)



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 was categorized as high risk, hence it is unlikely that the result is purely based on methodological flaws of the studies.

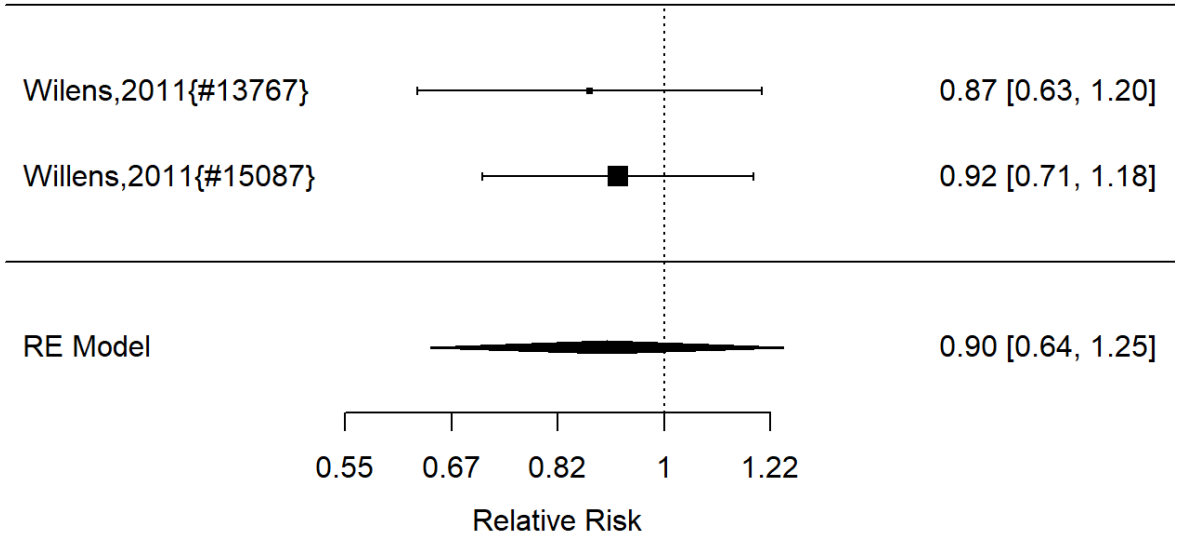
5.3.3.2 Tipepidine

Although two studies assessed tipepidine, the studies did not report on the same outcome measures. One study each found no difference in a broadband measure (SMD 0.38; CI -0.17, 0.93; 1 study, n=51)[223] or appetite suppression (RR 0.30; CI 0.01, 6.98; 1 study, n=105).[495] One of the studies reported on symptoms and found a significant effect on ADHD symptoms (SMD -0.58, CI -1.14, -0.02; 1 study, n=51).[223]

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.[112, 609] Both studies reported on a broadband measure but reported conflicting results and no meaningful summary measure could be derived (SMD 0.02, -2.58, 2.53; 2 studies, n=168). One of the studies reported on ADHD symptoms and found improvement (SMD -1.02; -1.46, -0.57; 1 study, n=88). Results for the number of participants reporting an adverse event are documented in Figure 49.

Figure 49. Effects of ABT-089 on Participants Reporting Adverse Events (RR)



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 was considered high risk.

5.3.3.4 Summary of Findings New 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 the evidence table in the appendix. The summary of findings table is limited to the agents assessed in multiple studies and Table 14 only shows results where effect size calculation was possible.

Table 14. KQ2Summary of Findings and Strength of Evidence for New Pharmacological Agents

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	SoE
KQ2 modafinil vs control	Broadband measures	3 RCTs[154, 155, 302]	No systematic effect detected (RR 0.49; CI -0.12, 2.07; 3 studies, n=539).	Low for no effect
KQ2 modafinil vs control	ADHD symptoms	4 RCTs[155, 302, 348, 561]	All individual studies were positive (SMD -0.76; CI -1.75, 0.23; 4 studies, n=667; RR 37.00; CI 2.36, 578.24; 1 study, n=46)	Low for benefit
KQ2 modafinil vs control	Appetite suppression	5 RCTs[154, 155, 302, 348, 561]	Intervention was associated with an effect (RR 4.44; CI 2.27, 8.69; 5 studies; n=780)	Moderate for effect
KQ2 ABT-089 vs control	Broadband measure	2 studies[112, 609]	No meaningful summary estimate could be derived (SMD 0.02, -2.58, 2.53; 2 studies, n=168)	Insufficient
KQ2 ABT-089 vs control	Number of participants reporting on the event	2 RCTs[112, 609]	No systematic effect (RR 0.90; CI 0.64, 1.25; 2 studies, n=171)	Low for no effect

Notes: CI 95% confidence interval, KQ key question, N/A not applicable, RR relative risk, RCT randomized controlled trial, SMD standardized mean differences, SoE strength of evidence

Modafinil was associated with positive effects on ADHD symptoms (low SoE, 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 Psychosocial Treatment

We identified 24 studies evaluating psychological, psychosocial, or behavioral interventions for children and adolescents with ADHD.[52, 113, 168, 208, 264, 324, 325, 330, 331, 351, 416, 420, 464, 469, 474, 510, 511, 520-523, 552, 581, 613] 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 unless the control group received the same medication.

The earliest identified eligible study was first published in 2009.[416] Evaluations were conducted in ten different countries, primarily the US.[113, 208, 242, 264, 324, 464, 469, 510] The populations studied were children and adolescents with ADHD between the ages of "preschool" and 18, with half of the studies including teenagers.[168, 257, 264, 350, 420, 520-523, 581] In studies that distinguished between ADHD presentations, the most prevalent type (ranging from 23.4%[330] to 100%[510] 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 patients with language difficulties,[613] homework problems,[469] and organizational deficits.[113] Race and ethnicity demographics were not mentioned in most studies.

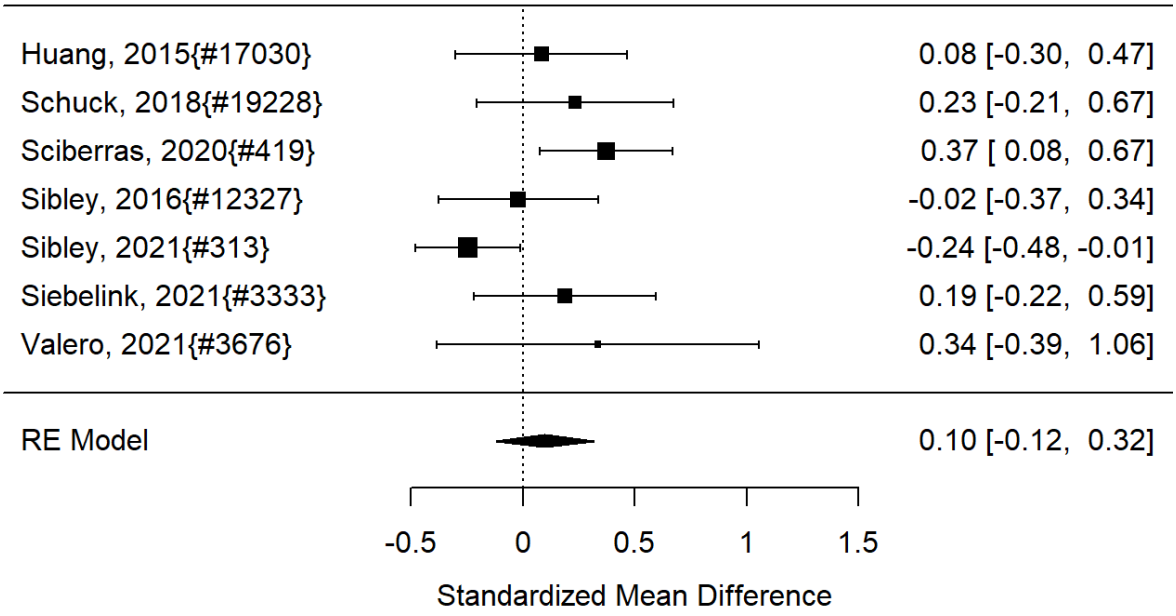
Interventions studied included skills training (e.g., homework and organizational skills),[113, 208, 469, 474] problem-solving coach and/or mentoring,[242, 416] social skills training,[331, 510, 552] sleep-focused intervention,[511] dialectical behavior therapy,[420] cognitive behavior therapy, [168, 548] and mindfulness training.[523, 581] Many interventions had multiple components[257, 330, 464, 469, 474, 510] that involving patients, parents, teachers, therapists, and counselors in addition to direct interventions for the participating children (interventions addressing parents exclusively are documented in the parent education and support section).

Of the identified studies, 19 reported on a control group, including attention-matched groups,[264, 510] no intervention (i.e., wait list), or treatment as usual where it varied what treatment individual children received.[113, 208, 242, 257, 330, 331, 350, 351, 416, 464, 474, 511, 520, 521, 523, 548, 552, 581, 613] One of those studies included an alternative psychological or behavioral intervention to test the comparative effectiveness of the intervention in addition to a control group comparison.[464] Four studies had no control group, only an alternative intervention in the form of another psychological approach[168, 469, 522] or a combined medication and behavioral support program.[325]

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

Figure 50 shows the effect of the intervention on individual problem behaviors such as tardiness, delinquency, and conduct problems, assessed in the individual studies.

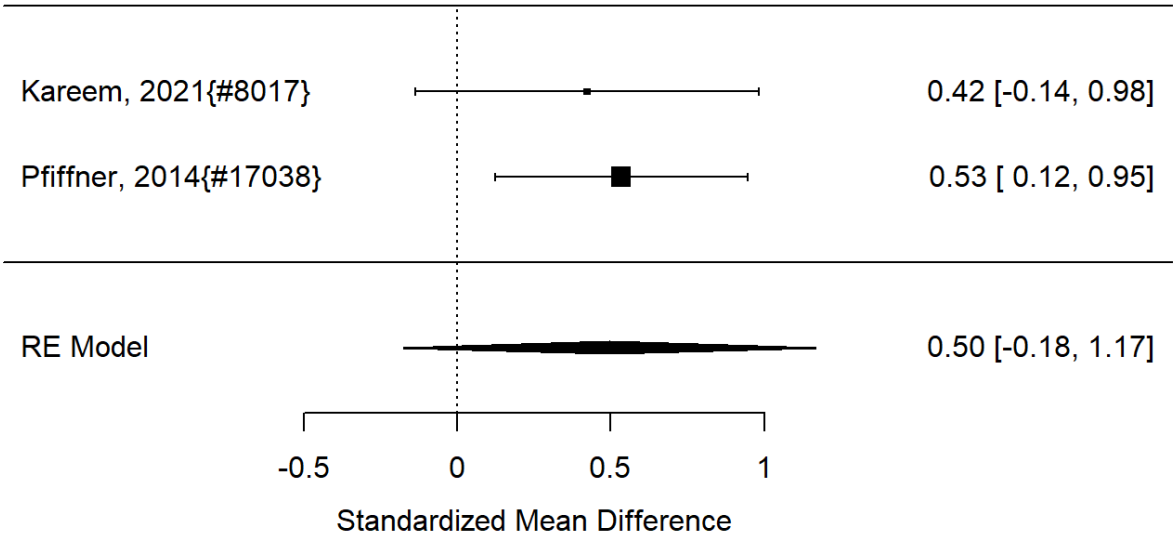
Figure 50. Effects of Psychosocial Interventions on Behavior (SMD)



Across studies, we did not detect a systematic effect of the interventions on problematic behaviors (SMD 0.10; CI -0.12, 0.32; 7 studies, n=897). The analysis did not detect substantial heterogeneity (I-squared 50%). We did not detect publication bias. Removing high risk of bias studies in a sensitivity analysis left only three studies and showed a different estimate with wide confidence intervals, but the effect was still not statistically significant (RR -0.06; CI -0.64, 5.2).

Studies reporting on broadband measure score changes are documented in Figure 51.

Figure 51. Effects of Psychosocial Interventions on Broadband Measures (SMD)

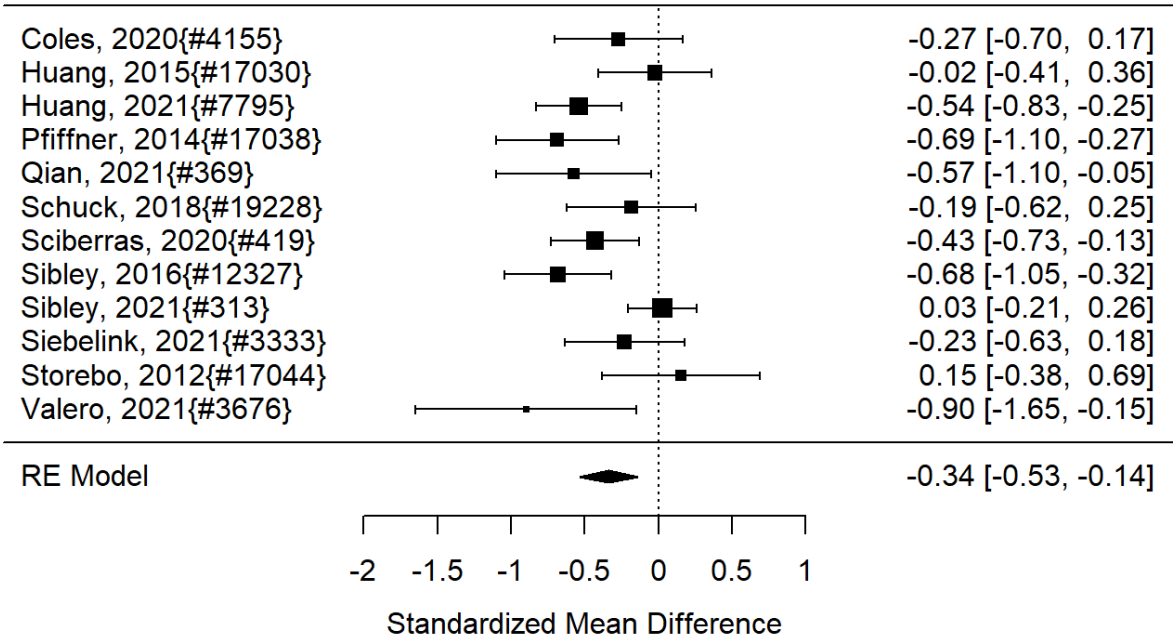


The small number of studies reported different estimates and, although both positive, the pooled effect was not statistically significant (SMD 0.50; -0.18, 1.17; 2 studies, n=170). In this

small set of studies, no heterogeneity was detected, there was no indications of publication bias, and no sensitivity analyses could be conducted. Removing high risk of bias studies in a sensitivity analysis left only one study; the study indicated a beneficial treatment effect.[464]

All studies reporting sufficient detail for changes on a continuous symptom scale are shown in Figure 52.

Figure 52. Effects of Psychosocial Interventions on ADHD Symptoms (SMD)



Analyses indicated a symptom reduction associated with the psychological or behavioral intervention (SMD -0.34; CI -0.53, -0.14; 12 studies, n=1450). Interventions were diverse and often included multiple components. Particularly successful interventions included social skills plus parent skills training (compared to no intervention),[331] a multi-component child life and attention skills program (compared to treatment as usual and a diagnostic report),[464] ecological executive skills training with parent components (compared to waitlist),[474] a family intervention focused on sleep (compared to usual care without focus on sleep management),[511] family therapy focused on teens' academic needs (compared to usual care without family therapy),[521] and mindfulness training for children and parents (compared to waitlist).[581] The youngest children included in the studies were five years old, and several studies targeted pre-teens and teenagers. Statistical heterogeneity was not remarkable, highlighting the diversity of the approaches. Statistical heterogeneity was not remarkable (I-squared 57%). There was some indication of publication bias (Begg p 0.31, Egger p 0.02) but an alternative effect estimate using the trim and fill method came to similar results (SMD -0.56; CI -1.02, -.09). Removing high risk of bias studies in a sensitivity analysis indicated a stronger treatment effect, but the confidence interval was wide and the effect was not statistically significant anymore (SMD -0.33; CI -0.71, 0.05).

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

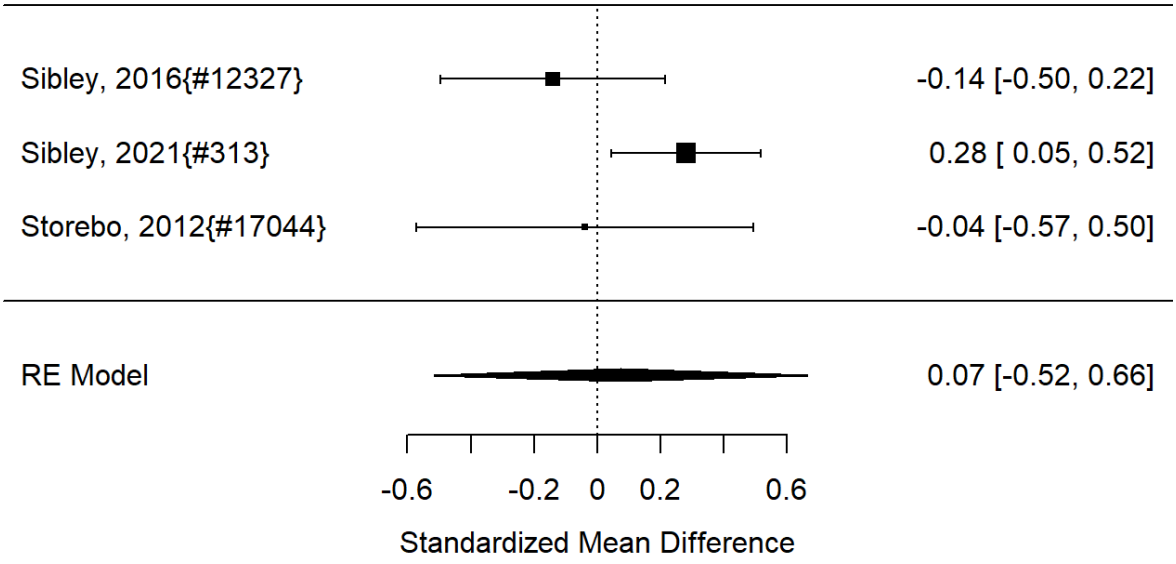
Life and Attention Skills) for youth with ADHD compared to families receiving a diagnostic report and a resource list (RR 0.69; CI 0.54, 0.88; 1 study, n=125).[464]

Very few studies reported on functional outcomes and two studies reporting on functional impairment as a categorical outcome could not be combined to a meaningful estimate (SMD 0.40; CI -1.16, 1.97; 2 studies, n=245).[474, 511]

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 (SMD 0.19; CI -0.12, 0.49; 1 study; n=164).[264]

Studies reporting on academic outcomes and reporting sufficient detail to compute effect sizes are shown in Figure 53.

Figure 53. Effects of Psychosocial Interventions on Academic Performance (SMD)



Across studies, we did not detect a systematic effect of the intervention on academic performance compared to control groups (SMD -0.07; CI -0.52, 0.66; 3 studies, n=459). The analysis detected little heterogeneity (I-squared 52%). 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 (RR 0.97; CI 0.02, 47.1; 1 study, n=55).[552]

5.3.4.1 Psychosocial Treatment Comparative Effects

We identified a small number of studies that compared diverse psychological and behavioral interventions to an alternative therapeutic approach.[52, 168, 325, 464, 469, 522]

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).[522] 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).[168]

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 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).[464] 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.[469] 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.[325]

One study addressed sequencing of interventions.[52] 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. 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=153).

5.3.4.2 Psychosocial Treatment Summary of Findings

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

Table 15. KQ2Summary of Findings and Strength of Evidence for Psychosocial Treatment

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	SoE
KQ2 psychosocial treatment vs control	Behavior	7 RCTs[331, 510, 511, 520, 521, 523, 581]	No systematic effect (SMD 0.10, CI -0.12, 0.32; 7 studies, n=897)	Low for no effect
KQ2 psychosocial treatment vs control	Broadband measures	3 RCTs[113, 351, 464]	Pooled result was not statistically significant (SMD 0.50, CI -0.18, 1.17; 2 studies, n=170)	Low for no effect
KQ2 psychosocial treatment vs control	ADHD symptoms	13 RCTs[208, 330, 331, 416, 464, 474, 510, 511, 520, 521, 523, 552, 581]	Results favored intervention (SMD -0.34, CI -0.53, -0.14; 12 studies, n=1450; RR 0.69; CI 0.54, 0.88; 1 study, n=125)	Moderate for benefit
KQ2 psychosocial treatment vs control	Functional impairment	4 RCTs[113, 464, 474, 511]	Pooled result was not statistically significant (SMD 0.40, CI -1.16, 1.97; 2 studies, n=245)	Insufficient
KQ2 psychosocial treatment vs control	Acceptability of treatment	4 RCTs[113, 264, 464, 520]	No systematic effect (SMD 0.22, CI -0.09, 0.53; 1 study, n=164)	Insufficient

5. Results: Treatment of ADHD

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	SoE
KQ2 psychosocial treatment vs control	Academic performance	4 RCTs[520, 521, 552]	No systematic effect (SMD 0.07, CI -0.52, 0.66; 3 studies, n=459)	Low for no effect
KQ2 psychosocial treatment vs control	Appetite suppression	0 studies	N/A	Insufficient
KQ2 psychosocial treatment vs control	Participants with adverse events	1 RCT[552]	No effect (RR 0.97; CI 0.02, 47.01; 1 study, n=55)	Insufficient
KQ2 intensive family-school intervention vs coping intervention	ADHD symptoms	1 RCT[469]	Results favored family-school success intervention (SMD -0.34; -.061, -0.06; 1 study, n=199)	Insufficient
KQ2 intensive family-school intervention vs coping intervention	Acceptability of treatment	1 RCT[469]	Results favored family-school success intervention (SMD -0.34; -.061, -0.06; 1 study, n=199)	Insufficient
KQ2 intensive family-school intervention vs coping intervention	Academic performance	1 RCT[469]	No difference detected (SMD -0.21; -0.49, 0.07; 1 study, n=199)	Insufficient
KQ2 intensive child life and attention skills intervention vs less intense intervention	Broadband measures	1 RCT[464]	No difference detected (SMD 0.20; CI -0.13, 0.52; 1 study, n=199)	Insufficient
KQ2 intensive child life and attention skills intervention vs less intense intervention	ADHD symptoms	1 RCT[464]	No difference detected (SMD -0.27; CI -0.60, 0.05 and RR 1.23; CI 0.89, 1.71; 1 study, n=199)	Insufficient
KQ2 planning CBT vs solution-focused CBT	ADHD symptoms	1 RCT[168]	No difference detected (SMD -0.14; CI -0.45, 0.17; 1 study, n=159)	Insufficient
KQ2 group parent and adolescent skills training vs dyadic skills training with motivational interviewing	ADHD symptoms	1 RCT[522]	No difference detected (SMD -0.23; CI -0.61, 0.16; 1 study, n=159)	Insufficient
KQ2 multi-component	Behavior	1 RCT[52]	Behavioral management intervention associated with fewer classroom rule	Insufficient

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	SoE
behavior management intervention vs methylphenidate			violations (incidence rate ratio 0.66, p<0.01; 1 study, n=152)	
KQ2 multi-component behavior management intervention vs methylphenidate	Symptoms	1 RCT[52]	No systematic difference (SMD -0.02; CI -0.34, 0.31; 1 study, n=152)	Insufficient
KQ2 multi-component behavior management intervention vs methylphenidate	Functional impairment	1 RCT[52]	No systematic difference (SMD -0.01; CI -0.33, 0.31; 1 study, n=152)	Insufficient

Notes: CI 95% confidence interval, KQ key question, N/A not applicable, RR relative risk, RCT randomized controlled trial, 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 most outcome data. We found low strength of evidence that psychological interventions do not improve problem behaviors across studies and we also found no effect on broadband measure scores. These findings were also downgraded for 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 insufficient due to inconsistency of direction, lack of precision, 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.

The comparative effectiveness results were downgraded due to study limitation and the lack of replication (downgraded by two for inconsistency) and strength of evidence was determined to be insufficient.

5.3.5 Cognitive Training

We identified 19 studies evaluating cognitive training to treat ADHD. The earliest identified study was from 2013.[59, 146, 156, 174, 203, 225, 226, 234, 247, 261, 310, 363, 366, 445, 446, 478, 518, 582, 602] Evaluations were published in 16 different countries, including the USA,[363, 366] China,[203, 518] Netherlands,[234, 582] and Spain.[156, 261]

5. Results: Treatment of ADHD

The populations studied were predominately males aged six to 17 years, with only one study including children as young as three years old.[478] 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 (ranging from 26%[203] to 100%[156, 226, 234, 247] of the ADHD participants) 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).[226, 582] Race and ethnicity demographics were not mentioned in almost all studies.

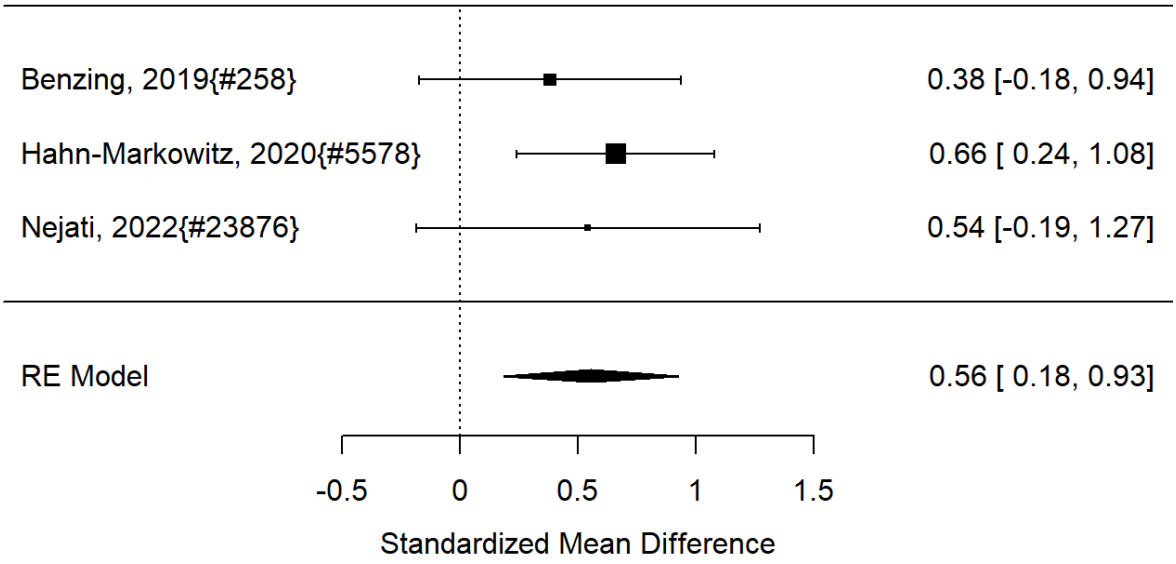
Cognitive training interventions were delivered across different settings, including home-based and hospital/clinic-based programs. More than half of the studies used a computerized video game format such as the Cogmed digital working memory training program.[59, 146, 156, 174, 226, 234, 247, 363, 366, 582] The other 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,[203, 261, 478, 518] or they employed functional cognitive rehabilitation paradigms used in occupational therapy settings[310, 445, 602] to improve ADHD. Some studies included a control group comprising demographically similar children and adolescents with ADHD. ADHD-matched control groups received treatment as usual,[59, 445, 518, 602] treatment as usual but then the targeted intervention during a crossover trial,[174, 310] non-adaptive/non-calibrated versions of the targeted cognitive intervention,[156, 226, 234, 366] cognitive training of a separate domain (e.g., training of working memory vs. training of inhibitory control),[363] or else they were randomized to a waitlist and received no extra intervention during the trial.[146, 203, 247, 261] Other studies reported on the comparative effects for two alternative interventions, such as a different modality (e.g., behavioral parent training)[478]; or cognitive training using a different intervention.[582]

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, symptom rating scale scores were most frequently reported.

Across identified studies, only two reported on a passive control group and reported on a problematic behavior, but the studies (although both favoring the intervention) reported very different treatment effects and could not be combined to a meaningful summary estimate (SMD 0.24; CI -0.31, 0.78; 2 studies, n=101).[156, 261]

Studies reporting on broadband measure scores as a continuous variable are documented in figure 54.

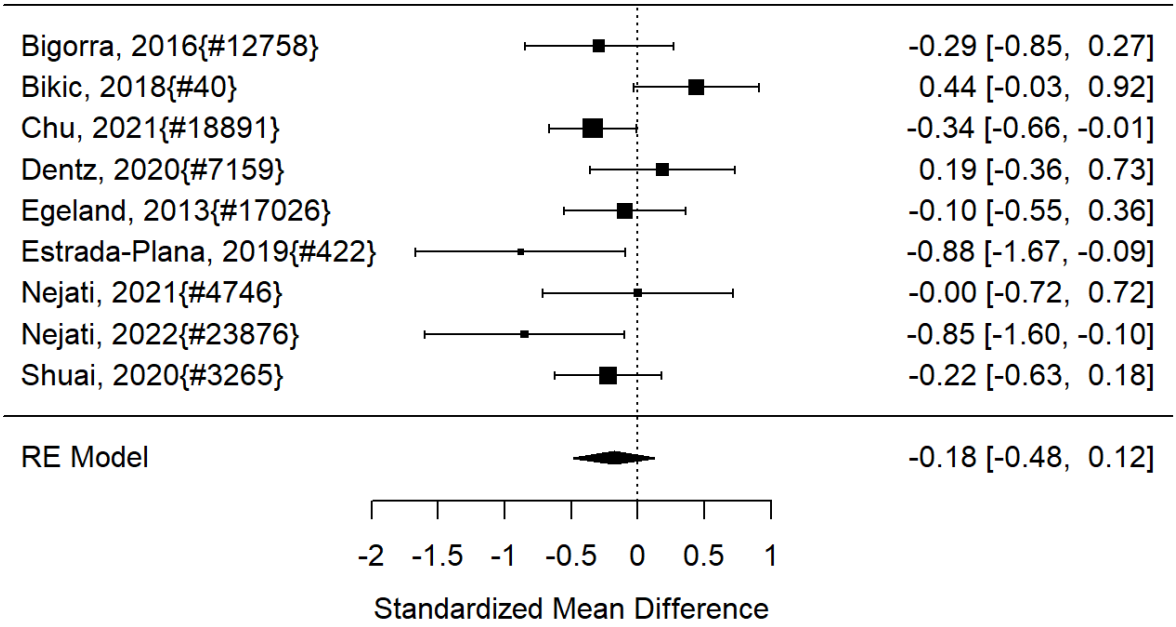
Figure 54. Effects of Cognitive Training on Broadband Measures (SMD)



The interventions were associated with an improvement in broadband measures (SMD 0.56; CI -0.18, 0.93; 3 studies, n=173). Children included in the studies were between six and seven, and seven and ten, where reported. The analysis did not detect statistical heterogeneity and there were too few studies for further analyses. 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).[366]

The studies reporting on the effect of cognitive training on ADHD symptoms are shown in Figure 55.

Figure 55. Effects of Cognitive Training on Symptoms (SMD)

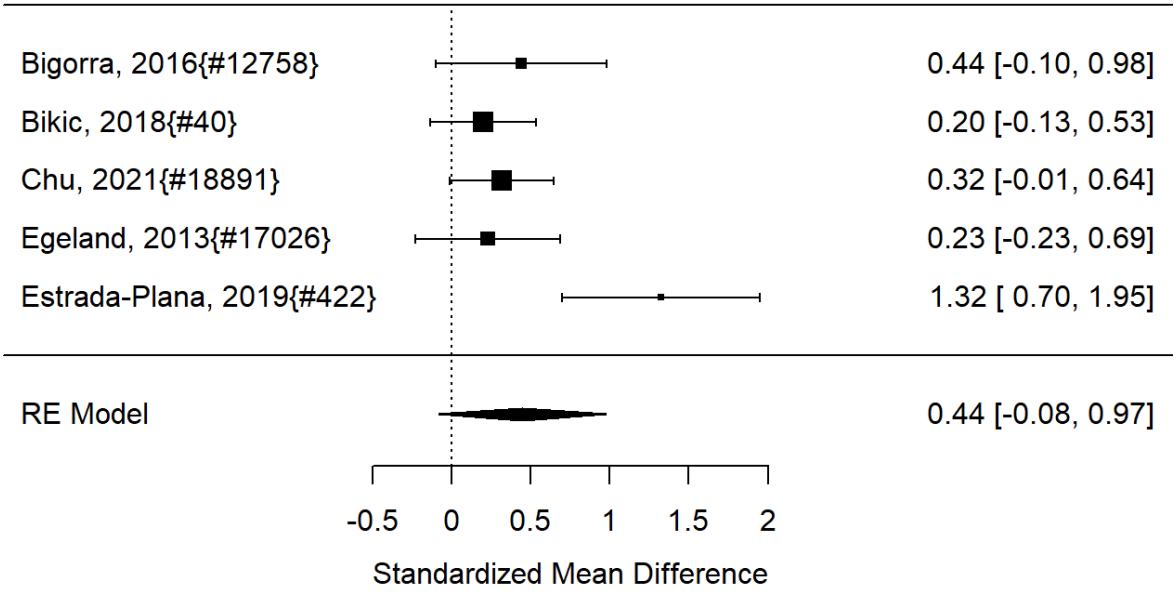


5. Results: Treatment of ADHD

Across studies, we did not identify a systematic improvement of ADHD symptoms associated with cognitive training compared to control groups not receiving cognitive training (SMD -0.18; CI -0.48, 0.12; 9 studies, n=574). The analysis did not detect substantial heterogeneity (I-squared 49%). There was no evidence of publication bias. Removing studies with high risk of bias indicated a similar lack of systematic effect (SMD -0.08; CI -0.65, 0.49). An additional study reporting on a categorical symptom outcome (number with at least 30% improvement) did not detect differences between groups (RR 1.28; CI 0.85, 1.94; 1 study, n=337).[366]

Studies reporting on effects of cognitive training on functional impairment are shown in Figure 56.

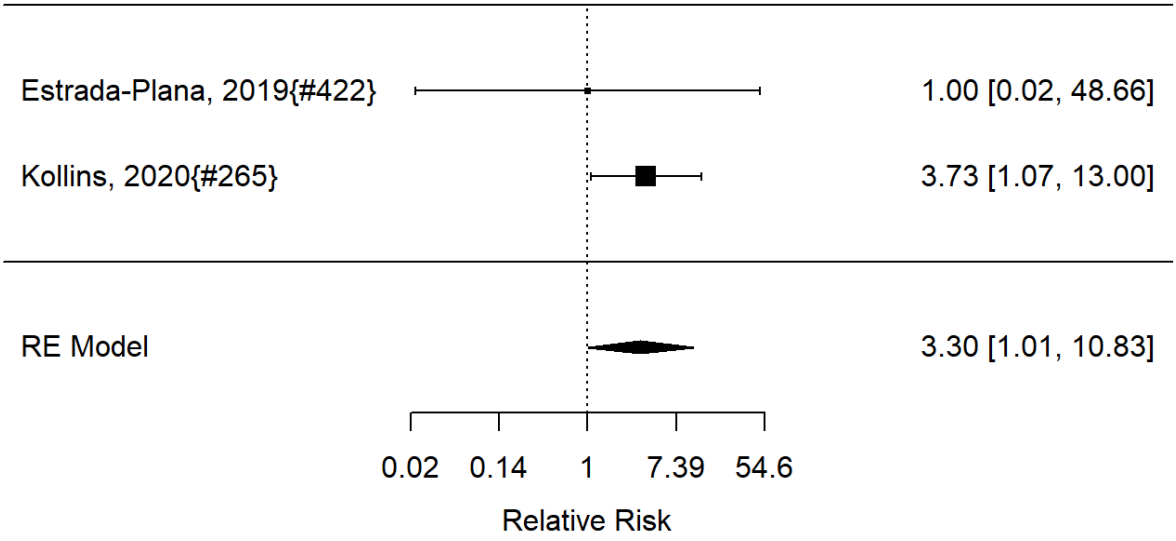
Figure 56. Effects of Cognitive Training on Functional Impairment (SMD)



Studies indicated an improvement in functional impairment, but the effect was not statistically significant (SMD 0.44; CI -0.08, 0.97; 5 studies, n=462). There was some heterogeneity and effect estimates varied somewhat (I-squared 67%). There was no indication of publication bias. Excluding high risk of bias studies in a sensitivity analysis (and thereby removing an outlier) did result in a smaller effect estimate (number of participants improved by 1 point on rating scale) but the effect was statistically significant (SMD 0.29; CI 0.03, 0.55). 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).[366]

We could not compute effect estimates for treatment satisfaction or academic performance ratings in this intervention subset. Appetite suppression was not assessed but the number of participants experiencing an adverse event is shown in Figure 57.

Figure 57. Effects of Cognitive Training on Participants with Adverse Events (SMD)



Only two studies reported clearly on the number of participants with adverse events in both treatment arms. Across studies, we did not detect a systematic effect of the intervention compared to a control group (RR 3.16; CI 0.96, 10.36; 2 studies, n=402). 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 in the intervention group (RR 3.73; CI 1.01, 10.83).[366]

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.[478] The study did not report on key outcomes but it concluded that working memory training is effective.

Three studies compared different cognitive training approaches.[234, 363, 582] 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.[363] Another study compared Cogmed working memory training versus a new active working memory and executive executive function compensatory training (paying attention in class).[582] The study found no difference in a broadband measure but 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.[234] The study did not report on key outcomes addressed in this review but concluded that there was no significant difference on any executive function measures.

5.3.5.1 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. KQ2Summary of Findings and Strength of Evidence for Cognitive Training

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	SoE
KQ2 cognitive training vs control	Behavior	3 RCTs[156, 261, 446]	Two studies favored the intervention, but estimates varied and could not be combined to a meaningful estimate (SMD 0.59; CI -3.75, 4.92; 2 studies, n=101)	Insufficient
KQ2 cognitive training vs control	Broadband measures	3 studies, 2 RCTs[146, 366] 1 CT[310]	Cognitive training was associated with positive effects in some studies (SMD 0.56; CI -0.18, 0.93; 3 studies, n=173; RR 0.96; CI 0.59, 1.55; 1 study, n=339)	Low for benefit
KQ2 cognitive training vs control	Symptoms	12 RCTs[146, 156, 225, 226, 261, 363, 366, 518]	No systematic effect (SMD -0.13; CI -0.41, 0.16; 8 studies, n=544; RR 1.28; CI 0.85, 1.93; 1 study, n=337)	Low for no effect
KQ2 cognitive training vs control	Functional impairment	6 RCTs[59, 156, 203, 247, 261, 366]	No systematic effect (SMD 0.44; CI -0.08, 0.97; 5 studies, n=462)	Low for no effect
KQ2 cognitive training vs control	Acceptability of treatment	0 studies	N/A	Insufficient
KQ2 cognitive training vs control	Academic performance	0 studies	N/A	Insufficient
KQ2 cognitive training vs control	Appetite suppression	0 studies	N/A	Insufficient
KQ2 cognitive training vs control	Participants with adverse events	2 RCTs[261, 366]	No systematic effect (RR 3.30; CI 1.01, 10.83; 2 studies, n=402)	Low for no effect

Notes: CI 95% confidence interval, KQ key question, N/A not applicable, RR relative risk, RCT randomized controlled trial, SMD standardized mean differences, SoE strength of evidence

The summary of findings table above 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 and imprecision. 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 15 studies using neurofeedback.[83, 110, 136, 219, 244, 291, 294, 301, 316, 390, 424, 472, 473, 550, 554] The earliest identified study was published in 2010 and studies came from ten different countries Almost all studies used a randomized control trial study design, except for one,[301] a non-randomized clinical trial. All children received a confirmatory ADHD diagnosis by a specialist and/or clinician. The populations studied were between the ages of six and 18 years. Female population proportions ranged from 15[390] to 37[301] percent; only two studies did not include females.[83, 219] 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[83] to 100[554] percent of ADHD participants, was the combined type. There were no reported systemic co-occurring disorders within the included study populations, though many

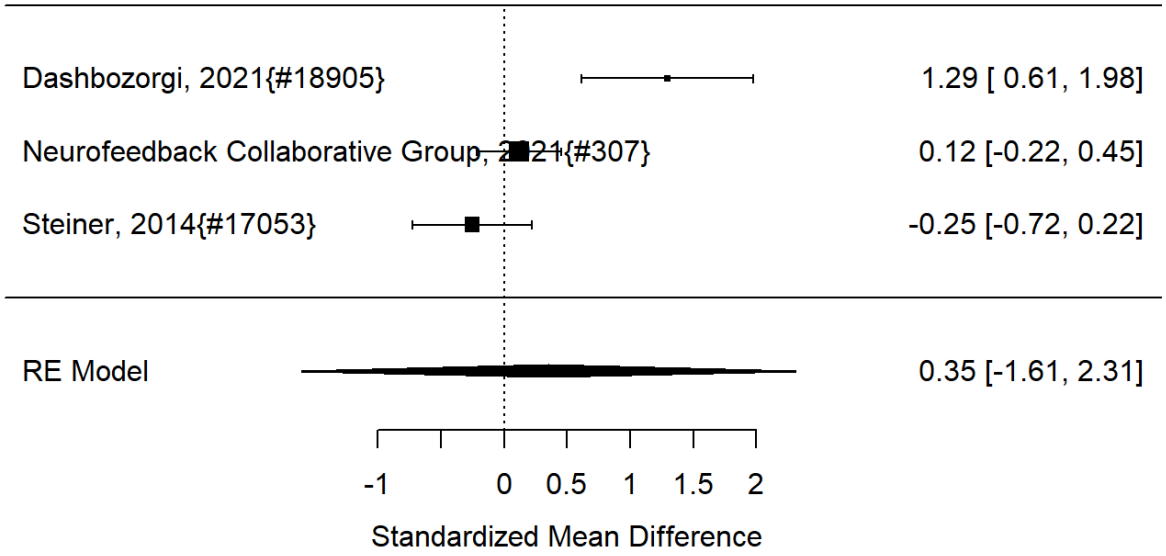
did not exclude commonly associated co-occurring disorders within their study population. Race and ethnicity demographics were described in few of the identified studies.[110, 550]

A variety of neurofeedback protocols were tested for their efficacy in treating ADHD symptoms. Two thirds of the neurofeedback protocols that were investigated involved theta/beta EEG marker modulation.[83, 110, 136, 180, 219, 244, 291, 294, 301, 390, 550] One third of protocols centered around modulation of slow cortical potentials.[294, 316, 424, 554] Among the neurofeedback studies, three quarters reported on a passive control group, including attention-matched task,[219, 291] waitlisted for intervention,[83, 390] and no intervention groups.[301, 550] Several studies reported efficacy results compared to an alternative intervention; methylphenidate[244, 291, 472] and cognitive trainings [294, 316, 424, 550] were the most common comparators.

Studies reported a variety of often study-specific outcomes, such as improvement in individual cognitive tasks as documented in the evidence table. 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 58.

Figure 58. Effects of Neurofeedback on Behavior (SMD)

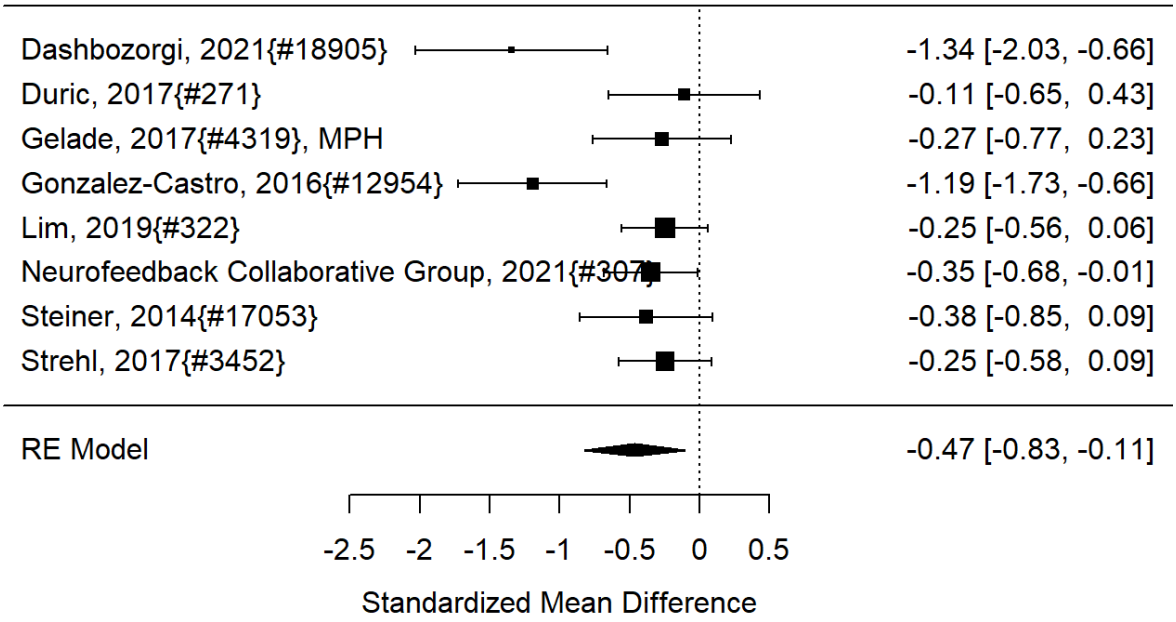


Study results varied considerably and no systematic effect was seen across studies (SMD 0.35; CI -1.61, 2.31; 3 studies, n=252). Despite the small number of studies, the analysis detected heterogeneity (I-squared 90%). There was no indication of publication bias. Removing one high risk of bias study did reduce heterogeneity but there was still no systematic positive effect on the intervention (SMD -0.03; CI -2.33, 2.27).

Two studies reported on broadband measure scores, but effect estimates varied so that the pooled estimate had very large confidence intervals (SMD 0.67; CI -2.65, 3.99; 2 studies, n=195). One of the studies also reported on a categorical broadband scale outcome (improvement of more than 2 on the CGI); the study did not find find a statistically significant difference between groups (RR 0.88; CI 0.66, 1.19; 1 study, n=142).[110]

Results for ADHD symptoms are reported in Figure 59.

Figure 59. Effects of Neurofeedback on Symptoms (SMD)



Across studies, neurofeedback was associated with a statistically significant ADHD symptom reduction compared to different passive control groups (SMD -0.47; CI -0.83, -0.11; 8 studies, n=736). The youngest children included in the studies were six years old. The analysis detected some heterogeneity (I-squared 69%). Excluding three high risk of bias studies found smaller but more precise and still statistically significant estimate (SMD -0.27; CI -0.35, -0.17) and there was no indication of heterogeneity anymore, suggesting that risk of bias was a key source of heterogeneity. We detected no evidence for publication bias.

Two studies reported on functional impairment outcomes but effect estimates varied considerably and no meaningful summary effect could be derived due to wide confidence intervals (SMD 0.19; CI -1.74, 2.13; 2 studies, n=212). We did not identify treatment satisfaction or academic performance estimates.

Appetite suppression was reported in one study; the Neurofeedback Collaborative group found no statistically significant difference between intervention and control group participants (RR 1.64; CI 0.77, 3.49; 1 study, n=142).[110] We could not determine the presence or absence of participants experiencing adverse events as none of the identified studies reported on the outcome.

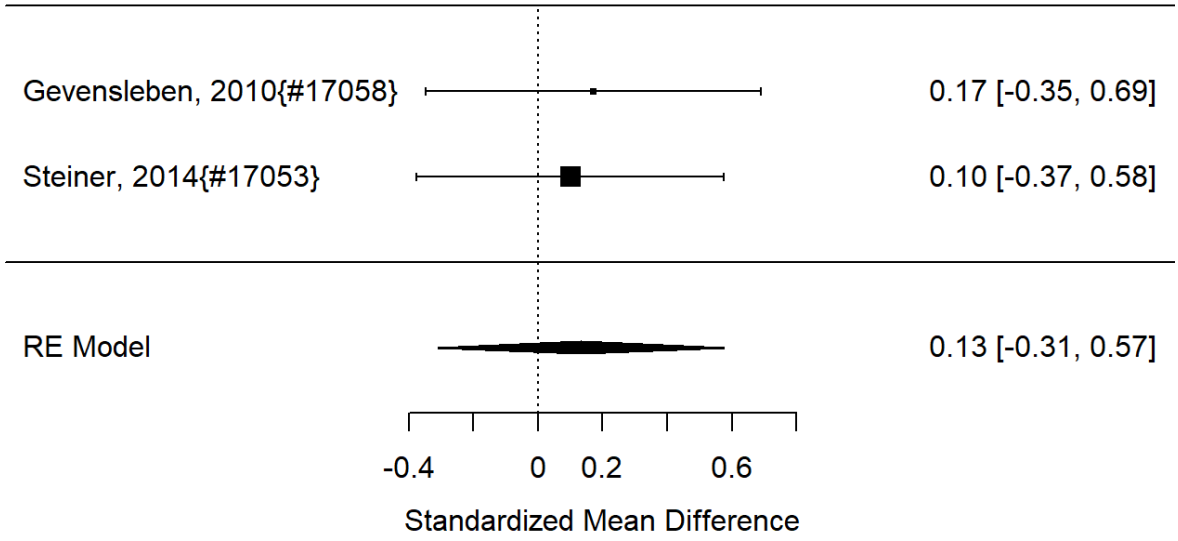
5.3.6.1 Neurofeedback Comparative Effects

Seven studies reported on active comparators, including cognitive training,[294, 316, 424, 550] medication with methylphenidate,[291, 472] and electromyographic biofeedback[219] as documented in the next subsections.

5.3.6.1.1 Neurofeedback Versus Cognitive Training

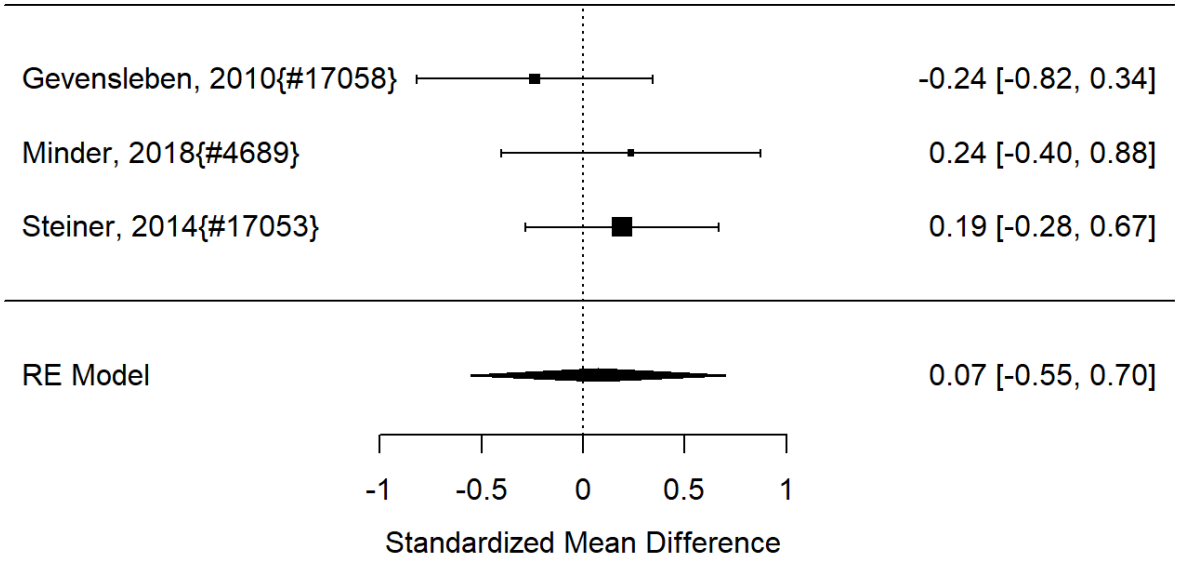
Two studies reported on individual behaviors as documented in Figure 60.

Figure 60. Neurofeedback versus Cognitive Training on Behaviors (SMD)



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. The identified studies did not report on broadband measures. Results for ADHD symptoms are shown in Figure 61.

Figure 61. Neurofeedback versus Cognitive Training on Symptoms (SMD)



Across studies, we found no systematic difference between interventions (SMD 0.07; CI -0.55, 0.70; 3 studies, n=167) and in the small set of studies, no heterogeneity was detected. Two of the studies were judged to be high risk of bias, leaving only one study for a sensitivity analysis. The study also detected no statistically significant difference between neurofeedback and cognitive training (SMD 0.19; CI -0.28, 0.67)

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 0.08; CI -1.27, 1.44; 2 studies, n=133) given the wide confidence intervals.[294, 550] 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.[472] 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, 472] Both studies found more improvement associated with methylphenidate but effect estimates differed and resulted in wide confidence intervals, precluding a meaningful effect estimate (SMD 0.57; CI -1.68, 2.81; 2 studies, n=209).

One of the studies reported adverse events; the study 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).[472]

5.3.6.1.3 Neurofeedback Versus Other Active Comparators

One study compared neurofeedback and electromyographic biofeedback.[136] 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.

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	SoE
KQ2 neurofeedback vs control	Behavior	3 RCTs[110, 219, 550]	No systematic effect (SMD 0.35; CI -1.61, 2.31; 3 studies, n=252)	Low for no effect
KQ2 neurofeedback vs control	Broadband measures	4 RCTs[83, 110, 390, 473]	The studies indicated improvements, but estimates varied or could not be computed and no meaningful summary estimate could be derived (SMD 0.77; CI -4.16, 5.7; 2 studies, n=195; RR 0.88; CI 0.66, 1.19; 1 study, n=142)	Insufficient
KQ2 neurofeedback vs control	ADHD symptoms	9 studies, 8 RCTs[219, 244, 291, 316, 390, 473, 550, 554] 1 CT[301]	Results favor intervention (SMD -0.45; CI -0.83, -0.08; 8 studies, n=736)	Moderate for benefit
KQ2 neurofeedback vs control	Functional impairment	2 RCTs,[110, 550]	1 study reported an improvement, 1 no difference and no summary estimate could be derived (SMD 0.2; -1.61, 2.00; 2 studies; n=212)	Insufficient
KQ2 neurofeedback vs control	Acceptability of treatment	0 studies	N/A	Insufficient

KQ2 neurofeedback vs control	Academic performance	0 studies	N/A	Insufficient
KQ2 neurofeedback vs control	Appetite suppression	1 study[110]	No systematic effect (RR 1.45; CI 0.68, 3.10; 1 study, n=142)	Insufficient
KQ2 neurofeedback vs control	Participants with adverse events	0 studies	N/A	Insufficient
KQ2 neurofeedback vs cognitive training	Behavior	2 studies[294, 550]	No systematic difference (SMD 0.13; CI -0.31, 0.57; 2 studies, n=129)	Low for no difference
KQ2 neurofeedback vs cognitive training	Symptoms	3 studies[294, 424, 550]	No systematic difference (SMD 0.07; CI -0.55, 0.70; 3 studies, n=167)	Low for no difference
KQ2 Neurofeedback vs methylphenidate	Broadband measures	1 study[472]	Results favored methylphenidate (RR 3.61; CI 2.36, 5.52; 1 study, n=149)	Low for favoring methylphenidate
KQ2 Neurofeedback vs methylphenidate	ADHD symptoms	2 studies[291, 472]	Both studies favored methylphenidate but no statistically significant difference between groups (SMD 0.57; CI -1.68, 2.81; 2 studies, n=209)	Insufficient
KQ2 Neurofeedback vs methylphenidate	Participants with adverse events	1 study[472]	Results favored neurofeedback (RR 0.23; CI 0.15, 0.35; 1 study, n=149)	Insufficient

Notes: CI 95% confidence interval, KQ key question, N/A not applicable, RR relative risk, RCT randomized controlled trial, SMD standardized mean differences, SoE strength of evidence

The summary of finding table shows an improvement for ADHD symptom scores compared to passive control (moderate strength of evidence, downgraded for study limitation). 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 imprecision. It should be noted that the included neurofeedback approaches varied by study and results of 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 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 Physical Exercise

We identified two studies reporting on physical exercise that met eligibility criteria.[243, 347] One RCT published in 2020[243] compared treadmill training plus whole body vibration training, versus treadmill training alone, in children with ADHD. Training took place three days per week for eight weeks. The study was conducted in Turkey; children ranged in age from 7 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 0.16; -0.55, 0.88; 1 study, n=30) for a broadband measure. A 2019 RCT (n=40) conducted in Tunisia evaluated the effect of Taekwondo exercises. The study reported on attentional inhibitory control and visual

attention and concluded that Taekwondo improved performance on measures of selective attention using the Stroop test in adolescents with ADHD.[347]

5.3.7.1 Exercise Comparative Effectiveness

We did not detect exercise studies comparing to different active treatments.

5.3.7.2 Exercise Summary of Findings

Table 18 below shows the results for the outcomes of interest.

Table 18. KQ2 Summary of Findings and Strength of Evidence for Physical Exercise

KQ2 Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	SoE
KQ2 exercise vs control	Behavior	0 studies	N/A	Insufficient
KQ2 exercise vs control	Broadband measures	1 RCT[243]	1 RCT[243] reported whole body vibration training plus treadmill training group improved more on Conners Parent Rating Scale-Revised/Long Form total score than the treadmill training alone group, but the difference did not reach statistical significance (p 0.055), the Intervention group had significantly more improvement in the teacher version of same instrument.	Insufficient
KQ2 exercise vs control	Symptoms	0 RCT	N/A	Insufficient
KQ2 exercise vs control	Functional impairment	0 RCT	N/A	Insufficient
KQ2 exercise vs control	Acceptability of treatment	0 studies	N/A	Insufficient
KQ2 exercise vs control	Academic performance	0 studies	N/A	Insufficient
KQ2 exercise vs control	Appetite suppression	0 studies	N/A	Insufficient
KQ2 exercise vs control	Participants with adverse events	0 studies	N/A	Insufficient

Notes: CI 95% confidence interval, KQ key question, N/A not applicable, RR relative risk, 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.

5.3.8 Nutrition and Supplements

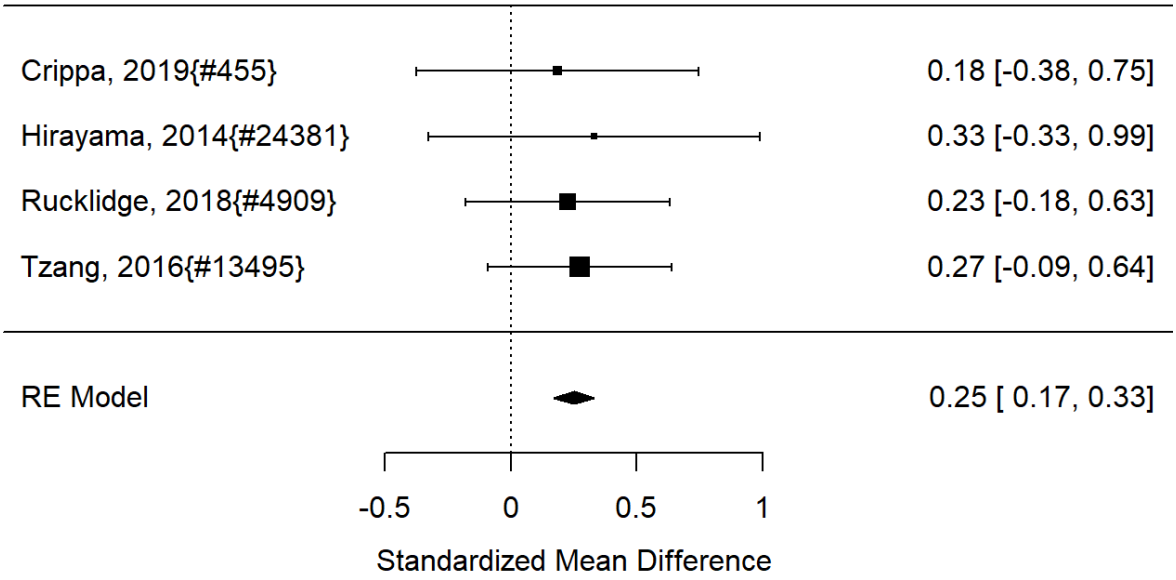
We identified 32 studies of nutrition or supplement interventions.[111, 123, 143, 157, 186, 214, 216, 265, 295, 308, 314, 320, 323, 343, 344, 353, 356, 358, 401, 428, 429, 431, 460, 466, 477, 493, 497, 498, 573, 577, 583, 596] The vast majority were placebo-controlled studies of dietary supplements; one of those was a crossover trial.[1] Two studies evaluated diets.[358, 460] 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 US.[344, 596] Most others were conducted in the Middle

East[265, 320, 353, 358, 401] or Europe.[157, 214, 216, 308, 343, 460, 573] All studies but one (which included children as young as four)[460] 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,[214, 358] one did not report sex,[308] and the rest were majority male. ADHD presentations were rarely reported. Children with psychological and psychiatric co-occurring disorders were excluded from at least half of the studies. One studied children with co-occurring epilepsy.[265]

The studies assessed a wide range of dietary and supplement approaches. However, Omega 3 fatty acid (DHA and/or EPA) was evaluated in more than one study.[186, 214, 216, 265, 308, 314, 343, 401, 429, 498] Other nutritional supplements included saffron,[143] zinc sulfate,[157] Vitamin D,[320] a multivitamin containing essential minerals, amino acids and antioxidants,[344] a different multivitamin,[493] a herbal preparation including spirulina,[353] pycnogenol (an extract from the bark of the French maritime pine),[573] and St. John's wort.[596] The DASH (Dietary Approaches to Stop Hypertension) diet[358] and an individually designed restricted elimination diet[460] were also studied. And one study each of saffron,[356] melatonin,[428] Ma'aljobon powder,[431, 1151] or iron.[466]

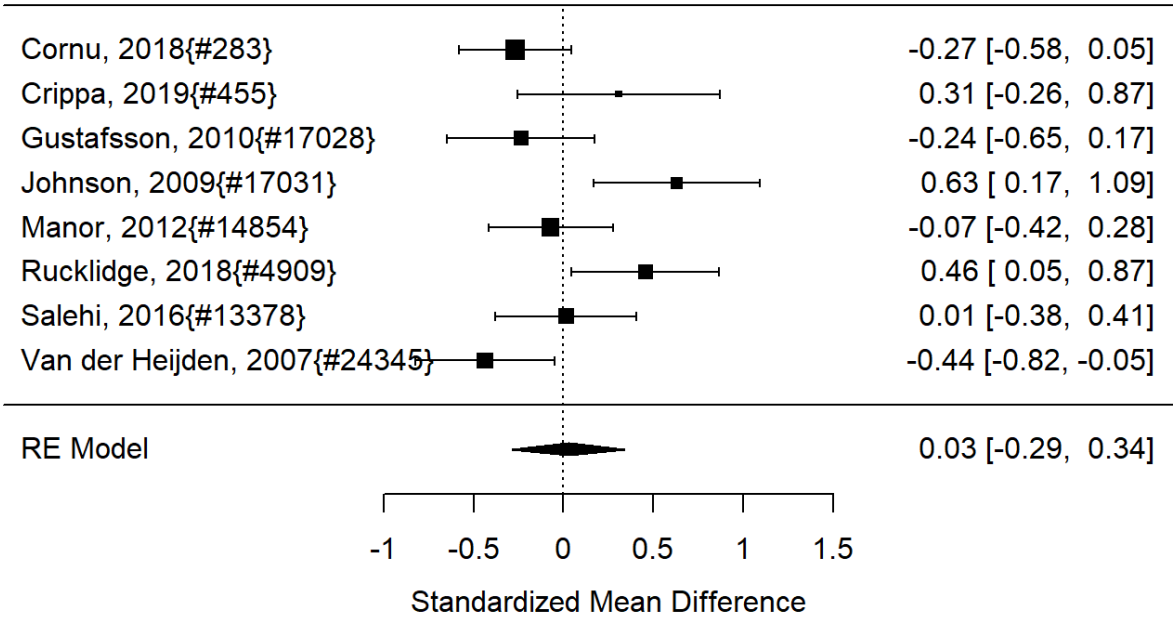
The most common categories of outcomes were broadband and ADHD symptom scores. In terms of instruments, Conners Parent Rating Scale (CPRS) and the ADHD Rating Scale, 4th Version (ADHD RS-IV) were the most frequently reported outcome measures. Figure 62 shows results for individual problem behavior such as teacher-reported conduct problems evaluated in individual studies.

Figure 62. Effects of Nutrition or Supplements on Behavior (SMD)



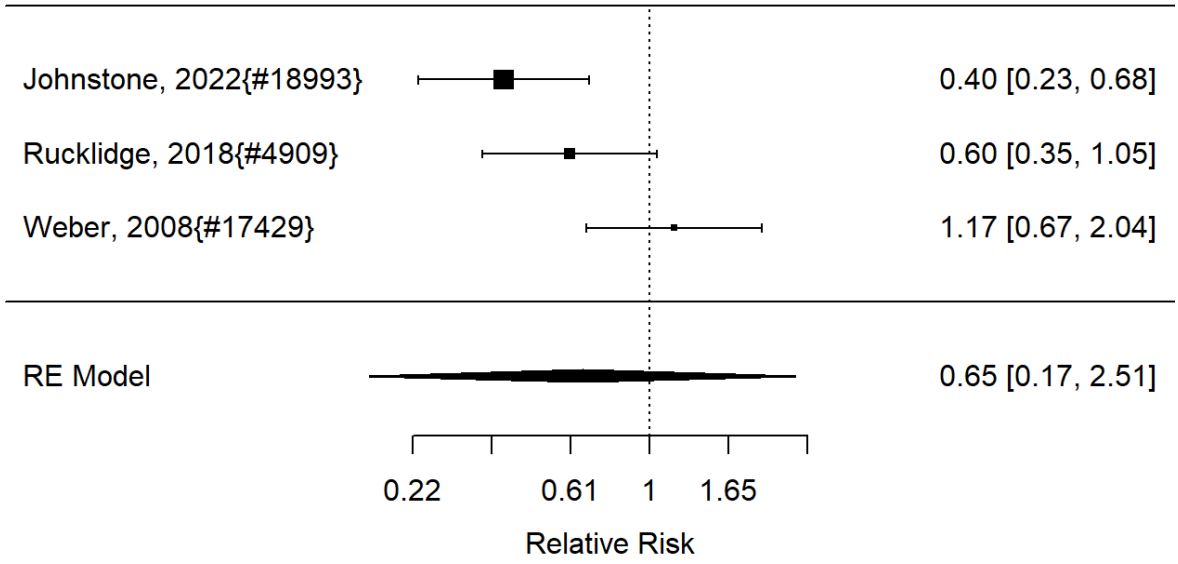
Across studies, nutritional approaches (docosahexaenoic acid, phosphatidylserine, vitamins and minerals, sarcosine), were associated with improvement in problem behavior compared to control (SMD 0.25; CI 0.17, 0.33; 4 studies, n=294). None of the studies included children under six years of age. There was no evidence of heterogeneity and publication bias was not detected. None of the included studies was considered high risk of bias. The included **Omega 3** study reported no statistically significant differences (SMD 0.15; CI -0.41, 0.72; 1 study, n=55).[216] Results of nutrition and supplements on broadband measures are shown in Figure 63.

Figure 63. Effects of Nutrition or Supplements on Broadband Measures (SMD)



Across studies, we did not detect a consistent effect of the intervention compared to control (SMD 0.03; CI -0.29, 0.34; 8 studies, n=818). There was evidence of heterogeneity (I-squared 70%). Heterogeneity was not explained by risk of bias. There was no evidence of publication bias. A few studies assessed the number of participants that improved according to a broadband measure as shown in Figure 64.

Figure 64. Effects of Nutrition or Supplements on Broadband Measures (RR)

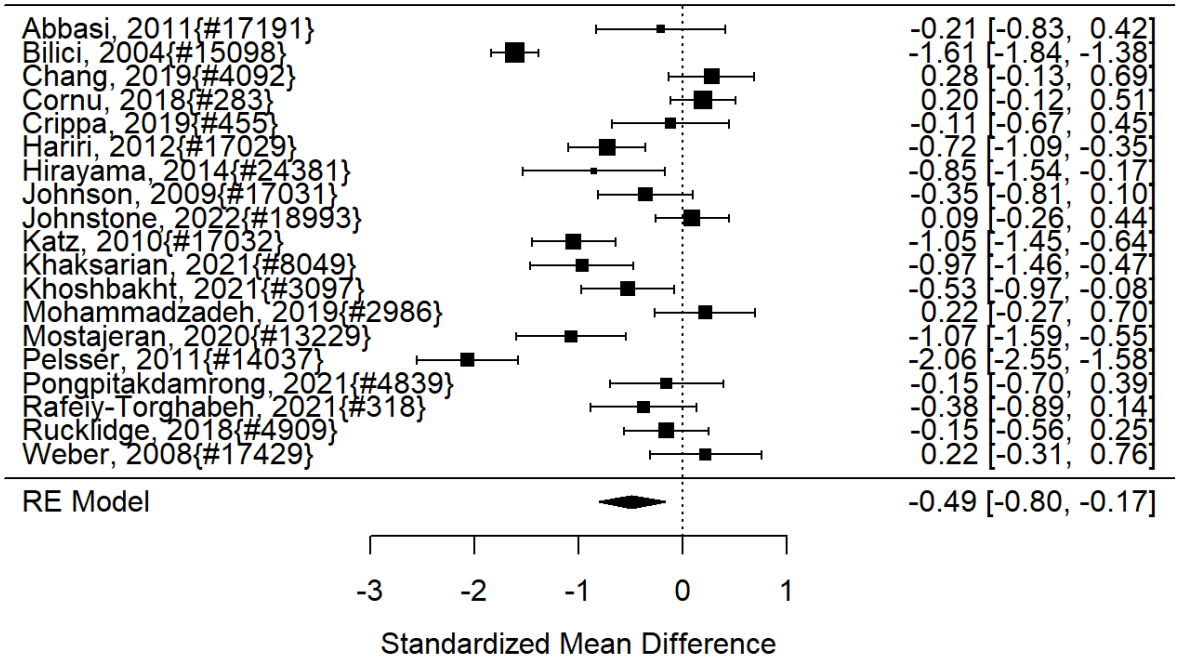


Similar effects are shows for broadband measures used as a categorical variable and the analysis did not detect a systematic treatment effect (RR 0.65; CI 0.35, 1.21; 3 studies, n=273). The three studies assessed different interventions, including micronutrients,[344] vitamin-mineral treatment,[493] and St. John's Wort[596] and there was some evidence of heterogeneity (I-squared 73%). None of the studies was judged to be high risk of bias. There was some evidence of publication bias for the categorical outcome but the alternative estimate based on the trim and fill method was unchanged from the original effect.

The most common supplement assessed in this category was **Omega 3**. Restricting to Omega 3 studies, results for broadband measures were similar to the overall analyses in that they did not show a systematic benefit compared to control groups (SMD 0.07; CI -0.39, 0.53; 6 studies, n=620).[214, 216, 308, 343, 401, 498]

All studies reporting on ADHD symptoms are shown in Figure 65.

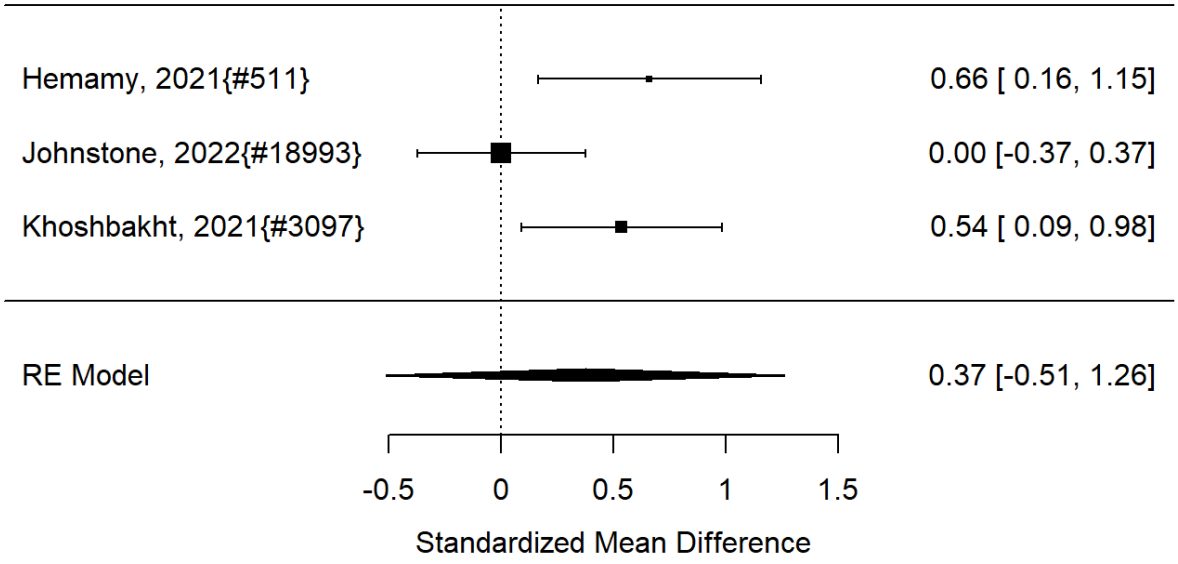
Figure 65. Effects of Nutrition or Supplements on ADHD Symptoms (SMD)



Across studies, analyses for the nutritional approaches and supplements showed a positive effect on ADHD symptoms compared to control (SMD -0.49; CI -0.80, -0.17; 19 studies, n=1854). 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[157] and a restricted elimination diet.[460] Excluding three high risk of bias studies suggested a smaller treatment effect and the result was not statistically significant anymore (SMD -0.65; CI -0.79, 0.10), but heterogeneity was still not reduced. There was no evidence of publication bias. An **omega 3** supplement was the only intervention that was studied in more than one of the otherwise very diverse studies. Restricting to Omega 3 studies did not find any benefits of the supplement (SMD -0.09; CI -0.53, 0.35; 6 studies, n=559).[186, 214, 216, 314, 343, 429] In this subset, heterogeneity was reduced, but still present (I-squared 75%). Two nutrition studies reported on symptom improvement as a categorical variable (i.e., number of participants showing a treatment response) but estimates varied and no meaningful effect estimate could be derived due to the large confidence interval (RR 1.88; CI 0.01, 678.58; 2 studies, n=256). Despite the small number of studies, some heterogeneity was detected (I-squared 43%). There was no evidence of publication bias either. One of the studies with a categorical ADHD symptom measure evaluated Omega 3; the study found no statistically significant effect (RR 3.93; 0.93, 16.95; 1 study, n=75)[343] and the estimate was imprecise.

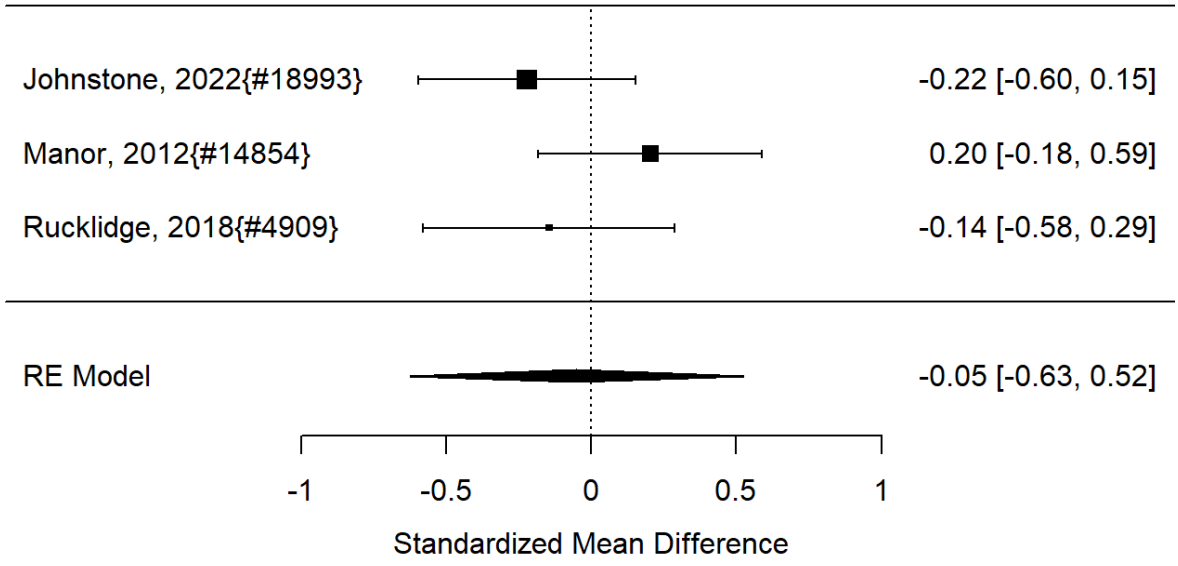
Effects of nutrition and supplements on functional outcomes are shown in Figure 66.

Figure 66. Effects of Nutrition or Supplements on Functional Impairment (SMD)



Across available studies reporting sufficient detail for effect size calculations, no systematic benefit was found on functional impairment (SMD 0.37; CI -0.51, 1.26; 3 studies, n=272). Studies evaluated different interventions, including vitamin D plus magnesium,[320] micronutrients,[344] and the DASH (dietary approach to stop hypertension) diet.[358] Despite the small number of studies, the analysis detected heterogeneity (I-squared 65%). There were no data for treatment satisfaction or academic performance. None of the omega 3 studies reported on these outcomes. A few studies addressed height, BMI, and weight changes as shown in Figure 67.

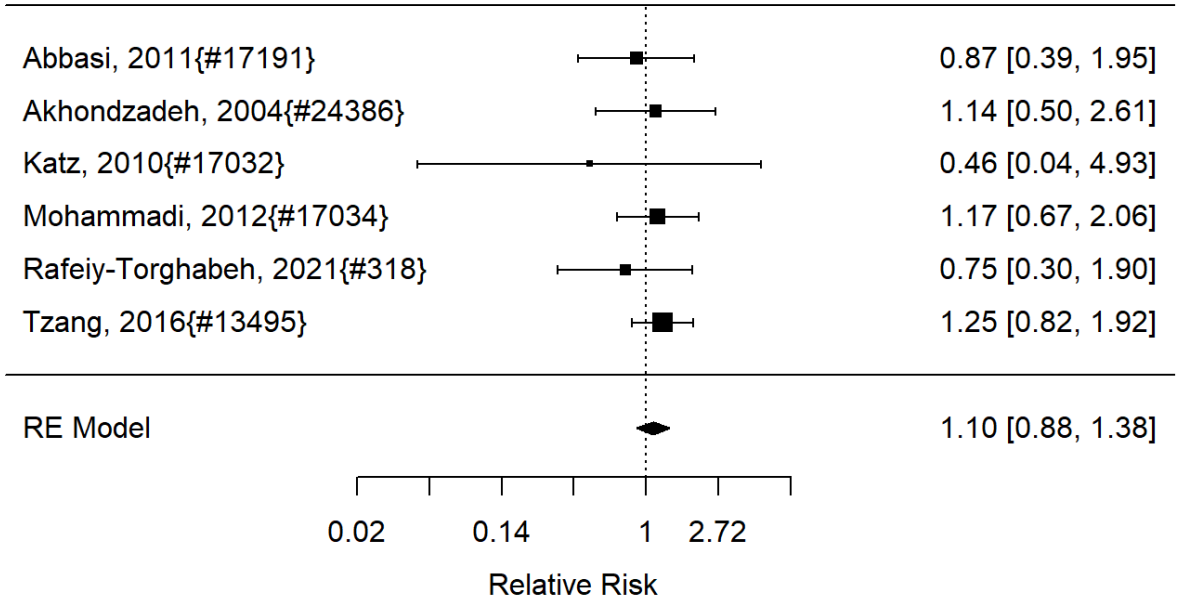
Figure 67. Effects of Nutrition or Supplements on Appetite Suppression (SMD)



5. Results: Treatment of ADHD

There were no differences between treatment arms (SMD -0.05; CI -0.63, 0.52; 3 studies, n=373) for appetite suppression. Heterogeneity was negligible (I-squared 26%). There was no indication of publication bias. Removing one high risk of bias study showed no effect either (SMD -0.19; CI -0.67, 0.29). One of the studies assessed **omega 3** specifically; the study did not detect a statistically significant effect (SMD 0.20; CI -0.18, 0.59; 1 study, n=200).[401] The equivalent analysis for a categorical outcome (number of participants reporting appetite suppression) is shown in Figure 68.

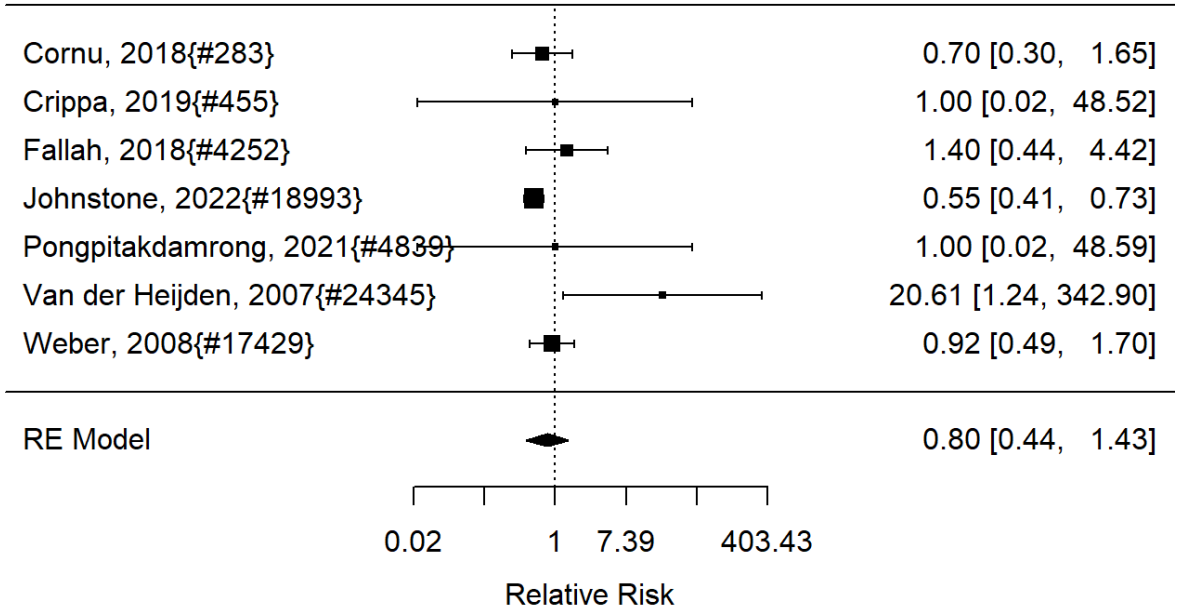
Figure 68. Effects of Nutrition or Supplements on Appetite Suppression (RR)



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 0.08, Egger p0.02). An alternative estimate using the trim and fill method also showed no systematic benefit (RR 1.16; CI 0.88, 1.54). Removing a high-risk of bias study in a sensitivity analysis found a similar effect (RR 1.14; CI 0.79, 1.64) suggesting that the result was not primarily driven by poor methodology.

Studies evaluating the effects on nutrition or supplements on adverse events are shown in Figure 69.

Figure 69. Effects of Nutrition or Supplements on Participants with Adverse Events (RR)



Across studies, there was no indication that the interventions were associated with a higher risk of experiencing an adverse event (RR 0.80; CI 0.44, 1.43; 7 studies, n=600). Heterogeneity was negligible (I-squared 33%), 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 three **omega 3** studies.[214, 216, 265] The result for this subset was similar to the overall analysis and omega 3 was also not associated with an increased risk of experiencing adverse events (RR 0.90; CI 0.46, 1.77; 3 studies, n=263).

5.3.8.1 Nutrition and Supplements Comparative Effects

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

Two studies compared to methylphenidate while the intervention group received saffron[143] or ginkgo biloba[497] Both 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 -4.79, 5.58; 2 studies, n=104). However, both studies reported also appetite suppression and found more events in the methylphenidate groups (RR 0.29; CI 0.14, 0.59; 2 studies, n=104).

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).[498]

5.3.8.2 Nutrition and Supplements Summary of Findings

Table 19 displays the findings for each outcome category along with the number of studies and study identifiers. All outcomes displayed are for the longest follow-up reported. The summary of findings table displays data for all outcomes of interest across nutrition/supplements and for specific supplements where more than one study reported on the particular agent for the outcome. Results of individual studies are documented in the evidence table in the appendix.

Table 19. 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	SoE
KQ2 nutrition/supplements vs control	Behavior	4 RCTs[216, 493, 573, 577]	Results favored intervention (SMD 0.25; CI 0.17, 0.33; 4 studies, n=294)	Low for benefit
KQ2 nutrition/supplements vs control	Broadband measures	10 RCTs[214, 216, 308, 343, 344, 401, 493, 498, 573, 596]	No systematic effect (SMD 0.03; CI -0.29, 0.34; 8 studies, n=818; RR 0.65; CI 0.35, 1.21; 3 studies, n=273)	Moderate for no effect
KQ2 nutrition/supplements vs control	ADHD symptoms	18 RCTs[295, 314, 356, 428, 429, 431, 466]	Positive effect (SMD -0.49; CI -0.80, -0.17; 19 studies, n=1854; RR 1.88; CI 0.01, 677.13; 2 studies)	Low for benefit
KQ2 nutrition/supplements vs control	Functional impairment	4 RCTs[320, 344, 358, 401]	No systematic effect (SMD 0.37; CI -0.52, 1.26; 3 studies, n=272)	Low for no effect
KQ2 nutrition/supplements vs control	Acceptability of treatment	0 studies	N/A	Insufficient
KQ2 nutrition/supplements vs control	Academic performance	0 studies	N/A	Insufficient
KQ2 nutrition/supplements vs control	Appetite changes and growth suppression	6 RCTs[344, 353, 401, 429, 493, 577]	No systematic effect (SMD -0.05; CI -0.63, 0.52; 3 studies, n=373; RR 1.10; CI 0.88, 1.38; 6 studies, n=439)	Low for no effect
KQ2 nutrition/supplements vs control	Number of participants with adverse events	9 RCTs[214, 216, 265, 314, 344, 401, 428, 466, 596]	No systematic effect (RR 0.80; CI 0.44, 1.43; 7 studies, n=600)	Moderate for no effect
KQ2 Omega 3 vs control	Broadband measures	6 RCTs[214, 216, 308, 343, 401, 498]	No systematic effect (SMD 0.03; CI -0.33, 0.38; 6 studies, n=620)	Moderate for no effect
KQ2 Omega 3 vs control	ADHD symptoms	6 RCTs[186, 214, 216, 314, 343, 429]	No systematic effect (SMD -0.08; CI -0.51, 0.34; 6 studies, n=559; RR 3.97; CI 0.93, 16.95; 1 study, n=64)	Low for no effect
KQ2 Omega 3 vs control	Number of participants with adverse events	3 RCTs[214, 216, 265]	No systematic effect (RR 0.90; CI 0.46, 1.77; 3 studies, n=263)	Low for no effect
KQ2 Supplement vs methylphenidate	ADHD symptom	2 RCTs[143, 497]	No systematic difference (SMD 0.40; CI -4.79, 5.58; 2 studies, n=104)	Insufficient
KQ2 Supplement vs methylphenidate	Appetite changes and grows suppression	2 RCTs[143, 497]	Supplements reported fewer events (RR 0.29; CI 0.14, 0.59; 2 studies, n=104)	Low for favoring supplements

Notes: CI 95% confidence interval, KQ key question, N/A not applicable, RR relative risk, RCT randomized controlled trial, 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 systematic effect on broadband measures or functional impairment but 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).

5.3.9 CAM

We identified four studies that evaluated complementary, alternative, or integrative medicine (CAM) interventions.[158, 280, 281, 327] Studies were published between 2001 and 2019; they were conducted in Switzerland,[280, 281] Iran,[158] and Korea.[327] All studies included both children and adolescents and participants were predominately male. Race or ethnicity was not reported, presumably because populations of these countries are fairly homogenous. ADHD presentations and presentations were not reported. Studies evaluated acupuncture and homeopathy. Three studies compared to a passive control group (waitlist, placebo, attention-matched control).

None of the studies reported on individual problem behaviors. One of the identified studies reported on a broadband measure in sufficient detail to calculate an effect size; the study found no systematic improvement associated with acupuncture compared to waitlist (SMD -0.19; CI -0.60, 0.22; 1 study, n=93).[327] One homeopathy study reported insufficient detail for effect size calculations but concluded that the intervention had improved the Conners Global Index compared to placebo.[280]

Two studies reported on ADHD symptoms, but the effects varied somewhat and no meaningful summary estimate could be derived (SMD 0.18; CI -1.66, 2.01; 2 studies, n=190).[158, 327] The studies evaluated traditional acupuncture and auricular acupuncture. 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=50).[158]

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, appetite suppression, or participants experiencing adverse events.

5.3.9.1 CAM Comparative Effects

One of the identified studies (n=115) compared homeopathy and methylphenidate.[281] The high risk of bias study used the Clinical Global Impression (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.

5.3.9.2 CAM Summary of Findings

Table 20 shows the findings for the outcomes of interest together with the number of studies and study identifiers.

Table 20. KQ2 Summary of Findings and Strength of Evidence for CAM

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	SoE
KQ2 CAM vs control	Behavior	0 studies	N/A	Insufficient
KQ2 CAM vs control	Broadband measures	2 RCTs[280, 327]	No systematic effect (SMD -0.19; -0.60, 0.22; 1 study, n=140)	Low for no effect
KQ2 CAM vs control	ADHD symptoms	2 RCTs[158, 327]	Conflicting results (SMD 0.19; CI 1.72, 2.11; 2 studies, n=190; RR 4.26; CI 1.42, 12.77; 1 study, n=44)	Insufficient
KQ2 CAM vs control	Functional impairment	0 studies	N/A	Insufficient
KQ2 CAM vs control	Acceptability of treatment	0 studies	N/A	Insufficient
KQ2 CAM vs control	Academic performance	0 studies	N/A	Insufficient
KQ2 CAM vs control	Appetite suppression	0 studies	N/A	Insufficient
KQ2 CAM vs control	Participants with adverse events	0 studies	N/A	Insufficient

Notes: CI 95% confidence interval, KQ key question, N/A not applicable, RR relative risk, RCT randomized controlled trial, SMD standardized mean differences, SoE strength of evidence

Very few studies reported on the key outcomes selected for the review and the conclusion for several outcomes was that the evidence base is insufficient because of lack of research. The strength of evidence was downgraded for broadband measure scores due to inconsistency and imprecision (both studies reported a positive effect but estimates varied). The strength of evidence was determined to be insufficient for symptoms because of conflicting results and it is unclear whether CAM interventions have an effect on ADHD symptoms.

Only one comparative effectiveness study was identified and the study reported insufficient details to compute effect sizes for the outcomes of interest.

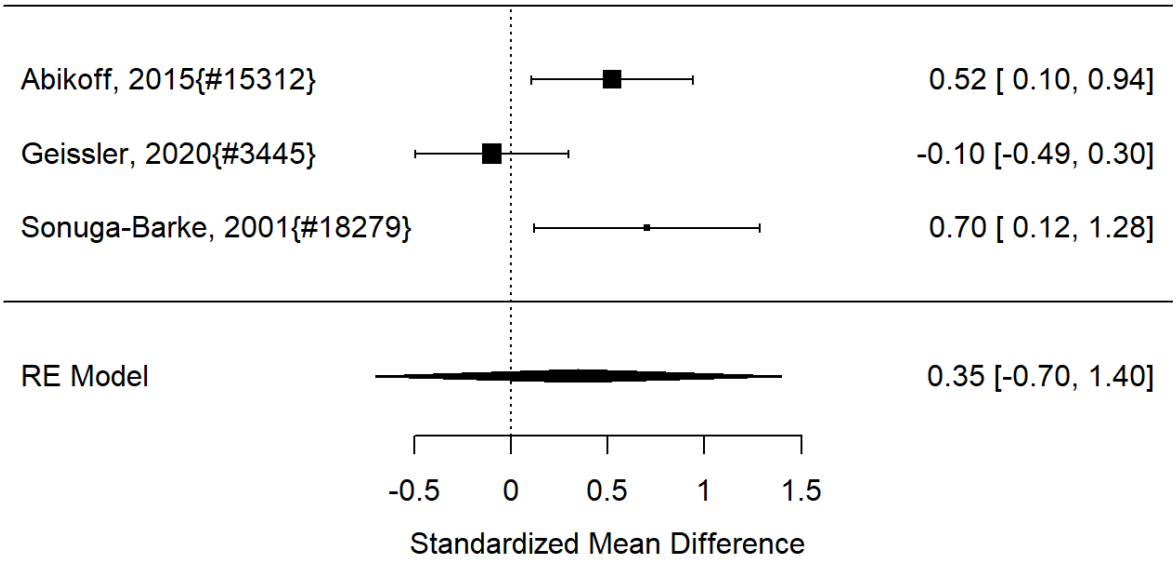
5.3.10 Parent Support

We identified 18 studies evaluating an intervention primarily targeting parents.[117, 184, 204, 228, 233, 260, 268, 269, 290, 328, 376, 418, 508, 533, 539-541, 572] Of note, some psychosocial studies presented earlier in the chapter also included a parent component, but in addition to targeting the children and adolescents directly. The earliest identified parent support study was published in 2001.[539] Evaluations were published in ten different countries, primarily the US[52, 117, 184, 204] and the UK.[269, 539-541] The populations studied were parents of children with ADHD between the ages of three and up to 18 years, but only three studies included teenagers.[204, 268, 269] For studies that distinguished between ADHD presentations, the most prevalent type (ranging from 33.5%[117] to 63%[328] of the ADHD participants) was the combined type. While ADHD participants with co-occurring disorders were not excluded from most of the studies, no studies purposely included specific co-occurring disorders such as oppositional defiant disorder or conduct disorder, i.e., where the children had a dual diagnosis. Two studies included children with sleep problems.[324, 418] Race and ethnicity demographics for the parents or children were not mentioned in most studies.

Interventions were diverse in terms of intervention 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,[268, 290] no intervention, waitlist, or treatment as usual.[233, 269, 324, 376, 508, 540, 572] Some studies included both a control group and an alternative psychological or behavioral intervention.[117, 184, 328, 539, 541] Three studies had no control group, only an alternative intervention.[52, 204, 533] Two studies compared parent training as stimulant augmentation to medication alone.[52, 418]

We only included studies that reported data on the effects on the children with ADHD; studies reporting only on parental outcomes were excluded (see eligibility criteria). 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 70 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.

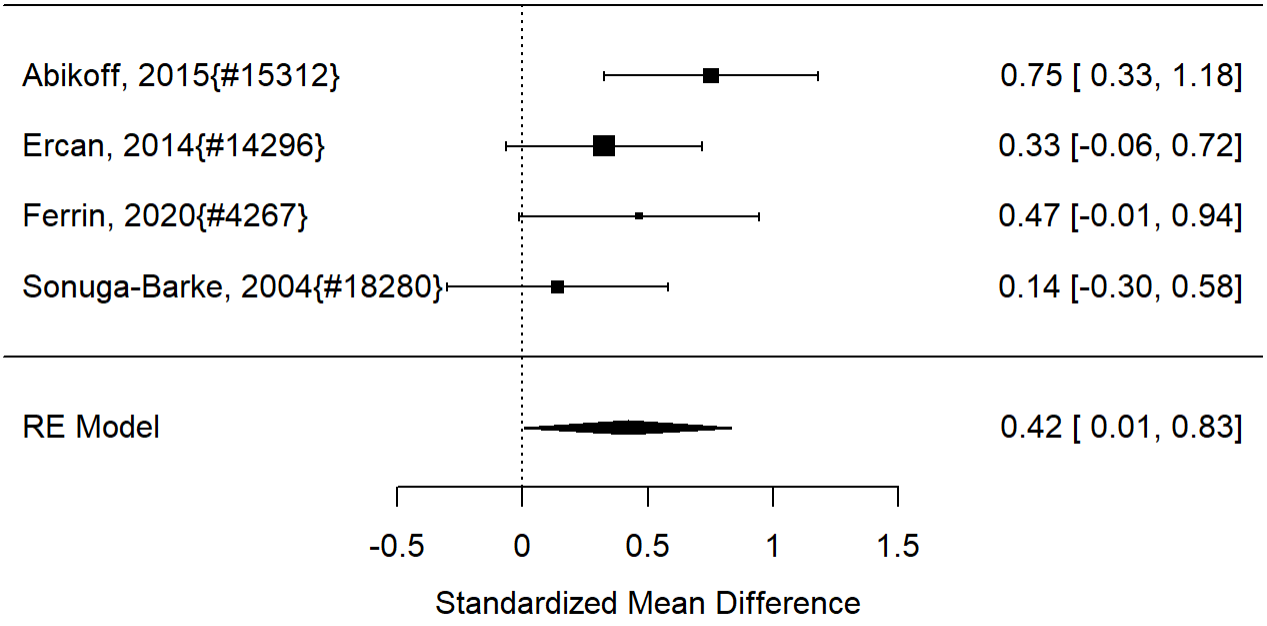
Figure 70. Effects of Parent Support on Behavior (SMD)



Across studies, we did not detect a systematic effect of the parent-oriented interventions (SMD 0.35; CI -0.70, 1.40; 3 studies, n=252). The analysis did detect statistical heterogeneity (I-squared 70%). None of the studies was considered high risk. There was no evidence of publication bias.

Results for broadband measures are shown in Figure 71.

Figure 71. Effects of Parent Support on Broadband Measures (SMD)

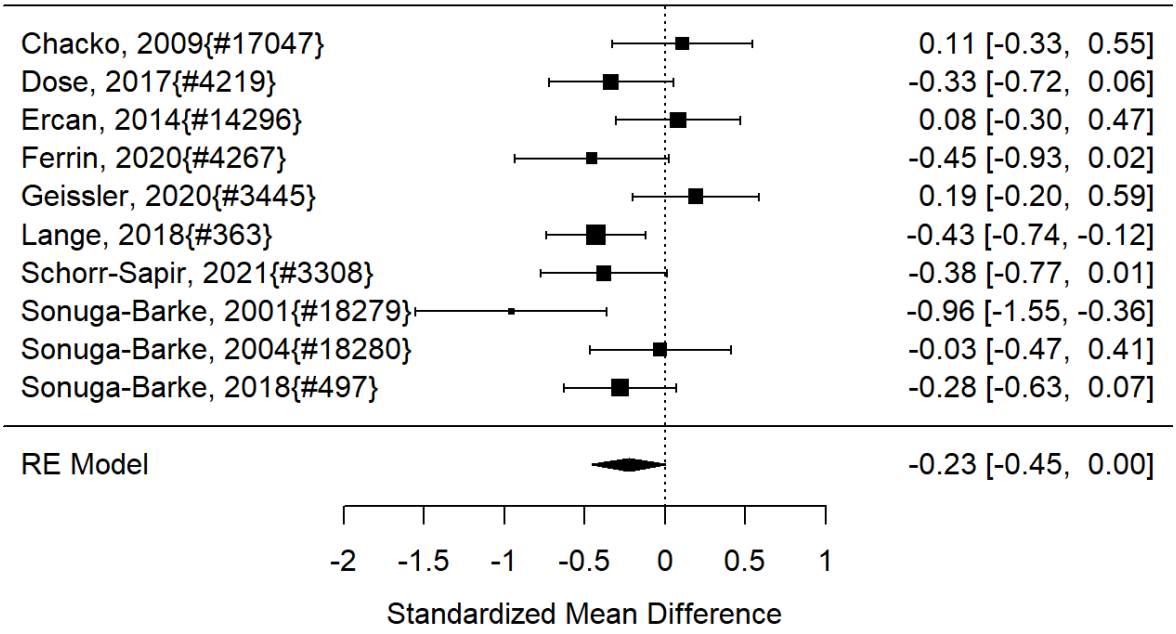


Analyses found positive effects of parent support interventions but the effect was only borderline statistically significant (SMD 0.42; CI 0.01, 0.83; 4 studies, n=379). The youngest children included in the studies were three years old, the oldest were 18. The included

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,[117] a combination of methylphenidate plus parental training and support versus medication alone,[260] a psychoeducation interventions versus treatment as usual,[269] and parent training for mothers versus waitlist,[540] in the individual studies. Heterogeneity was unremarkable (I-squared 28%). There was no evidence of publications bias and none of the studies was considered high risk of bias.

A number of studies reported on ADHD symptom measures (Figure 72).

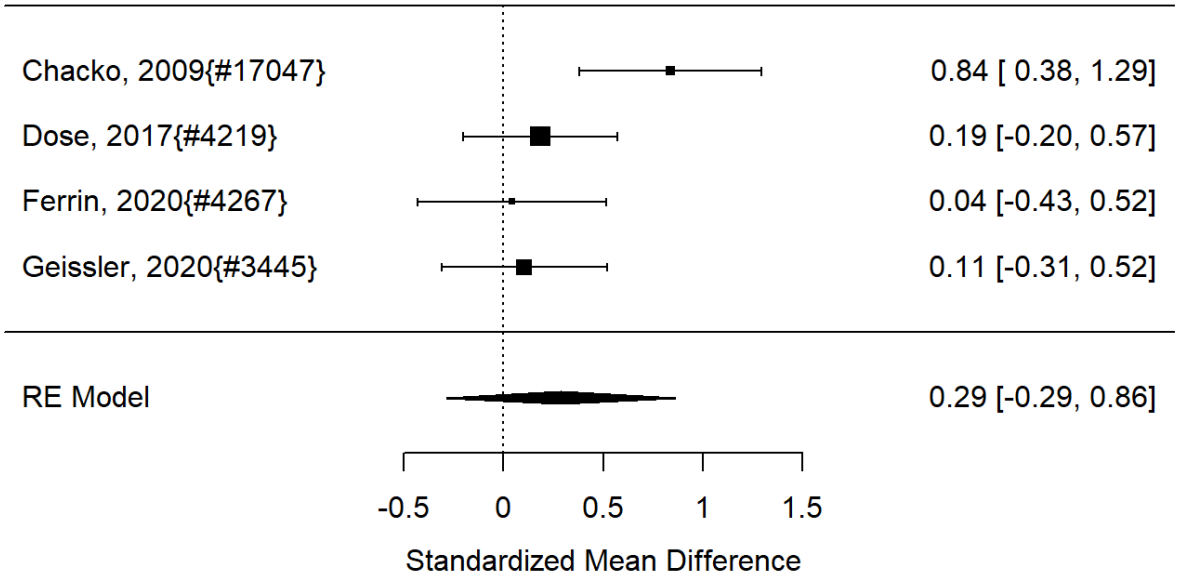
Figure 72. Effects of Parent Support on Symptoms (SMD)



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 -0.23; CI -0.45, -0.00; 10 studies; n=1053). The youngest children included in the studies were three years old, the oldest were 18. There was little statistical heterogeneity (I-squared 51%) 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,[539] psychoeducation for families,[269] and the New Forest Parenting Package for parents of preschoolers,[376] specifically. Removing high risk of bias studies suggested a smaller, not statistically significant effect (SMD -0.20; CI -1.00, 0.60) but heterogeneity increased in this sensitivity analysis. There was no evidence of publication bias. 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 0.47; CI 0.20, 1.07; 1 study, n=50).

Functional impairment outcomes were also frequently reported in identified studies as shown in Figure 73.

Figure 73. Effects of Parent Support on Functional Impairment (SMD)



Pooled effect estimates showed no systematic effect of the intervention on functional impairment (SMD 0.29; CI -0.29, 0.86; 4 studies, n=344). There was some heterogeneity (I-squared 61%). Removing two high risk of bias studies reported also a non-significant effect with wide confidence intervals (SMD 0.47; CI -4.18, 5.11). There was no evidence of publication bias. There were insufficient data to calculate effects on treatment satisfaction or academic outcomes.

One study reported on appetite suppression and found no systematic effect (RR 7.14; CI 0.38, 134.71; 1 study, n=99) but the estimate was very imprecise. The study also reported on the number of participants with adverse events, but results were likely driven by the pharmacological component of the intervention: the study found more events in psychoeducation for parents plus atomoxetine versus psychoeducation for parents plus placebo (RR 1.21; CI 1.00, 1.47; 1 study, n=92).[560]

5.3.10.1 Parent Support Comparative Effectiveness

Multiple studies compared 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).[117] One study compared the New Forest Parenting program with the Incredible Years alternative parenting program.[541] 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.[539] The study found no differences in 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 favored

the parent training when comparing the parental account of childhood symptom score 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; -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.[268]

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.[328] 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).[204] A study (n=172) comparing a parental friendship coaching intervention versus psychoeducation and social support found no significant differences in aggressive behaviors in the children with ADHD and did not report sufficient detail for effect size calculations, but the study concluded that the coaching intervention showed parents providing more emotion strategies and praise.[533]

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).[184]

5.3.10.2 Parent Support 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 Parent Interventions

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	SoE
KQ2 parent support vs control	Behavior	5 RCTs[117, 290, 328, 376, 539]	No systematic effect (SMD 0.35; CI -0.70, 1.40; 3 studies, n=252)	Low for no effect
KQ2 parent support vs control	Broadband measures	6 RCTs[117, 260, 269, 539, 540, 560]	Results favor intervention (SMD 0.42; CI 0.01, 0.83; 4 studies, n=379)	Low for benefit
KQ2 parent support vs control	ADHD symptoms	14 RCTs[184, 233, 260, 269, 290, 328, 376, 508, 539-541, 560, 572]	Results favor intervention (SMD -0.23; CI -0.45, -0.00; 10 studies, n=1053; RR 0.47, CI 0.20, 1.07; 1 study, n=50)	Low for benefit
KQ2 parent support vs control	Functional impairment	4 RCTs[184, 233, 269, 290]	No systematic effect (SMD 0.29; CI -0.29, 0.86; 4 studies, n=344)	Low for no effect
KQ2 parent support vs control	Acceptability of treatment	0 studies	N/A	Insufficient
KQ2 parent support vs control	Academic performance	0 studies	N/A	Insufficient
KQ2 parent support vs control	Appetite suppression	1 RCT[560]	No systematic effect (RR 7.14; CI 0.38, 134.71; 1 study, n=99)	Insufficient

5. Results: Treatment of ADHD

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	SoE
KQ2 parent support vs control	Participants with adverse events	0 studies	N/A	Insufficient
KQ2 New Forest Parenting program vs Helping the Noncompliant Child	Behavior	1 RCT[117]	No systematic difference (SMD 0.05; CI -0.29, 0.40; 1 study, n=164)	Insufficient
KQ2 New Forest Parenting program vs Helping the Noncompliant Child	Broadband measures	1 RCT[117]	Results favored the helping-the-noncompliant-child intervention (SMD -0.41; CI 0.76, -0.07; 1 study, n=164)	Insufficient
KQ2 New Forest Parenting program vs Helping the Noncompliant Child	Functional impairment	1 RCT[117]	No systematic difference (SMD -0.13; CI -0.48, 0.21; 1 study)	Insufficient
KQ2 New Forest Parenting program vs The Incredible Years	ADHD symptoms	1 RCT[541]	No systematic difference (SMD 0.09; CI -0.33, 0.15; 1 study, n=307)	Insufficient
KQ2 Parent training vs parent counseling	Behavior	1 RCT[539]	No systematic difference (SMD 0.36; CI -0.16, 0.88; 1 study, n=78)	Insufficient
KQ2 Parent training vs parent counseling	Broadband measures	1 RCT[539]	No systematic difference (SMD 0.74; CI 0.42, 1.30; 1 study, n=78)	Insufficient
KQ2 Parent training vs parent counseling	ADHD symptoms	1 RCT[539]	Results favored the parent training intervention (SMD -0.69; CI -1.22, -0.16; 1 study, n=78)	Insufficient
KQ2 Parent friendship coaching vs psychoeducation	Behavior	1 RCT[533]	No systematic difference (SMD 0.14; CI -0.16, 0.43; 1 study, n=172)	Insufficient
KQ2 Parent psychoeducation vs parent counseling	ADHD symptoms	1 RCT[268]	No systematic difference (SMD -0.32; CI -0.77, 0.13; 1 study, n=81)	Insufficient
KQ2 Parent psychoeducation vs parent counseling	Functional impairment	1 RCT[268]	No systematic difference (SMD 0.07; CI -0.38, 0.52; 1 study, n=81)	Insufficient
KQ2 Strategies to Enhance Positive Parenting Program vs traditional parent behavior training	ADHD symptoms	1 RCT[184]	No systematic difference (SMD -0.16; CI -0.28, 0.60; 1 study, n=120)	Insufficient
KQ2 Strategies to Enhance Positive Parenting Program vs traditional parent behavior training	Functional impairment	1 RCT[184]	Results favored the positive parenting program (SMD 0.51; CI 0.07, 0.96; 1 study, n=120)	Insufficient

Notes: CI 95% confidence interval, KQ key question, N/A not applicable, RR relative risk, RCT randomized controlled trial, SMD standardized mean differences, SoE strength of evidence

Across studies, parent training interventions were associated with improvements in broadband measure scores (low strength of evidence, downgraded for inconsistency given the variation and small number of studies and imprecision) and standardized symptom scores (moderate strength of evidence, downgraded for inconsistency and imprecision) as well as. 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 (inconsistency). Evidence was insufficient to determine acceptability of treatment, academic performance, and participants with adverse events due to lack of research reporting on the outcome. Although one study reported on appetite suppression, the estimate was so imprecise and the study did not assess parent interventions per se (it assessed the combinations parent training plus atomoxetine versus parent training plus placebo) that we also determined the evidence base as insufficient for that outcome (downgraded due to study limitation, inconsistency as no replication could be evaluated, and imprecision due to the wide confidence intervals).

The comparative studies were downgraded to 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 (downgraded for inconsistency, study limitation).

5.3.11 School Interventions

We identified ten studies reporting on teacher or school environment interventions.[171, 213, 242, 262, 509, 517, 519, 564, 590, 628] The earliest study was published in 2009.[590] Interventions were evaluated in four different countries, predominantly the US. The populations studied were most often children attending elementary through middle school between the ages of six and 14, with only one study including adolescents up to 17 years old.[509] In two studies, participants were required to demonstrate an IQ of 80 or higher.[171, 262] 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.[213] 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.[564] 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.[171, 517, 519, 564, 590]

Approximately half of the studies used a multimodal intervention strategy comprising both teacher training and parent training,[509, 517, 519, 628] with some studies also including intervention components targeting children with ADHD.[171, 262, 519, 564] Two studies examined teacher-specific interventions. One[213] tested a web-based online learning modules for elementary-school teachers, while the other[590] 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,[171, 213, 509] no intervention,[262, 519] and ADHD medication only (compared to other modes of active treatment).[517, 628] Some studies reported on an alternative intervention, such a lower intensity intervention[519] or a modified version of an original intervention,[262] or multimodal intervention packets targeted at both parents and teachers[509] and evaluated the comparative effectiveness of these interventions.

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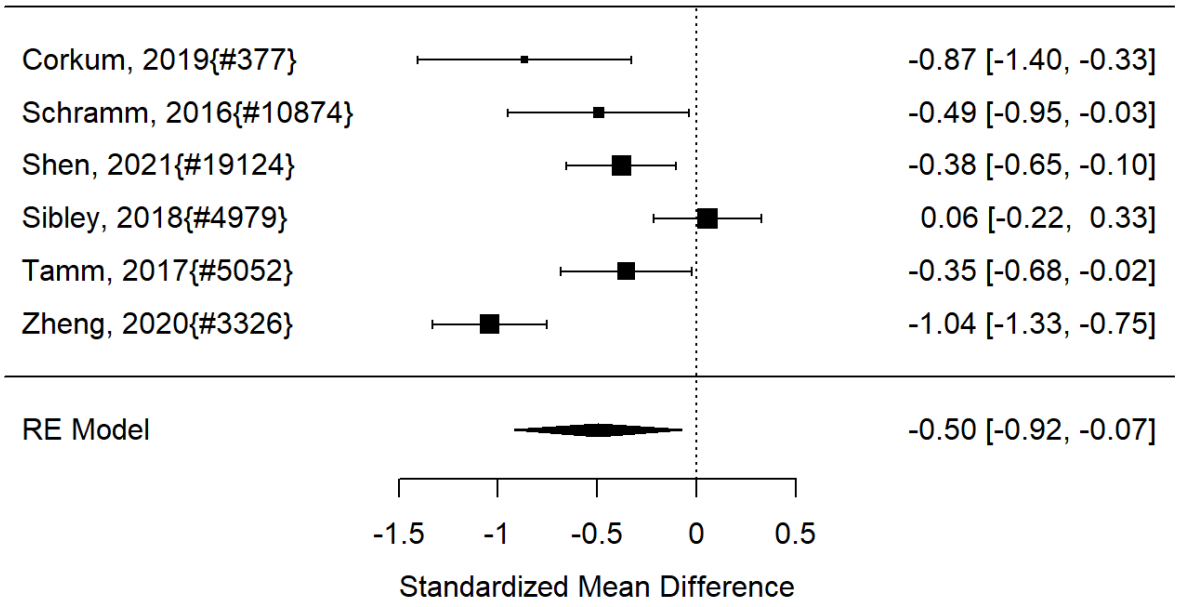
Studies reported a variety of often study-specific outcomes, such as improvement in individual cognitive tasks. In terms of pre-specified outcomes, symptom scores, functional impairment, and academic scores were the most frequently reported outcomes. Two studies reported on individual problem behaviors, but results were conflicting and could not be combined to a meaningful summary estimate (SMD 0.01; CI -1.36, 1.38; 2 studies, n=395).[242, 519] We did not identify studies reporting on broadband measure scores. Studies reporting on ADHD symptoms are shown in Figure 74.

Figure 74. Effects of School Interventions on ADHD Symptoms (SMD)

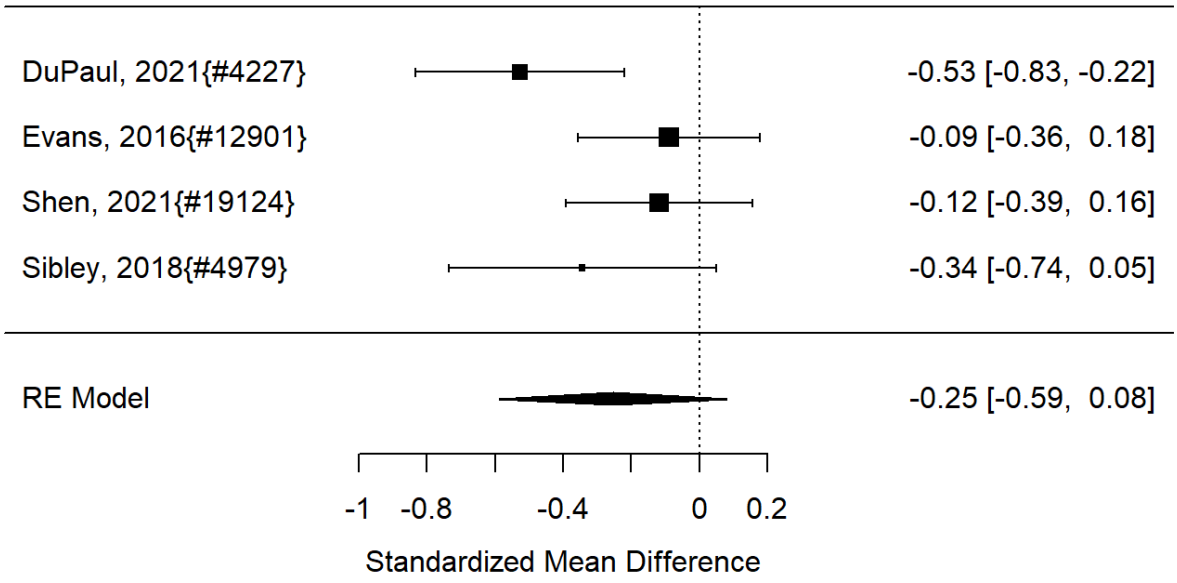


Across studies, school interventions were associated with a reduction in ADHD symptoms (SMD -0.50; CI -0.92, -0.07; 6 studies, n=898). The age of the children in the included studies ranged from six to 17. There was evidence of heterogeneity (I-squared 82%). We found no indication of publication bias. Removing high risk of bias studies in a sensitivity analysis left only three studies; the effect estimate was smaller and was not statistically significant anymore (SMD -0.24; CI -1.00, 0.48). Heterogeneity was reduced, suggesting that the methodological rigor of the study is one source of heterogeneity.

Two studies reported on functional outcomes, however, they reported conflicting results and could not be combined to a meaningful estimate (SMD 0.22; CI -4.39, 4.82; 2 studies; n=274).[213, 262] There was heterogeneity (I-squared 83%) but no further analyses could be performed due to the small number of studies. One study evaluated a web-based intervention for teachers of elementary students with ADHD[213] and reported improvements. The other assessed a school-based training intervention program for adolescents but found no differences compared to community care in the relation with peer scale domain of the IRS (Impairment Rating Scale).[262]

A small number of studies reported on academic performance measures as shown in Figure 75.

Figure 75. Effects of School Interventions on Academic Performance (SMD)



Although all individual studies reported a reduction, across studies, the effect was not statistically significant (SMD -0.25; CI -0.59, 0.08; 4 studies, n=691). There was little heterogeneity (I-squared 47%). We did not detect potential publication bias. Removing one high-risk of bias study found a smaller effect that was not statistically significant (SMD -0.15; CI 0.44, 0.14) and the analysis detected no heterogeneity, suggesting that methodological rigor of the studies was a source of heterogeneity. Identified studies did not report on other prespecified outcomes for the review.

5.3.11.1 School Interventions Comparative Effects

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; the authors found no differences in school disciplinary incidents (SMD 0.01; CI -0.26, 0.28; 1 study, n=325), ADHD symptom assessments (SMD 0.01; CI -0.26, 0.29; 1 study, n=325), functional impairment (SMD -0.14; CI -0.42, 0.13; 1 study, n=325), or academic performance (SMD -0.25; -0.64, 0.14; 1 study, n=325) but concluded that the high intensity intervention was superior in engagement and uptake of selected skills.[519]

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.[171] The study found 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.[262] Another 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).[590]

One study compared an academic problem solving and organization skill intervention versus progressive muscle relaxation and found no statistically significant difference in ADHD symptoms (SMD -0.29; CI -0.74, 0.16; 1 study, n=113).[509]

5.3.11.2 School Interventions 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 School Interventions

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	SoE
KQ2 school intervention vs control	Behavior	2 RCTs[242, 519]	Conflicting results (SMD 0.01; CI -1.36, 1.38; 2 studies, n=395)	Insufficient
KQ2 school intervention vs control	Broadband measures	0 studies	N/A	Insufficient
KQ2 school intervention vs control	ADHD symptoms	7 RCTs[213, 262, 509, 517, 519, 564, 628]	Results favor interventions (SMD -0.50; CI -0.92, -0.07; 6 studies, n=898)	Moderate for benefit
KQ2 school intervention vs control	Functional impairment	2 RCTs[213, 262]	Conflicting results (SMD 0.22; CI -4.39, 4.82; 2 studies, n=274)	Insufficient
KQ2 school intervention vs control	Acceptability of treatment	3 RCTs[213, 517, 519]	Studies reported favorable results but effect could not be estimated	Low for benefit
KQ2 school intervention vs control	Academic performance	4 RCTs[171, 262, 517, 519]	No statistically significant difference but all studies positive (SMD -0.25; CI -0.59, 0.08; 4 studies, n=691)	Insufficient
KQ2 school intervention vs control	Appetite suppression	0 studies	N/A	Insufficient
KQ2 school intervention vs control	Participants with adverse events	0 studies	N/A	Insufficient
KQ2 contingency-management based vs planning skills homework program	Academic performance	1 RCT[171]	No systematic difference (SMD 0.12; CI -0.14, 0.39; 1 study, n=222)	Insufficient
KQ2 After school program vs mentoring program	Functional impairment	1 RCT[262]	No systematic difference SMD 0.02; CI -0.24, 0.28; 1 study, n=326)	Insufficient

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	SoE
KQ2 After school program vs mentoring program	Academic performance	1 RCT[262]	No systematic difference SMD -19; CI -0.46, 0.07; 1 study, n=376)	Insufficient
KQ2 Consultant and data-driven interventions vs teacher selected interventions	Academic performance	1 RCT[590]	No systematic difference SMD -0.26; CI -0.56, 0.05; 1 study, n=326)	Insufficient
KQ2 School skills training vs progressive muscle relaxation	ADHD symptoms	1 RCT[509]	No systematic difference (SMD -0.29; CI -0.74, 0.16; 1 study, n=113)	Insufficient

Notes: CI 95% confidence interval, KQ key question, N/A not applicable, RR relative risk, RCT randomized controlled trial, SMD standardized mean differences, SoE strength of evidence

School interventions showed favorable results for ADHD symptoms (moderate strength of evidence) but we downgraded the effect for study limitations (effects were lower and not statistically significant when removing high risk of bias studies). Identified studies showed conflicting results for behavior and functional impairment, and given the small number of studies, we were not able to determine whether school interventions improve these outcomes and judged the evidence base to be insufficient. Treatment acceptability (low strength of evidence) was favorable across multiple studies, but no effect estimate could be determined (downgraded by two 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 studies were downgraded to insufficient as evaluations had not been replicated yet and all results were unique to the reported study, the specific intervention and the specific comparator, and the robustness of results could not be further evaluated(downgraded for inconsistency, study limitation).

5.3.12 Provider Interventions

We identified eight studies[257-259, 306, 365, 378, 440, 454] evaluating provider interventions or interventions changing how ADHD care is delivered. The earliest study was published in 2007.[259] All evaluations were conducted in the US. The populations studied were children with ADHD; no studies included teenagers. Only one study[378] 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[306] reported that 46 percent of patients were African American. The majority of patients in the other studies were White.

Of the identified studies, five reported on a control group that underwent treatment as usual.[258, 259, 306, 378, 454] 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.[259] Another study[258] 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.[306] 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.[378] Another created a web-based platform that enabled clinicians to administer online clinical questionnaires to

parents and teachers to monitor patients remotely between visits.[454] 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.[365]

The studies are difficult to compare and assessed unique interventions. In addition, many used study-specific evaluation measures and rarely reported on key outcomes for this review or did not report sufficient detail to compute effect sizes. One study reported on a broadband measure and indicated children under the care of providers that used a trigger algorithm and alert resolution process to facilitate online clinical questionnaires to monitor patients remotely between visits, reported less improvement in global functioning (SMD -0.36; CI -0.65, -0.07; 1 study, n=263) than control group participants.

Parent-reported outcomes were the only outcomes reported in more than one study. Studies reported conflicting results and no meaningful summary estimate could be derived (SMD 0.26; CI -4.79, 5.31; 2 studies, n=537).[306, 454] This included the trigger algorithm study which did not find positive effects[454] 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.[306]

5.3.12.1 Provider Interventions Comparative Effects

Two studies also compared provider interventions 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.[365] 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.[440] The study reported improvement in symptom measures in the telehealth intervention (SMD -0.54; CI -0.81, -0.27; RR 1.64; CI 1.09, 2.47; 1 study, n=223) and functional impairment (SMD 0.27; CI 0.01, 0.54; 1 study, n=223).[440]

5.3.12.2 Provider Interventions Summary of Findings

Table 23 displays the findings for the outcomes of interest together with the number of studies and study identifiers. Comparative effectiveness results are only shown for outcomes where effect sizes could be calculated.

Table 23. KQ2 Summary of Findings and Strength of Evidence for Provider Interventions

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	SoE
KQ2 provider interventions vs control	Behavior	0 studies	N/A	Insufficient
KQ2 provider interventions vs control	Broadband measures	1 RCT[454]	Results favored intervention (SMD -0.36; CI -0.65, -0.07; 1 study, n=263)	Insufficient
KQ2 provider interventions vs control	ADHD symptoms	5 RCTs[258, 259, 306, 378, 454]	Conflicting results (SMD 0.26; CI -4.79, 5.31; 2 studies; n=537)	Insufficient

5. Results: Treatment of ADHD

Intervention and Comparison	Outcome	Number of Studies; Study Design and IDs	Findings	SoE
KQ2 provider interventions vs control	Functional impairment	0 studies	N/A	Insufficient
KQ2 provider interventions vs control	Acceptability of treatment	0 studies	N/A	Insufficient
KQ2 provider interventions vs control	Academic performance	0 studies	N/A	Insufficient
KQ2 provider interventions vs control	Appetite suppression	0 studies	N/A	Insufficient
KQ2 provider interventions vs control	Participants with adverse events	0 studies	N/A	Insufficient
KQ2 Tele-psychiatry program vs single consultation	ADHD symptoms	1 RCT[440]	Results favored the tele-psychiatry program (SMD -0.54; CI -0.81, -0.27; RR 1.64; CI 1.09, 2.47; 1 study, n=223)	Insufficient
KQ2 Tele-psychiatry program vs single consultation	Functional impairment	1 RCT[440]	Results favored the tele-psychiatry program (SMD 0.27; CI 0.01, 0.54; 1 study, n=223)	Insufficient

Notes: CI 95% confidence interval, KQ key question, N/A not applicable, RR relative risk, RCT randomized controlled trial, SMD standardized mean differences, SoE strength of evidence

Studies reported on very different intervention approaches and studies were difficult to compare and 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 difficult to determine whether interventions do affect the outcomes of interest (ADHD symptoms).

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

5.4.1 Key Points KQ2a Effect of Presentation

- We did not detect differential treatment effects associated with ADHD presentation, but analyses were based on indirect comparisons and should be interpreted with caution.
- We identified only a small number of studies systematically addressing co-occurring disorders, and evidence is insufficient for concrete evidence statements.

Table 24 documents the results across studies.

Table 24. KQ2a Summary of Findings and Strength of Evidence for ADHD Interventions

Intervention and Comparison	Outcome	Number of Studies; Study	Findings	SoE
KQ2a effect modifier ADHD presentation	Behavior changes	N/A	Indirect comparisons did not suggest an effect	Low for no effect
KQ2a effect modifier ADHD presentation	Broad-band scale score	N/A	Indirect comparisons did not suggest an effect	Low for no effect
KQ2a effect modifier ADHD presentation	Standardized symptom scores	N/A	Indirect comparisons did not suggest an effect	Low for no effect
KQ2a effect modifier ADHD presentation	Functional impairment	N/A	Indirect comparisons did not suggest an effect	Low for no effect
KQ2a effect modifier ADHD presentation	Acceptability of treatment	N/A	Indirect comparisons did not suggest an effect	Low for no effect
KQ2a effect modifier ADHD presentation	Academic performance	N/A	Indirect comparisons did not suggest an effect	Low for no effect
KQ2a effect modifier ADHD presentation	Appetite suppression	N/A	Indirect comparisons did not suggest an effect	Low for no effect
KQ2a effect modifier ADHD presentation	Participants with adverse events	N/A	Indirect comparisons did not suggest an effect	Low for no effect
KQ2a effect modifiers co-occurring disorders	Behavior changes	N/A	Indirect comparisons did not detect effects, but few studies addressed co-occurring disorders systematically	Insufficient
KQ2a effect modifiers presentation and co-occurring disorders	Broad-band scale score	N/A	Indirect comparisons did not detect effects, but few studies addressed co-occurring disorders systematically	Insufficient
KQ2a effect modifiers presentation and co-occurring disorders	Standardized symptom scores	N/A	Indirect comparisons did not detect effects ,but few studies addressed co-occurring disorders systematically	Insufficient

Intervention and Comparison	Outcome	Number of Studies; Study	Findings	SoE
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	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	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	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	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	Insufficient
KQ2b diversion	Misuse	2 studies[444, 485]	Did not indicate any issues	Insufficient

Notes: CI 95% confidence interval, KQ key question, N/A not applicable, RR relative risk, RCT randomized controlled trial, SMD standardized mean differences, 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.

5.5 KQ2a. How do outcomes vary by presentation 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.

5.5.1 ADHD Presentation

Most studies included a range of ADHD presentations. However, we identified one study that only included participants with inattentive ADHD presentation.[464] The study evaluated an integrated psychosocial treatment approach; results are documented in the evidence table in the appendix. A number of studies included only children with combined presentation.[111, 156, 234, 264, 295, 348, 427, 432, 496, 497, 510, 554, 624] The studies evaluated diverse interventions. Half of the studies

restricting to the combined presentation evaluated FDA-approved pharmacological treatments, and 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 the presentation in indirect comparisons across studies and we documented results of subgroup analyses as reported by the individual authors.

5.5.1.1 Indirect analyses

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 0.09), hyperactive (p 0.23), or combined (p 0.32) 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 0.74, categorical data p 0.90), hyperactive (continuous data p 0.67, categorical data p 0.92), or combined (continuous data p 0.34, 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 0.55), hyperactive (p 0.70), or combined (p 0.52) 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). Results for hyperactive (p 0.17) and combined (p 0.41) presentation were not statistically significant.

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 or 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 in the continuous data analyses, i.e., results for inattentive (p 0.39), hyperactive (p 0.24), or combined presentation (p 0.52) were not significant across all included interventions. However, for the equivalent analyses for the more commonly reported outcome analyzing appetite suppression as categorical data, effects for the combined presentation was borderline (p 0.05). Results for inattentive (p 0.18) or hyperactive (p 0.31) presentation did not indicate a systematic effect. Similarly, across studies, 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.

5.5.1.2 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,[115, 172, 304, 430, 526, 545] a new pharmaceutical agent,[625] psychosocial interventions;[171, 511] cognitive training;[174] nutritional supplements;[308, 343, 401, 498] and provider training,[378] 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.[174] 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).[343] One omega 3 and zinc study[498] 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[115] 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. A further study reported no significant treatment interaction between relapse and the ADHD presentation.[172] 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).[304] A study assessing the effects of omega 3[308] 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.[378]A study of atomoxetine[430] 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[545] 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 ($p<.01$) on the ADHD-RS-IV scale and for doses above 10mg on CGI Impression Scores ($p<.01$). One study evaluating pantogam[378] 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 Rating Scale-IV Scores explored whether children rated with abnormal scores in 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.[401] A behavioral sleep intervention for children with ADHD[511] 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. 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).[526]

5.5.2 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 defiance disorder or conduct disorder,[159, 182, 211, 224, 231, 260, 267, 317, 422, 612] learning disabilities,[225, 469, 514, 526, 564, 590, 613] sleep conditions,[324, 418, 501, 511] mood disorders such as depression and anxiety,[138, 292, 371] tic disorders,[125, 374, 528, 544] traumatic brain injury,[375] epilepsy,[265] substance use disorder,[485] iron deficiency,[466] genetic disorders,[120] or organizational deficits,[113] 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 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;[339] children with comorbid anxiety, particularly those with overlapping disruptive disorder comorbidities, showed preferential benefits to the intervention;[835] no detrimental effect of anxiety on medication response for core ADHD or other outcomes in anxious or non-anxious ADHD children was demonstrated[876]; 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[908]; 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% of the MTA sample without anxiety at baseline displayed a response to treatment that was close to that of the overall sample, the 34% with comorbid anxiety showed a relatively better response to the behavioral aspects of the MTA treatments.[802] Parent-reported anxiety and ODD/CD 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.[834] 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.[835] A further study[449] 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.[139] 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 the evidence table.

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 0.93, ODD p 0.32). For broadband scale scores, we also found no systematic effect (sleep p 0.85, ODD p 0.68, learning disability p 0.11). Symptom scores provided the most data for the comparisons; however, the analysis did not detect systematic effects (sleep p 0.61, ODD p 0.66, learning disability p 0.83, coordination disorder p 0.77). For functional outcomes also, results were not statistically significant (sleep p 0.93, ODD p 0.57). Treatment satisfaction could not be evaluated due to the small number of studies. Appetite suppression was not significant (ODD p 0.69, learning disability p 0.24), nor was adverse events (sleep p 0.94, ODD p 0.87).

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?

5.6.1 Key Points KQ2b

Only two studies reported on diversion and it was not possible to quantify the risk of diversion of pharmacological treatment

Only two studies met inclusion criteria for KQ2b.[444, 485] One was an RCT evaluating either 200 or 400 mg viloxazine vs placebo and found no evidence for misuse.[444] Viloxazine, however, is a non-stimulant (SNRI) 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 .[485] 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. On the other hand, 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.

6. Results: Monitoring ADHD

6.1 KQ3 ADHD Monitoring Key Points

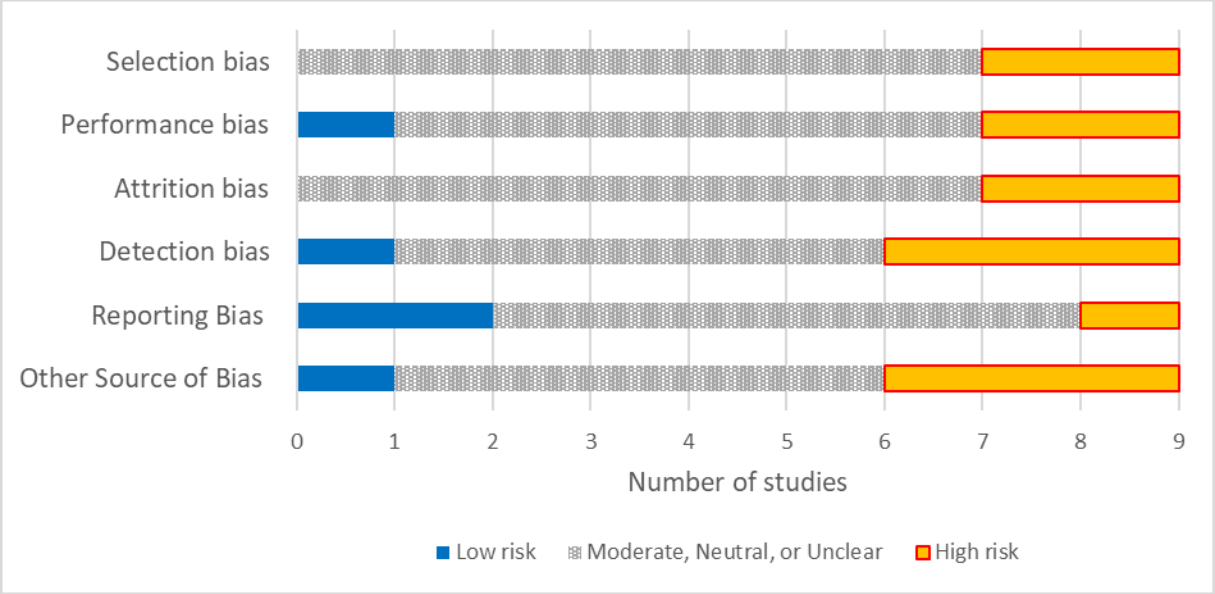
- Very few monitoring studies have been reported and more research is needed on how youth with ADHD should be monitored over time.
- Different assessment modalities may provide valid but different perspectives and more than a single assessment modality may be required for comprehensive and effective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

6.2 KQ 3 ADHD Monitoring Summary of Findings

We identified a small number of studies addressing a monitoring strategy.[181, 207, 258, 259, 271, 277, 454, 534, 617] Results of the individual studies are shown in the evidence table in the appendix. 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 76. The critical appraisal for the individual studies is in Appendix D.

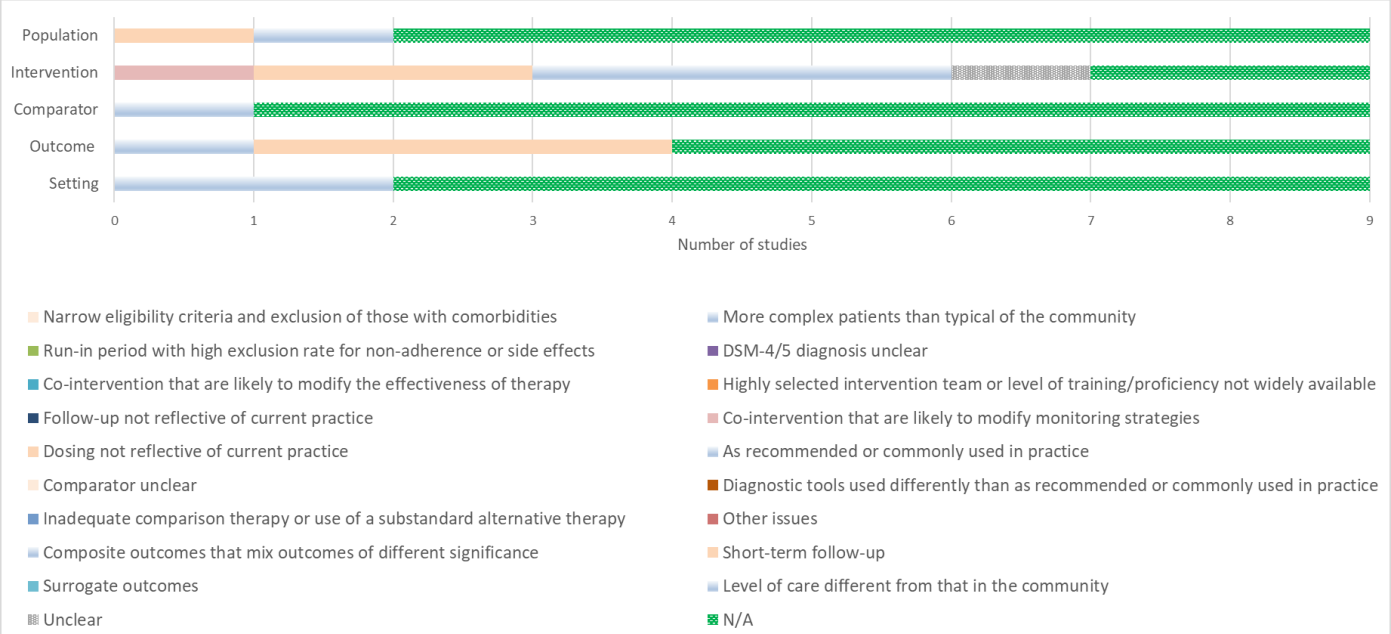
Figure 76. Risk of Bias in KQ3 Studies



Across studies, selection bias was likely present in two studies.[277, 454] Performance bias was present in two studies.[271, 277] Attrition bias was also present in two of the identified studies.[181, 207] Detection bias was determined to be present in three studies.[181, 277, 454] Reporting bias was likely in one study.[534] In the small set of studies, a third were rated as high risk of bias for other sources.[258, 271, 617]

Figure 77 shows the distribution of applicability issues in KQ3 studies. The applicability for the individual studies is in Appendix D.

Figure 777. KQ3 Applicability Rating



Given the small number of available studies, results of the different monitoring strategies are documented in Table 25.

Table 25. KQ3 Monitoring Strategies Evidence

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[181] Göteborg University, 2017[768] 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	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 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.

6. Results: Monitoring of ADHD

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**
	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		
Cohen, 1989[207] 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, short-acting methylphenidate administered twice daily for 1 month, with measures collected at baseline, 1	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; 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**
		month (the time of crossover), and 2 months (endpoint).	
Epstein, 2007[259] 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.	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.

6. Results: Monitoring of ADHD

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
		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	
Epstein, 2016[258] Childrens Hospital Medical Center, Cincinnati, 2010[692] ID: NCT01143701 Cluster RCT Multicenter N = 577 US Setting: Primary Care	**Target:** 577 patients in grades 1 through 5, presenting for ADHD evaluation, and were ADHD medicaInaive 50 community-based pediatric primary care practices with ≥2 physicians (213 providers), 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 **Co-occurring disorders:** N/A **Female:** 29.5 % **Age mean:** 7.8 (1.4) **Minimum age:** **Maximum age:** **Ethnicity:** Other info on race or ethnicity: Other : 36.7% were –on-white – unspecified	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[271] Childrens Hospital of Philadelphia, 2014[693] ID: NCT02271386	**Target:** Children aged 5-12 years with ADHD diagnosis; children with autism spectrum disorder excluded. 105 clinicians practicing at 19 sites within a	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	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-

6. Results: Monitoring of ADHD

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**
Cluster RCT Multicenter N = 790 US Setting: Primary Care	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:	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	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[277] 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	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	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

6. Results: Monitoring of ADHD

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
	Minimum age: **Maximum age:** **Ethnicity:** Other info on race or ethnicity: N/A	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	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[454] Boston Childrens Hospital, 2014[678] 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.
Smith, 2000[534] ID: N/A Cohort study Single center N = 36	**Target:** 36 adolescents who completed a summer treatment program; 12 years and older; diagnosis meets DSM-III criteria; verbal IQ higher	**Intervention:** assessed the reliability, validity, and unique contributions of self-reports by adolescents receiving treatment for ADHD in a summer treatment program that	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

6. Results: Monitoring of ADHD

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**
US Setting: Specialty care	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:	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	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 intormation about improved interactions with others in response to treatment.
Yang, 2012[617] 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	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.

6. Results: Monitoring of ADHD

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
	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		

We identified 9 studies addressing some type of monitoring strategy for ADHD.[181, 207, 258, 259, 271, 277, 454, 534, 617] 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[534] or between assessment modalities (e.g., rating scale vs computerized performance test).[181, 207] Both subjective assessment modalities (e.g., self-report, parent, teacher, and clinician rating scales)[181, 207, 534] and more objective measurement modalities (e.g., continuous performance task)[181] 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.[207]

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,[259] and two assessed the impact of a quality improvement intervention on outcome monitoring[271, 692] or ADHD symptoms.[692] Collectively, the studies showed that medication prescribers (mostly pediatricians) exhibited poor compliance in attending training programs for quality improvement in treating ADHD.[259, 271] 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,[259, 271] even when the intervention increased the collection of ratings compared with waitlist controls.[271] Moreover, pediatricians often did not prescribe stimulant medication for youth who met diagnostic criteria for ADHD,[258, 259] and when they did prescribe, the doses were sub-optimal,[258] even when provided intensive advice and support services from mental health specialists.[259] Youth whose prescribers participated in the consultative services from specialists, however, had greater reductions in ADHD symptom severity.[259] 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.[454] 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.[277] 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 assessed the use of an electronic bottle cap (the Medication Event Monitoring System) for stimulant medication to monitor treatment adherence.[617] 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 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 400 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 is good; 70 to 80 fair; 60 to 70 poor; and 50 to 60 indicates failed performance.

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.

AUCs for parent rating scales ranged widely from "poor"[335] to excellent,[620] with a low strength of evidence (SoE) due to imprecision and inconsistency. Only one study reported inter-rater reliability (between mothers and fathers), with an intraclass correlation coefficient of 0.51 for inattention, 0.56 for hyperactivity, and 0.58 for impulsivity, indicating moderate inter-rater reliability. Internal consistency for rating scale items was generally high across most rating scales.

AUCs for teacher rating scales ranged from "failed performance" (distinguishing ADHD from other patients[480]) to "good" (distinguishing ADHD from healthy controls or from patients with reading disability[352]) to "excellent" (distinguishing ADHD from typically developing controls),[455] again with a low SoE due to imprecision and consistency. The internal consistency for scale items was generally high. Teacher ratings demonstrated very low inter-rater reliability 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 poor specificity (35.7 per cent with associated sensitivity of 83.5 per cent) when using the Conners to distinguish ADHD from other clinically referred youth,[17] and a machine learning study reporting a diagnostic accuracy of 0.93 when using the BRIEF to distinguish ADHD youth from typically developing controls.[455]

Though data are limited, self-reports from youth seem to perform less well than corresponding parent and teacher reports, with AUCs ranging from 0.56 ("fail" for CBCL/ASEBA distinguishing ADHD from other patients)[480] to 0.71 ("fair" for the SWAN distinguishing ADHD from community controls).[176, 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 EEG biomarker for that patient (the reference standard was a consensus diagnosis from a panel of ADHD experts).**[26]** These findings were not independently replicated, and no test-retest reliability was reported.

AUCs for all biomarkers ranged from 0.68 (serum miRNAs)**[623]** to 1.00 (erythropoietin and erythropoietin receptors levels)**[307]** but with a low SoE. 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 7 year of age (Table 3).[175, 193, 326, 402, 406, 455] 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 ("good" AUC 0.83);[175] 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 ("good" AUC 0.81);[175] or the BRIEF to distinguish ADHD from typically developing controls (average diagnostic accuracy of 0.93). 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 7, though the two studies of rating scales suggest that performance may be comparable to performance of similar scales in youth older than 7.

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 0.63[201] to 0.97.[402] SoE is low due to large variations in diagnostic performance across studies, and often the methods for classification were not well described. The ICC for the Theta/Beta ratio, based on repeated measures on two different visits,[26] was 0.83.

AUCs ranged from "poor" for distinguishing ADHD youth without co-occurring disorders from healthy controls[1153] to "excellent" for distinguishing ADHD youth from healthy controls[567] in the neuroimaging studies. 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 a corresponding specificity of 80%)[187] to 98 percent (with a corresponding specificity of 92% or 99%).[165, 180] Using MRI data, sensitivity ranged from 61 percent (with a corresponding specificity of 68%)[1153] to 99 percent (with a corresponding specificity of 99%).[567] 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 SoE 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"[23, 266] to "excellent",[147] with a low SoE due to imprecision and inconsistency. 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 measures make the results of meta-analyses difficult to interpret. Extracting specific, comparable measures of inattention and impulsivity from CPTs yielded only fair diagnostic performance.[20, 23, 170] Only one diagnostic study assessed test-retest reliability, which was poor. No studies provided an independent replication of diagnosis using the same measure. SoE for CPT measures is low due to imprecision. Thus, despite the widespread use of neuropsychological testing in the evaluation of youth suspected as having ADHD, often at

considerable expense, 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 SOE 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.[455, 712]

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 (with a mode at 80%) was much narrower in community settings, 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 in their presentations than those presenting in clinical settings. We also found that the population appeared to modify diagnostic performance, in that specificity (the rate of identifying true negatives) was significantly lower when discriminating ADHD youth from neurotypical developing youth. A lower true negative rate indicated that clinically identified youth who did not have ADHD were mistakenly diagnosed as having ADHD, likely because they had symptoms or other non-specific aspects of clinical "caseness" that were confused with those of ADHD. Thus, the diagnostic group being differentiated from ADHD – whether it is a neurotypical "healthy" control, or youth who have a different emotional/behavioral/psychiatric disorder -- has a critical role in diagnostic performance. We found some indication that diagnostic performance was better for youth who were older compared with younger than 7 years of age (Figure 9), 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, 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.

Numerous classes of intervention yielded significant effects on measures of *ADHD symptom severity*. These included: FDA-approved medications collectively; psychosocial treatment; neurofeedback; nutrition or supplements; school interventions; and parent support. All had medium effect sizes, except small effects were observed for psychosocial interventions, parent support, neurofeedback, and nutrition and supplements. The SoE for effects on ADHD symptoms is high for FDA-approved medications; moderate for psychosocial interventions, neurofeedback, parent support, and school interventions; and low for nutritional interventions. We note that many of the studies for psychosocial interventions and parent support 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. Other studies compared the active intervention against one that did not adequately blind either participants or study assessors to the treatments and hypotheses.[1163, 1164] These limitations in study design considerably undermines the SOE for psychosocial and parent interventions. Similar considerations limit the SOE for studies of neurofeedback and nutrition and supplements.

For *broadband measures*, FDA-approved medications collectively yielded significant, medium-sized effects, parent support had significant small effects across four studies (low SOE), and cognitive training had medium effects across three studies (low SOE). For *disruptive behaviors*, only nutrition or supplements yielded significant but small effects across four different supplements (low SOE). For *functional impairments*, only FDA-approved medications collectively yielded significant effects that were medium-sized. No treatment modality yielded significant 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, with all individual studies yielding nonsignificant improvements of small effect size). We found only two studies for the effects of exercise, and two for the effects of complementary and alternative medicines, that met our inclusion criteria, and they did not yield significant improvement in any ADHD outcome domain. Thus, the large number of studies combined with their medium-to-large effect sizes allow us to conclude with a high SOE 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. Only one study assessed the effectiveness of an FDA-approved medication in improving academic performance, and it reported large, significant, and positive effects.

We also found benefits from more specific medication classes. *Stimulant medications*, for example, significantly improved broadband scale scores with medium effect sizes, with comparable effects for amphetamine and methylphenidate derivatives, though amphetamines yielded much more variable effects across studies. Only one study included children younger than six years of age.[116] Similarly, stimulants significantly improved ADHD symptoms, with modest but homogeneous effects across methylphenidate studies and large but highly variable effects across amphetamine studies. Stimulants significantly improved functional impairment, with large effect sizes. A newer stimulant medication, modafinil, produced significant

improvement in ADHD symptoms in each of four studies, though in aggregate the improvement was not statistically significant, due to effect size heterogeneity.

Non-stimulant medications collectively yielded significant improvements in ADHD symptom scores with a medium effect size; similar effect sizes were observed separately for the SNRIs and alpha agonists compared with placebo. Non-stimulants also improved broadband scale scores, with similar effects observed for the SNRI subclass. Only one study included children younger than six years old.[372] Non-stimulants reduced functional impairment with a significant but small effect size, and comparable effects observed for SNRIs alone (the effects of alpha agonists could not be assessed).

Medication therapies reported substantially more adverse events than did the other interventions, including appetite suppression, with a high SoE. Stimulants were associated with an increased reporting of adverse events compared with placebo, with a similar but nonsignificant effect of methylphenidate and a similar though significant effect of amphetamines on adverse events. Stimulants were associated with appetite suppression compared to placebo, with somewhat smaller effects for methylphenidate than for amphetamines. Modafinil significantly suppressed appetite, with very large effect sizes. Non-stimulants compared with placebo were associated with an increased number of participants reporting adverse events, with comparable rates in SNRI studies and alpha agonists. Non-stimulants were also associated with suppressed appetite compared to placebo, with significant appetite suppression from SNRIs but much weaker and non-significant effects from alpha agonists.

The most common head-to-head comparison between two alternative medication treatments was atomoxetine vs methylphenidate,[144, 370, 448, 500, 513, 527, 593, 632] which did not detect significant differences in effects on ADHD symptoms,[144, 370, 448, 527, 593, 632], broadband measures,[370, 448, 527, 593] behavioral problems[448, 513], functional impairment, appetite suppression,[370, 500, 527, 593, 632] or the number of patients experiencing adverse events, though the direction of effects consistently favored methylphenidate. Indirect comparison of studies evaluating stimulants and non-stimulants compared to control groups, however, showed larger reported effect sizes for stimulants providing much greater improvement for ADHD symptoms and functional impairment, while effect sizes for broadband measures and appetite suppression were comparable. We did not identify head-to-head comparisons of SNRIs versus alpha agonists that met eligibility criteria.

We found no evidence that interventions are better when delivered in combination than as monotherapies. Furthermore, our findings suggest that combined medication and behavioral therapies do not improve ADHD symptoms better than either medication or behavioral therapy alone. We note, however, that these analyses do not consider the possibility that exact sequencing of psychological and medication therapies may produce differential effects on outcomes.[52, 208]

Variation in Outcomes by Clinical Presentation

We found little evidence that treatment outcomes varied by ADHD presentation.

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 RCT comparing stimulant plus 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 nine 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[534] or between different assessment modalities (e.g., rating scale with computerized performance test).[181, 207] 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.[181, 534] 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.[207]

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.[258, 259, 271] Despite very extensive training efforts, and even when expert support and consultation was available,[259] pediatricians exhibited poor compliance in attending training programs for treating ADHD,[259, 271] 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.[259]

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.[277] 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.[617]

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 AHRQ reviews on ADHD.[11, 50] 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)[1165], which in turn was the primary source for the recommendations from the US Center for Disease Control for the diagnosis and treatment of ADHD.[1166]

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.[25, 26] 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 SOE 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 provided showed that stimulant and non-stimulant medications yielded comparable effects on most effectiveness outcomes when these medications were compared head-to-head, though the overall direction of effects across all outcomes tended to favor stimulant medications. Clinical guidelines advise starting treatment for youth older than 6 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 many studies that did not meet criteria for inclusion in our review. The 2018 review also found that parent training improved ADHD symptoms, though 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. We found low SoE that cognitive training does not improve ADHD symptoms, and moderate SOE that neurofeedback does. Clinical guidelines do not currently recommend neurofeedback as a second line treatment, but should consider doing so. We also found, with low SOE, that nutritional supplements and dietary interventions improve

ADHD symptoms and problem behaviors. The SOE for nutritional interventions is still too low to recommend 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 9 such papers. The APA and CDC clinical guidelines do not include recommendations for monitoring strategies.

Implications

ADHD treatment guidelines should educate clinicians on 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 symptom 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 MRI are not yet close to being ready to aid clinical diagnosis. Ultimately, a valid and reliable diagnosis of ADHD requires the judgement 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 SNRIs atomoxetine and viloxazine, as well as the alpha agonists clonidine and guanfacine), individual psychosocial treatments, neurofeedback, nutritional interventions, and school interventions (often combined with parent training). 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 SNRI 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[1165, 1167, 1168] should consider that successful combinations showing clear superiority still need to be explored and identified. A further finding of this review with clinical implications is that only FDA-approved medications have been shown to 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 400 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.

Space limitations precluded a more detailed parsing of putative diagnostic tools (such as similar rating scales or specific domains of cognitive functioning) and medication classes across the large number of available treatments. Those finer-grained analyses will be the subject of future publications. Moreover, 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 more smaller 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. 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 (KQ1c 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. Because studies did not compare effects in direct, head-to-head comparisons, we had to explore modifiers indirectly, across studies. Future studies of ADHD should more systematically address the modifier effects of these patient characteristics. Much more research is needed in the use of diagnostic tools, effectiveness of medication and other therapies, and monitoring strategies in preschool youth 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.[181] 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.[1169] 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 SOE for the effectiveness of the interventions assessed, including active attention comparator conditions and effective blinding of participants and assessors to study interventions and hypotheses.[1163, 1164] 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, treatment effectiveness across a wide array of interventions and outcomes, medication diversion, and adverse effects associated with treatment.

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, 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 treatment and outcomes in ADHD youth. The temporal stability of outcome measures and their sensitivity to change in response to treatment should be assessed. Future synthetic studies should 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.

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Abbreviations and Acronyms

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
e.g.	exempli gratia
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
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	The 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 Risks
SEADS	Submit Supplemental Evidence and Data for Systematic Reviews
SMART	Sequential Multiple Assignment Randomized Trial
SMD	standardized mean differences

SNAP-IV	Swanson, Nolan, and Pelham (SNAP) Questionnaire
SNRI	Serotonin and norepinephrine reuptake inhibitor
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
TEP	Technical Expert Panel
TOO	Task Order Officer
TRF	Teacher Report Form
UK	United Kingdom
US	United States

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 "Diagnostic and Statistical Manual of Mental Disorders"[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 DSM[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 accuracy[tiab] OR accurate[tiab] OR accurately[tiab] OR misdiagnos*[tiab] OR (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 "cohort studies"[MeSH] OR cohort[tiab] OR "longitudinal studies"[MeSH] OR "longitudinal"[tiab] OR longitudinally[tiab] OR "prospective"[tiab] OR prospectively[tiab] OR "comparative study"[pt] OR "comparative study"[tiab] OR systematic[sb] 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])
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
humans[mh]
8
English[la]
9
#1 AND #2 AND #3 AND #4 NOT #5 NOT #6 NOT #7 AND #8
PUBLICATION DATE RANGE: 2016 to Jan 2023

KQ #2

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 "retrospective"[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
humans[mh]
7

English[la]
8
#1 AND #2 AND #3 NOT #4 NOT #5 NOT #6 AND #7
PUBLICATION DATE RANGE: 1980 to Jan 2023

PsycInfo

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 "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

(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

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(((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)

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"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)))) 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
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
'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"]
#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

ADHD 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: To January 2023

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") AND (RTYPE "journal article")
#5
#1 AND #2 AND #3 AND #4
#6
#5, English
Publication Date Range: To 2021

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 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

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 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)
#5
#1 AND #2 AND #3 AND #4
#6
#5 AND [humans]/lim
#7
#6 AND [embase]/lim NOT [medline]/lim

Publication Date Range: To 2021

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
#10
Limit to CDSR

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

Appendix B. List of Excluded Studies

This appendix shows the list of excluded studies with reasons for exclusion. We only recorded one reason per publications.

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. 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*

15. Abadi MS, Madgaonkar J, Venkatesan S. Effect of yoga on children with attention deficit/hyperactivity disorder. Psychological Studies. 2008;53:154-9. *Power*

16. 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*

17. 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*

18. 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*

19. 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*

20. 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*

21. 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. *Outcome*

22. 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*

23. 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*

24. 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*

25. 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*

26. 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*

27. 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*

28. 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*

29. 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*

30. 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*

31. 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*

32. 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*

33. 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*

34. 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*

35. 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*

36. 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*

37. 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*

38. 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*

39. 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. *Design*

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Background

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Appendix C. Evidence Tables

Table C.1. KQ1 evidence table
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Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
Activity	Amado-Caballero, 2020[128] Case series N = 148 Spain Setting: N/A	**Target:** 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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Clinicians diagnosis using DSM-5 Timing: Prior diagnosis **Index test:** 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 PPV: 100 70%/30% train/test with 300 second window size NPV: 98 70%/30% train/test with 300 second window size LR+: 21 70%/30% train/test with 300 second window size LR-: 0.0238 70%/30% train/test with 300 second window size	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Accuracy: 99 70%/30% train/test with 300 second window size AUC: 0.9993 70%/30% train/test with 300 second window size Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Specificity: PPV: NPV: AUC: **Index text 5:**
Activity	Lindhiem, 2022[394] Case series N = 30 US Setting: N/A	**Target:** Recruited via a web-based research registry through the University of Pittsburgh's Clinical and Translational Science Institute program; not on medication during the testing period **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%	**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 **Index test:** Activity LemurDx app prototype on Apple smarwatch tracking motion, heart rate, and location of participants paired with acitivity labels in 30 minute increments reported by the parents; random forest classifier, leave-one-participant-out cross validation; pilot study	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		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 info on race or ethnicity: Other : 7% race not reported	Sensitivity: 93 Specificity: 86 PPV: 87 NPV: 92 LR+: LR-: Accuracy: 89 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Activity	Martin-Martinez, 2012[406] 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	**Reference standard:** Clinical diagnosis Diagnosed as having the combined kind of ADHD according to the DSM-IV criteria. Timing: Prior diagnosis **Index test:** Activity Nonlinear signal processing of 24 h-long actigraphic registries Sensitivity: 97 By means of multidimensional classifiers driven by	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Age mean: N/A **Min age:** 6 **Max age:** 6 **Ethnicity:** Other info on race or ethnicity: N/A	combined features from different time intervals Specificity: 84 By means of multidimensional classifiers driven by combined features from different time intervals PPV: NPV: LR+: LR-: 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 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
Biomarker	Das, 2021[218] Case series N = 50 Multiple countries Setting: Mixed	**Target:** Not on stimulant medication; recruited from elementary schools in Chile **Other:** Healthy children **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 14% **Age mean:** N/A **Min age:** 10 **Max age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Diagnosis of ADHD and ADHD-C according to DSM-IV criteria Timing: Prior diagnosis **Index test:** Biomarker 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. Support vector machine (SVM) classifier, nested 10-fold cross validation Sensitivity: 77 Support vector machine classifier Specificity: 75 Support vector machine classifier PPV: NPV: LR+: LR-: Accuracy: 76 Support vector machine classifier AUC: 0.856 Support vector machine classifier Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Misdiagnosis: Labeling: Costs:	**Index text 5:**
Biomarker	Gungor, 2021[307] Case series N = 70 Turkey Setting: N/A	**Target:** 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 info on race or ethnicity: Other	**Reference standard:** Clinical diagnosis Clinical diagnosis using DSM-5 Timing: Prior diagnosis **Index test:** Biomarker Serum erythropoietin levels Sensitivity: 100 Specificity: 97 PPV: NPV: LR+: LR-: Accuracy: AUC: 0.980 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs:	**Index test 2:** Biomarker Serum erythropoietin receptor levels Sensitivity: 100 Specificity: 100 PPV: NPV: LR+: Accuracy: AUC: 1.00 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Misdiagnosis: Labeling: Costs:	LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Biomarker	Roessner, 2007[489] Case series N = 66 Germany Setting: Specialty care	**Target:** Children and Adolescents in Germany who were patients of specialty clinics, 18 of the 42 ADHD participants were on stimulant medication at the day of urine sampling; 16 had one or more coexisting psychiatric problems including conduct disorder (n=13), learning disorders (n=4), tic disorders (n=2), and others (n=5) **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:**	**Reference standard:** Clinical diagnosis All children were referred and fulfilled DSMIV-TR criteria for ADHD. Timing: Prior diagnosis **Index test:** Biomarker tetrahydroisoquinolines (TIQ) urine levels: Salsolinol (free) Sensitivity: 56 Specificity: 95 PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement: Kappa:	**Index test 2:** Biomarker tetrahydroisoquinolines (TIQ) urine levels: N-methyl-Salsolinol (free) Sensitivity: 93 Specificity: 94 PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Other info on race or ethnicity: N/A	ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 3:** biomarker tetrahydroisoquinolines (TIQ) urine levels: Norsalsolinol (free) Sensitivity: 88 88 Specificity: 80 PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** biomarker tetrahydroisoquinolines (TIQ) urine levels: N-methyl-Norsalsolinol (free) Sensitivity: 69 Specificity: 94 PPV: NPV: AUC: **Index text 5:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
Biomarker	Stepanova, 2021[551] Case series N = 64 US Setting: School	**Target:** Recruited from community advertisements and physician referrals; not currently taking psychostimulants, 46% provided another blood draw 30 days after receiving psychostimulants; children with bipolar disorder excluded **Other:** Children without ADHD **ADHD presentation:** inattentive : 33.3,hyperactive : 0,combined : 66.7 **Diagnosed by:** Provider **Comorbidity:** N/A **Female:** 33.3% **Age mean:** 11.61(3.30) **Min age:** 6 **Max age:** 17 **Ethnicity:** % Hispanic or Latino : 12.5 % Black/African American : 70.8 % Asian : 0 % White : 8.3 Other info on race or ethnicity: Other : 20.8	**Reference standard:** Clinical diagnosis Completed Mini-International Neuropsychiatric Interview 7 and was evaluated by a clinical psychiatrist Timing: Prior diagnosis **Index test:** Biomarker Membrane potential ratio (MPR). ADHD cutoff score provided by the MPR™ test developers of >0.75 is considered positive for ADHD. Sensitivity: 79 Specificity: 25 PPV: NPV: LR+: LR-: Accuracy: 55 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Index text 5:
Biomarker	Wang, 2018[592] Case series N = 40 Taiwan Setting: Specialty care	**Target:** Medication naive; no major physical illnesses (such as genetic, metabolic, or infectious conditions) or a history of comorbid major neuropsychiatric diseases (such as intellectual disabilities, autism spectrum disorder, bipolar disorders, major depressive disorders, psychotic disorders, substance use disorders, epilepsy, or severe head trauma) **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	**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-based diagnostic panel using 13 miRNA candidate biomarkers, SVM classifier Sensitivity: 90 For test group Specificity: 80 For test group PPV: NPV: LR+: LR-: Accuracy: 85 For test group AUC: 0.91 Test set Rater agreement: Kappa: ICC:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		Ethnicity: % Asian : 100,Other : Han Chinese Other info on race or ethnicity:	Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Biomarker	Zadehbagheri, 2019[623] 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 of the participants 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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Diagnosed with ADHD based on DSM-IV with structured interview Timing: Concurrent **Index test:** Biomarker Biomarker miRNA: hsa-miR101-3p Sensitivity: 82 Specificity: 95 PPV: NPV: LR+: LR-: Accuracy: AUC: 0.959 Rater agreement: Kappa: ICC: Internal consistency:	**Index test 2:** Biomarker Biomarker miRNA: hsa-miR-106b-5p Sensitivity: 86 Specificity: 82 PPV: NPV: LR+: Accuracy: AUC: 0.942 Rater agreement: Kappa: Internal consistency: Alpha: Costs:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 3:** biomarker Biomarker miRNA: hsa-miR-138-5p Sensitivity: 82 82 Specificity: 79 PPV: NPV: LR+: Accuracy: AUC: 0.856 Rater agreement: **Index text 4:** biomarker 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 PPV: NPV: AUC: 0.68 **Index text 5:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
Clinician rating scale	Lau, 2018[377] Case series N = 3,464 Canada Setting: Specialty care	**Target:** Data were collected from 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:** Other info on race or 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 rating scale The 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 (n=2849) 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 PPV: NPV: LR+: LR-: Accuracy: AUC: 0.79 Rater agreement: Kappa: ICC:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Internal consistency: Standardized Cronbach's Alpha (using polychoric correlations) Alpha: 0.86 Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index text 5:**
Clinician rating scale	Robles, 2021[487] Case series N = 52 Mexico Setting: Specialty care	**Target:** Those without the presence of communication difficulties, cognitive dysfunctions, and disabilities; seeking mental health services at two specialized psychiatric care facilities in Mexico City **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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Two psychiatrists independently established diagnosis, blind to each others evaluation Timing: Concurrent **Index test:** Clinician rating scale 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. Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			AUC: Rater agreement: 2 clinicians, one conducted the interview, the other was observer Kappa: 0.46 ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Combined rating	Francois-Sevigny, 2022[279] 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 a mental health disorder such as anxiety and depression were included; children with ASD or intellectual disablility were excluded **Other:** Gifted children;IQ>=130 on the Full-Scale Intelligence Quotient or the General Aptitude Index of the Wechsler Intelligence Scale for Children 5th edition **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** 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 **Index test:** Combined rating Conners 3 content scales teacher and parent ratings; discriminant function analysis with 3 categories (ADHD+gifted vs ADHD vs gifted)	**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) Sensitivity: 70% of the ADHD+gifted children were correctly classified, 66% of the ADHD children were correctly classified Specificity: 100 PPV: NPV: LR+: Accuracy: 76

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Female: 29% **Age mean:** 9.85 (2.51) **Min age:** 6 **Max age:** 16 **Ethnicity:** Other info on race or ethnicity: N/A	Sensitivity: 72% of the ADHD+gifted children were correctly classified, 68% of the ADHD children were correctly classified Specificity: 100 PPV: NPV: LR+: LR-: Accuracy: 78 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Gifted children may exhibit behaviors that look similar to the characteristics of ADHD, contributing to misdiagnosis. The fact that the only differences between gifted/ADHD children and ADHD children were observed in terms of hyperactive–impulsive symptom Labeling: Costs:	AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
Combined rating	Gibbons, 2020[297] Case series N = 801 US Setting: Specialty care	**Target:** English speakers only. Children were excluded if they had 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 Other info on race or ethnicity:	**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 Kiddie-Computerized adaptive test (K-CAT) 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 PPV: NPV: LR+: LR-: Accuracy: 86 AUC: 0.86 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 2:** Parental rating scale Kiddie-Computerized adaptive test (K-CAT) using combined item response scale scores from parent. The test was administered using tablet computers. 3-fold cross validation Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: 0.85 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Teen/child self report Kiddie-Computerized adaptive test (K-CAT) using combined item response scale scores from child. The test was administered using tablet computers. Items were tested for readability using the Flesch-

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Kincaid reading grade level. The overall average reading Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: 0.71 Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Combined rating	Longridge, 2019[396] Case series N = 288 UK Setting: Specialty care	**Target:** Secondary analysis of a cohort of children attending two child and adolescent mental health serivices between 2006 and 2009 **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%	**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	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 info on race or ethnicity: Other : 31% Black and Minority ethnicity	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 Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC: 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 ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
Combined rating	Oztekin, 2021[455] Case series N = 162 US Setting: Mixed	**Target:** IQ>=70. No confirmed history of Autism Spectrum Disorder. 70% had a comorbid oppositional defiant disorder or conduct disorder diagnosis. Recruited from local schools and mental health agencies via brochures, radio and newspaper ads, and open houses/parent workshops **Other:** Typically developing children **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 26% **Age mean:** mean 5.55 **Min age:** 4 **Max age:** 7 **Ethnicity:** % Hispanic or Latino : 82.6 Other info on race or ethnicity:	**Reference standard:** Clinical diagnosis Computerized-Diagnostic Interview Schedule for Children and Disruptive Behavior Disorders Rating Scale, Impairment Rating Scale Timing: Prior diagnosis **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 vector machine (SVM) classifier, 5-fold cross validation Sensitivity: 74 Specificity: PPV: 94 NPV: LR+: LR-: Accuracy: 93 AUC: 0.982 Rater agreement: Kappa: ICC: 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. Alpha:	**Index test 2:** neuropsychological,EF Executive function tasks: Flanker task, the Dimensional Change Card Sorting task, and the Head-Toes-Knees-Shoulders task. Support vector machine (SVM) classifier, 5-fold cross validation Sensitivity: 64 Specificity: PPV: 71 NPV: LR+: Accuracy: 67 AUC: 0.738 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Imaging Structural MRI scans assessing neural measures of cortical thickness in target regions that support executive function. Support vector machine (SVM) classifier, 5-fold cross validation Sensitivity: 65 65 Specificity:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Test-retest: Costs: Misdiagnosis: Labeling: Costs:	PPV: 64 NPV: LR+: Accuracy: 61 AUC: 0.624 Rater agreement: **Index text 4:** Imaging Full model includes demographics, parent/teacher 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 structural Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
Combined rating	Parker, 2016[17] McGonnell, 2009[882]; Davidson, 2016[712] Case series N = 279 Canada Setting: Specialty care	**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 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:** Other info on race or 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 **Index test:** Combined rating Teacher Telephone Interview and Parent Interview for Child Symptoms combined Sensitivity: 92 Specificity: 71 PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling:	**Index test 2:** Combined rating Conners Teacher Rating Scale and Conners Parent Rating Scale combined Sensitivity: 84 Specificity: 36 PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Teacher rating scale The Behavior Rating Inventory of Executive Functioning teacher rating[712] Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Costs:	**Index text 4:** Parental rating scale The Behavior Rating Inventory of Executive Functioning parent rating[712] Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Combined rating	Sullivan, 2007[557] Case series N = 92 US Setting: Other	**Target:** Subset of participants 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 **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	**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 Behavior Rating Inventory of Executive Function (BRIEF) parent and teacher forms Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC:	**Index test 2:** Combined rating Conners' Parent Rating Scale-Short Form (CPRS) and Conners' Teacher Rating Scale- Short Form (CTRS) Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Parent ratings on the Conners' scales were significantly correlated with teacher ratings on the same scales Kappa: Internal consistency:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Ethnicity: % Hispanic or Latino : 8 % Black/African American : 11 % Asian : 1 % White : 80 Other info on race or ethnicity:	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) Kappa: ICC: Range 0.31 to 0.59 (median 0.48) over 11 subscales Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Abramov, 2019[118] Case series N = 39 Brazil Setting: N/A	**Target:** ADHD boys without a history of chronic diseases, and without suspicion of psychiatric disorders other than ADHD (psychosis, affective, obsessive-compulsive and tic disorders, phobic and post-traumatic stress conditions, anorexia, bulimia, encopresis, or enuresis) as screened by K-SADS-PL; (2) No use of any psychotropic medicines for at least 30 days; (3) estimated Intelligence Quotient (I.Q.) equal or lower than 80; and (4)no less	**Reference standard:** Clinical diagnosis Classified as ADHD in accordance with the DSM-IV-TR Timing: Prior diagnosis **Index test:** EEG Attentional Network Test with recordings of event-related potentials from the mid-frontal, mid-parietal, right frontal, and central scalp areas (C3-C4, F8, F4, Fz, Pz) for a biological classification	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		than 6 h of regular sleep and (5)no report of somnolence before the ANT testing **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:** Other info on race or ethnicity: N/A	using the clustering of variables method. 80/20 train/test split repeated 100 times. Sensitivity: 89 Specificity: 75 PPV: NPV: LR+: LR-: Accuracy: 82 AUC: Rater agreement: Agreement between DSM and behavioral/psychological/neurophysiological data Kappa: 0.75 ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
EEG	Ahmadi, 2021[122] Case series N = 40 Iran Setting: Specialty care	**Target:** Right handed children, none had any neuro-feedback or any other neuro-modulation treatment, none had been treated with methylphenidate, 13 with ADHD combined and 12 with ADHD inattention presentation; all selected from Hamrah Child and Adolescent Multidisciplinary Neuropsychiatric Center, Tabriz, Iran **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:** Other info on race or 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 blind Timing: Prior diagnosis **Index test:** EEG EEG, eyes open resting-state; spatial and frequency band feature extraction and classification 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 PPV: NPV: LR+: LR-: Accuracy: 99 AUC: Rater agreement: Comparison of model accuracy with expected accuracy (chance level) Kappa: 0.99 ICC: Internal consistency:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index text 5:**
EEG	Altınkaynak, 2020[127] Case series N = 46 Turkey Setting: Specialty care	**Target:** ADHD referrals from university hospital psychiatry department, all were drug-naïve, without neurological conditions or hearing problems, all were 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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Psychiatrists used DSM-IV to diagnose patients with ADHD Timing: Prior diagnosis **Index test:** EEG Time and frequency analysis of Event Related Potentials (ERP) obtained from EEG signals while participants performed an auditory oddball task; multilayer Perception classifier, leave-one out cross validation Sensitivity: 91 Specificity: 91 PPV: NPV: LR+: LR-: Accuracy: 91 AUC: 0.91 Rater agreement: Inter-rater reliability for the classifier Kappa: 0.82	**Index test 2:** EEG Time and frequency analysis of Event Related Potentials (ERP) obtained from EEG signals while participants performed an auditory oddball task; support vector machine (SVM) classifier, leave-one out cross validation Sensitivity: 95 Specificity: 82 PPV: NPV: LR+: Accuracy: 89 AUC: 0.89 Rater agreement: Inter-rater reliability for the classifier Kappa:0.78 Internal consistency: Alpha:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Costs: **Index test 3:** EEG Time and frequency analysis of Event Related Potentials (ERP) obtained from EEG signals while participants performed an auditory oddball task; naïve Bayes classifier, leave-one out cross validation Sensitivity: 86 86 Specificity: 86 PPV: NPV: LR+: Accuracy: 87 AUC: 0.94 Rater agreement: Inter-rater reliability for the classifier **Index text 4:** EEG Time and frequency analysis of Event Related Potentials (ERP) obtained from EEG signals while participants performed an auditory oddball task; k-nearest neighbor classifier, leave-one out cross validation Sensitivity: 91 Specificity: 82 PPV:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				NPV: AUC: 0.89 **Index text 5:**
EEG	Beriha, 2018[150] Case series N = 297 India Setting: School	**Target:** Children recruited from 15 elementary schools, 5 of which were particularly for children with disorders, 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 **Female:** % N/A **Age mean:** N/A **Min age: Max age:** **Ethnicity:** Other info on race or 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 **Index test:** 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 optimization tuned back propagation neural network (PSO-BPNN) classifier Sensitivity: 100 Specificity: 100 PPV: NPV: LR+: LR-: Accuracy: 100 AUC: Rater agreement:	**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 optimization tunedradial basis function (PSO-RBF) classifier Sensitivity: 90 Specificity: 89 PPV: NPV: LR+: Accuracy: 97 AUC: Rater agreement: Kappa: Internal consistency: Alpha:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Boroujeni, 2019[165] 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:**	**Reference standard:** Clinical diagnosis Diagnosis confirmed by neurologist using DSM-IV criteria Timing: Concurrent **Index test:** EEG EEG signals obtained during eyes open, eyes closed, and a Continuous Performance Test (CPT), combination of non-linear features, support vector machine (SVM) classification, 70/30 training/testing split. Best results obtained from combination of correlation dimension	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Min age: 4 **Max age:** 15 **Ethnicity:** Other info on race or ethnicity: N/A	and fractal dimension in FP2 channel, and correlation dimension and sample entropy in Fz channel. Sensitivity: 98 Specificity: 92 PPV: NPV: LR+: LR-: Accuracy: 96 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
EEG	Catherine Joy, 2021[180] 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:** Other info on race or 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 Eyes-open and eyes-closed resting state EEG, permutation entropy feature extraction and artificial neural network (ANN) classifier. Leave-one-out cross validation Sensitivity: 98 Specificity: 99 PPV: NPV: LR+: LR-: Accuracy: 99.82 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Index text 5:
EEG	Chang, 2019[187] Case series N = 60 Taiwan Setting: Specialty care	**Target:** IQ > 80. All male, 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:** Other info on race or 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 Quantitative EEG (qEEG), eyes closed, 21 electrodes for 20 minutes at a sampling rate 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 PPV: NPV: LR+: LR-: Accuracy: AUC: 0.8778	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Chen, 2019[191] Case series N = 108 China Setting: Mixed	**Target:** IQ>80; drug naive, right-handed, no lifetime history of head trauma with loss of consciousness, no history of neurological illness or other severe 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:**	**Reference standard:** Clinical diagnosis Diagnosis based on CDIS structured and interviewer-administered scale based on DSM-IV criteria Timing: Prior diagnosis **Index test:** EEG 10 minute eyes closed resting-state EEG using relative spectral power, spectral power ratio, complexity analyses, and 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. Sensitivity: Specificity: PPV: NPV: LR+:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		10.44 (0.75) for ADHD group, 10.92 (0.69) for control group **Min age: Max age:** **Ethnicity:** Other info on race or ethnicity: N/A	LR-: Accuracy: 85 Classifier model which selected from all tested features AUC: 0.9158 Classifier model which selected from all tested features Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Chen, 2019[192] Case series N = 107 China Setting: Specialty care	**Target:** 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. Recruited from the outpatient clinic at Beijing Children's Hospital, Capital Medical University **Other:** Handedness and age matched typically developing children recruited from local schools **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A	**Reference standard:** Clinical diagnosis Psychiatrist diagnosis using DSM-IV criteria Timing: Prior diagnosis **Index test:** EEG Ten-minute resting state EEG. Convolutional neural network (CNN) classifier, 10 fold cross validation. Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 95	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		Female: 18% **Age mean:** 10.44 (0.75) for ADHD group, 10.92 (0.69) for control group **Min age: Max age:** **Ethnicity:** Other info on race or ethnicity: N/A : Assume Chinese ethnicity	AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: N/A Costs:	**Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Chen, 2021[193] Case series N = 70 Taiwan Setting: Specialty care	**Target:** 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:**	**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,1 minute eyes open resting EEG, and 7.5 minute EEG recording during Conners Kiddie Continuous Performance	**Index test 2:** EEG EEG data, independent testing data (n=9) used for cross validation Sensitivity: 95 Specificity: 38 PPV: 64 NPV: 86 LR+: Accuracy: 69

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		5.68 (0.52) for ADHD group, 5.72 (0.46) for control group **Min age:** 5 **Max age:** 7 **Ethnicity:** Other info on race or ethnicity: N/A	Test, independent testing data (n=9) used for cross validation Sensitivity: 87 Specificity: 84 PPV: 87 NPV: 84 LR+: LR-: Accuracy: 86 AUC: 0.926 0.950 in independent cross validation test sample n=9 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: 0.677 0.55 in independent cross validation test sample n=9 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **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 66 Specificity: 84 PPV: 83 NPV: 68 LR+: Accuracy: 74 AUC: 0.812 Rater agreement: **Index text 4:** CPT Conners Kiddie Continuous Performance Test, independent testing data (n=9) used for cross validation Sensitivity: 42 Specificity: 97

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
				PPV: 94 NPV: 58 AUC: 0.737 **Index text 5:**
EEG	Chiarenza, 2018[196] 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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Diagnoses were based on a DSM-V criteria Timing: Prior diagnosis **Index test:** EEG Quantitative EEG, Quantitative EEG Tomographic Analysis, and the Junior Temperament Character Inventory to classify ADHD only from ADHD+ODD Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 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	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			sources (quantitative EEG tomographic analysis) Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Chow, 2019[201] Chow, 2019[699] 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:**	**Reference standard:** Clinical diagnosis Clinical diagnosis from a pediatric neurologist or psychiatrist using DSM-V criteria Timing: Prior diagnosis **Index test:** EEG 20 minutes, eyes closed, Hjorth Mobility analysis of EEG, dataset randomly spilt 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: 80 Specificity: 80 PPV: NPV:	**Index test 2:** EEG 20 minutes, eyes closed, Theta/Beta ratio (TBR) of the EEG band, dataset randomly spilt 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 reducti Sensitivity: 46 Specificity: 74 PPV: NPV: LR+: Accuracy: 57.5 AUC: 0.633

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Other info on race or ethnicity: N/A	LR+: LR-: Accuracy: 79.2 AUC: 0.885 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** EEG 20 minutes, eyes closed, approximate entropy analysis of EEG,dataset randomly spilt 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, Sensitivity: 85 85 Specificity: 82 PPV: NPV: LR+: Accuracy: 82 AUC: 0.862 Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Index text 5:
EEG	Ekhlasi, 2022[249] Case series N = 121 Iran Setting: Specialty care	**Target:** Children with ADHD symptoms **Other:** Neurotypical developing children **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % N/A **Age mean:** 9.73 (1.76) **Min age: Max age:** **Ethnicity:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Diagnosed by an experienced psychiatrist Timing: Prior diagnosis **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; Local graph measures in-degree and strength in the theta band Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 89 AUC: Rater agreement: Kappa: ICC:	**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 measures (local efficiency, clustering coeffici Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 91 AUC: Rater agreement: Kappa: Internal consistency: Alpha:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Costs: **Index test 3:** 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 coeffici Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 90 AUC: Rater agreement: **Index text 4:** EEG EEG recorded during a visual attention task; weighted directed graphs constructed using the Phase Transfer Entropy measure; K-Nearest Neighbor classifier, 10-fold cross validation; Feature matrix of all global graph measures (global efficiency, characteri Sensitivity:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Hager, 2021[309] Case series N = 130 Multiple countries Setting: Specialty care	**Target:** Free of somatic conditions that could alternatively explain symptoms such as a diagnosed brain injury/ neurological disorder, and/or autism spectrum disorder. IQ must be >=70. Patients were not excluded if they had common comorbidities such as learning disabilities, language disorders, Tourette syndrome, behavioral- and emotional disorders . Patients were 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)	**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 3 min eyes-closed condition, 3 min eyes-opened, and 20 min during a cued go/no-go task. Combined behavioral test scores from a cued visual go/no-go task and Event Related Potentials Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 98 AUC: Log10 Index AUC 0.977 Rater agreement:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		Min age: 9 **Max age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A	Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Helgadottir, 2015[318] Case series N = 661 Iceland Setting: Mixed	**Target:** Diagnosed with ADHD and free of moderate or severe intellectual disability. No exclusions due to medication status: included medication-naïve patients, patients receiving treatment at the time of the recording , and patients on medication but not actually receiving treatment at the time of the recording. Children with comorbidities included. Recruited in two specialised centres in Reykjavik, Iceland **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:** %	**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 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. Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 76 Independent test cohort, 81% cross validation	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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:** Other info on race or ethnicity: N/A	AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Jahanshahloo, 2017[336] Castro-Cabrera, 2010[687]; Ghasemi, 2022[764] Case series N = 60 Colombia Setting: School	**Target:** Nothing abnormal in their physical, normal hearing/vision and and IQ of 80 or higher, those on medication were not to take medication for 24 hours before test. Comorbidities were accounted for; ODD, phobias, and learning problems. **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	**Reference standard:** Clinical diagnosis Medical diagnosis determined using neurophysiological examination based on the criteria in DSM-4. Timing: Prior diagnosis **Index test:** EEG Event-related Potential signals were recorded by three electrodes located in the midline 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. Fra-wave characterization with v_SVM classifier, 10 fold cross validation. Sensitivity: Specificity: PPV: NPV:	**Index test 2:** EEG EEG event-related potentials using 3 sets of features: morphological, wavelets, and nonlinear dynamics based, best combination of features. Support vector machine (SVM) classification, leave one out cross validation[687] Sensitivity: 96 Specificity: 87 PPV: NPV: LR+: Accuracy: 91 AUC: 0.94 Rater agreement:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Min age: 4 **Max age:** 15 **Ethnicity:** Other info on race or ethnicity: N/A	LR+: LR-: Accuracy: 99 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Kappa: Internal consistency: Alpha: Costs: **Index test 3:** EEG Event-related potential (ERP) signals were recorded according to the criteria of the Oddball 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 Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 100 AUC: 0.9995 Rater agreement: **Index text 4:** EEG Event-related potential (ERP) signals were recorded according to the criteria of the Oddball paradigm in two modes of auditory and visual stimulation; Deep learning classifier using the

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				features Absolute Band Power that is normalized by maximum power (ABP Sensitivity: Specificity: PPV: NPV: AUC: 0.9995 **Index text 5:**
EEG	Johnstone, 2021[345] Case series N = 214 China Setting: Other	**Target:** 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:** 18.9% **Age mean:** 8.85 (range 7-12) Control mean age 8.92 years (range 7-12) **Min age:** 7 **Max age:** 12 **Ethnicity:** % Asian : 100 Other info on race or ethnicity:	**Reference standard:** Clinical diagnosis DSM-V diagnosis, using the KSADS Timing: Concurrent **Index test:** EEG Contributions to classification were from child tasks assessing working memory, inhibitory control, and task-shifting, child questionnaires, parent questionnaires including the SNAP-IV, and EEG. Stepwise discriminant function analysis, leave-one-out cross validation Sensitivity: 91 After leave- one-out cross-validation, 85% sensitivity Specificity: 94 After leave- one-out cross-validation, 92% specificity PPV: NPV: LR+: LR-: Accuracy: 93 AUC:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Rater agreement: Kappa: ICC: Internal consistency: Internal consistency reported for the Children's Report of Sleep Patterns (CRSP), Basic Psychological Needs Scale (BPNS-Child), IOWA Conners Rating Scale, Child Self-Regulation and Behaviour Questionnaire (CSBQ), and modified version of the Basic Psychol Alpha: unclear Test-retest: CRSP (all subscales) r >0.80, EQ-5D-Y: moderate test-retest, 69-99%; IOWA Conners Rating Scale: "good" test-retest Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Khoshnoud, 2018[359] Case series N = 24 Iran Setting: Specialty care	**Target:** Right-handed **Other:** Healthy age-matched right-handed children **ADHD presentation:** N/A : included hyperactive-impulsive, inattentive, and combined subtypes **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** %	**Reference standard:** Clinical diagnosis Diagnosed with ADHD at Atieh Comprehensive Centre for Psychology and Nerve Disorders, Tehran, Iran Timing: Prior diagnosis **Index test:** 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	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		N/A **Age mean:** N/A **Min age:** 7 **Max age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A	height and width of the multifractal singularity spectrum of the EEG time series. Classification using support vector machine (SVM) classifier, 4 fold cross validation. Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 83 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
EEG	Kim, 2015[362] Case series N = 97 Korea Setting: Specialty care	**Target:** Attending a camp for hyperactive children; IQ>70; no brain damage, a neurological disorder, 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 **Min age: Max age:** **Ethnicity:** Other info on race or 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 Theta-phase gamma-amplitude coupling Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 72 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
				Index text 5:
EEG	Kim, 2015[361] Case series N = 157 Korea Setting: Other	**Target:** 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; children diagnosed with ADHD-not otherwise specified were excluded from the study **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:**	**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 Quantitative electroencephalography Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 61% for the delta power and 56% for the theta wave AUC: Rater agreement: Kappa: ICC:	**Index test 2:** CPT Integrated Visual and Auditory Continuous Performance Test Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 82% for commission error, and 79% for omission error AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		9.25 (1.63) for the ADHD group, 9.56 (1.98) for the control group **Min age: Max age:** **Ethnicity:** Other info on race or ethnicity: N/A	Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Li, 2005[386] Case series N = 113 China Setting: Specialty care	**Target:** Outpatient children in Psychology Hyperactivity Department of the Central Hospital of Anshan City diagnosed with ADHD; excluding those with nervous system organic disease, 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%	**Reference standard:** Clinical diagnosis Diagnosed with ADHD according to DSM-IV criteria Timing: Prior diagnosis **Index test:** EEG Sensitivity: 84 Specificity: 83 PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement: Kappa:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Age mean: 10 (3) **Min age:** 6 **Max age:** 14 **Ethnicity:** Other info on race or ethnicity: N/A	ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Li, 2018[385] Case series N = 141 China Setting: Mixed	**Target:** IQ>=80. Free of other neurological disease or serious head injuries. Normal or corrected vision. recruited from Changzhou NO.1 people's hospital affiliated with Suzhou university **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:**	**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. Sensitivity: Specificity: PPV: NPV:	**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. Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 95

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Other info on race or ethnicity: N/A	LR+: LR-: Accuracy: 97 Stroop Incongruent experiment pattern on feature channel in inferior parietal cortex using multiple features to train the support vector machine classifier. AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **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. Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 94 AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Index text 5:
EEG	Liechti, 2013[388] Case series N = 62 Switzerland Setting: Other	**Target:** 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:** Other info on race or 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 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 PPV: NPV: LR+: LR-: Accuracy: 73 Stepwise selection of all resting EEG and event related potential variables	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Luo, 2022[399] Case series N = 161 China Setting: Specialty care	**Target:** 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:** Other info on race or 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 Resting-state eye-closed EEG; microstate features (temporal microstate dynamics) and delta 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 PPV: NPV:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			LR+: LR-: Accuracy: 73 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Marcano, 2018[402] Case series N = 7 US Setting: Other	**Target:** Children part of an ongoing longitudinal study focused on frontal lobe development from infancy through childhood 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 **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 0% **Age mean:** N/A	**Reference standard:** Other Diagnosis of ADHD was obtained via maternal report Timing: Prior diagnosis **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) and 3 for validation (2 ADHD, 1 control) Sensitivity: Specificity: PPV: NPV:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Min age: 6 **Max age:** 6 **Ethnicity:** Other info on race or ethnicity: N/A	LR+: LR-: Accuracy: AUC: 0.97 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Markovska-Simoska, 2017[403] Case series N = 60 Macedonia Setting: Specialty care	**Target:** All male, right handed with no serious medical or neurological problems like seizures, or recent head trauma<6 months; not on 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:**	**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 5 minute eyes open resting state EEG, absolute theta central Sensitivity: 100 Specificity: 71 PPV: NPV:	**Index test 2:** EEG 5 minute eyes open resting state EEG, theta/beta ratio at Cz Sensitivity: 59 Specificity: 92 PPV: NPV: LR+: Accuracy: AUC: 0.810 Rater agreement:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		9 (2.44) for ADHD group, 10.46 (2.27) for control group **Min age:** 6 **Max age:** 14 **Ethnicity:** Other info on race or ethnicity: N/A	LR+: LR-: Accuracy: AUC: 0.876 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
EEG	Martín-Brufau, 2017[405] Case series N = 50 Spain Setting: Specialty care	**Target:** EEG records from 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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Diagnosed with ADHD Timing: Prior diagnosis **Index test:** EEG Eyes-closed resting EEG. Direct analysis of EEG specific montages performed by untrained individuals in EEG interpretation. Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 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%. Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 2:** EEG Eyes-closed resting EEG analyzed by the Theta/ Beta Ratio method after decomposition with the Fast Fourier Transformation. Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: 0.929 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** EEG Eyes-closed resting EEG analyzed with the Delta + Theta / Alpha index obtained by visual position decomposition-Verley method. Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				AUC: 0.917 Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Moghaddari, 2020[426] National Brain Mapping Lab, 2019[915]; Mohammadi, 2016[898]; Allahverdy, 2016[650]; Sho'ouri, 2022[1029] 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:** Other info on race or 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. Sensitivity: Specificity: PPV: NPV:	**Index test 2:** EEG Non linear functions were extracted from EEG, and the data was selected as inputs to the multi-layer perceptron neural network using double input symmetrical relevance and the minimum redundancy maximum relevance to select best features for distinguishing Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 94 AUC: Rater agreement: Kappa: Internal consistency:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			LR+: LR-: Accuracy: 98 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Alpha: Costs: **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[650] Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 97 AUC: Rater agreement: **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

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Sensitivity: 85 Specificity: 79 PPV: NPV: AUC: 0.82 **Index text 5:**
EEG	Muthuraman, 2019[438] Case series N = 22 Germany Setting: N/A	**Target:** All male, right handed, with normal or corrected-to-normal vision. (I) ADHD without conduct disorders or tic disorders as diagnosed by an experienced child and adolescent psychiatrist; (II) No other neuropsychiatric as well as no documented comorbidities in a structured psychiatric interview 'Kinder-DIPS'29; (III) Sufficient compliance of child and family; (IV) Normal school achievement; (V) IQ>85; and (VI) No MEG exclusion criteria (i.e. ferromagnetic body objects, or a history of claustrophobia). 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:**	**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 Multimodal electroencephalography (EEG): Eyes closed, resting state. 56 channels were selected 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 five frequency bands (delta, theta, alpha, beta, and gamma). 10-fold cross validation. Sensitivity: Specificity:	**Index test 2:** EEG Multimodal magnetoencephalography (MEG): Eyes closed, resting state recordings were performed using a whole-head system at a sampling rate of 1200Hz in a synthetic third-order gradiometer configuration. Support vector machine (SVM) classifier using renorm Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 97 AUC: Rater agreement: Kappa: Internal consistency:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		13.1 (1.8) and 13.2 (1.5) **Min age:** 10 **Max age:** 17 **Ethnicity:** Other info on race or ethnicity: N/A	PPV: NPV: LR+: LR-: Accuracy: 98 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Ogrim, 2012[453] Case series N = 101 Norway Setting: Mixed	**Target:** IQ>=70 **Other:** Normal gender and age-matched controls with no psychiatric diagnosis, developmental disorders, learning disability, or brain injury **ADHD presentation:** inattentive : 32,combined : 68 **Diagnosed by:** Specialist **Comorbidity:** 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 **Index test:** EEG Quantitative EEG Sensitivity:	**Index test 2:** CPT,EF Go/NoGo task recording omission and commission errors, reaction time, and variability of response Sensitivity: Specificity: PPV: NPV: LR+:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Female: 32% **Age mean:** 11 (3) **Min age:** 7 **Max age:** 16 **Ethnicity:** Other info on race or ethnicity: N/A	Specificity: PPV: NPV: LR+: LR-: Accuracy: 63% for theta, 58% for theta/beta ratio AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Accuracy: 85 For omission errors AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
EEG	OÖztoprak, 2017[456] Case series N = 108 Turkey Setting: N/A	**Target:** Male unmedicated first referrals, 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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis ADHD-C subtype was diagnosed using the DSM-IV Timing: Prior diagnosis **Index test:** EEG Event-related potentials (ERPs) extracted from EEG recordings during performance of 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. Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 100 Test dataset, N=10. Training dataset: 99.5% with the use of 5 features. AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Misdiagnosis: Labeling: Costs:	**Index text 5:**
EEG	Pereda, 2018[461] Gonzalez, 2013[767] Case series N = 33 Spain Setting: Specialty care	**Target:** All males with combined type ADHD **Other:** Male children of hospital staff **ADHD presentation:** combined : 100 **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 0% 100% male **Age mean:** 8(0.3) for ADHD group, 8.1 (0.48) for control group **Min age:** 6 **Max age:** 10 **Ethnicity:** Other info on race or 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 1.5 hour eyes open and eyes closed resting-state EEG recordings at 256 Hz, international 10/20 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 PPV: NPV: LR+: LR-: Accuracy: 94	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Rezaeezadeh, 2020[482] Case series N = 24 Iran Setting: Specialty care	**Target:** Patients of Atieh Comprehensive Centre for Psychology and Nerve Disorders, Tehran, Iran **Other:** Age-matched neurotypical children **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** % N/A **Age mean:** NA **Min age:** 7 **Max age:** 12 **Ethnicity:** Other info on race or 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 Resting state eyes closed EEG, classification by Radial Basis Function support vector machine (RBF SVM) based on a combination of non-linear univariate features, 75/25 training/testing split rearranged randomly 20 times for validation Sensitivity: Specificity: PPV: NPV: LR+: LR-:	**Index test 2:** 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 Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 90.63 AUC: Rater agreement: Kappa:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Accuracy: 99.58 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
EEG	Smith, 2003[535] 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 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:** Other info on race or 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 inter Timing: Prior diagnosis **Index test:** EEG Event-related potential data collected using EEG while participants completed two blocks of an auditory odd-ball task; discriminant function analysis using 7 variables; leave-one-out cross-validation; children 8-12 years old Sensitivity: 71 Specificity: 77 PPV: NPV: LR+: LR-: Accuracy: 73 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs:	**Index test 2:** EEG Event-related potential data collected using EEG while participants completed two blocks of an auditory odd-ball task; discriminant function analysis using 4 variables; leave-one-out cross-validation; adolescents 13-18 years old Sensitivity: 57 Specificity: 63 PPV: NPV: LR+: Accuracy: 59 AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Misdiagnosis: Labeling: Costs:	Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Snyder, 2008[537] Case series N = 159 US Setting: Specialty care	**Target:** Presented to one of four psychiatric and pediatric clinics because of the suspected presence of attention and behavior problems; diagnosed with ADHD; 66% had comorbidities; study required medication wash out (>72 hours) so patients stabilized by multiple medications and individuals on non-stimulants directed toward conditions other than ADHD were excluded **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:**	**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 disord Timing: Concurrent **Index test:** EEG Eyes-open and eyes-closed resting state EEG (N= 159); theta/beta ratio, compared to normative database values with ADHD predicted at a standard deviation cutoff of 1.5 Sensitivity: 87 Specificity: 94 PPV: 95 NPV: 82 LR+: LR-: Accuracy: 89	**Index test 2:** Combined rating ADHD Rating Scales-IV (N=101) Sensitivity: 55 Specificity: 43 PPV: 63 NPV: 36 LR+: Accuracy: 50 AUC: Rater agreement: Parent versus teacher ratings Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Combined rating Conners Rating Scales-Revised (N=103)

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		% Hispanic or Latino : 3 % Black/African American : 37 % Asian : 1 % White : 59 Other info on race or ethnicity:	AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Sensitivity: 72 72 Specificity: 19 PPV: 62 NPV: 27 LR+: Accuracy: 53 AUC: Rater agreement: Parent versus teacher ratings **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
EEG	Snyder, 2015[26] Case series N = 275 US Setting: Mixed	**Target:** Children and adolescents consecutively presenting with attentional and behavior concerns to 13 geographically distinct clinics who were diagnosed with ADHD by reference standard; participants needed to be 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 **Other:** Children and adolescents consecutively presenting with attentional and behavior concerns to 13 geographically distinct clinics	**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 **Index test:** EEG Combination of theta/beta ratio (TBR) from EEG with a clinician's regular ADHD evaluation. Ten minute eyes open resting-state EEG. Clinical evaluation included: (1) Physical examinations, (2) Clinician interviews, with initial impressions	**Index test 2:** Clinician rating scale Clinician ADHD evaluation only Sensitivity: 89 (83, 93) Specificity: 36 (29, 44) PPV: 56 NPV: 79 LR+: Accuracy: 61 AUC: Rater agreement: Kappa: Internal consistency:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 Other info on race or ethnicity: N/A : 4	and reference to DSM-IV-TR criteria, (3) Kiddie-Schedule of Affective Disorders and Schizophrenia–Present and Lifetime Version (K-SADSPL) and Supplements with interviewer notes, (4) Children's Global Assessment Scale, (5) Clinical Global Impression-Severity subscale, (6) ADHD-IV Rating Scales completed by investigator with parent informant and 1–2 teachers, (7) Wechsler Abbreviated Scale for Intelligence-long version, (8) Wide Range Achievement Test-4, (9) Questionnaires on socioeconomic status, education and family histories, and (10) 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 result categories were labeled for reference as "low", "moderate", or "high" for TBR level. Sensitivity: 82 (74, 87) Specificity: 94 (89, 97) PPV: 92 NPV: 85 LR+: LR-: Accuracy: 88 AUC: Rater agreement: Theta/Beta ratio repeated measures collected on two different visits	Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			(n=198). ICC model chosen was two-way, random, single-measure, consistency Kappa: ICC: 0.83 Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Missing data analysis was conducted to evaluate the 32 subjects who did not have “complete” EEG recordings, by which “complete” refers to a quality standard set prior to study initiation requiring at least 15 epochs (30 sec) with minimal to no artifact. O Labeling: Costs:	
EEG	Vahid, 2019[580] Case series N = 144 Germany Setting: N/A	**Target:** No other severe or acute psychiatric comorbidities (e.g., autism, tics, depressive episode, etc.). Either diagnosed as ADD (ICD-10 F9838) or ADHD (ICD-10 F90.0 or F90.1) **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%	**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 Event-related EEG recording during an interval-timing task, deep learning (EEGNet) classifer, leave one out subject (LOOS) cross validation, 2 class problem classification ADHD inattentive type from healthy control	**Index test 2:** EEG Event-related EEG recording during an interval-timing task, deep learning (EEGNet) classifer, leave one out subject (LOOS) cross validation, 2 class problem classification ADHD combined type from healthy control Sensitivity: 83 Specificity: 82 PPV: NPV:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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:** Other info on race or ethnicity: N/A	Sensitivity: 89 Specificity: 84 PPV: NPV: LR+: LR-: Accuracy: 83 2 class classification AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	LR+: Accuracy: 80 2 class classification AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** EEG Event-related EEG recording during an interval-timing task, deep learning (EEGNet) classifer, leave one out subject (LOOS) cross validation, 3 class problem classification ADHD inattentive type, ADHD combined type, healthy control Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 69 AUC: Rater agreement: **Index text 4:** Sensitivity:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Specificity: PPV: NPV: AUC: **Index text 5:**
Imaging	Bansal, 2012[27] Case series N = 83 US Setting: Specialty care	**Target:** Children with no lifetime diagnosis of Obsessive Compulsive Disorder, Tourette Syndrom 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 ChADD (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:** Other info on race or 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 Anatomical MRI 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 then we applied 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	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			PPV: 89 NPV: LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Imaging	Chen, 2020[195] Wang, 2018[1120]; Wang, 2018[1121] Case series N = 86 China Setting: Other	**Target:** ADHD-200 dataset, Peking University subset 1 only (PU_1) **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	**Reference standard:** Clinical diagnosis ADHD-200 Dataset Diagnosis Timing: Prior diagnosis **Index test:** Imaging fMRI resting-state functional connectivity, feature selection via support vector machine with recursive feature elimination (SVM-RFE), deep learning dual subspace classification algorithm (binary hypothesis testing), leave one out cross-validation Sensitivity: 100 Range 69%-95% [Subset Analysis]	**Index test 2:** Imaging 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 (SVMs), leave-one-out cross-validation and 10-folds cross-validations; be Sensitivity: 76 Specificity: 81 PPV:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Ethnicity: Other info on race or ethnicity: N/A	Specificity: 100 Range 82%-96% [Subset Analysis] PPV: Range 81%-92% [Subset Analysis] NPV: LR+: LR-: Accuracy: 99.6 AUC: 0.996 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	NPV: LR+: Accuracy: 79 AUC: 0.84 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Imaging Individual interregional morphological connectivity, support vector machine classification, leave one out cross validation[1121] Sensitivity: 75 75 Specificity: 74 PPV: NPV: LR+: Accuracy: 75 AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
				Index text 5:
Imaging	Crippa, 2017[215] Case series N = 44 Italy Setting: Mixed	**Target:** 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 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 Other info on race or ethnicity:	**Reference standard:** Clinical diagnosis Diagnosis of ADHD based on DSM-IV TR Timing: Prior diagnosis **Index test:** Imaging Multi-domain profile of measures including blood fatty acid profiles, neuropsychological measures, and functional measures from near-infrared spectroscopy. Feature extraction using principal components analysis, support vector machine (SVM) 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 PPV: NPV:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			LR+: LR-: 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: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Imaging	Gao, 2020[283] Bethlehem, 2017[669]; Qureshi, 2016[958]; Qureshi, 2017[959]; Riaz, 2018[970]; Miao, 2019[889]; Zou, 2017[1158]; Dey, 2014[715] Case series N = 83 US	**Target:** Children age 8-13, 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	**Reference standard:** Clinical diagnosis Diagnosed with ADHD from the ADHD-200 datasets Timing: Prior diagnosis **Index test:** Imaging Combination of functional connectivity from resting state fMRI and phenotypic data (phenotypic-attribute attentional brain connectivity, age, and gender), support vector machine (SVM)	**Index test 2:** Imaging Fusion of fMRI and non-imaging data, functional connectivity calculation, feature selection, fusion of non-imaging data (age, gender, IQ), and classification, SVM classifier[970] Sensitivity: 90 Specificity: 77 PPV: NPV:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
	Setting: Other	**Min age:** 8 **Max age:** 13 **Ethnicity:** Other info on race or ethnicity: N/A	classification. Used ADHD-200 provided KKI test dataset for validation Sensitivity: 93 Specificity: 95 PPV: NPV: LR+: LR-: Accuracy: 95 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	LR+: Accuracy: 87 AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Imaging Fractional amplitude of low-frequency fluctuation reflecting intensity of spontaneous neuronal activity combined with feature selection on fMRI[889] Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 82 AUC: Rater agreement: **Index text 4:** Imaging Deep learning-based classification method via 3-D convolutional neural networks applied to MRI, first extracting meaningful 3-D low-level features from fMRI and structural MRI (sMRI),

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				investigating local spatial patterns of MRI features, multi-modality co Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Imaging	Hasaneen, 2017[315] Case series N = 35 Egypt Setting: Specialty care	**Target:** IQ<=80; no comorbid neuropsychiatric 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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Diagnosis completed using examination with criteria of fourth edition of DSM. Physical and neurological exams completed by trained pediatric neurologist Timing: Prior diagnosis **Index test:** Imaging T2*-MRI used to assess brain Iron content levels, and R2* value calculated (Transverse relaxation rates-T2*, or its inverse R2*) Sensitivity: 71 Specificity: 94 PPV: 92 NPV: 77 LR+: LR-: Accuracy: 82.9 AUC: 0.863 Rater agreement: Kappa:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Imaging	Lin, 2023[392] Zhou, 2021[1153] Case series N = 7,805 US Setting: Other	**Target:** U.S. population-based cohort from longitudinal Adolescent Brain and Cognitive Development (ABCD) 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	**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 **Index test:** Imaging Neuroimaging features selected from multimodal MRI data (resting-state fMRI, structural MRI, and diffusion MRI); RIDGE regularized logistic regression feature selection, extreme gradient boosting (XGB) classifier; 4:1 training/ testing split with 5 repeats of 10-fold cross validation; N=1,561 in validation test set Sensitivity: 57 Specificity: 65 PPV: NPV: LR+: LR-:	**Index test 2:** Imaging Combined clinical features (age, sex, race, highest parental education, and handedness) and neuroimaging features selected from multimodal MRI data (resting-state fMRI, structural MRI, and diffusion MRI); Hierarchical Clustering feature selection, Support Sensitivity: 60 Specificity: 56 PPV: NPV: LR+: Accuracy: AUC: 0.613 Rater agreement: Kappa:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Other info on race or ethnicity: Other : Undetermined <1%	Accuracy: AUC: 0.576 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Internal consistency: Alpha: Costs: **Index test 3:** Imaging Integration of multimodal features of structural and functional MRIs and Diffusion Tensor Images, Boruta based feature selection, multiple kernel learning, and support vector machine classifier, 10-fold cross validation and repeated nested 5-fold cross v Sensitivity: 61 61 Specificity: 68 PPV: NPV: LR+: Accuracy: 64 AUC: 0.698 Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
Imaging	Riaz, 2020[483] Riaz, 2018[971]; Itani, 2019[823]; Sun, 2020[1057]; Itani, 2018[822] Case series N = 222 US Setting: Other	**Target:** Children 7-18, 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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis ADHD-200 dataset Timing: Prior diagnosis **Index test:** Imaging End-to-end deep learning model using pre-processed fMRI time-series signals. Used ADHD-200 provided NYU test set for validation. Sensitivity: 66 Specificity: 92 PPV: NPV: LR+: LR-: Accuracy: 73 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 2:** Imaging Decision tree machine learning predictive models based on phenotypic characteristics and resting-state functional Magnetic Resonance Images, validated using test set[823] Sensitivity: 79 Specificity: 58 PPV: NPV: LR+: Accuracy: 73 AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Imaging Whole-brain resting-state functional connectivity patterns, support vector machine (SVM) classification, leave one out cross validation[1057] Sensitivity: 82 82 Specificity: 88 PPV: NPV: LR+:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Accuracy: 85 AUC: Rater agreement: **Index text 4:** Imaging Computer-aided diagnosis, multi-level decision tree[822] Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Imaging	Schirmer, 2021[506] Case series N = 100 US Setting: Other	**Target:** 25 children with primary diagnosis of Autism spectrum disorder who met diagnostic criteria for ADHD and 25 children with ADHD in test set. Part of The Connectomics in NeuroImaging Transfer Learning Challenge using data amassed retrospectively across multiple studies conducted by the Center for Neurodevelopmental and Imaging andResearch (CNIR) at the Kennedy Krieger Institute (KKI) in Baltimore, MD. Considered high-functioning based on having a full-scale 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	**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 Sca Timing: Prior diagnosis **Index test:** Imaging fMRI, resting state, support vector machines (SVMs), 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	**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 PPV: 71 NPV: 74 LR+: Accuracy: 73 53% in test set AUC: 0.85 0.54 in test set

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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:** Other info on race or ethnicity: N/A	Specificity: 55 25% in test set PPV: 68 50% in test set NPV: 92 50% in test set LR+: LR-: Accuracy: 75 50% in test set AUC: 0.73 0.48 in test set Rater agreement: Matthews correlation coefficient 0.55 in validation set Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Rater agreement: Matthews correlation coefficient 0.45 in validation set Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Imaging fMRI, resting state, mean and standard deviation, Pearson correlation, Tangent, covariance, and Tangent Pearson Sensitivity: 80 80 Specificity: 85 PPV: 84 NPV: 81 LR+: Accuracy: 83 AUC: 0.89 Rater agreement: Matthews correlation coefficient 0.65 in validation set **Index text 4:** Imaging fMRI, resting state, long short-term memory network was used, AAL ROIs were first selected based on consistent connectivity differences

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				between ADHD and controls in bootstrapped samples, time-series from these ROIs were input to an LSTM, with the demograp Sensitivity: 70 Specificity: 65 PPV: 67 NPV: 68 AUC: 0.72 **Index text 5:**
Imaging	Serrallach, 2016[512] Case series N = 147 Germany Setting: Specialty care	**Target:** Part of a larger longitudinal project addressing the effects of musical practice on the brain and cognition from the primary school age to adolescence; ADHD group broken into separate categories, 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	**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 structural magnetic MRI was performed to investigate the anatomy of the auditory cortex; Neuromag-122 whole-head MEG system was used to measure and analyze 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.	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Min age: Max age: **Ethnicity:** Other info on race or ethnicity: N/A	Pooled disorder group (dyslexia, ADHD, and ADD) vs control group Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 84.4% pooled disorder group vs controls AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
Imaging	Soliva, 2010[538] Tremols, 2008[1085] Case series N = 78 Spain Setting: Specialty care	**Target:** 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; all on methylphenidate **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:** Other info on race or 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 the right caudate nucleus body volume/ total bilateral caudate volume and right caudate nucleus body volume/ bilateral caudate body volume ratios. Split sample for training/testing. 40 participants in training group, 38 in test group. 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 PPV: 89 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	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			For optimal cut-off value <=0.4818 of the right caudate nucleus body volume/ bilateral caudate body volume ratio in the test group LR+: LR-: Accuracy: AUC: 0.84 For optimal cut-off value <=0.4818 of the right caudate nucleus body volume/ bilateral caudate body volume ratio in the test group Rater agreement: Inter-rater reliability of the caudate segmentation procedure Kappa: ICC: 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) Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index text 5:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
Imaging	Sun, 2018[558] Case series N = 170 China Setting: Mixed	**Target:** Newly diagnosed and never-treated, consecutively recruited from September 2009 to October 2015 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 affect brain anatomy and function (including neurologic illness; head injury; and liver, renal or cardiac abnormalities); 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:** Other info on race or 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 **Index test:** Imaging Structural 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 PPV: NPV: LR+: LR-: Accuracy: 74 AUC: Rater agreement: 100 runs of 10-fold cross-validation (1000 training-testing cycles) Kappa: 0.47 ICC: Internal consistency: Alpha: Test-retest: Costs:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Misdiagnosis: Labeling: Costs:	**Index text 5:**
Imaging	Tang, 2022[567] Case series N = 194 China Setting: Other	**Target:** Children age 8 to 17 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:** Other info on race or 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 PPV: NPV: LR+: LR-: Accuracy: 99.6 AUC: 0.997 Rater agreement: Kappa: ICC:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Imaging	Yao, 2018[618] Case series N = 62 China Setting: Mixed	**Target:** Children: male drug-naive, right handed, 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% all male in children dataset **Age mean:** 9.79 (1.86) for ADHD group, 10.29 (1.67) for control group **Min age: Max age:** **Ethnicity:** Other info on race or 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 Functional connectivity pattern derived from resting-state fMRI. Used novel Feature Selection method based on Relative Importance and Ensemble Learning (FS_RIEL), 10-fold cross validation Sensitivity: 95 Using FS_RIEL feature selection method Specificity: 76 Using FS_RIEL feature selection method PPV: NPV: LR+: LR-:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Accuracy: 86.36 Using FS_RIEL feature selection method AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Imaging	Yasumura, 2020[619] Yasumura, 2014[1149] Case series N = 99 Japan Setting: Mixed	**Target:** No severe comorbidities (e.g., ASD or learning disability); IQ >=80 **Other:** Typically developing children without ADHD **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 15.0% 15% female in ADHD training group, gender not reported for test group **Age mean:** Test set: 10.27 (2.2) for ADHD group, 10.16 (1.55) for control group **Min age: Max age:**	**Reference standard:** Clinical diagnosis The Japanese version of the 26-item Swanson, Nolan and Pelham–IV + neurologist evaluation Timing: Prior diagnosis **Index test:** Imaging Near-infrared spectroscopy (NIRS) was used 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,	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		Ethnicity: Other info on race or ethnicity: N/A	and interference ratio on the interference condition) and NIRS data. Sensitivity: 89 Specificity: 84 PPV: NPV: LR+: 5.47 LR-: 0.13 Accuracy: 86 AUC: 0.898 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Imaging	Yoo, 2020[621] Seoul National University Childrens Hospital, 2015[1001] Case series N = 130 Korea Setting: Other	**Target:** 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,	**Reference standard:** Clinical diagnosis DSM-IV criteria confirmed with the Korean Kiddie Schedule for Affective Disorders and Schizophrenia – Present and Lifetime version Timing: Prior diagnosis **Index test:** Imaging Structural, functional, and diffusion-tensor MRI, age, sex, and IQ.	**Index test 2:** Imaging Structural, functional, and diffusion-tensor MRI, age, sex, and IQ. Lesser feature with Equivalent performance (LE): Machine learning algorithms on multi-measures, multi-modal neuroimaging data (structural

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		obsessive-compulsive disorder, and no history of methylphenidate treatment for >1 year or having taken methylphenidate in the previous 4 weeks; test set subjects were selected from independent neuroimaging data called “A cohort study for neurodevelopmental disorder” **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:** % 33% female in test set, 21% female in training set **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:** Other info on race or ethnicity: N/A	Best Accuracy Model: Machine learning algorithms on multi-measures, multi-modal neuroimaging data (structural MRI, 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. Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 78 AUC: 0.70 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: 23.4% misclassification error Labeling:	MRI, Resting-state fMRI, diffusion tensor imaging Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 69 AUC: 0.65 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Costs:	AUC: **Index text 5:**
neuropsychological	Li, 2016[384] Yale University, 2012[1147] Case series N = 60 China Setting: Other	**Target:** Selected to participate if they met diagnostic criteria for any presentation of ADHD or who were considered to be subthreshold for ADHD, defined as one symptom short of meeting diagnostic criteria. Free of any other co-morbid psychiatric ondition. Mediation 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:**	**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 PPV: NPV: LR+: LR-: Accuracy: AUC: 0.904 Rater agreement: Kappa:	**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 PPV: NPV: LR+: Accuracy: AUC: Between 0.867 and 0.932 for the 15 frequency band measures Rater agreement: Kappa: Internal consistency:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		% Asian : 100,Other : All participants were of Han ancestry Other info on race or ethnicity:	ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Alpha: Costs: **Index test 3:** neuropsychological,activity Performance measures on the Go/No-Go task, 6 measures omission errors, commission errors, accuracy, multiple response errors, reaction time, and reaction time variability Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** neuropsychological Go/No-Go task accuracy Sensitivity: Specificity: PPV: NPV: AUC: 0.844 **Index text 5:** Neuropsychological

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Attention,Impulsivity,Response variability,Reaction time
neuropsychological,CPT	Adams, 2009[119] Case series N = 35 US Setting: Specialty care	**Target:** Boys diagnosed with ADHD recruited through newspaper advertising, children with comorbidities excluded, 10 of the 19 participants were on medication on the day of testing **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 Other info on race or ethnicity:	**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 The Virtual Classroom virtual reality continuous performance test including visual and/or auditory distracters; logistic regression with percent correct as the predictor (difference between ADHD and control groups trended toward significance) Sensitivity: 50 Specificity: 88 PPV: NPV: LR+: LR-: 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 PPV: NPV: LR+: Accuracy: 59 AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,CPT	Berger, 2010[148] Hadassah Medical Organization, 2008[782] Case series N = 58 Israel Setting: Specialty care	**Target:** All the children in the study 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:**	**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	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		9.86 (1.89) in the ADHD group, 10.50 (1.81) in the control group **Min age:** 6 **Max age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A	Specificity: PPV: NPV: LR+: LR-: Accuracy: 95 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,CPT	Berger, 2017[147] Case series N = 798 US Setting: N/A	**Target:** 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 (e.g., depression, anxiety, and psychosis) **Other:** Randomly recruited typically developed children who study in regular classes at primary schools **ADHD presentation:** N/A **Diagnosed by:** Specialist	**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	**Index test 2:** neuropsychological MOXO-Continuous Performance Test (CPT) Total Score including 4 indices: attention, timing, hyperactivity, and impulsivity for 12 year old participants Sensitivity: Specificity: PPV:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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:** Other info on race or ethnicity: N/A	Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC: 0.92 0.91-0.96 over the 6 age groups Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	NPV: LR+: Accuracy: AUC: 0.92 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **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 Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: 0.80 Rater agreement: **Index text 4:** MOXO-Continuous Performance Test (CPT) Hyperactivity for 12 year old participants; the number of

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				all types of commission responses that are not coded as impulsive responses Sensitivity: Specificity: PPV: NPV: AUC: 0.82 **Index text 5:** Neuropsychological Attention,Impulsivity
neuropsychological,CPT	Bledsoe, 2020[160] Case series N = 35 US Setting: N/A	**Target:** Did not meet diagnostic criteria for other psychiatric or psychological disorder including Learning Disorders, Anxiety Disorders, Mood Disorder, or Oppositional Defiant Disorder. IQ>=80. ADHD participants who were prescribed stimulant medication were subjected to at least a 24- to 48-hr washout period prior to testing, and were 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:**	**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/ Impulsive composite 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 PPV: NPV: LR+:	**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 PPV: NPV: LR+:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		N/A **Min age: Max age:** **Ethnicity:** Other info on race or ethnicity: N/A	LR-: Accuracy: 100 After leave-one-(participant)-out cross-validation AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Accuracy: 97 After leave-one-(participant)-out cross-validation AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
neuropsychological,CPT	Bloch, 2012[161] Case series N = 34 Israel Setting: Specialty care	**Target:** Children referred by a neurologist or a child psychiatrist for a neurocognitive evaluation in order to substantiate a possible diagnosis of ADHD; no known diagnosis of mental retardation or major psychopathology (namely, major affective disorder, psychotic disorder, pervasive developmental disorder, substance abuse, posttraumatic stress disorder, obsessive-compulsive disorder, panic disorder) **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:** Other info on race or 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 The Test of Variables of Attention (TOVA) Sensitivity: 63 Specificity: 85 PPV: 94 NPV: 37 LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**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 PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
				Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,CPT	Chen, 2022[190] Case series N = 109 China Setting: School	**Target:** Recruited from 6 primary schools and 6 junior high schools 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	**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	**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 develop Sensitivity: Specificity: PPV: NPV:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Min age: 6 **Max age:** 13 **Ethnicity:** Other info on race or ethnicity: N/A	Capacity (the relationship between response accuracy and information rate), 10-fold cross validation, binary classification ADHD versus typically developing peers Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 60 SD 2.6% AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	LR+: Accuracy: 64 SD 1.5% AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **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 re Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 65 AUC: Rater agreement:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				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 Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,CPT	Chu, 2017[202] 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:**	**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	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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:** Other info on race or ethnicity: N/A	PPV: 82 NPV: 67 LR+: LR-: Accuracy: 78 AUC: 0.867 Rater agreement: Kappa: ICC: 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. Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
neuropsychological,CPT	Emser, 2018[256] Case series N = 60 Germany Setting: Mixed	**Target:** 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 as long as ADHD was the primary diagnosis; participants taking medication were asked to stop taking it 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:** Other info on race or 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 PPV: NPV: LR+: LR-: Accuracy: 87 AUC: Rater agreement: Kappa: ICC: 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 Alpha: Test-retest: Costs:	**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 PPV: NPV: LR+: Accuracy: 78 AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Misdiagnosis: Labeling: Costs:	Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,CPT	Hall, 2016[312] Pre-post study N = 80 UK Setting: Specialty care	**Target:** Pre vs post-test audit design, case records were examined in 40 cases diagnosed without the QbTest [pre-QbTest group] and 40 cases diagnosed with the QbTest [QbTest group] **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:** QbTest group - 9.2 (2.3) / pre-QbTest group - 8.1 (2.4) **Min age:** 4.5 **Max age:** 14.6	**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 Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: pounds **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		Ethnicity: Other info on race or ethnicity: N/A	Internal consistency: Alpha: Test-retest: Costs: 31 Misdiagnosis: Labeling: Costs: 31108 British pounds	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,CPT	Heller, 2013[319] 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 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	**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 **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= presence/absence of hyperactivity Sensitivity: 77 Specificity: 81 PPV: NPV: LR+:	**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 decision tree algorithms tested, binary classification = binary classification= presence/absence of inattentio Sensitivity: 59 Specificity: 83 PPV: NPV: LR+: Accuracy: 78 AUC: Rater agreement:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Min age: 6 **Max age:** 17 **Ethnicity:** % Hispanic or Latino : 2 % Black/African American : 15 % White : 77 Other info on race or ethnicity: Other : 6% Other Race	LR-: Accuracy: 75 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
neuropsychological,CPT	Hult, 2018[23] 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 **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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Diagnosis of ADHD performed by a multi-professional team, based on DSM-IV behavioral criteria Timing: Concurrent **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% PPV: 76%-86% NPV: 37%-50% LR+: LR-: Accuracy: AUC: 0.62-0.76 over three test parameters with cutoff set at recommended 1.25 Q-Score Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Misdiagnosis: Labeling: Costs:	**Index text 5:** Neuropsychological Attention,Impulsivity,Other : Activity parameters
neuropsychological,CPT	Matier-Sharma, 1995[407] 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 info on race or 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 PPV: NPV: LR+: LR-: Accuracy: 72 AUC: Rater agreement: Kappa:	**Index test 2:** neuropsychological,CPT,activity 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 PPV: NPV: LR+: Accuracy: 66 AUC: Rater agreement: Kappa: Internal consistency: Alpha:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Costs: **Index test 3:** activity Actigraph measures taken during CPT task; ADHD versus neurotypical controls Sensitivity: 25 25 Specificity: 94 PPV: 91 NPV: 36 LR+: Accuracy: AUC: Rater agreement: **Index text 4:** activity Actigraph measures taken during CPT task; ADHD versus non-ADHD Sensitivity: 25 Specificity: 95 PPV: 77 NPV: 63 AUC: **Index text 5:** Neuropsychological,CPT Attention,Impulsivity,Other : Dyscontrol

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
neuropsychological,CPT	Mitchell, 1990[425] Case series N = 204 US Setting: School	**Target:** Selected from five elementary schools, in special education placement or regular class with resource specialist, no coexisting major medical problems or centrally acctive 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:** Other info on race or 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 percentle with a cutoff point of 4 of 21 measures Sensitivity: 60 Specificity: 95 Allowed false positive rate of 5% PPV: NPV: LR+: LR-: Accuracy: AUC: 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	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Agreement = 75% Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index text 5:** Neuropsychological Attention,Impulsivity,Response variability,Reaction time,Other : Hand errors
neuropsychological,CPT	Mwamba, 2019[439] Case series N = 30 South Africa Setting: Specialty care	**Target:** No known history of severe mental illness **Other:** Controls, non-ADHD youth **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 54% Gender ratio was kept as closely as possible to 1:1 **Age mean:** 10 **Min age:** 5 **Max age:** 16 **Ethnicity:** Other info on race or 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 **Index test:** neuropsychological,CPT Paediatric Attention-Deficit/Hyperactivity DisorderApplication Software (PANDAS): Tablet-based game, Support vector machine (SVM) classifier. 75/25 train/test split Sensitivity: 75 Specificity: 100 PPV: 100 NPV: 75 LR+: LR-: Accuracy: 86	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,CPT	Park, 2019[457] Case series N = 114 Korea Setting: Specialty care	**Target:** 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. May have comorbid disorders such as tics, and depressive or anxiety disorder; consecutively 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	**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 The Advanced Test of Attention Sensitivity: 85 Specificity: 46 PPV: 78 NPV: 57 LR+: LR-: Accuracy: 72.8 AUC: 0.653	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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:** Other info on race or ethnicity: N/A	Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Test-retest no ICC greater than 0.5 was found in ADHD retest participants Costs: Misdiagnosis: Labeling: Costs:	Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,CPT	Rodríguez, 2018[488] Case series N = 338 Spain Setting: Mixed	**Target:** Stopped medication 72 hours before testing; IQ>=70 and <=130; no comorbid disorders. **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:**	**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 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 Sensitivity:	**Index test 2:** neuropsychological,CPT Test of Variables of Attention (TOVA); discrimination between ADHD-IH vs ADHD-I vs ADHD-C vs controls Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 34 Discrimination between ADHD-IH vs ADHD-I vs ADHD-C vs controls AUC:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Other info on race or ethnicity: N/A	Specificity: PPV: NPV: LR+: LR-: Accuracy: 57 Discrimination between ADHD-IH vs ADHD-I vs ADHD-C vs controls AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: 0.72 Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
neuropsychological,CPT	Schatz, 2001[503] 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 Other info on race or ethnicity:	**Reference standard:** Clinical diagnosis Medical history, neurological exam, parent and teacher historical reports, and psychological testing Timing: Prior diagnosis **Index test:** neuropsychological,CPT Test of Variables of Attention (TOVA), cutoff at least one T score >=65 Sensitivity: 86 Specificity: 70 PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: TOVA miss rate 14.3% and false positive rate 30.0%, Conners Hyperactivity Index miss rate 21.4% and false positive rate 0% Labeling: Costs:	**Index test 2:** Parental rating scale Conners Parent Rating Scale, Hyperactivity Index, cutoff T score >=65 (1.5 SD above the mean) Sensitivity: 79 Specificity: 100 PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,CPT	Simões, 2021[525] Case series N = 160 Brazil Setting: School	**Target:** Drug naïve, no comorbidities, normal or corrected-to-normal vision; students with developmental delays, poor academic performance, epilepsy, previous history of traumatic brain injury, psychosis, mood disorders, or learning disabilities (including dyslexia, dysgraphia, and dyscalculia) were excluded **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:**	**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 obser 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 PPV: NPV: LR+: LR-:	**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 PPV: NPV: LR+: Accuracy: 66 AUC: Rater agreement: Kappa: Internal consistency:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		Other info on race or ethnicity: Other : Sample size is all Brazilian	Accuracy: 70 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,CPT	Slobodin, 2020[532] Berger, 2020[668] 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 (e.g., depression, anxiety, and psychosis). **Other:** Typically developed children recruited from regular primary schools	**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	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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:** Other info on race or ethnicity: N/A	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) PPV: NPV: LR+: LR-: Accuracy: 87 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
neuropsychological,CPT	Yeh, 2020[620] 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:** Other info on race or 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 Virtural 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 extreme gradient boosing (XGB) machine learning classifier. 5-fold cross validation with 5 repeats Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 82 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs:	**Index test 2:** neuropsychological,CPT Virtural 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-fol Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 83 AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** neuropsychological,CPT Virtural Reality (VR) classroom: VR cognitive tasks, continuous performance tests, and audio tests were embedded into the virtual environment. Captured

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Misdiagnosis: Labeling: Costs:	task performance and neuro-behavior data. Analyzed with logistic regression. 5-fold cross validation w Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 72 AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,CPT	Zelnik, 2012[627] Case series N = 230 Israel Setting: Specialty care	**Target:** No major psychiatric conditions, mental retardation, autistic spectrum disorder, and epilepsy and children treated with psychotropic drugs (including central nervous system stimulants); referred to ADHD clinic **Other:** Children referred to ADHD clinic not diagnosed with ADHD **ADHD presentation:** inattentive : 39,hyperactive : 15,combined : 46 **Diagnosed by:** Specialist	**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, Timing: Concurrent	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Comorbidity: N/A **Female:** % 29% in entire sample **Age mean:** 10.0 (2.7) **Min age:** 6 **Max age:** 17 **Ethnicity:** Other info on race or ethnicity: N/A	**Index test:** neuropsychological,CPT Test of Variables of Attention Sensitivity: 91 Specificity: 22 PPV: 80 NPV: 41 LR+: LR-: Accuracy: AUC: Rater agreement: Test of Variables of Attention versus reference standard Kappa: 0.152 ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
neuropsychological,CPT	Zulueta, 2019[634] Case series N = 407 Spain Setting: Mixed	**Target:** Clinical sample of children, with normal IQ >80 **Other:** Typically developing children **ADHD presentation:** inattentive : 49.30,combined : 50.70 **Diagnosed by:** Specialist **Comorbidity:** N/A **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:** Other info on race or ethnicity: N/A	**Reference standard:** Other EDAH Rating Sale a revised Spanish version of the Conners Teacher Rating Scale-Revised Timing: Concurrent **Index test:** neuropsychological,CPT AULA is a Virtual Reality based neuropsychological test Sensitivity: 68 Specificity: 75 PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Index text 5:
neuropsychological,CPT,Activity	Gilbert, 2016[298] Clinical trial N = 70 China Setting: Mixed	**Target:** 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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Diagnosed by clinician using DSM-IV criteria Timing: Prior diagnosis **Index test:** neuropsychological,CPT,Activity Stepwise discriminant function analysis with 5 variables: Full-Scale Response Control Quotient 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 Sensitivity: 80 Specificity: 90 PPV: NPV: LR+: LR-: 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 PPV: NPV: LR+: Accuracy: 70 AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 3:** neuropsychological,CPT,activity Continuous performance test quotient scores (Full-Scale Response Control Quotient from the Integrated Visual and Auditory Test, Full-Scale Response Attention Quotient) plus actigraph data (converted into kilocalories, i.e., units of energy expenditure) Sensitivity: 83 83 Specificity: 91 PPV: NPV: LR+: Accuracy: 84 AUC: Rater agreement: **Index text 4:** activity Continuous performance test scores (Full-Scale Response Control Quotient from the Integrated Visual and Auditory Test, Full-Scale Response Attention Quotient) plus actigraph data (converted into kilocalories, i.e., units of energy expenditure) plus age g Sensitivity: 80 Specificity: 90

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				PPV: NPV: AUC: **Index text 5:**
neuropsychological,CPT,Activity	Luo, 2022[398] 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	**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:** neuropsychological,CPT,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 ten 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	**Index test 2:** Parental rating scale SNAP-IV Sensitivity: 80 (67, 89) Specificity: 76 (63, 86) PPV: 79 NPV: 78 LR+: Accuracy: 78 AUC: 0.907 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Ethnicity: Other info on race or ethnicity: N/A	Random forest and Bayesian network were employed to build diagnosis models Sensitivity: 98 (89, 100) Specificity: 95 (84, 99) PPV: 98 NPV: 95 LR+: 52 LR-: 0.06 Accuracy: 96 AUC: 0.964 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,CPT, EF	Breaux, 2016[170] Case series N = 168 US Setting: Primary Care	**Target:** Children presenting with elevated levels of externalizing problems at age 3 who were diagnosed with ADHD or ADHD+ODD at age 6; no intellectual disability, deafness, blindness, language delay, cerebral palsy, epilepsy, autism, and/or psychosis; children were not asked to discontinue medication **Other:** Children presenting with elevated levels of externalizing problems at age 3 who were	**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 (fo Timing: Concurrent	**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 PPV: 63

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 Other info on race or ethnicity:	**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 PPV: 67 NPV: 72 LR+: LR-: Accuracy: 70 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	NPV: 71 LR+: Accuracy: 67 AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** neuropsychological Delay Aversion: Present task Sensitivity: 55 55 Specificity: 66 PPV: 57 NPV: 64 LR+: Accuracy: AUC: Rater agreement: **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,

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				attentiveness, and reaction time by block Sensitivity: 62 Specificity: 68 PPV: 61 NPV: 69 AUC: **Index text 5:** Neuropsychological Attention,Impulsivity,Working memory
neuropsychological,CPT,EF	Faraone, 2016[266] Case series N = 113 US Setting: Specialty care	**Target:** Consecutive patients referred to a child psychiatrist 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; participants did not take stimulant medication on the testing days **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:**	**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 **Index test:** neuropsychological,CPT,EF The Groundskeeper game was designed to measure attention capabilities on a go/no go task, with the addition of visual, auditory, and visuo-spatial distractions at various frequencies. Sensitivity: Specificity: PPV: NPV: LR+: LR-:	**Index test 2:** Parental rating scale Parent-rated Conners subscales as a predictor of ADHD diagnoses Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: 0.76 Rater agreement: Kappa: Internal consistency: Alpha: Costs:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 Other info on race or ethnicity:	Accuracy: AUC: 0.79 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) Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 3:** neuropsychological,CPT Conners Continuous Performance Test II (CPT II) Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: 0.62 Rater agreement: **Index text 4:** neuropsychological,CPT,EF Combined the significant Groundskeeper factors with the Conners inattention subscale and the CPT percent correct in the same model Sensitivity: Specificity: PPV: NPV: AUC: 0.87 **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
neuropsychological,CPT,EF	Jimenez-Figueroa, 2017[341] Case series N = 103 Colombia Setting: School	**Target:** Spanish native speakers; attend school of medium socio-economic stratum in Barranquilla, Colombia; both parents alive; parents and teachers complete the screening ADHD checklist; IQ >=70; no clinical history of any major neurologic disease and/or developmental disorders or psychotic disorders **Other:** Children without ADHD **ADHD presentation:** inattentive : 30.1,combined : 69.9 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 29.1% **Age mean:** 7.75 (1.46) ADHD group, 8.84 (1.54) control group **Min age:** 6 **Max age:** 11 **Ethnicity:** Other info on race or 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 Diagnosis made by neuropsychologist using DSM-V criteria Timing: Concurrent **Index test:** neuropsychological,CPT,EF Multi-operational apparatus for reaction times (MOART): the visual signal reaction times for prepotent response (PR–RT) and Go/No-Go tasks. PR-based variables were used in a predictive setting to determine their potential for discriminating ADHD-affected individuals from healthy controls. Sensitivity: 68 (60, 80) Specificity: 84 (74, 93) PPV: 90 NPV: 55 LR+: 4.16 LR-: 0.38 Accuracy: 79 AUC: 0.73 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Costs:	**Index text 5:**
neuropsychological,CPT,EF	Newman, 2017[450] Case series N = 152 US Setting: N/A	**Target:** 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 Other info on race or ethnicity:	**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 The Pediatric Attention Disorders Diagnostic Screener (PADDS) 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	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			PPV: 85 NPV: 88 LR+: LR-: Accuracy: 86 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,CPT,EF	Peijnenborgh, 2016[459] 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 **Female:** 25% **Age mean:** 6.90 (0.74) **Min age:** 6 **Max age:** 8	**Reference standard:** Clinical diagnosis Diagnosis of ADHD according to DSM-V Timing: Prior diagnosis **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 PPV:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		Ethnicity: Other info on race or ethnicity: N/A	NPV: LR+: LR-: Accuracy: 78 (76/97) of the children were correctly classified as being in the ADHD group or in the control group AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,CPT,EF	Williams, 2010[20] 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	**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" from Brain Resource Ltd. Combination of sustained attention, impulsivity, intrusions, inhibition,	**Index test 2:** neuropsychological,CPT,EF Cognitive and brain-function assessments using proprietary testing software "IntegNeuro" and "LabNeuro" from Brain Resource Ltd. Combination of sustained attention, impulsivity, intrusions, inhibition, and response variablility. Severity threshold for det

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 Other info on race or ethnicity:	and response variablility. Severity threshold for determining impairment <= 1.0 SD below the mean. Sensitivity: 88 Specificity: 91 PPV: 96 NPV: 88 LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Sensitivity: 84 Specificity: 94 PPV: 88 NPV: 95 LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Index text 5: Neuropsychological Attention
neuropsychological,EF	Boucugnani, 1989[167] 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:** Other info on race or 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 Timing: **Index test:** neuropsychological,EF Stepwise discriminant function analysis: final multivariate linear equation included the Trail-Making test- Part B and the Wisconsin Card Sorting Test perseverative responses, failure to maintain set, and perseverative errors Sensitivity: Specificity: PPV: NPV: LR+: LR-:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Accuracy: 79 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,EF	Canivez, 2016[178] Case series N = 40 US Setting: School	**Target:** 15% receive special education **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	**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 The Das–Naglieri Cognitive Assessment System is a test of cognitive abilities based on the Planning, Attention, Simultaneous, and Successive Theory Sensitivity: 80 Specificity: 75 PPV: 76 NPV: 79 LR+: LR-:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		% Multiracial : 15 Other info on race or ethnicity: Other : 5% No response for race/ethnicity	Accuracy: 78 AUC: 0.846 Rater agreement: Cognitive Assessment System discriminant function analysis classifications versus a priori diagnosis Kappa: 0.550 ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,EF	Chan, 2022[185] Case series N = 188 China Setting: Other	**Target:** Recruited through posting ads at parent groups of various social media and mass mail; diagnosed with ADHD; 30.85% comorbid with special learning difficulties including dyslexia, 10.64% had other comorbidities including special language impairment, emotional disorders, gross and fine motor difficulties, oppositional defiant disorder, limited intelligence, and social and communication disorder **Other:** Age- and gender-matched typically developing children without any reported diagnosis of developmental disorders, psychiatric disorders, and subjective complaints	**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	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		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:** Other info on race or ethnicity: N/A	and ISI passing threshold in the CV task, ROC analysis Sensitivity: 76 Specificity: 51 PPV: NPV: LR+: LR-: Accuracy: AUC: 0.67 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,EF	Chelune, 1986[189] Case series N = 48 US Setting: N/A	**Target:** 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	**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 c Timing:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Female: 29% **Age mean:** 9.4 **Min age:** 6 **Max age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A	**Index test:** neuropsychological,EF Stepwise discriminant function analysis; final variables in the multivariate linear equation 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. Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 85 AUC: 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 ICC: Internal consistency: Alpha: Test-retest:	Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Costs: Misdiagnosis: Labeling: Costs:	
neuropsychological,EF	Culbertson, 1998[217] 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; comorbidities present in 46 of the ADHD children including oppositional defiant/conduct disorders, anxiety disorders, depressive disorders, adjustment disorders, and learning disabilities **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	**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 PPV: 85 NPV: LR+: LR-: Accuracy: 70 AUC: Rater agreement: Kappa: ICC:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		Ethnicity: % White : 96 Other info on race or ethnicity:	Internal consistency: 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 Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,EF	El-Sayed, 1999[250] Case series N = 159 Sweden Setting: Mixed	**Target:** Consecutive cases with ADHD selected from 3 sites **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:** Other info on race or 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 PPV: NPV: LR+: LR-: Accuracy:	**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 PPV: NPV: LR+: Accuracy: AUC: 0.72 Rater agreement:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			AUC: 0.72 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Kappa: Internal consistency: Alpha: Costs: **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 51 Specificity: 85 PPV: NPV: LR+: Accuracy: AUC: 0.73 Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
neuropsychological,EF	Ferrin, 2012[270] Case series N = 1,185 Australia Setting: Mixed	**Target:** All 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:** Other info on race or 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 PPV: 98 NPV: 25 LR+: 6.16 LR-: 0.37 Accuracy: AUC: 0.779 (95% CI 0.742–0.816) Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Index text 5:
neuropsychological,EF	Garcia-Sanchez, 1997[284] Case series N = 60 Spain Setting: School	**Target:** Teenagers diagnosed with ADD with hyperactivity or ADD without 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:** Other info on race or 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 **Index test:** neuropsychological,EF Neuropsychological tests developed for the assessment 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	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			PPV: NPV: LR+: LR-: Accuracy: 65 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,EF	Geurts, 2004[293] Case series N = 136 Netherlands Setting: Mixed	**Target:** Children with ADHD and children with ADHD+ODD/CD; recruited from parents affiliated with the national parent association of children with ADHD or from 11 special educational services for children with extreme behavioral problems; 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	**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	**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 Ca Sensitivity: Specificity:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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:** Other info on race or ethnicity: N/A	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 Specificity: PPV: NPV: LR+: LR-: Accuracy: 61 56% using leave-one-out cross validation AUC: 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 ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	PPV: NPV: LR+: Accuracy: 71 69% using leave-one-out cross validation AUC: 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:0.38 Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,EF	Grodzinsky, 1992[305] Case series N = 130 US Setting: Specialty care	**Target:** Consecutive referrals to an outpatient unit specializing in the treatment of hyperactive children diagnosed with ADHD; children with language-based learning disabilities or clinically significant conduct disorder were excluded; all male; FSIQ between 85 and 125 **Other:** "Snowball" technique: Parents of ADHD boys referred peer(s) of their son's, parents of these children 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:** Other info on race or 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 **Index test:** neuropsychological,EF Stepwise discriminant function analysis; variables included are commissions and omissions scores from the vigilance portion of the Gordon Diagnositc System and the Interference subtest of the Stroop test Sensitivity: 82 Specificity: 80 PPV: NPV: LR+: LR-: Accuracy: 81	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,EF	Hinshaw, 2002[322] Case series N = 228 US Setting: Other	**Target:** Recruited from multiple sources to attend one of three consecutive summer research programs; all female; testing performed without stimulant medication (minimum 24 hour washout period); IQ>=70; common comorbidities not excluded (disruptive behavior disorders, anxiety disorders, depression) **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	**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	**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 PPV: NPV: LR+: Accuracy: 57 AUC: Rater agreement: Kappa:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Female: 100% **Age mean:** **Min age:** 6 **Max age:** 12 **Ethnicity:** % Hispanic or Latino : 11 % Black/African American : 27 % Asian : 9 % White : 53 Other info on race or ethnicity:	PPV: NPV: LR+: LR-: Accuracy: 78 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
neuropsychological,EF	Juneja, 2019[346] Case series N = 100 India Setting: Specialty care	**Target:** Children presenting with features suggestive of ADHD at a pediatric outpatient department; IQ>=70; No neurological disorders likely to affect upper limb motor performance or compliance with directions for the test, and 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:** Other info on race or 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 **Index test:** neuropsychological,EF Children's Color Trails Test (CCTT) was administered to all the subjects by a blinded clinical psychologist. This test has two parts – Part 1 (CCTT1) is 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. CCTT takes 15-20 minutes for administration. The examiner records the time taken to complete each trail and errors committed, to arrive at the score of each part. Sensitivity: 74 (60, 85) Specificity: 74 (60, 85) PPV: NPV: LR+: LR-: Accuracy: AUC: 0.800 Rater agreement:	**Index test 2:** neuropsychological,EF In part 2 (CCTT2) of the test, 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. CCTT takes 15-20 minutes for administrat Sensitivity: 84 (71, 93) Specificity: 72 (58, 84) PPV: NPV: LR+: Accuracy: AUC: 0.854 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,EF	Krieger, 2021[373] Case series N = 260 Spain Setting: Specialty care	**Target:** 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 (General Ability Index) > 85. Participants taking psychostimulant medication were asked to withhold medication 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)	**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 PPV: NPV: LR+: LR-: Accuracy:	**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 PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		Min age: 8 **Max age:** 16 **Ethnicity:** Other info on race or ethnicity: N/A	AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,EF	Mayes, 2004[412] Case series N = 809 US Setting: Specialty care	**Target:** IQ>=80, referred for learning, attention, and/or behavior problems, off medication for testing, and no head injury with loss of consciousness, 54% had a comorbid mood or behavior disorder, 76% had a comorbid learning disorder **Other:** Children with autism, brain injury, or mood and behavior disorders with or without learning disorders	**Reference standard:** Clinical diagnosis DSM-IV diagnoses agreed upon by both a child psychologist and child psychiatrist Timing: Prior diagnosis **Index test:** neuropsychological,EF 12 Wechsler Intelligence Scale for Children-Third Edition (WISC-III} subtests comprising the four Indexes, Verbal Comprehension, Perceptual Organization, Freedom from	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 info on race or ethnicity: Other : 8% were Black, Hispanic, or Asian	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 LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
neuropsychological,EF	Moura, 2017[434] Case series N = 116 Portugal Setting: Specialty care	**Target:** Children with ADHD only and with ADHD+developmental dyslexia; (a)IQ ≥ 85; (b) native speakers of European Portuguese; (c) absence of a visual, hearing, or motor handicap; and (d) 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:** Other info on race or 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 (Ameri Timing: Prior diagnosis **Index test:** neuropsychological,EF Shifting - Trail-B: The Trail–B subtest from the BANC 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 PPV: NPV: LR+: LR-: Accuracy: AUC: 0.727 Rater agreement: Kappa: ICC: Internal consistency:	**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 PPV: NPV: LR+: Accuracy: AUC: 0.744 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **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

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	quickly as possible, which were randomly displayed on a card in a 10 × 5 matrix. Sensitivity: 75 75 Specificity: 88 PPV: NPV: LR+: Accuracy: AUC: 0.844 Rater agreement: **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 PPV: NPV: AUC: 0.825 **Index text 5:** Neuropsychological Processing speed,Working memory

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
neuropsychological,EF	Moura, 2019[433] 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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Diagnosed using the DSM-5, ADHD confirmed by psychologist Timing: Prior diagnosis **Index test:** neuropsychological,EF Wechsler Intelligence Scale for Children (WISC-III) Freedom from Distractibility Index, 4 lowest subtests Sensitivity: 28 Specificity: 95 PPV: 87 NPV: 52 LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**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 PPV: NPV: LR+: Accuracy: AUC: 0.781 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Index text 4: Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,EF	Pauli-Pott, 2021[458] Case series N = 138 Germany Setting: Community	**Target:** Children who scored in the upper quartile an ADHD screening questionnaire completed by their parent at age 4-5; IQ>=80; no chronic diseases involving brain functions, any continuous pharmacological treatment, and insufficient German language skills of the parent or child; diagnosed with ADHD at age 8 **Other:** Children who scored in the upper quartile an ADHD screening questionnaire completed by their parent at age 4-5; not diagnosed with ADHD at age 8 **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 41% in entire sample **Age mean:** 4.9 (0.5) Age at follow up assessment 8.4 (0.3) **Min age:** 4 **Max age:** 5 **Ethnicity:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Parents and child care teachers completed the ADHD rating scale (FBB-ADHS-V) of the Diagnostic System for Psychiatric Disorders (DISYPS-II) done at first assessment at 4 to 5 years old. Investigator (psychologist), who was blind to all data of the first a Timing: Later diagnosis **Index test:** neuropsychological,EF Task-based neuropsychological impulsivity measure. Two tasks on hot inhibitory control and one task on behavioral approach tendency done at first assessment at 4 to 5 years old. Impulsivity measure cut-point used to predict ADHD diagnosis at 8 years old Sensitivity: 76 Specificity: 70 PPV: NPV: LR+:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,EF	Pineda, 2011[465] Case series N = 288 Colombia Setting: Specialty care	**Target:** Children with 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 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	**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	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		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 info on race or ethnicity: Other : 100% Paisa	Specificity: 81 at 0.2759 cutoff PPV: NPV: LR+: LR-: Accuracy: AUC: 0.862 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,EF	Qin , 2018[475] Case series N = 275 China Setting: Mixed	**Target:** 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:**	**Reference standard:** Clinical diagnosis Clinical diagnosis made by psychiatrists using DSM-IV criteria Timing: Prior diagnosis **Index test:** neuropsychological,EF The Das-Naglieri Cognitive Assessment System (DN: CAS). Test of cognitive abilities based on four cognitive processes. 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	**Index test 2:** neuropsychological,EF The Das-Naglieri Cognitive Assessment System (DN: CAS). Test of cognitive abilities based on four cognitive processes. Two different sets of tests were carried out according to various age groups (5–7 year-olds and 8–17 year-olds). Classification performa Sensitivity: 79

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		9.1 (2.1) for ADHD group, 9.3 (1.5) for control group **Min age: Max age:** **Ethnicity:** Other info on race or ethnicity: N/A	Planning subscale when the cut-off point was set at 25-points. Sensitivity: 73 Specificity: 79 PPV: NPV: LR+: LR-: Accuracy: AUC: 0.808 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Specificity: 58 PPV: NPV: LR+: Accuracy: AUC: 0.730 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
neuropsychological,EF	Skogli, 2013[529] Case series N = 130 Norway Setting: Specialty care	**Target:** Recruited as 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 **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:** Other info on race or 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 **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 performed 5,000 times on different random splits; ADHD boys versus control boys Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 73 SD 7.8 AUC: Rater agreement: Observed classification results versus expected classification results Kappa: 0.466 (SD 0.152) ICC: Internal consistency: Alpha: Test-retest:	**Index test 2:** neuropsychological,EF Random Forest classification using EF tests assessing working memory, inhibition, cognitive flexibility, planning, and verbal fluency; 75/25 testing/validation split performed 5,000 times on different random splits; ADHD girls versus control girls Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 79 SD 7.8 AUC: Rater agreement: Observed classification results versus expected classification results Kappa:0.507 (SD 0.175) Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Costs: Misdiagnosis: Labeling: Costs:	LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,EF	Webster, 2000[597] Case series N = 132 US Setting: Specialty care	**Target:** Children referred to a private clinic for psychoeducational evaluations who had been previously identified by at least two professionals as having 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:**	**Reference standard:** Clinical diagnosis ADHD group had been previously diagnosed by at least 2 professionals as having the disorder Timing: Prior diagnosis **Index test:** neuropsychological,EF Learning Efficiency Test -II Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 84 AUC: Rater agreement: Kappa:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		% Hispanic or Latino : 1 % Black/African American : 34 % White : 65 Other info on race or ethnicity:	ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,EF	Westerberg, 2004[603] 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:** Other info on race or 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 LR+: LR-: Accuracy:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
neuropsychological,EF	Weyandt, 1994[604] 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	**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 Six executive function tasks: Visual search, verbal fluency, the Wisconsin Card Sorting Test, Matching Familiar Figures Test, Tower of Hanoi, and mazes; Two nonexecutive function tasks: Peabody Picture Vocabulary	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Female: 0% **Age mean:** **Min age:** 6 **Max age:** 12 **Ethnicity:** % White : 100 Other info on race or ethnicity:	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 PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
neuropsychological,EF	Wodka, 2008[614] Case series N = 123 US Setting: Specialty care	**Target:** Participants were recruited from outpatient clinics at the Kennedy Krieger Institute, and from local area pediatricians, local chapters of Children and Adults with Attention Deficit/Hyperactivity Disorder (CHADD), schools, social/service organizations (e.g., Boy/Girl Scouts), and advertisements in the community (e.g., postings at libraries) as part of a larger project examining brain–behavior relationships in children; 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; oversampling for the type of ADHD less likely to occur in each sex (combined presentation for girls and inattentive presentation for boys); participants taking stimulant mediation were asked to withold 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:**	**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 Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		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 info on race or ethnicity: Other : 5% Other race	Costs:	**Index text 5:**
Observation	Bunte, 2013[175] Case series N = 251 Netherlands Setting: N/A	**Target:** Referred preschool children with externalizing behavioral problems; IQ>=70; no current medications; diagnosed with ADHD or disruptive behavior disorder plus ADHD **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:** 54.7 (8.8) **Min age:** 3.5 **Max age:** 5.5 **Ethnicity:** % Black/African American : 2 % Asian : 0.5 % White : 86 % Multiracial : 12,Other : Turkish/Moroccan Other info on race or ethnicity:	**Reference standard:** Clinical diagnosis Clinical diagnosis made by child psychiatrist and child psychologist Timing: Prior diagnosis **Index test:** Observation Disruptive Behavior Diagnostic Observation Schedule Sensitivity: 87 Specificity: 79 PPV: NPV: LR+: LR-: Accuracy: AUC: 0.92 Rater agreement: Interrater reliability between researchers administering test Kappa: ICC: 0.92 Internal consistency:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Alpha: 0.82 ICC; children retested after 8 weeks Test-retest: 0.64 Costs: Misdiagnosis: Labeling: Costs:	Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Other : Claim-based algorithms	Straub, 2021[553] Case series N = 350 US Setting: Other	**Target:** Children 14 years or younger identified from a medical encounter in hospitals who met a clinical definition for specific neurodevelopmental disorders including ADHD; required 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:**	**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:** Other : Claim-based algorithms Claim-based algorithms for neurodevelopmental disorders including ADHD Sensitivity: Specificity: PPV: 88 NPV: LR+: LR-: Accuracy:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		N/A **Min age:** 1 **Max age:** 14 **Ethnicity:** Other info on race or ethnicity: N/A	AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Other : ECG	Koh, 2022[364] Raine, 2019[960]; Tor, 2021[1083] Case series N = 123 Singapore Setting: Specialty care	**Target:** ADHD only (45 participants), ADHD + conduct disorder (62 participants), subset from the randomized Omega-3 Supplements and Social Skills Intervention Study (ClinicalTrials.gov Identifier: NCT00819429) **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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Primary diagnosis made by child's attending physician Timing: Prior diagnosis **Index test:** Other : 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 PPV: NPV: LR+:	**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 PPV: NPV: LR+: Accuracy: 84 AUC: Rater agreement:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			LR-: Accuracy: 88 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Kappa: Internal consistency: Alpha: Costs: **Index test 3:** EEG Electroencephalogram (EEG) during resting-state, eyes open for 3 minutes, K-nearest neighbor three class classification (ADHD vs ADHD+CD vs CD only), 10-fold cross validation[1083] Sensitivity: 97 97 Specificity: 100 PPV: NPV: LR+: Accuracy: 98 AUC: Rater agreement: **Index text 4:** EEG Electroencephalogram (EEG) during resting-state, eyes open for 3 minutes, bagged tree three class classification (ADHD vs ADHD+CD vs CD only), 10-fold cross validation[1083] Sensitivity: 94

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Specificity: 100 PPV: NPV: AUC: **Index text 5:**
Other : EHR phenotype algorithm	Slaby, 2022[530] Case series N = 27,270 US Setting: Other	**Target:** Mined EHRs from 2009 to 2016 using ICD codes, medication history and keywords specific to ADHD, and comorbid psychiatric disorders; subjects that were cases of both ADHD and one or more psychiatric disorders were considered comorbid ADHD cases **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	**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. The numb Timing: Prior diagnosis **Index test:** Other : EHR phenotype algorithm Multi-source/multi-approach electronic health record (EHR) rule-based phenotype algorithm with natural language processing text mining developed to discriminate cases with ADHD in isolation from cases with ADHD with comorbidities Sensitivity: Specificity: PPV: 95 NPV: LR+: LR-: Accuracy:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		Other info on race or ethnicity: Other : 4% Other	AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Other : Electro interstitial scans (EIS)	Caudal, 2011[263] Case series N = 112 France Setting: N/A	**Target:** Participants 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; children needed to have diagnosis of ADHD following psychiatric examination **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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Diagnosed with ADHD according to the DSM-IV and further examinations Timing: Prior diagnosis **Index test:** Other : Electro interstitial scans (EIS) Electro interstitial scans to measure bioimpedance Sensitivity: 80 Cutoff 7.4 micro Siemens Specificity: 98 Cutoff 7.4 micro Siemens PPV: NPV: LR+: LR-: Accuracy: AUC: 0.876 Rater agreement: Kappa:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Other : Eye movement	Merzon, 2022[419] Case series N = 73 Other Setting: N/A	**Target:** No medication within 24 hours prior to assessment; comorbidities present in some participants include oppositional defiant disorder, unspecified conduct disorder, panic disorder, unspecified affective disorders, and chronic motor or vocal tic disorder **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	**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 : 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	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		Min age: 9 **Max age:** 13 **Ethnicity:** Other info on race or ethnicity: N/A	PPV: NPV: LR+: LR-: Accuracy: AUC: 0.91 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: 16% false negatives, 22% false positives Labeling: Costs:	Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Other : Eye vergence	Varela Casal, 2019[586] Case series N = 92 Spain Setting: Mixed	**Target:** 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	**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 : 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	**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 routin

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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:** Other info on race or ethnicity: N/A	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. Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 96 AUC: 0.99 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 86 AUC: 0.90 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Index text 5:
Other : Medical record data	Mikolas, 2022[423] 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:** Other info on race or 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 attentio Timing: Later diagnosis **Index test:** Other : Medical record data 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	**Index test 2:** Other : Medical record data 19 most predictive features selected from the original 30 using sequential floating forward selection, linear support vector machine classifier, 10-fold cross-validation Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: 68 AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Sensitivity: 67 Specificity: 65 PPV: NPV: LR+: LR-: Accuracy: 66 AUC: 0.66 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: SVM classifier using all 30 features: 18% false negatives, 16% false positives Labeling: Costs:	**Index test 3:** Other : Medical record data Secondary classification without demographic features: linear support vector machine classifier, 10-fold cross-validation, non-demographic features only Sensitivity: 65 65 Specificity: 65 PPV: NPV: LR+: Accuracy: 65 AUC: 0.663 Rater agreement: **Index text 4:** Other : Medical record data 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 PPV: NPV:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				AUC: 0.696 **Index text 5:**
Other : Parent + Teacher rating	Vogt, 2011[588] 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 (CAMHS) clinic over 2 years; ADHD assessments in the year prior to using objective measurements (2006-2007 control group, n = 46) were compared with ADHD assessments in the first year of adding objective measures to the assessment (2007-2008 QbTest group, n = 62) **Other:** Individuals from same referral group not diagnosed with ADHD **ADHD presentation:** N/A : QbTest group: 16% combined, 14% 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	**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 **Index test:** Other : Parent + Teacher rating Strengths and Difficulties Questionnaire (SDQ) parent and teacher ratings compared to clinical diagnosis for QbTest group (n= 62, 43 ADHD, 19 no ADHD) Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC:	**Index test 2:** Other : Parent + Teacher rating Strengths and Difficulties Questionnaire (SDQ) parent and teacher ratings compared to clinical diagnosis for control group (n=46, 27 ADHD, 19 no ADHD) Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Follow-up over 1 year of the participants referred for an

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Min age: Max age: **Ethnicity:** Other info on race or ethnicity: N/A	Rater agreement: Mixed SDQ rating (disagreement between parent and teacher ratings) versus clinician's diagnosis 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 Kappa: ICC: Internal consistency: Alpha: 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 Costs: Misdiagnosis: The results from this audit suggest that through greater symptom specification with the use of objective measurements clinical decisions remained more consistent and were less likely to be revised over 1 year Labeling: Costs:	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) Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
Parent interview guide	Ickowicz, 2006[334] 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:** Other info on race or 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 Parent Interview for Child Symptoms (PICS) Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement: 48 randomly selected, videotaped interviews were rescored by an independent reviewer blinded to original ratings Kappa: 0.73 ICC: 0.93 for ADHD inattentive, 0.97 for ADHD hyperactive-impulsive Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Labeling: Costs:	**Index text 5:**
Parent rating	Algorta, 2016[124] Case series N = 18,232 UK Setting: Other	**Target:** Children with ADHD; all participants 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 Other info on race or ethnicity:	**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 Strengths and Difficulties Questionnaire Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC: Range 0.81-0.96 for hyperactivity/inattention, conduct problems and total difficulties scales in male and	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			female subsamples and at different age ranges Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Babinski, 2021[135] Case series N = 1050 US Setting: N/A	**Target:** Participation not limited by gender, race, income, or geography due to desire of sample to represent US population; all participants had ADHD **Other:** None **ADHD presentation:** N/A **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 48.5% **Age mean:** 8.42 (2.31) **Min age:** 5 **Max age:** 12 **Ethnicity:** % White : 78.8% Other info on race or ethnicity: Other : Non-Hispanic: 84.2%	**Reference standard:** Other Disruptive Behavior Disorders Rating Scale-Parent rating Timing: Prior diagnosis **Index test:** Parent rating ROC analysis was conducted to examine the optimal ADHD symptom count cutoff for girls and boys, the criterion was defined as an impairment score of 5 or more on the Impairment Rating Scale. Sensitivity: Specificity: PPV: NPV: LR+: LR-:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Accuracy: AUC: Reported for girls inattention, Inattention boys=0.87, hyperactivity/impulsivity girls=0.90, hyperactivity/impulsivity boys=0.87 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Burton, 2019[176] Case series N = 15560 Canada Setting: Mixed	**Target:** Population-based sample: reported a diagnosis of ADHD, self-report only completed by those ages 13-17 years. ADHD clinic sample (validation sample): IQ >=80, children and adolescents diagnosed with ADHD by a psychiatrist and clinical psychologist, self-reports not done in this sample **Other:** Population-based sample: did not report a diagnosis of ADHD. Clinic sample (validation sample): children and adolescents not diagnosed with ADHD, IQ>=80 **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** 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 **Index test:** Parent rating Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Rating Scale (SWAN) Parent rating, optimal cut-point >0.74. Cut-	**Index test 2:** Teen/child self report Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Rating Scale (SWAN) Self report, optimal cut-point >0.81. Self-reports done by adolescents ages 13-17 from population-based sample only. Sensitivity: 57 Specificity: 81 PPV: NPV: LR+:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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:** Other info on race or ethnicity: N/A	point created using population-based sample tested using validation sample. Sensitivity: 82 84% in clinical validation sample Specificity: 81 92% in clinical validation sample PPV: NPV: LR+: LR-: Accuracy: AUC: 0.88 Rater agreement: Kappa: ICC: Internal consistency: Alpha: 0.95 Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Accuracy: AUC: 0.71 Rater agreement: Kappa: Internal consistency: Alpha: 0.88 Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
Parent rating	Bussing, 1998[177] Case series N = 499 US Setting: School	**Target:** Total special ed population in one school district. 70% participation rate. All underwent Diagnostic Interview Schedule for Children (DISC) for DSM IV diagnosis plus two index instruments. **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 info on race or ethnicity: Other : 49% "non-white"	**Reference standard:** Clinical diagnosis ADHD per DSM IV diagnosis Timing: Concurrent **Index test:** Parent rating Attention Deficit Disorders Evaluation Scale (ADDES), parent rating Data abstracted 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. 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. LR+: LR-: Accuracy: 73 "Efficiency" = 73% at 2 months before DSM-IV administered. Data is for 15th percentile on ADDES AUC:	**Index test 2:** Parental rating scale Conners Abbreviated Symptom Questionnaire (ASQ), parent rating Data abstracted for 60 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. PPV: NPV: LR+: Accuracy: 76% "efficiency" when administered simultaneous with DISC for DSM IV, 76% "efficiency" to discriminate from other special ed students. AUC: Rater agreement: Kappa: Internal consistency: Alpha:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Chen, 1994[194] Doyle, 2000[721] Case series N = 260 US Setting: Mixed	**Target:** All male, met diagnostic criteria for current ADHD at time of clinical referral 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 sesorimotor handicaps (paralysis, deafness, blindness), psychosis, autism; IQ>80 **Other:** Children without ADHD selected from active outpatients at pediatric medical clinics;	**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 Child Behavior Checklist (CBCL) Attention Problems Scale, T score cutoff of 55; logistic regression,	**Index test 2:** Parental rating scale Child Behavior Checklist (CBCL) Attention Problems Scale, T score cutoff of 55; logistic regression, validation using brothers of ADHD and pediatric comparison probands Sensitivity: 61 Specificity: 94 PPV: 65

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 Other info on race or ethnicity:	split-half cross validation sample using ADHD and pediatric comparison probands Sensitivity: 84 Specificity: 93 PPV: 93 NPV: 84 LR+: LR-: Accuracy: AUC: 0.925 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	NPV: 93 LR+: Accuracy: AUC: 0.855 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Parental rating scale Child Behavior Checklist (CBCL) Attention Problems Scale,T score cutoff of 55; logistic regression, validation using sisters of ADHD and pediatric comparison probands Sensitivity: 67 67 Specificity: 94 PPV: 50 NPV: 97 LR+: Accuracy: AUC: 0.902 Rater agreement: **Index text 4:** neuropsychological,CPT,EF Neuropsychological tests administered to ADHD and pediatric comparison probands

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				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 Specificity: 46 PPV: 63 NPV: 62 AUC: 0.69 **Index text 5:**
Parent rating	Deb, 2008[222] Case series N = 151 UK Setting: Specialty care	**Target:** Children who received clinical assessments for ADHD and intellectual disabilities in a specialist outpatient clinic; Intellectual disability defined as IQ <=70 associated with inadequte adaptive functioning, borderline IQ defined as IQ above 70 but below 80 on either verbal or performance tasks **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	**Reference standard:** Clinical diagnosis Timing: Prior diagnosis **Index test:** Parent rating Conners' Parent Rating Scales-Revised, cut-off score of 50 Sensitivity: 83 Specificity: 89 PPV: NPV: LR+: LR-: Accuracy: AUC: 0.875 Rater agreement: Parent versus teacher total scores Kappa: ICC: 0.19	**Index test 2:** Teacher rating scale Conners' Teacher Rating Scales-Revised, cut-off score of 48 Sensitivity: 56 Specificity: 83 PPV: NPV: LR+: Accuracy: AUC: 0.665 Rater agreement: Kappa: Internal consistency: Alpha: 0.80 Costs:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Age mean: **Min age:** 3 **Max age:** 17 **Ethnicity:** Other info on race or ethnicity: N/A	Internal consistency: Alpha: 0.84 Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Deserno, 2022[227] Case series N = 434 Netherlands 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; a third had an additional diagnosis such as oppositional defiant disorder, autism spectrum disorder, specific learning disorder with impairment in reading, language disorder, and generalized anxiety disorder; replication sample from the Oregon ADHD and Autism project **Other:** Children with autism spectrum disorder, neurotypical developing children	**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 The Strengths and Weaknesses of ADHD symptoms and Normal-behaviors ratings scale (SWAN)	**Index test 2:** Parental rating scale The Strengths and Weaknesses of ADHD symptoms and Normal-behaviors ratings scale (SWAN) hyperactivity/impulsivity subscale and the Social Responsiveness Scale restricted interests and repetitive behaviors, social

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		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:** Other info on race or ethnicity: N/A	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 PPV: NPV: LR+: LR-: Accuracy: 76 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	awareness, social cognition, social commun Sensitivity: 67 For ADHD diagnostic group, recall = 79% Specificity: 84 For ADHD diagnostic group PPV: NPV: LR+: Accuracy: 72 AUC: Rater agreement: Predicted diagnostic group versus actual diagnostic group Kappa:0.56 Internal consistency: Alpha: Costs: **Index test 3:** Parental rating scale The Strengths and Weaknesses of ADHD symptoms and Normal-behaviors ratings scale (SWAN) hyperactivity/impulsivity subscale and the Social Responsiveness Scale restricted interests and repetitive behaviors, social awareness, social cognition, social commun

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
				Sensitivity: 77 77 Specificity: 74 PPV: NPV: LR+: Accuracy: 71 AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Duda, 2016[239] Case series N = 2925 US Setting: Other	**Target:** Mainly siblings of the autism probands that reported a prior clinical diagnosis of 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:**	**Reference standard:** Clinical diagnosis Parent-reported clinical diagnosis Timing: Prior diagnosis **Index test:** Parent rating Social Responsiveness Scale, Support Vector Classification, 10-fold cross validation, classification of ADHD vs ASD Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Ethnicity: Other info on race or ethnicity: N/A	AUC: 0.965 5 of 65 features used Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Duda, 2017[238] Case series N = 422 US Setting: Mixed	**Target:** Selected the subset of responses from parents of children with only ADHD (n = 174) to serve as the survey sample; for this survey data set, 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	**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 Subset of items from the Social Responsiveness Scale (SRS). Best AUC obtained with Elastic Net and Linear discriminant analysis classifiers. Machine-learning pipeline consisted of three	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Female: 34.5% **Age mean:** 10.4 (3.6) **Min age: Max age:** **Ethnicity:** Other info on race or ethnicity: N/A	trials using subsamples of archival data, survey data, or a mixture of both. Model used to discriminate between ADHD and ASD Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC: 0.89 ADHD versus ASD Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
Parent rating	Ebesutani, 2010[245] 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 **Comorbidity:** N/A **Female:** % 32.8% female in entire sample **Age mean:** 11.4 (2.5) **Min age:** 6 **Max age:** 18 **Ethnicity:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Children's Interview for Psychiatric Syndromes, Parent Version (P-ChIPS) Timing: Concurrent **Index test:** Parent rating Child Behavior Checklist (CBCL) DSM-oriented ADH Problems scale, ADHD vs No ADHD Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC: 0.75 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 2:** Parental rating scale Child Behavior Checklist (CBCL) Attention Problems syndrome scale, ADHD vs No ADHD Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: 0.76 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Eiraldi, 2000[248] 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	**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 Devereux Scales of Mental Disorders (DSMD) Attention subscale; children with any presentation of ADHD versus controls, cutoff T>=65 Sensitivity: 77 Specificity: 78 PPV: 95 NPV: 39 LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC:	**Index test 2:** Parental rating scale Child Behavior Checklist (CBCL) Attention Problems subscale; children with any presentation of ADHD versus controls, cutoff T>=70 Sensitivity: 51 Specificity: 83 PPV: 94 NPV: 24 LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		% White : 76 Other info on race or ethnicity:	Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Elkins, 2014[254] 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 **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** Mood disorder **Female:** 54%	**Reference standard:** Clinical diagnosis Diagnosed with ADHD per DSM-IV-R Timing: Prior diagnosis **Index test:** Parent rating Attention Problems Scale of the Child Behavior Checklist (CBCL) Sensitivity: 73.9 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 PPV: 89.5 NPV: 77.8 LR+:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Age mean: 12.03 (3.3) **Min age:** 7 **Max age:** 18 **Ethnicity:** % White : 80.4 Other info on race or ethnicity:	LR-: Accuracy: 82.6 Overall Correct Classification AUC: 0.84 SE 0.06 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Gardner, 2007[285] Case series N = 269 US Setting: Primary Care	**Target:** Children and adolescents diagnosed with ADHD who consecutively presented at primary care offices for well-child care, the evaluation of recurrent abdominal pain, or the assessment and management of other minor illnesses. Participants selected into one of two studies based on positive screening results for the conditions of interest for each study. Sample includes more children with psychosocial problems, particularly anxiety and depression, than would be found in an unselected primary care sample.	**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 17-item Pediatric Symptom Checklist (PSC-17) Attention subscale, cut score >=7 Sensitivity: 58 Specificity: 91 PPV: 25 5% prevalence	**Index test 2:** Parental rating scale Child Behavior Checklist (CBCL) Attention subscale Sensitivity: 68 Specificity: 90 PPV: 26 NPV: 98 LR+: Accuracy: AUC: 0.88 Rater agreement:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 info on race or ethnicity: Other : 4	NPV: 98 5% prevalence LR+: LR-: Accuracy: AUC: 0.86 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
Parent rating	Gargaro, 2014[287] Case series N = 49 Australia Setting: N/A	**Target:** Children with ADHD (N = 13) or ADHD plus autism (N = 12). Participants were excluded if they had previously experienced the following conditions: comorbid medical (e.g. tuberous sclerosis), hearing or visual, neurological (e.g. Epilepsy), psychiatric (e.g. Tourette's, Conduct Disorder, Oppositional Defiant Disorder) or genetic disorders (e.g. Fragile X disorder), 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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Diagnosed with ADHD per DSM IV TR Timing: Prior diagnosis **Index test:** Parent rating Developmental Behaviour Checklist Hyperactivity Index (DBC-HI), parent version, cut 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 PPV: NPV: LR+: LR-: Accuracy: AUC: 0.997 AUC 0.722 (CI .507–.937) for discriminating autism + ADHD from autism alone Rater agreement: Kappa: ICC: Internal consistency: Alpha: 0.931 Test-retest: Costs: Misdiagnosis: Labeling:	**Index test 2:** Parental rating scale Conner's Parent Rating Scale-Revised Short Form (CPRS-R S) 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 PPV: NPV: LR+: Accuracy: AUC: 0.994 AUC 0.782 (CI 0.596–0.979) for discriminating autism + ADHD from autism alone Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Costs:	NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Gomez, 2018[299] Cohort study N = 217 Australia Setting: Specialty care	**Target:** Archival records of patients referred to an outpatient psychiatric unit between 2008 and 2016 **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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis DSM-IV TR Timing: Prior diagnosis **Index test:** Parent rating Modified version of the Strengths and Weaknesses of ADHD-Symptoms and Normal Behavior (SWAN-M) Scale, all maternal ratings, test-retest study of measurement invariance over a 12-month interval Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			AUC: Rater agreement: Kappa: ICC: 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 Costs: Misdiagnosis: For the bifactor model, measurement invariance testing using multiple-group confirmatory factor analysis (CFA) indicated support for configural and full scalar test-retest invariance when the chi-square difference test was applied. Labeling: Costs:	Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
Parent rating	Hong, 2019[326] Case series N = 44 US Setting: Specialty care	**Target:** Children presenting to university affiliated outpatient clinics with early disruptive behavior problems diagnosed with ADHD+ disruptive behavior disorder **Other:** Children presenting to university affiliated outpatient clinics with early disruptive behavior problems 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 Other info on race or ethnicity:	**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 **Index test:** Parent rating Child Behavior Checklist for ages 1.5 to 5 Attention-Deficit/Hyperactivity Problems scale Sensitivity: 71 Specificity: 91 PPV: 88 NPV: 78 LR+: LR-: Accuracy: 80 AUC: 0.83 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Index text 5:
Parent rating	Hudziak, 2004[332] Case series N = 370 US Setting: Mixed	**Target:** Probands participating in a family genetic study of attention and aggressive behavior problems; lives with at least one biological parent, has at least one sibling between ages 6 and 18, IQ>=70, T-scores above 67 on the attention problems syndrome and/or the aggressive behavior syndrome scales of the Child Behavior Checklist **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	**Reference standard:** Clinical diagnosis Vermont Structured Diagnostic inverview with mothers of the probands and siblings Timing: Prior diagnosis **Index test:** Parent rating Child Behavior Checklist (CBCL) attention problems scale, T-score cutoff= 55, ROC analysis using attention problems syndrome scale Sensitivity: 83 Sibling group Specificity: 88 Sibling group PPV: 80 Sibling group NPV: 90 Sibling group LR+: LR-: Accuracy: AUC: 0.841 for proband group, 0.904 for sibling group Rater agreement: Kappa:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Ethnicity: Other info on race or ethnicity: N/A	ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Jacobson, 2020[335] 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	**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 neurops Timing: Concurrent **Index test:** Parent rating Behavior Rating Inventory of Executive Function, Second Edition (BRIEF2) global executive composite summary score Sensitivity: 38 Specificity: 96 PPV: 93 NPV: 54 LR+: LR-: Accuracy: 63	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		% Asian : 2.3 % White : 59.63 % Multiracial : 5.45 Other info on race or ethnicity: Other : 4.8% unknown	AUC: 0.806 Rater agreement: Kappa: ICC: Internal consistency: Alpha: 0.965 Test-retest: Costs: Misdiagnosis: Labeling: Costs:	LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Jensen-Doss, 2013[340] Case series N = 82 US Setting: Community	**Target:** 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 **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:** Provider **Comorbidity:** N/A **Female:** %	**Reference standard:** Clinical diagnosis 15 clinicians conducted the initial eligibility evaluations for the clients; Four of them were licensed mental health professionals, five were interns, and six were called ''Qualified Mental Health Professionals'' by the state, representing individuals wi Timing: Concurrent **Index test:** Parent rating Child Behavior Checklist Attention deficit/ hyperactivity problems subscale Sensitivity: Specificity: PPV: NPV: LR+: LR-:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		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 Other info on race or ethnicity:	Accuracy: AUC: 0.55 Rater agreement: Child Behavior Checklist score versus clinical chart diagnosis Percent disagreement= 45.1 Kappa: 0.10 ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Levy, 2017[382] Case series N = 139 US Setting: Specialty care	**Target:** Validation sample consisted of consecutive patients seen in a comprehensive psychological testing clinic (for cognitive and/or personality assessment) over approximately an 8-year period of time **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_other : 42,combined_other : 36 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** %	**Reference standard:** Clinical diagnosis SI-4 scores for parent and teacher Timing: Prior diagnosis **Index test:** Parent rating Conduct-Hyperactive-Attention Problem-Oppositional Symptom (CHAOS) scale parent. Subscales include attention problems, hyperactivity-impulsivity, oppositional behavior, and conduct problems. Sensitivity: Specificity: PPV: NPV:	**Index test 2:** Teacher rating scale Conduct-Hyperactive-Attention Problem- Oppositional Symptom (CHAOS) scale teacher. Subscales include attention problems, hyperactivity-impulsivity, oppositional behavior, and conduct problems. Sensitivity: Specificity: PPV: NPV: LR+:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		41% female in entire validation sample **Age mean:** 10.7(3.1) **Min age:** 6 **Max age:** 17 **Ethnicity:** % Black/African American : 7.19 % Native Hawaiian or Pacific Islander : 0.719 % White : 91.367 % Multiracial : 0.719 Other info on race or ethnicity:	LR+: LR-: Accuracy: AUC: Rater agreement: Mother versus father rating Ranged from 0.58 to 0.63 over three subscales, the fourth subscale, conduct problems , interrater agreement was not statistically signficant Kappa: ICC: Internal consistency: Cronbach's alpha ranged from 0.80 to 0.91 over four subscales Alpha: Test-retest between 1 and 829 days Test-retest: Ranged from 0.74 to 0.87 over four subscales Costs: Misdiagnosis: Labeling: Costs:	Accuracy: AUC: Rater agreement: Teacher versus parent rating Ranged from 0.28 to 0.41 over three subscales. The fourth subscale, oppositional behavior, was only marginally statistically significant (r=0.17,p<0.1) Kappa: Internal consistency: Cronbach's alpha ranged from 0.64 to 0.91 over four subscales Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Mayfield, 2018[413] Case series N = 337 US Setting: Other	**Target:** Children with no co-morbid intellectual disability, pervasive developmental disorder, or history of neurological disorder including seizures, convulsions, epilepsy, cerebral palsy, encephalitis, traumatic brain injury, and loss of consciousness, and a standardized rating scale for the assessment of ADHD symptoms was completed by both the mother and the father **Other:** None; study comparing mother and father ratings **ADHD presentation:** inattentive : 62.9,combined : 37.1 **Diagnosed by:** Unclear/NR **Comorbidity:** N/A **Female:** 27.9% **Age mean:** 10.3 (2.83) **Min age:** 6 **Max age:** 16 **Ethnicity:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis DSM-IV diagnosis of ADHD Timing: Concurrent **Index test:** Parent rating DSM-ADHD-SRS (symptom rating scale) total score mother rating Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement: DSM-ADHD-SRS (symptom rating scale) mother-rating versus father-rating Mother and father ratings (ICC) correlated .51 for inattention, .56 for hyperactivity, and .58 for impulsivity. Kappa:	**Index test 2:** Parental rating scale DSM-ADHD-SRS (symptom rating scale) total score father rating Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: 0.91 Costs: **Index test 3:** Sensitivity: Specificity:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			ICC: Internal consistency: Alpha: 0.90 Test-retest: Costs: Misdiagnosis: Labeling: Costs:	PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	McCarthy, 2016[414] 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	**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-typ Timing: Concurrent **Index test:** Parent rating The Pediatric Symptom Checklist (PSC) Attention Subscale parent-completed measure of child and adolescent psychosocial functioning Sensitivity: 55 Specificity: 81	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Ethnicity: Other info on race or ethnicity: N/A	PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: 0.90 Test-retest: BPRS-C-PE and PSC-AS correlated 0.56 at intake and 0.53 at a 3-month follow up appointment. Costs: Misdiagnosis: Labeling: Costs:	Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	McIntosh, 1995[417] Case series N = 265 US Setting: School	**Target:** Selected from two suburban public school districts, no other medical problems (i.e. Tourettes, seizures, cerebral palsy, mental retardation), 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	**Reference standard:** Clinical diagnosis Diagnosed by physicians and licensed psychologists and verified by the investigators through school health and testing records Timing: Prior diagnosis **Index test:** Parent rating The Maternal Perinatal Scale consisting of questions and a condition checklist	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 info on race or ethnicity: Other : 5% Other	Sensitivity: 61 Specificity: 73 PPV: 69 NPV: 66 LR+: LR-: Accuracy: 67 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
Parent rating	Mouti, 2019[435] Case series N = 162 Australia Setting: Mixed	**Target:** Children with ADHD and 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:** Other info on race or 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 Social Communication Questionnaire- Lifetime version, total score cutoff of 13 to differentiate between autism spectrum disorder and ADHD Sensitivity: 96% autism spectrum disorder vs ADHD groups Specificity: 87% autism spectrum disorder vs ADHD groups PPV: NPV: LR+: LR-: Accuracy: AUC: AUC 0.96 (0.91, 1.0) autism spectrum disorder vs ADHD groups Rater agreement: Kappa: ICC: Internal consistency: Alpha: 0.93 Test-retest: Costs:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Misdiagnosis: In Australia, given the introduction of a new funding scheme (i.e., the National Disability Insurance Scheme), a "missed" diagnosis would have implications for accessing funding and treatments. Labeling: Costs:	**Index text 5:**
Parent rating	Mukherjee, 2014[436] Case series N = 156 India Setting: Specialty care	**Target:** Recruited from the Child Development/Neurology outpatient clinics **Other:** Children with various Neurodevelopmental Disorders were recruited from the Child Development/Neurology outpatient clinics; those with typical development were recruited from the pediatric outpatient departments. **ADHD presentation:** inattentive : 46,hyperactive : 19,combined : 35 **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** % 31% female in entire sample **Age mean:** 7.4 (0.99) **Min age:** 6 **Max age:** 9 **Ethnicity:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Each child was assessed by a two member expert team (pediatric neurologist and child psychiatrist) who based their diagnosis on DSM-IV-TR criteria comprising interviews and direct observations; each evaluator was blinded to original diagnosis and to the a Timing: Concurrent **Index test:** Parent rating INCLEN Diagnostic Tool for ADHD (INDT-ADHD); ADHD versus typically developing children Sensitivity: 88 (81, 89) Specificity: 97 (87, 100) PPV: 98 NPV: 83 LR+: 31.5 LR-: 0.12 Accuracy: AUC: Rater agreement:	**Index test 2:** Parental rating scale INCLEN Diagnostic Tool for ADHD (INDT-ADHD); ADHD versus other neuro-developmental disorders Sensitivity: 88 (79, 94) Specificity: 43 (35, 49) PPV: 58 NPV: 79 LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Parental rating scale INCLEN Diagnostic Tool

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Convergent validity with Conner's Parents Rating Scale was moderate (r =0.73, P= 0.001). Kappa: ICC: Internal consistency: Alpha: 0.91 Test-retest: Costs: Misdiagnosis: Labeling: Costs:	for ADHD (INDT-ADHD); total score >=8 Sensitivity: 88 88 Specificity: 96 PPV: 38 NPV: 11 LR+: Accuracy: AUC: 0.98 Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Mulhern, 1994[437] 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	**Reference standard:** Clinical diagnosis Clinical diagnosis from a Pediatrician, using DSM-III-R Criteria Timing: Concurrent **Index test:** Parent rating Parental concern for one or more major symptoms of ADHD Sensitivity: 87 Specificity: 41 PPV: 47 NPV: 84 LR+:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		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 Other info on race or ethnicity:	LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Nolan,1999[451] 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:**	**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 psychoeduca Timing: Concurrent	**Index test 2:** Teacher rating scale Symptom Inventories- Teacher rating Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 info on race or ethnicity: Other : 2% Other race	**Index test:** Parent rating Symptom Inventories- Parent rating Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement: Parent versus Teacher Kappa: Inattentive category 0.68, Hyperactive-impulsive category 0.42, Combined category 0.56 ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
Parent rating	O'Neill, 2021[452] 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 Other info on race or ethnicity:	**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 Conners 3 Parent Rating Scale Inattention and Hyperactivity/Impulsivity scores and Behavioral Regulation Index of the Behavior Rating Inventory of Executive Function (BRIEF2) used to discriminate between children with ADHD+Prenatal alcohol exposure and typically developing children Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC: 0.90 All 3 scale measures alone AUC >0.90, p<0.0005 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs:	**Index test 2:** Parental rating scale Conners 3 Parent Rating Scale Inattention (CIn) and Hyperactivity/Impulsivity (CHp) scores and Behavioral Regulation Index (BRI) of the Behavior Rating Inventory of Executive Function (BRIEF2) used to discriminate between children with ADHD+familial histo Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: 0.95 All 3 scale measures alone AUC >0.95, p<0.0005 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Imaging Magnetic resonance spectroscopy (MRS) and diffusion tensor imaging (DTI) used to discriminate between children with

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Misdiagnosis: Labeling: Costs:	ADHD+Prenatal alcohol exposure and typically developing children Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: 0.68 Rater agreement: **Index text 4:** Imaging Magnetic resonance spectroscopy (MRS) and diffusion tensor imaging (DTI) used to discriminate between children with ADHD+familial history of ADHD (no prenatal alcohol exposure) and typically developing children Sensitivity: Specificity: PPV: NPV: AUC: 0.70 **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
Parent rating	Quintana, 2007[476] 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 info on race or ethnicity: 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 The Attention-Deficit/Hyperactivity Disorder Rating Scale, Version-IV Sensitivity: 81 Specificity: 22 PPV: 65 NPV: LR+: LR-: Accuracy: 60 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 2:** 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 PPV: NPV: LR+: Accuracy: 96 AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Index text 4: Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Rishel, 2005[486] Case series N = 236 US Setting: Community	**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 Other info on race or ethnicity:	**Reference standard:** Clinical diagnosis DSM IV per Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) Timing: Concurrent **Index test:** Parent rating Child Behavior Checklist (CBCL), 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 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 LR+: LR-: Accuracy: 77.8% overall correct	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			AUC: .83 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Scheeringa, 2020[504] Case series N = 58 US Setting: Specialty care	**Target:** Children recruited from one private outpatient child and adolescent psychiatry clinic that specialized in very young children without primary diagnosis of ASD **Other:** None **ADHD presentation:** N/A **Diagnosed by:** Researcher **Comorbidity:** N/A **Female:** 25% **Age mean:** 4.67(1.15) **Min age:** 1 **Max age:** 6 **Ethnicity:** % Hispanic or Latino : 8 % Asian : 1 % White : 87 % Multiracial : 4	**Reference standard:** Other ADHD measured using SNAP and administered by trained RA Timing: Concurrent **Index test:** Parent rating The Diagnostic Infant and Preschool Assessment was revised to include Likertratings(DIPA-L) all cases Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement:	**Index test 2:** Parental rating scale The Diagnostic Infant and Preschool Assessment was revised to include Likertratings(DIPA-L) <= 30 days between interviews Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Other info on race or ethnicity:	Kappa: ICC: Internal consistency: 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 Kappa 0.79 Costs: Misdiagnosis: Labeling: Costs:	Alpha: The Diagnostic Infant and Preschool Assessment including Likertratings (DIPA-L) first interview versus second interview. Interval between interviews <=30 days ICC 0.91 Kappa 0.84 Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
Parent rating	Silverstein, 2016[524] Cohort study N = 156 US Setting: Mixed	**Target:** Children whose primary care providers initiated an ADHD evaluation between September 2010 and June 2013; enrolled from a pediatric primary care clinic of an urban safety-net hospital or an urban, federally qualified community health center **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 info on race or ethnicity: Other : 22% Other	**Reference standard:** Clinical diagnosis ADHD assessment complied with DSM-IV guidelines Timing: Concurrent **Index test:** Parent rating Best performing model contained: parent Vanderbilt scale plus child age, history of grade retention, the presence of child anxiety or depression, the presence of clinically significant oppositional defiant symptoms, and history of parental substance abuse. Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: 84 AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Index text 5:
Parent rating	Spencer, 2018[542] Case series N = 41 US Setting: Community	**Target:** Children recruited during a well-child visit at an urban pediatric practice and diagnosed with ADHD; 55% comorbid with ODD, 30% with two or more comorbidities **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:** Other (specify) Staff **Comorbidity:** N/A **Female:** 49.3% **Age mean:** 7.0 (1.4) **Min age:** 6 **Max age:** 10 **Ethnicity:** % Hispanic or Latino : 84.7 % Black/African American : 4.3 % American Indian or Alaska Native : 0.5 % Asian : 0.0 % Native Hawaiian or Pacific Islander : 1.0 % White : 9.6	**Reference standard:** Other MINI-KID (Miniature International Neuropsychiatric Interview) for Children Timing: Later diagnosis **Index test:** Parent rating Pediatric Symptom Checklist (PSC-35) Sensitivity: 82 Specificity: 50 PPV: 64 NPV: 73 LR+: LR-: Accuracy: AUC: 0.700 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest:	**Index test 2:** Parental rating scale Child Behavior Checklist (CBCL) Sensitivity: 80 Specificity: 81 PPV: 80 NPV: 81 LR+: Accuracy: AUC: 0.837 Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		% Multiracial : 7.7 Other info on race or ethnicity:	Costs: Misdiagnosis: Labeling: Costs:	NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Sprafkin, 2007[546] 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	**Reference standard:** Clinical diagnosis Timing: Concurrent **Index test:** Parent rating ADHD Symptom Checklist-4 Parent, randomized-order version given to cohort 2 (N=104) Sensitivity: 58 Specificity: 60 PPV: 68 NPV: 49 LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC:	**Index test 2:** Parental rating scale ADHD Symptom Checklist-4 Parent, standard diagnostic-cluster version given to cohort 1 (N=103) Sensitivity: 61 Specificity: 59 PPV: 67 NPV: 53 LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Coefficient alpha 0.95 for inattentive scale,

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Ethnicity: % Hispanic or Latino : 4 % Black/African American : 7 % White : 88 Other info on race or ethnicity: Other : 1% Other	Internal consistency: Coefficient alpha 0.92 for inattentive scale, 0.87 for hyperactive/impulsive scale Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	0.95 for hyperactive/impulsive scale Alpha: Costs: **Index test 3:** Teacher rating scale ADHD Symptom Checklist-4 Teacher, randomized-order version given to cohort 2 (N=104) Sensitivity: 66 66 Specificity: 57 PPV: 75 NPV: 57 LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Teacher rating scale ADHD Symptom Checklist-4 Teacher, standard diagnostic-cluster version given to cohort 1 (N=103) Sensitivity: 70 Specificity: 59 PPV: 67 NPV: 62 AUC: **Index text 5:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
Parent rating	Thompson, 2017[569] Case series N = 393 UK Setting: Other	**Target:** Recruitment specialists identified participants (parents of individuals aged 5-19 with ADHD) through advertising, patient advocacy groups, and treating physicians; each individual ADHD status was recorded based on a self-report by a parent or caregiver **Other:** Age matched healthy children **ADHD presentation:** N/A **Diagnosed by:** Provider **Comorbidity:** N/A **Female:** 20% **Age mean:** Control: 11.5 (3.4); ADHD: 11.4 (3.4) **Min age:** 5 **Max age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Self-Report physician-diagnosed ADHD Timing: Prior diagnosis **Index test:** Parent rating The Weiss Functional Impairment Rating Scale Parent Form (WFIRS-P) , a tool to differentiate ADHD from normal controls based on functional impairment scores Sensitivity: 83 Specificity: 85 PPV: NPV: LR+: LR-: Accuracy: AUC: 0.91 Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Index text 5:
Parent rating	Tillman, 2005[571] Case series N = 264 US Setting: Specialty care	**Target:** Consecutive new case ascertainment from outpatient child psychiatric and pediatric sites; IQ>=70; no current or past mania, hypomania, or major depressive disorder **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:** Other info on race or 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 **Index test:** Parent rating Conners' Abbreviated Parent Questionnaire; diagnostic performance outcomes calculated by using data for all 10 items from the ADHD subjects and the healthy comparison subjects Sensitivity: 99 Specificity: 95 PPV: NPV: LR+: LR-: Accuracy:	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Wassenberg, 2004[595] Case series N = 72 US Setting: Primary Care	**Target:** Children 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 second matched control group of subjects who sustained an orthopaedic injury with no evidence of traumatic brain injury; most of the ADHD children had at least one comorbid disorder including depression and/or anxiety disorders, ODD, or CD **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	**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 Child Behavior Checklist; scores for ADHD (n=19) versus no ADHD (n=51) groups, social problems subscale, cutoff t>=60 Sensitivity: 74 Specificity: 86 PPV: NPV: LR+: LR-: Accuracy: 83	**Index test 2:** Parental rating scale Child Behavior Checklist; scores for ADHD (n=19) versus no ADHD (n=51) groups, attention problems subscale, cutoff t>=60 Sensitivity: 84 Specificity: 84 PPV: NPV: LR+: Accuracy: 84 AUC: Rater agreement: Kappa: Internal consistency:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 Other info on race or ethnicity:	AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Parent rating	Zelko, 1991[626] 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	**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 Conners Abbreviated Rating Scale (ARS) parent Sensitivity:	**Index test 2:** Parental rating scale Child Behavior CheckList (CBCL) parent Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Diagnosed by: Specialist **Comorbidity:** N/A **Female:** 0% All male **Age mean:** 9.71 (1.1) **Min age: Max age:** **Ethnicity:** % Hispanic or Latino : 3.4 % Black/African American : 6.7 % White : 84.3 Other info on race or ethnicity: Other : 5.6% other	Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Parental rating scale Self Control Rating Scale (SCRS) parent Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
Teacher rating scale	Alloway, 2009[126] Case series N = 91 UK Setting: School	**Target:** Only included children who score in the normal range on the Developmental, Diagnostic and 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:** Other info on race or ethnicity: N/A	**Reference standard:** Clinical diagnosis Comprehensive clinical diagnostic assessment by pediatric psychiatrists and community pediatricians Timing: Concurrent **Index test:** Teacher rating scale Conners' Teacher Rating Scale (CTRS) short form; discriminant function analysis ADHD index Sensitivity: 72 Specificity: 95 PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 2:** Teacher rating scale The Behavior Rating Inventory of Executive Function (BRIEF) teacher rating; discriminant function analysis all three indices Sensitivity: 78 Specificity: 90 PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Teacher rating scale The Working Memory Rating Scale (WMRS) teacher rating; discriminant function analysis Sensitivity: 82 82 Specificity: 100 PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				AUC: Rater agreement: **Index text 4:** neuropsychological,CPT The Conners' Continuous Performance Test; The K test was administered to assess performance on a vigilance task; discriminant function analysis Sensitivity: 41 Specificity: 65 PPV: NPV: AUC: **Index text 5:**
Teacher rating scale	Edwards, 2015[246] Case series N = 95 US Setting: Specialty care	**Target:** Consecutively 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:** %	**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:** Teacher rating scale Teacher Report Form (TRF) Attention Problems Scale; cutoff T-score 65 Sensitivity: 78 Specificity: 76 PPV: 75	**Index test 2:** Parental rating scale Child Behavior Checklist (CBCL) Attention Problems Scale; cutoff T-score 65 Sensitivity: 87 Specificity: 53 PPV: 64 NPV: 81 LR+: Accuracy: AUC:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 Other info on race or ethnicity:	NPV: 79 LR+: LR-: Accuracy: AUC: Rater agreement: Cohen's kappa; recalibrated efficiency (adjusted for base rates; 0= random test, 1.0= perfect test) Kappa: 0.537 (95% CI: 0.519, 0.567) ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Rater agreement: Cohen's kappa; recalibrated efficiency (adjusted for base rates; 0= random test, 1.0= perfect test) Kappa:0.396 (95% CI: 0.375, 0.424) Internal consistency: Alpha: Costs: **Index test 3:** Teacher rating scale Teacher Report Form (TRF) Attention Problems Scale; cutoff T-score 67 Sensitivity: 57 57 Specificity: 88 PPV: 81 NPV: 68 LR+: Accuracy: AUC: Rater agreement: Cohen's kappa; recalibrated efficiency (adjusted for base rates; 0= random test, 1.0= perfect test) **Index text 4:** Parental rating scale Child Behavior Checklist (CBCL) Attention Problems Scale; cutoff T-score 67

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Sensitivity: 78 Specificity: 63 PPV: 67 NPV: 76 AUC: **Index text 5:**
Teacher rating scale	Gomez, 2021[300] Case series N = 264 Australia Setting: Specialty care	**Target:** Children referred to a hospital outpatient psychiatric who were diagnosed with ADHD; more individuals in the ADHD group with comorbid-specific phobia, panic disorder, ODD and conduct disorder compared to those without 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:** Other info on race or 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:** Teacher rating scale Conners 3 Teacher Short Form and Teacher's Report Form, score of 17 used as cut-off Sensitivity: 72 (64, 79) Specificity: 75 (59, 87) PPV: 92 NPV: 41 LR+: LR-: Accuracy: AUC: 0.77 Rater agreement: Kappa: ICC: Internal consistency: Alpha:	**Index test 2:** Parental rating scale Conners 3 Parent Short Form and Child Behavior Checklist Sensitivity: 79 (73, 85) Specificity: 77 (63, 87) PPV: 92 NPV: 50 LR+: Accuracy: AUC: 0.85 Child Behavior Checklist parent 0.86 (95% CI: 0.81, 0.90) Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Parental rating scale Child Behavior Checklist aggressive behavior scale Sensitivity: 60 60 Specificity: 75

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			Test-retest: Costs: Misdiagnosis: Labeling: Costs:	PPV: 83.9 NPV: 46.9 LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Teacher rating scale Teacher's Report Form = aggressive behavior scale; Sensitivity: 48 Specificity: 91 PPV: 91.5 NPV: 44.9 AUC: **Index text 5:**
Teacher rating scale	Hall, 2020[311] RCT 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; participants and their assessing clinician were randomized to either immediately receiving the QbTest report (QbOpen group) or having the report withheld until the study end (QbBlind group) **Other:** None **ADHD presentation:** N/A **Diagnosed by:** Provider **Comorbidity:** N/A **Female:** 21%	**Reference standard:** Clinical diagnosis Clinician's diagnosis was made in accordance with DSM-IV/DSM-5 criteria using a short clinical record pro forma after each consultation Timing: Concurrent **Index test:** Teacher rating scale SNAP-IV teacher rating Sensitivity: 97 Specificity: 26 PPV: 83 NPV: 67 LR+: LR-:	**Index test 2:** Parental rating scale SNAP-IV parental rating Sensitivity: 100 Specificity: 4 PPV: 82 NPV: 100 LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Age mean: 9.5(2.8) **Min age:** 5.9 **Max age:** 17.4 **Ethnicity:** % White : 89 % Multiracial : 6 Other info on race or ethnicity: Other : 5	Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Teacher rating scale	Jarrett, 2018[338] Case series N = 388 US Setting: Specialty care	**Target:** Consecutive referrals to an outpatient clinic diagnosed with ADHD; 18.3% taking stimulant medication, instructed not to take medication on day of assessment. 5.8% on nonstimulant medication, not asked to stop medication for assessment **Other:** Children referred from community pediatricians, schools, and mental health professionals presenting at an outpatient clinic	**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 **Index test:** Teacher rating scale Teacher Report Form Attention Problems Sensitivity:	**Index test 2:** Parental rating scale Child Behavior Checklist Attention Problems Sensitivity: Specificity: PPV: NPV: LR+: Diagnostic likelihood ratio of 1.98 for individuals in the

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 info on race or ethnicity: Other : 1.5% Race other	Specificity: PPV: NPV: LR+: Diagnostic likelihood ratio of 1.55 for individuals in the highest risk group (scores >=66.28) LR-: Accuracy: AUC: 0.65 Rater agreement: Kappa: ICC: Internal consistency: Alpha: 0.95 Test-retest: Costs: Misdiagnosis: Labeling: Costs:	highest risk group (scores >=71) Accuracy: AUC: 0.66 Rater agreement: Kappa: Internal consistency: Alpha: 0.76 Costs: **Index test 3:** CPT Conners CPT Hit Reaction Time Standard Error Sensitivity: Specificity: PPV: NPV: LR+: Diagnostic likelihood ratio of 1.87 for individuals with high scores (>=74.5) Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Index text 5:
Teacher rating scale	Karr, 2021[352] Kibby, 2015[852]; Kibby, 2014[853] Case series N = 223 US Setting: Community	**Target:** IQ >=80, diagnosed with ADHD or ADHD with comorbid reading disorder (children with comorbidities not included in ROC analysis) **Other:** Healthy children; study also included children with reading disorder and children with "other diagnoses" but they were not part of ROC analysis **ADHD presentation:** N/A : n=85 children in sample w/ADHD **Diagnosed by:** Specialist **Comorbidity:** Learning disability : Reading disability **Female:** 43.1% **Age mean:** 9.49 (1.35) **Min age:** 8 **Max age:** 12 **Ethnicity:** % Hispanic or Latino : 2.7 % Black/African American : 4.9 % White : 85.8 Other info on race or ethnicity: Other : 6.7	**Reference standard:** Clinical diagnosis Clinical neuropsychologist conducted assessment according to DSM-IV criteria Timing: Prior diagnosis **Index test:** Teacher rating scale Behavior Assessment System for Children, Second Edition, Executive Function screener (BASC-2-EF) teacher rating scale global sum score; analysis of ADHD vs healthy children Sensitivity: 79 Specificity: 71 PPV: NPV: LR+: LR-: Accuracy: AUC: 0.831 Rater agreement: Kappa: ICC:	**Index test 2:** Parental rating scale Behavior Assessment System for Children, Second Edition, Executive Function screener (BASC-2-EF) parent rating scale global sum score; analysis of ADHD vs healthy children Sensitivity: 91 Specificity: 84 PPV: NPV: LR+: Accuracy: AUC: 0.919 Rater agreement: Kappa: Internal consistency: Alpha: 0.91 Costs:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Internal consistency: Alpha: 0.95 Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Teacher rating scale	Kennerley, 2018[355] Case series N = 55 New Zealand Setting: Specialty care	**Target:** Recruited from a preexisting database within the Department of Psychology at the University of Otago, New Zealand or referred from the Southern District Health Board's Paediatric Outpatients and Child and Family Mental Health Services; 15 children were on medication (Ritalin, Rubifen, Concerta, and Methamphetamine) **Other:** None **ADHD presentation:** inattentive : 43,hyperactive : 11,combined : 39,N/A : 7% ADHD-not otherwise specified	**Reference standard:** Clinical diagnosis Kiddie Schedule for Affective Disorders and Schizophrenia Timing: Prior diagnosis **Index test:** Teacher rating scale Attention-Deficit/Hyperactivity Disorder Rating Scale–Fourth edition teacher rating Sensitivity: Specificity: PPV: NPV:	**Index test 2:** Parental rating scale Attention-Deficit/Hyperactivity Disorder Rating Scale–Fourth edition parent rating Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 info on race or ethnicity: Other : 5.5% Maori	LR+: LR-: Accuracy: AUC: 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 ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Observation Behavioral Observation of Students in Schools Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Clinician versus parent and clinician versus teacher Significant positive correlation between teacher-rated total symptoms and clinician-total off-task behavior (r = .264, p < .05) but not between parent-rated total symptoms and clinician-total off-task behavior (i.e., motor, verbal, and passive off-task be **Index text 4:** Sensitivity:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
				Specificity: PPV: NPV: AUC: **Index text 5:**
Teacher rating scale	Raiker, 2017[480] Case series N = 620 US Setting: Specialty care	**Target:** Recruited using a prospective, consecutive case series design from all intakes at an urban, community mental health center; youth self-report only completed by adolescent group age 12-18 **Other:** Children and adolescents recruited using a prospective, consecutive case series design from all intakes at an urban, community 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:**	**Reference standard:** Clinical diagnosis Diagnoses of ADHD were made in accordance with DSM-IV-TR Timing: Prior diagnosis **Index test:** Teacher rating scale Teacher Report Form Achenbach System of Empirically Based Assessment (ASEBA) Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC: Age 5 to 11: AUC 0.62 (0.55-0.70), age 12 to 18: AUC 0.56 (0.50-0.62) Rater agreement: Kappa: ICC: Internal consistency:	**Index test 2:** Parental rating scale Child Behavior Checklist Achenbach System of Empirically Based Assessment (ASEBA) Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Age 5 to 11: AUC 0.72 (0.65-0.80), age 12 to 18: AUC 0.0.73 (0.67-0.78) Rater agreement: Kappa: Internal consistency: Alpha: Costs:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 info on race or ethnicity: Other : Ethnicity Other age 5 to 11: 4%. Age 12 to 18: 4%.	Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 3:** Teen/child self report Youth Self-Report Achenbach System of Empirically Based Assessment (ASEBA) Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: 0.56 Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Teacher rating scale	Schneider, 2020[507] Case series N = 84 US Setting: Mixed	**Target:** ADHD symptoms present 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	**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 Timing: Prior diagnosis	**Index test 2:** Parental rating scale Behavior Rating Inventory of Executive Function- Preschool Version (same form for teachers and parents) Sensitivity: Specificity: PPV:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		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 info on race or ethnicity: Other : Other 1%	**Index test:** Teacher rating scale Behavior Rating Inventory of Executive Function-Preschool Version (same form for teachers and parents) Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: AUC: 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). In con Kappa: ICC: Internal consistency: Alpha: Test-retest:	NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Costs: Misdiagnosis: Labeling: Costs:	
Teacher rating scale	Shemmassian, 2016[515] Shemmassian, 2012[1008] Case series N = 195 US Setting: Other	**Target:** Youths recruited through talks at self-help groups for ADHD, and study fliers distributed to local mental health service providers with language specifically targeting youth 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:**	**Reference standard:** Clinical diagnosis Any subtype of ADHD according to DISC-IV Timing: Concurrent **Index test:** Teacher rating scale Teacher Disruptive Behavior Disorder (DBD) Ratings Scale Sensitivity: 48 Specificity: 70 PPV: 65 NPV: 54 LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest:	**Index test 2:** Parental rating scale Parent Disruptive Behavior Disorder (DBD) Ratings Scale Sensitivity: 73 Specificity: 93 PPV: 93 NPV: 75 LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Parent-rated inattention Cronbach's alpha 0.94, Parent rated hyperactivity/impulsivity Cronbach's alpha 0.91 Alpha: Costs:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		% Hispanic or Latino : 10 % Black/African American : 7 % White : 53 % Multiracial : 22 Other info on race or ethnicity: Other : 4	Costs: Misdiagnosis: Labeling: Costs:	**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: 88 88 Specificity: 63 PPV: 73 NPV: 83 LR+: Accuracy: AUC: Rater agreement: **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: 25 Specificity: 98 PPV: 93 NPV: 53 AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
Teacher rating scale	Shemmassian, 2017[516] Case series N = 151 US Setting: Mixed	**Target:** IQ>=70, free from a previous pervasive developmental, seizure, or neurological disorder, or any medical condition that prevented full participation in the study; recruited through presentations to self-help groups and advertisements mailed to 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 info on race or ethnicity: Other : 2% race category other	**Reference standard:** Clinical diagnosis Diagnostic Interview Schedule for Children, 4th edition Timing: Prior diagnosis **Index test:** Teacher rating scale Disruptive Behavior Disorder Rating Scale, teacher rating. Total predictive value (TPV) was 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 endorsed at their highest TPV level. Sensitivity: 82 Specificity: 55 PPV: 67 NPV: 73 LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Cronbach's alpha 0.94 for both teacher-rated inattention and hyperactivity symptom counts on the Disruptive Behavior Disorder Rating Scale Alpha:	**Index test 2:** Parental rating scale Disruptive Behavior Disorder Rating Scale, parent rating. Total predictive value (TPV) was 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 o Sensitivity: 88 Specificity: 80 PPV: 82 NPV: 87 LR+: Accuracy: AUC: Rater agreement: Kappa: 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 Alpha: Costs: **Index test 3:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Teacher rating scale	Tripp, 2006[574] Case series N = 184 New Zealand Setting: Specialty care	**Target:** Children diagnosed with ADHD at specialized clinic. No exclusion criteria listed. **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	**Reference standard:** Clinical diagnosis DSM IV by clinical psychologist experienced in ADHD assessment Timing: Concurrent **Index test:** Teacher rating scale Teacher Report Form (TRF) Sensitivity: 78.7 Specificity: 63.5 PPV: NPV: LR+: LR-: Accuracy: 72.5	**Index test 2:** Parental rating scale Child Behavior Checklist (CBCL), parent rating Sensitivity: 76.9 Specificity: 32.9 PPV: NPV: LR+: Accuracy: 58.7 AUC: Rater agreement: Kappa: Internal consistency:

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
		Ethnicity: % Native Hawaiian or Pacific Islander : 12.0 % White : 76.1 Other info on race or ethnicity: N/A : 8.7,Other : Other 3.2	AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	Alpha: Costs: **Index test 3:** Teacher rating scale Conners Teacher Rating Scale Sensitivity: 81.3 81.3 Specificity: 69.3 PPV: NPV: LR+: Accuracy: 76.4 AUC: Rater agreement: **Index text 4:** Parental rating scale Conners Parent Rating Scale Sensitivity: 78.5 Specificity: 32.4 PPV: NPV: AUC: **Index text 5:**

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
Teacher rating scale	Zhou, 2018[629] Case series N = 339 US Setting: Mixed	**Target:** Children diagnosed with ADHD diagnosed in multiple clinics across the United States by the practicing clinicians in these clinics; 68% prescribed medication; 22% had at least one comorbid psychiatric diagnosis **Other:** A population proportion stratified random sample of the US child and adolescent population 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 info on race or ethnicity: Other : other 5%	**Reference standard:** Clinical diagnosis Diagnosed by practicing clinicians using DSM criteria Timing: Prior diagnosis **Index test:** Teacher rating scale The Behavior Assessment System for Children-Third Edition (BASC-3) teacher rating scale Sensitivity: 70 Specificity: 73 PPV: NPV: LR+: LR-: Accuracy: AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	**Index test 2:** Parental rating scale The Behavior Assessment System for Children-Third Edition (BASC-3) parent rating scale Sensitivity: 94 Specificity: 51 PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:**

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
				Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Teen/child self report	Bergeron, 2017[149] 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:**	**Reference standard:** Other Schedule for Affective Disorders and Schizophrenia for School-Aged Children (KIDDIE-SADS) Timing: Concurrent **Index test:** Teen/child self report Dominic Interactive for Adolescents-Revised (DIA-R); ADHD scale 18 items, cutoff >=10 Sensitivity: 86 (62, 100) Specificity: 70 (65, 74) PPV: NPV: LR+: 2.8 LR-: Accuracy: AUC: 0.85 Rater agreement: Kappa: ICC: Internal consistency: Cronbach's alpha: >0.80 for the total sample	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
		Other info on race or ethnicity: N/A	Alpha: 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) Costs: Misdiagnosis: Labeling: Costs:	AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Teen/child self report	Doyle, 2007[236] Case series N = 251 US Setting: Other	**Target:** Probands and siblings participating in a longitudinal study of youth 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 Other info on race or ethnicity:	**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 Achenbach youth self-report (YSR) Sensitivity: Specificity: PPV: NPV: LR+: LR-: Accuracy: Total predictive value ranged from 85% to 90% over 8 subscales	**Index test 2:** Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Sensitivity: Specificity: PPV:

Index Type	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	Results: Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	Additional index tests
			AUC: Rater agreement: Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	NPV: LR+: Accuracy: AUC: Rater agreement: **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**
Teen/child self report	Slobodin, 2022[531] Case series N = 190 Israel Setting: Specialty care	**Target:** Referred to a private pediatric neurologic clinic between January 2018 and December 2020; exclusion criteria were an intellectual disability, severe neurological or developmental disabilities, and psychosis **Other:** **ADHD presentation:** N/A **Diagnosed by:** Specialist **Comorbidity:** N/A **Female:** 40% **Age mean:** 8.48 (0.90) **Min age:** 7 **Max age:** 10 **Ethnicity:** Other info on race or ethnicity: Other : All of Jewish background living in northern Israel	**Reference standard:** Clinical diagnosis Interview with the child and the parents, medical/neurological examination, CPT administration, and ADHD diagnostic questionnaires (Conners ADHD Index Rating scales, 3rd edition, short-form-parent and teacher, Child Behavior Checklist and Teacher's Repor Timing: **Index test:** Teen/child self report Child self-report ratings compared to parent ratings (Conners and Child Behavior Checklist) Sensitivity: Specificity: PPV: NPV: LR+:	**Index test 2:** Teen/child self report Child self-report ratings compared to teacher ratings (Conners and Teacher's Report Form) Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Child self-report versus teacher reports Spearman correlation: Inattention self-report with

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
			LR-: Accuracy: AUC: Rater agreement: Child self-report versus parent reports Spearman correlation: Inattention r= 0.179, p<0.05; hyperactivity r= 0.246, p <0.01; social problems r=0.206, p<0.01; child self-report of social problems with parent report of anxiety r=0.164, p<0.05; anxiety r=0.178, p<0.05; child self-report of depress Kappa: ICC: Internal consistency: Alpha: Test-retest: Costs: Misdiagnosis: Labeling: Costs:	social problems teacher report r=0.174, p<0.05; social problems r=0.283, p <0.01; children's self-report of social problems with teacher's report of depression r=0.270, p <0.01; learning difficulties r= 0 Kappa: Internal consistency: Alpha: Costs: **Index test 3:** Teen/child self report Child self-report ratings compared to performance on MOXO-CPT indices Sensitivity: Specificity: PPV: NPV: LR+: Accuracy: AUC: Rater agreement: Child self-report versus MOXO-CPT performance Spearman correlation: child self-report of inattention with at least one impaired CPT index r=0.211, p< 0.01; child self-report of learning difficulties with CPT

Index Type	**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	**Results:** Reference standard; Index test; Diagnostic accuracy; Rater agreement; Other outcomes	**Additional index tests**
				accuracy r= -0.162, p<0.05 and CPT impulsivness r= 0.212, p<0.01; child self-report of disli **Index text 4:** Sensitivity: Specificity: PPV: NPV: AUC: **Index text 5:**

Table C.2. KQ2 evidence table
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Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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[158] Research Institute for Islamic and Complementary Medicine, 2019[965] ID: IRCT20090527001957N9 RCT Single center N = 50 Iran Setting: N/A	**Target:** Children aged 6–14 years diagnosed with ADHD according to DSM-5 criteria, their CSI-4 score, clinical judgment of a psychiatrist, and a family physician; scores on the CSI-4 questionnaire scores for the AD section needed to exceed 6, and the HA section needed to exceed 5 to meet the inclusion criteria **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:** Other info on race or ethnicity: N/A	**Intervention:** Auricular therapy was performed at six ear acupoints, stimulated bilaterally for 20 sec at each point, each participant evaluated and received stimulation for 15 min, repeated once a week for 6 weeks, after stimulation, 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 **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 ($p < .05$).
CAM	Frei, 2001[281] ID: NA Clinical trial Single center N = 115	**Target:** Patients ADHD with a CGI of 14 or higher were included in the study; if there was any doubt concerning the diagnosis of ADHD, patients were referred to a child and adolescent psychiatrist or	**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	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**
	Switzerland Setting: Specialty care	psychologist or a pediatric neurologist for further testing **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:** Other info on race or ethnicity: N/A	**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	
CAM	Frei, 2005[280] ID: NA Crossover trial Single center N = 83 Switzerland Setting: Specialty care	**Target:** Children with ADHD with neuropsychological correlates (greater difficulty in learning, memory, non-automated language tasks, and traditional frontal executive measures), 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	**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**
		Female: 12.8 % Arm 1= 14.81% / Arm 2= 10.71% **Age mean:** Arm A: 10 (range 7–15); Arm B: 10 (range 7–15) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** Other info on race or ethnicity: N/A		
CAM	Hong, 2016[327] Cochrane Central Register of Controlled Trials, 2010[701] ID: KCT0000019 RCT Single center N = 93 Korea Setting: Specialty care	**Target:** ADHD diagnosis (of any subtype); any intervention (pharmacological, psychosocial therapy, educational, occupational therapies etc.) without change in ADHD treatments/ symptoms for last 2 weeks or no current treatment. Exclusion criteria: diagnosis of mental retardation or pervasive developmental disorders; past history of epilepsy or other neurotic disorder; pregnancy; any 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	**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**
		Comorbidity: N/A **Female:** 18.7 % **Age mean:** 11.0 (2.8) **Minimum age:** 7 **Maximum age:** 18 **Ethnicity:** % Asian : 100 Other info on race or ethnicity:		
Cognitive training	Benzing, 2019[146] Universität Bern, 2016[1091] ID: KEK 393/15, DRKS00010171 RCT Single center N = 51 Switzerland Setting: Other	**Target:** Children between the ages of 8 and 12 who had been previously diagnosed with the ADHD by a medical professional based upon the ICD-10; should not suffer from a 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:** Xbox Kinect exergaming training for 8 weeks, 3 times a week for at least 30 minutes **Control:** Wait list 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
		Other info on race or ethnicity:		
Cognitive training	Bigorra, 2016[156] Bigorra, 2016[674] ID: ISRCTN00767728 RCT Single center N = 66 Spain Setting: Specialty care	**Target:** Children with ADHD, comorbidity with other disruptive behavior disorders was accepted, all diagnoses were confirmed using the semi-structured Kiddie-Schedule for Affective Disorders and Schizophrenia, Present and Lifetime Version (K-SADS-PL) interview that was administered to parents; 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	**Intervention:** Adaptive training with Cogmed Working Memory 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 5 sessions per week over a 5-week period for a total of 25 sessions **Control:** Attention-matched control 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) 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
		Ethnicity: % Hispanic or Latino : 95.4 Other info on race or ethnicity:		
Cognitive training	Bikic, 2018[59] Region Syddanmark, 2012[963] ID: NCT01752530 RCT Multicenter N = 78 Denmark Setting: Mixed	**Target:** Children fulfilling DSM-IV criteria for ADHD (in DAWBA interview, and verified with K-SADS); age between 6 and 13 years; access to a computer and internet connection; no diagnosis of comorbid conduct disorder, autism spectrum disorders, depression or schizophrenia; no medical history of head injury or a verified neurological disorder; intelligence quotient (IQ) not less than 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	**Intervention:** Computer program ACTIVATE used 6 times a week for 8 weeks using only used the cognitive computer games part, not use the physical exercises, the group received ADHD treatment as usual **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
		Disorders and Schizophrenia (K-SADS) **Comorbidity:** N/A **Female:** 16 % **Age mean:** 9.95 (1.7) **Minimum age:** 6 **Maximum age:** 13 **Ethnicity:** Other info on race or ethnicity: N/A		
Cognitive training	Bul, 2016[174] Bul, 2018[684] 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 (determined by health care professionals on the basis of medication data and behavioral observation) **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	**Intervention:** Game intervention in addition to treatment as usual for the first 10 weeks, maximum of 65 minutes approximately 3 times per week **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 school activities; there were 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
		Ethnicity: Other info on race or ethnicity: N/A		
Cognitive training	Chu, 2021[203] Shanghai Childrens Hospital, 2021[1006] ID: ChiCTR2100052803 RCT Unclear/Not reported N = 145 China Setting: N/A	**Target:** IQ should be 70 or above established with the Wechsler Intelligence Scale for children–fifth edition (WISC-V). Moreover, parents or primary caregivers did not want to receive drug therapy, could read and write the Chinese language, were legally able to sign informed consent, and signed the informed consent. Children with autism spectrum disorder, schizophrenia, epilepsy, head injury, or verified neurological disorder, intellectual disability (IQ <70, based on WISC-V), and sensory impairment (hearing/vision problems) and those receiving other ADHD treatments were excluded. Neither the intervention nor waitlist group were treated with medication. **Other:** **ADHD presentation:** inattentive : 60,hyperactive : 14,combined : 26 **Diagnosis:** Confirmation by specialist DSM-V	**Intervention:** Eight weekly sessions of a hospital-based executive function training program for participants, each session 90 minutes long, and an online parent training program, each session 30 minutes long **Control:** Wait list **Comparator:** NA **Follow-up:** 2 months	SNAP- IV total score (Chinese version), parent There was no significant difference between groups. Weiss Functional Impairment Scale, parent The intervention had significantly greater differences of improvement compared to control ($p = 0.009$). The intervention group had greater reduction in the scores of 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
		Comorbidity: N/A **Female:** 25 % **Age mean:** Intervention: 7.10 (0.47) Waitlist: 7.04 (0.61) **Minimum age:** 6 **Maximum age:** 8 **Ethnicity:** Other info on race or ethnicity: N/A		
Cognitive training	Denton, 2020[225] The University of Texas Health Science Center, Houston, 2010[1082]; Dvorsky, 2021[727] 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	**Intervention:** Reading intervention plus medication plus parent training; the reading intervention was provided individually or in groups of two students in 45- minute lessons, 4 days per week, a possible total of 64 lessons over 16 weeks; 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 **Control:** Other	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).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		% White : 19.6 % Multiracial : 6.4 Other info on race or ethnicity:	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	
Cognitive training	Dentz, 2020[226] Université du Québec a Montréal, 2017[1092] ID: NCT03335748 RCT Single center N = 52 Canada Setting: Other	**Target:** Youths 7-13 years of age diagnosed with ADHD combined type with comorbid learning disability, oppositional defiance disorder, or Tourette syndrome, and under pharmacological treatment for ADHD, which had been stabilized for at least the past 2 months **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 13 % **Age mean:** Intervention: 10.44 (1.18), control: 9.60 (2.08) **Minimum age:** 7	**Intervention:** Cogmed program: a cognitive training software designed with exercises targeting the verbal and visuospatial components of working memory specifically, each training session lasted from 30 to 45 min, participants had to complete at least five sessions per week for five consecutive weeks **Control:** Placebo Comparison version of the Cogmed program with a low and invariable level of difficulty, which was expected to dampen the program's effects. **Comparator:** NA **Follow-up:** 2.5 months	Inattention, Conners 3 There was no significant difference between groups (p=0.18).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Maximum age: 13 **Ethnicity:** % White : 86.5 Other info on race or ethnicity:		
Cognitive training	Dovis, 2015[234] Dovis, 2015[720] ID: NTR2728 RCT Multicenter N = 89 Netherlands Setting: Specialty care	**Target:** DSM-IV-TR diagnosis of ADHD combined time 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 (WISC-III); Exclusion criteria - conduct disorder, autism spectrum disorder, neurological disorder, sensory or motor impairment reported by parents, medications other than methylphenidate or dextroamphetamine **Other:** **ADHD presentation:** combined : 100 **Diagnosis:** No Prior diagnosis per DSM-IV confirmed by child psychologist or	**Intervention:** Executive functioning training ("Braingame Brian") total of 25 training sessions, each session taking between 35-50 minutes each, all tasks were in training mode and level is adjusted to child's level of performance **Control:** Placebo Braingame Brain in placebo 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 leve **Comparator:** Cognitive trainingPartially-active condition in which the working memory tasks were in placebo mode which did not adjust difficultly to performance while the inhibition and cognitive-flexibility tasks were in training mode **Follow-up:** 4.25 months	There was no signifcant difference of treatment outcome on any executive function 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
		psychiatrist, but did not describe process of confirmation **Comorbidity:** N/A **Female:** 20 % **Age mean:** Table 1 labeled value as "M", suspect this is the "mean age,"; mean age of full-active intervention 10.6 (SD 1.4), partially-active intervention 10.3 (SD 1.3), and placebo group 10.5 (SD 1.3) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A		
Cognitive training	Egeland, 2013[247] Hovik, 2013[811] ID: ISRCTN19133620 RCT Single center N = 75 Norway Setting: School	**Target:** Children in treatment for ADHD, exclusion criteria were IQ below 70, or a comorbid diagnosis of Pervasive Developmental Disorders, Tourette's Disorder, evidence of psychosis or Bipolar Disorder and Conduct Disorder **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist F-90 ICD-10 Hyperkinetic Disorder (equivalent to DSM-IV) **Comorbidity:** N/A **Female:** 24 %	**Intervention:** The Working Memory training (RoboMemo) performed on a daily basis at school for 5–7 weeks, sessions last for 30–45 minutes **Control:** Wait list Offered the possibility to train after the completion of the study **Comparator:** NA **Follow-up:** 8 months	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. Training group had significant gains in working memory performance 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
		Age mean: 10.4 (0.7) **Minimum age:** 10 **Maximum age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A		
Cognitive training	Estrada-Plana, 2019[261] ID: NA RCT Single center N = 29 Spain Setting: Other	**Target:** Attending primary school, and having diagnosis of ADHD, without having any other mental disorders, and having an IQ of more than 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 info on race or ethnicity: Other : Does not specify the other 3%	**Intervention:** Cognitive training based on board games, closed groups of 6-8 participants, 5 weekly training sessions, 60 minutes each, 1 game per week **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. 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[310] Hahn-Markowitz, 2017[786]; Hadassah Medical Organization, 2013[783] ID: NCT01792921 Crossover trial Multicenter N = 107 Israel Setting: Mixed	**Target:** Children in second to fourth grade 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:** Other info on race or 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.
Cognitive training	Kofler, 2020[363] ID: NA RCT Single center N = 54	**Target:** DSM-5 diagnosis of ADHD by the directing clinical psychologist based on K-SADS; and clinical/borderline elevations on at least 1 parent and one teacher ADHD rating scale, or previous psychoeducational	**Intervention:** Inhibitory control training: 10-week protocol included weekly in-office sessions with the child (1 hour), combined with parent-supervised, in-home training (goal: 15-min/day, 2–3 days/week) **Control:** NA	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), and executive function training was superior for teacher-reported ADHD-RS-5 Attention Problems (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**
	US Setting: Other	evaluation documenting cross-informant symptoms; children with scores in the average range or higher on all pretreatment working memory tests were excluded; no inhibitory control thresholds were set **Other:** **ADHD presentation:** inattentive : 28,hyperactive : 3.7,combined : 69 **Diagnosis:** Confirmation by specialist K-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 Other info on race or ethnicity:	**Comparator:** Cognitive trainingCentral executive training targeting central executive working memory deficits in ADHD; each matched pair of ICT/CET training games is identical in terms of website address, name, art, animations, storylines, layouts, interfaces, and use of adaptive train **Follow-up:** 2.5 months	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).
Cognitive training	Kollins, 2020[366] Akili Interactive Labs, Inc., 2016[646] ID: NCT02674633 RCT Multicenter	**Target:** Children aged 8–12 years with a confirmed diagnosis of ADHD according to DSM-5 and Intelligence Quotient 80 or above; no significant comorbid psychiatric diagnoses and no use of ADHD	**Intervention:** Digital therapeutic AKL-T01 at home for 5 sessions per day (total time on task about 25 min), 5 days per week, for 4 weeks **Control:** Attention-matched control Control was designed to match AKL-T01 on expectancy,	CGI (Clinical Global Impressions) scoring 2 or more No difference in improvement between groups. ADHD-RS-IV, number with at least 30% 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
	N = 348 US Setting: Other	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:** Other info on race or ethnicity: N/A	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	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.
Cognitive training	Nejati, 2021[445] Nejati, 2020[921] ID: NA RCT Single center N = 30 Iran Setting: Specialty care	**Target:** Children with ADHD. Those with psychiatric comorbidities excluded. **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	**Intervention:** Cognitive training with paper and pencil tasks, twelve to fifteen sessions of intervention, three sessions per week during 4–5 weeks, each session took about 40–50 minutes **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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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: 47 % **Age mean:** 10.74 (1.81) Poor reporting. Authors report mean age for experimental group = 11.16 (1.52), control group = 11.40 (1.99). Yet mean age for total = 10.74 (1.81). **Minimum age:** 8 **Maximum age:** 14 **Ethnicity:** Other info on race or ethnicity: N/A,Other : Presumably 100% Persian		
Cognitive training	Nejati, 2022[446] ID: RCT Multicenter N = 35 Iran Setting: School	**Target:** Children with ADHD; in each kindergarten children with behavioral problems were selected by their teachers for the study and then clinically assessed **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:**	**Intervention:** PARISA (Program for Attentive Rehabilitation of Inhibition and Selective Attention), 6 progressive computerized tasks targeting 3 types of inhibitory control, 10-12 sessions, each 30-45 minutes, over a 4 to 5 week period **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
		Other info on race or ethnicity: N/A		
Cognitive training	Raghuveer, 2020[478] 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:** % Not reported **Age mean:** 4.5 (1.06) **Minimum age:** 3 **Maximum age:** 6 **Ethnicity:** Other info on race or 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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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	Shuai, 2020[518] Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, 2018[1146] ID: NCT03515135 RCT Unclear/Not reported N = 96 China Setting: N/A	**Target:** 96 native Chinese speaking preschool children with DSM-V diagnosed ADHD, ranging from ages 4 years 0 months to 5 years 11 months. No major sensory-motor disorders, no history of brain damage, epilepsy, no diagnosis of autism spectrum disorder, no intelligence quotient (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	**Intervention:** Executive Function Training for Preschool is structured psychotherapy 90-min sessions (60-min for children, 30-min for parents) once a week for 8 weeks. Sessions contained four 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). **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
		Ethnicity: Other : Presumably 100% Chinese Other info on race or ethnicity:		
Cognitive training	van der Donk, 2015[582] ID: NA RCT Single center N = 105 Netherlands Setting: School	**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 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:** Other info on race or ethnicity: N/A	**Intervention:** Combined working memory and compensatory training (Paying Attention in Class): participants trained individually outside the classroom for 5 weeks, five times a week, about 45 min a day **Control:** NA **Comparator:** Cognitive trainingCogmed Working Memory 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	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 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[602] ID: NA RCT Multicenter N = 46 Sweden Setting: N/A	**Target:** Diagnosis of ADHD, age 9–15 years and parent-reported difficulties with daily time management, despite medication for ADHD. No autism spectrum disorder; no intelligence quotient <70; able to answer questions in Swedish. **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:** Other info on race or ethnicity: N/A	**Intervention:** Compensation and remediation lasted about 12 weeks: compensation were 1.5-hour sessions with 3-4 sessions in the study period, remediation training sessions were 3 times per week with 20 minutes per day assigned outside of sessions **Control:** Other Received standard methods of care alone. **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[616] ID: Clinical trial Single center N = 127 China Setting: Specialty care	**Target:** Children with ADHD; those with serious medical conditions or neuropsychiatric diseases were excluded, as were those on any ADHD meds **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 Other info on race or ethnicity:	**Intervention:** Executive function training (AET), designed and developed by Infinite Brain Technology, is a battery of 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 a two-month period **Control:** **Comparator:** Cognitive trainingGeneral executive function training (GET) is 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 training sess **Follow-up:** 2 months	CBCL-attention problems 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[114] Hechtman, 2004[798]; Klein, 2004[855] 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 Other info on race or ethnicity:	**Intervention:** Methylphenidate plus 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), treatment period of 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:** NA **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. ADHD diagnosis 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.
Combined pharmacological +	Blader, 2021[159] Joseph Blader, 2008[841] ID: NCT00794625 RCT Multicenter N = 175	**Target:** Diagnosed with ADHD (any subtype) and either oppositional defiant disorder or conduct disorder according to DSM-IV-TR; required an R-MOAS total score >24 at both the initial telephone screening and the in-person evaluation with recent or	**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	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

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
	US Setting: Specialty care	current treatment with stimulant medication at a minimum daily total dose equivalent of 30 mg of immediate-release methylphenidate for at least 30 days; required 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, and IQ greater than or equal to 70, no seizure disorders; no pregnancy; and 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)	**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	remission from aggression-remission was met by 69% of the risperidone group, 40% of the divalproex There were no instances of 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
		Minimum age: 6 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 30.29 % Black/African American : 16.57 % White : 46.29 Other info on race or ethnicity: Other : 6.86 other		
Combined pharmacological + behavioral	Coelho, 2017[205] ID: NA Crossover trial Unclear/Not reported N = 67 Brazil Setting: Specialty care	**Target:** 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:** Group cognitive-behavioral therapy and medication, prolonged-release methylphenidate 20 mg for 20 weeks, group cognitive-behavioral therapy attended by parents and children, family sessions lasted 40 minutes and sessions with children about 80 minutes **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
		Other info on race or ethnicity:		
Combined pharmacological + behavioral	David, 2021[220] Babes-Bolyai University, 2018[657] ID: ISRCTN92640175 RCT Single center N = 59 Romania Setting: Specialty care	**Target:** Diagnosed with ADHD by a child psychiatrist and/or certified psychologist; attending elementary school (6–11 years old); with sufficient understanding of the Romanian language; with an 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:** Other info on race or ethnicity:	**Intervention:** Cognitive-behavioral psychological treatment and rational emotive behavior therapy plus 0.8 mg/kg/day and 1.2 mg/kg/day of atomoxetine (pharmacological non-stimulant treatment); weekly psychotherapy session with parents alone (30 min) and with child alone (30 min), treatment over a period of 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	Jensen, 2007[339] No author, 2011[656]; Abikoff, 2001[637]; Acosta, 2016[639]; Arnold, 1997[651]; Arnold, 1997[652]; Arnold, 2004[653]; Arnold, 2003[654]; Babinski, 2019[658]; Brinkman, 2018[682]; Carey, 2000[686]; Conners, 2001[706] ID: NCT00000388 (MTA) RCT Multicenter N = 579 US Setting: N/A	**Target:** Children with ADHD combined type (MTA) **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 info on race or ethnicity: Other : 10.7%	**Intervention:** Multimodal Treatment Study of Children With ADHD (MTA), intensive multicomponent behavior therapy consisting of medication management and behavior modification, treatment period of 36 months **Control:** TAU Usual community care **Comparator:** NA **Follow-up:** 36 months	Parent and teacher average rating of oppositional defiant disorder symptoms from the SNAP Ratings were similar across groups. SWAN Both groups improved from baseline. Columbia Impairment Scale (CIS) 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[656]; 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[759].

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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	Karakaya, 2019[350] 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 **Female:** 19.5 % **Age mean:** 13.2 (1.25) **Minimum age:** 12 **Maximum age:** 18 **Ethnicity:** Other info on race or ethnicity: N/A	**Intervention:** Solution-focused approach comprised of 6 sessions, each 45-60 minutes, 1 per week for 6 weeks, individually and face-to-face, in addition to ADHD medication treatment with psychostimulants and clinic follow-up **Control:** Other No intervention, but ADHD medication treatment with psychostimulants as usual **Comparator:** NA **Follow-up:** 3 months	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).
Combined pharmacological + behavioral	Perez-Alvarez, 2009[462] ID: NA RCT Single center N = 96 Spain Setting: Specialty care	**Target:** Children and adolescents with SNAP IV teacher rating scores of at least 2.5 and parent ratings of at least 1.8, all had planning dysfunction according to PASS (planning, attention, successive and simultaneous) scales; patients with medical and psychiatric comorbidities were excluded **Other:** Parents and teachers provided some outcome data **ADHD presentation:** inattentive : 79,hyperactive : 0,combined : 21	**Intervention:** Methylphenidate plus humanistic intervention; extended release methylphenidate hydrochloride administered at an optimal dose plus humanistic psychological intervention conducted as 24 sessions, 1 every 15 days, treatment followed up for 12 months **Control:** Other Extended release methylphenidate hydrochloride alone	Swanson, Nolan, and Pelham scale 18 (SNAP-IV-18), number in remission (score <= 1.0) Intervention scored better than control (p < .05). 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**
		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:** Other info on race or ethnicity: N/A	**Comparator:** NA **Follow-up:** 12 months	
Combined pharmacological + behavioral	Riggs, 2011[485] University of Cinncinnati, 2006[1095] ID: NCT00264797 RCT Multicenter N = 303 US Setting: Specialty care	**Target:** Adolescents meeting DSM-IV criteria for current ADHD and at least one nontobacco Substance User Disorder (SUD). Exclusion criteria were 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:**	**Intervention:** Cognitive behavioral therapy plus osmotic-release methylphenidate (OROS); 72mg methylphenidate 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	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).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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 : 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 Other info on race or ethnicity:	**Comparator:** NA **Follow-up:** 4 months	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,
Combined pharmacological + behavioral	Sprich, 2016[548] Massachusetts General Hospital, 2009[877] ID: NCT01019252 Crossover trial Single center N = 46 US Setting: Specialty care	**Target:** Adolescents 14-18, with ADHD on a stable dose (defined as no change in dose for at least 2 months) of an FDA-approved medication without severe comorbid disorders that could interfere with participation, active suicidality, conduct disorder, active substance abuse or dependence, organic mental disorder, mental retardation, pervasive	**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 **Control:** Wait list Wait list received no psychosocial treatment for 4 months but continued to receive FDA-approved medication	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**
		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 Other info on race or ethnicity:	**Comparator:** NA **Follow-up:** 4 months	
FDA-approved pharmacological	Abikoff, 2007[116] Greenhill, 2006[772]; Ghuman, 2007[766]; Swanson, 2006[1071]; Wigal, 2006[1140]; Kollins, 2006[856] ID: N/A	**Target:** Children between the ages of 3-5.5 years and an impairment scale score of less than or equal to 55 on the Children Global Assessment Scale **Other:** Parents and teachers of the children	**Intervention:** Methylphenidate 1.25, 2.5, 5, or 7.5 mg 3 times per day for 4 weeks **Control:** Placebo Placebo treatment **Comparator:** NA	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

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
	RCT Multicenter N = 114 US Setting: School	**ADHD presentation:** hyperactive : 29.51,combined : 70.49 **Diagnosis:** Confirmation by specialist Used the DSM-IV edition, the psychiatrists interviewed children and make them take examinations to determine their scale scores. **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 Other info on race or ethnicity:	**Follow-up:** 1 month	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 in treatment group and placebo group for parents.[116] Social Skills Rating System (Parent) (SSRS-P) change, measures social function Effect size 0.14, ANCOVA treatment effect not statistically significant.[116] There was no significant difference in parental stress across the treatment and placebo groups. Growth rates During methylphenidate treatment, slope indicated a reduction of growth rates.[1071] 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.[772]
FDA-approved pharmacological	Abikoff, 2009[115] NA ID: Crossover trial Single center N = 19 US	**Target:** Medication naive children with ADHD who had problems with organization, time management, and planning. **Other:** Parents and teachers provided outcome data **ADHD presentation:** inattentive : 58,hyperactive : 0,combined : 42	**Intervention:** Methylphenidate osmotic-release oral system 48.3 mg (range 18-54 mg) daily for 2 weeks **Control:** Placebo Placebo **Comparator:** NA	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 lower in intervention group at follow-up ($p < .005$ for both outcomes). Lower is better.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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	**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:** Other info on race or ethnicity: N/A	**Follow-up:** 2 months	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[125] ID: NA RCT Multicenter N = 148 US Setting: Mixed	**Target:** Children 7-17 years old with diagnosis of ADHD according to DSM-IV and concurrent Tourette syndrome or chronic motor tic disorder, have scores on the Attention Deficit/Hyperactivity Disorder Rating Scale-IV-Parent Version: Investigator Administere and Scored (ADHDRS-IV-Parent:Inv) had to be at least 1.5 SD above the age and sex norm, have scores of at least 5 on the Yale Global Tic Severity Scale (YGTSS). Exclusion: have a Children's Yale–Brown Obsessive Compulsive Scale (C-YBOCS) total score larger or equal to 15, have a	**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 Patients randmonly assigned to matching placebo taking 2 times a day for an 18-week treatment period. **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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		Children's Depression Rating Scale–Revised (CDRS-R) total score of larger than 40, have a 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 info on race or ethnicity: Other : Other: 4/148 (2.7%)		

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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	Ashkenasi, 2011[133] ID: N/A RCT Single center N = 26 US Setting: Other	**Target:** Children aged 6-12 years who met the DSM IV Edition criteria for attention deficit hyperactivity disorder (any subtype) and who demonstrated difficulty sleeping (as reported by the caregiver) were eligible; patients with previous intolerance, adverse response, or allergy to methylphenidate or skin sensitivity to the methylphenidate transdermal system, and those with severe comorbid psychiatric disorders were excluded **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:** Other info on race or ethnicity: N/A	**Intervention:** Methylphenidate transdermal patch sequence of 9 hours, 10 hours, 11 hours, and 12 hours for 4 week, 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 Sunday **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	Connor's Global Impression-Parent There was no significant difference between groups (p=0.114). 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[137] Coghill, 2013 [702]; Coghill, 2014[703]; Coghill, 2021[705]; Shire, 2008[1015] ID: NCT00763971 RCT Multicenter N = 336 Multiple countries Setting: Mixed	**Target:** Children and adolescents 6-17 years old who meet DSM-IV criteria for ADHD diagnosis, with baseline ADHD-RS-IV total score of 28 or higher. Key exclusion criteria included failure to respond to a previous course of OROS-MPH (but not of other formulations of methylphenidate) and the presence of a comorbid psychiatric diagnosis with significant symptoms (not including oppositional defiant disorder); patients whose current ADHD medication provided effective control of symptoms with acceptable tolerability were also excluded **Other:** **ADHD presentation:** inattentive : 15.96,hyperactive : 3.01,combined : 80.72 **Diagnosis:** Confirmation by specialist ADHD-RS-IV **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	**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.[702] Participants experiencing treatment emergent adverse events The rate was 72.1% for LDX, 64.9% for OROS-MPH, and 57.3% for placebo.[702] The proportion of patients who reported serious treatment emergent adverse events were low across all groups.[702]

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		Maximum age: 17 **Ethnicity:** % Hispanic or Latino : 1.20 % Black/African American : 0.30 % Asian : 0.30 % White : 97.0 Other info on race or ethnicity: Other : 2.41		
FDA-approved pharmacological	Bangs, 2007[138] ID: N/A RCT Multicenter N = 142 US Setting: N/A	**Target:** Adolescents aged 12–18 years who met the criteria for both ADHD and major depressive disorder per DSM–IV; patients beginning structured psychotherapy for ADHD and/or depression less than 1 month before trial entry were excluded **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:** Other info on race or 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[139] RCT Multicenter N = 226 Other Setting: Specialty care	**Target:** Children with ADHD and oppositional defiance disorder (ODD). 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 Other info on race or ethnicity:	**Intervention:** Atomoxetine, 1.2 mg/kg per day for ~8 weeks **Control:** Placebo Placebo daily for ~8 weeks. **Comparator:** NA **Follow-up:** 2 months (8 weeks)	Clinical Global Impression - Improvement (CGI-I) Atomoxetine group improved more on CGI-I (p = 0.037) and CGI-Severity (p=0.013). SNAP-IV 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 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[144] Mount Sinai, 2005[818] ID: NCT00183391 Crossover trial Unclear/Not reported N = 102 US Setting: Other	**Target:** Youth with ADHD, excluded were IQ below 75, non-English speaking parent or child, neurological dysfunction, systemic medical illness, uncorrected sensory impairments, and history of psychosis or bipolar disorder; other comorbidity was permitted provided ADHD was the primary disorder and the comorbid condition did not require medication treatment; participants may have been previously treated with ATX or MPH, but must not have been nonresponders to an adequate trial 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	**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**
		% Black/African American : 31 % Asian : 1 % White : 36 % Multiracial : 12 Other info on race or ethnicity:		
FDA-approved pharmacological	Biederman, 2007[152] ID: RCT Multicenter N = 290 US Setting: N/A	**Target:** Children aged 6-12 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 Other info on race or ethnicity:	**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, 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, 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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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, 2008[153] Shire, 2003[1022] ID: NCT00152009 RCT Multicenter N = 345 US Setting: N/A	**Target:** Children with ADHD, patients were excluded for a current, uncontrolled, comorbid psychiatric diagnosis (except oppositional defiant disorder) with significant symptoms, or when other symptomatic manifestations would contraindicate GXR treatment or confound efficacy or safety assessments; patients who weighed<55 lb or were morbidly overweight or obese, pregnant, lactating, or hypertensive were also excluded, patients were not enrolled when they had any of the following: QTc interval of >440 milliseconds, history of seizure during the past 2 years (exclusive of febrile seizures), 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 that would require exclusion, who had taken an investigational drug within 28 days, were taking medications that affect BP or heart rate, or were taking other medications that have central nervous system effects or affect performance were also not eligible **Other:**	**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, and 5.7% in the 2mg group. Participants experiencing treatment emergent adverse events The rate as 87.2% in the intervention, 64% in the placebo, and 77.0% in the 2mg 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 (n=2), and insomnia (n=2)).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 : 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 info on race or ethnicity: Other : 5.8		
FDA-approved pharmacological	Block, 2009[162] ID: N/A RCT Single center N = 288 US Setting: Primary Care	**Target:** Children, 6 to 12 years old 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	**Intervention:** Atomoxetine 1.25mg/kg/day each morning for 6 weeks **Control:** Placebo Placebo in the morning or evening for 6 weeks	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

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 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 Other info on race or ethnicity:	**Comparator:** MedicationEvening dosing, 1.26mg/kg/day of atomoxetine for 6 weeks **Follow-up:** 1.5 months	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 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).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
				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 atomoxetine in the incidence of any particular adverse event were observed.
FDA-approved pharmacological	Brams, 2018[169] Shire, 2015[1020] 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:** % Hispanic or Latino : NR % Black/African American : 28.5 % Asian : 0.3 % White : 61.2 % Multiracial : 8.0 Other info on race or ethnicity:	**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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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	Buitelaar, 2007[172] Trzepacz, 2011[1088]; Michelson, 2004[892] ID: N/A RCT Multicenter N = 163 Multiple countries Setting: Other	**Target:** Children with ADHD; patients with bipolar disorder or psychotic illness were excluded, as were patients with 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:** Other info on race or 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).[1088] 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,

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
				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 subjects, and none were reported significantly more often by those taking atomoxetine.
FDA-approved pharmacological	Cetin, 2015[183] ID: N/A RCT Single center N = 145 Turkey Setting: Specialty care	**Target:** Patients 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 info on race or ethnicity: Other : Ethnicity, Turkish patients but not sure of race	**Intervention:** Atomoxetine, mean dose 1.14±0.13 mg/kg/day **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.
FDA-approved pharmacological	Childress, 2009[199] ID: RCT Multicenter N = 253	**Target:** Children with ADHD who were drug naıve or not treated with any MPH-related medication in the month prior to the study; those with serious psyc disorders were excluded.	**Intervention:** 30 mg extended release Dexmethylphenidate daily. **Control:** Placebo Placebo capsule daily	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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
	US Setting: Specialty care	**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 info on race or ethnicity: Other : Other 12.6%	**Comparator:** Medication10 mg extended release Dexmethylphenidate daily. **Follow-up:** 1 month	Conners'- ADHD DSM-IV Scales (CADS), teacher report Patients in medication groups demonstrated a significant improvement as compared to placebo (all $p < 0.001$) on both CADS-T and CADS-P (parent report). Deceased appetite, number Significantly more medication patients experienced appetite decease. Number with any adverse event "Overall incidence of adverse events was generally higher" in medication groups; p values not reported. " Adverse events were mild to moderate in severity"
FDA-approved pharmacological	Childress, 2019[197] Tris Pharma, Inc., 2017[1086] ID: NCT03088267 RCT Single center N = 36 US Setting: Other	**Target:** Scored greater or equal to the 90th percentile for sex and age on the ADHD rating scale-5, and needed to have no other disorder included in the DSM-V with the exception of a few other disorders including specific phobias and learning disorders, and have no comorbid medical illnesses such as hypertension, and thyroid disease or family history of sudden death	**Intervention:** Amphetamine, optimized dose of 5–20 mg/day of amphetamine extended-release oral suspension for 5 days, and then crossed over on day 6 **Control:** Placebo Matching placebo drug **Comparator:** NA **Follow-up:** 0.5 month	SKAMP-C (Swanson, Kotkin, Agler, M-Flynn, Pelham-Combined) Rating Scale score at 30 minutes postdose At both 30 minutes and 3 hours postdose, changes from baseline in SKAMP-C for AMPH EROS versus placebo were statistically significant ($p<0.01$ and $p=0.0002$, respectively). AEs (>10%) during the open-label phase included upper respiratory tract infection, fatigue, upper abdominal pain, headache,

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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:** inattentive : 16.7,combined : 83.3 **Diagnosis:** Confirmation by specialist diagnosed with ADHDPychiatrist, psychologist, developmental pediatrician, or an experienced licensed allied health professional according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria **Comorbidity:** N/A **Female:** 22.2 % **Age mean:** 9 (1.71) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Black/African American : 11.1 % White : 88.9 Other info on race or ethnicity:		decreased appetite, and affect lability. There were two subjects (11.1%) who reported decreased appetite and no reports of insomnia. No serious AEs or AEs leading to premature withdrawal were reported.
FDA-approved pharmacological	Childress, 2022[198] Shire, 2017[1021] ID: NCT03260205 RCT Multicenter N = 199 US	**Target:** ADHD diagnoses per DSM-IV, baseline scores of 28 (boys) or 24 (girls) on the parent reported ADHD-RS-IV-PS-TS and 4 on the Clinical Global Impression–Severity (CGI-S) scale. Required to have undergone nonpharmacologic treatment or to have had symptoms severe	**Intervention:** Lisdexamfetamine 30 mg/day for 6 weeks **Control:** Placebo Matching placebo for 6 weeks **Comparator:** MedicationTreatment with 5 mg lisdexamfetamine for 6 weeks	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

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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	enough to warrant enrollment without prior nonpharmacologic treatment and to be 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/LAR for 6 months; excluded if need meds for CNS, have a concurrent illness, disability or comorbidity. **Other:** **ADHD presentation:** combined : 91.6 **Diagnosis:** No **Comorbidity:** N/A **Female:** 32.3 % depends on placebo/tx group/pooled **Age mean:** 5.1 (6.54) **Minimum age:** 4 **Maximum age:** 5 **Ethnicity:** Other info on race or ethnicity: Other : depends on tx/placebo/pooled	**Follow-up:** 1.5 months	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 comparator receiving 5mg, 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[200] ID: N/A RCT Multicenter N = 153 Korea Setting: N/A	**Target:** Children aged 6 to 18 years with a diagnosis of ADHD as defined by DSM-IV-TR, enrolled patients had to meet all of the following criteria: 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-RS-IV-Parent:Inv and CGI-S 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 (along with parents or legal guardian) to keep appointments for clinic visits and all examinations as required by the protocol **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	**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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Ethnicity: % Asian : 100 Other info on race or ethnicity:		
FDA-approved pharmacological	Coghill, 2014[206] Banaschewski, 2014[660]; Shire, 2009[1017] 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-RS-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 Other info on race or ethnicity:	**Intervention:** Lisdexamfetamine dimesylate optimal dose for up to 6 weeks orally **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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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	Concordia Pharmaceuticals, 2011[209] ID: NCT01439126 RCT Multicenter N = 135 US Setting: Mixed	**Target:** Children and adolescents ages 6-17 years old who meet DSM-IV-TR criteria for primary diagnosis for ADHD, IQ at least 70 or higher; exclusion: 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 **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	**Intervention:** Clonidine hydrochloride 0.1 mg, 0.2 mg, 0.3 mg, or 0.4 mg taken daily for 26 weeks **Control:** Placebo Subjects randomized to the placebo arm were 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, and then received only placebo for the rest of the study. **Comparator:** NA **Follow-up:** 6.5 months	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 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
		% Multiracial : 7.4 Other info on race or ethnicity:		
FDA-approved pharmacological	Connor, 2010[211] Shire, 2006[1013] ID: NCT00367835 RCT Multicenter N = 217 US Setting: Specialty care	**Target:** Children with ADHD and oppositional symptoms. Those with other psychiatric co-morbidities excluded. **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	**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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		% Native Hawaiian or Pacific Islander : 0.5 % White : 66.4 Other info on race or ethnicity: Other : 7.9% other		
FDA-approved pharmacological	Corkum, 2020[212] ID: NA RCT Unclear/Not reported N = 26 Canada Setting: Specialty care	**Target:** ADHD participants with or without periodic limb movements during sleep (PLMS) **Other:** **ADHD presentation:** inattentive : 34.6,combined_other : hyperactive-impulsive 65.4% **Diagnosis:** Confirmation by specialist psychologists and pediatricians. DSM-IV-TR **Comorbidity:** N/A **Female:** 11.5 % **Age mean:** 8.57 (2.0) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** % Hispanic or Latino : 3.8 % White : 88.8 Other info on race or ethnicity: N/A,Other : Aboriginal 7.7%	**Intervention:** Methylphenidate hydrochloride for 2 weeks, <20 kg = 20 mg daily dose, 20-30 kg = 30 mg, >30 kg = 40 mg **Control:** Placebo Placebo **Comparator:** NA **Follow-up:** 1 month	ADHD symptoms index, Conners Parent and Teacher Rating Scale-Revised (Long Form) (CP/TRS-R:L) Univariate analyses indicated that CPRS-R:L and CTRS-R:L T-scores were both significantly reduced during MPH treatment compared to placebo: CPRS-R:L: F (1, 25) = 8.11, p = .009; partial η2 = .25; CTRS-R:L: F (1, 25) = 5.64, p = 0.03, partial η2 = .18 Increased sleep onset latency resulting in reduced total sleep time, which has been linked to poorer daytime functioning, is a potential adverse effect of stimulant medication which may require management to optimize outcome.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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	Daviss, 2008[221] Palumbo, 2008[943]; University of Cincinnati, 1999[1096] ID: NCT00031395 RCT Multicenter N = 122 US Setting: Other	**Target:** All ADHD subtypes who had a designated parent in daily contact with the patient had previously used methylphenidate or clonidine; with no history of the following disorders: tic disorder, major depression, pervasive developmental disorder, autism, psychosis, mental retardation, anorexia nervosa, bulimia, a serious cardiovascular (e.g., significant hypotension, congenital heart disease) 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	**Intervention:** Clonidine plus methylphenidate adjusted to optimal doses and continued for 8 weeks; 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) **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. 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). Participants with any adverse event Subjects taking clonidine had higher rates of any AE reported (75%) than those not treated with clonidine (41%; p=.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
		Other info on race or ethnicity: Other : 4		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 clonidine (p<0.0001); fatigue: subjects treated with clonidine experienced higher rates of fatigue than subjects not treated with clonidine (p=0.03); nervousness: subjects treated with clonidine experienced higher rates of nervousness than subjects not treated with clonidine (p=0.04); Pittsburg Side Effects Rating Scale Parent & Teacher: dull/tired/listless subjects treated with clonidine experienced higher rates (p<0.0001), drowsiness/sedation subjects treated with clonidine experienced higher rates (p<0.0001).
FDA-approved pharmacological	Dell'Agnello, 2009[224] 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)	**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

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		Comorbidity: ODD **Female:** 7.1 % **Age mean:** mean 9.9 **Minimum age:** 6 **Maximum age:** 15 **Ethnicity:** Other info on race or ethnicity: N/A		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[228] ID: RCT Unclear/Not reported N = 91 Canada Setting: N/A	**Target:** Children aged 6 to 12 years old 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 **Other:** **ADHD presentation:** N/A **Diagnosis:** No DSM-III-R, methods only state "interviewer" **Comorbidity:** Mood disorder **Female:** 0.2 %	**Intervention:** Methylphenidate 0.7 mg/kg twice daily with parental training/support **Control:** Other Placebo with parental training/support **Comparator:** NA **Follow-up:** 4 months	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
		Age mean: 8.65 (1.8) and 8.07 (1.3) **Minimum age:** **Maximum age:** **Ethnicity:** Other info on race or ethnicity: N/A		
FDA-approved pharmacological	Dittmann, 2011[231] ID: NA RCT Multicenter N = 181 Germany Setting: N/A	**Target:** Children with ADHD, patients with a history of bipolar I or II disorder, psychosis, pervasive developmental disorder, or seizure disorder (other than febrile seizures), or at serious suicidal risk, or likely to require psychotropic medications other than study drug or a structured psychotherapy were excluded; psychotherapy initiated before study participation was acceptable **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	**Intervention:** Atomoxetine fast titration, 0.5 mg/kg for 7 days, then 1.2 mg/kg for 8 weeks,once daily in the morning **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 (15.0/13.1% vs. 0.0%), and anorexia (15.0/11.5% vs.1.7%).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Maximum age: 17 **Ethnicity:** Other info on race or ethnicity: N/A		
FDA-approved pharmacological	Dittmann, 2013[230] Shire, 2010 [1018] ID: NCT01106430 RCT Multicenter N = 267 Multiple countries Setting: Mixed	**Target:** Male and female patients (aged 6–17 years) 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 (ADHD-RS-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	**Intervention:** Atomoxetine, mean optimal dose 40.2 mg/day (SD 20.05) **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**
		% White : 88.95 Other info on race or ethnicity:		
FDA-approved pharmacological	Dreakhshanpour, 2022[237] 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 were excluded, as were those who using any psychotropic drug during the two prior weeks or with co-psychiatric disorders such as bipolar mood disorder, mental retardation, and autism **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:** Other info on race or ethnicity: N/A	**Intervention:** Daily risperidone: started at 0.25 mg/day in one dose and increased based on response and tolerance by 0.25 mg weekly increments, to a maximum dose of 1.25 mg/day **Control:** **Comparator:** MedicationAripiprazole 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 **Follow-up:** 3 months	Strengths and Difficulties Questionnaire (SDQ), pro-social behavior scale 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. Number with adverse events "No statistically significant differences observed 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**
FDA-approved pharmacological	Duke University, 2009[578] ID: NCT00889915 RCT Unclear/Not reported N = 228 US Setting: N/A	**Target:** Children 6-17 years old 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; patients with inpatient status are excluded, cannot take another medication for ADHD (psychostimulant, atomoxetine, bupropion); those with psychosis or autism spectrum disorder are excluded **Other:** **ADHD presentation:** N/A **Diagnosis:** **Comorbidity:** N/A **Female:** 31.6 % **Age mean:** 10.3 (3.1) 10.3 (3.2), 10.6 (3.1), 10.0 (3.2), Adderall 10.4 (3.0) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** Other info on race or ethnicity: N/A	**Intervention:** Methylphenidate transdermal system, optimal dose received for 6 weeks **Control:** NA **Comparator:** MedicationMixed amphetamine salts extended release (dosage not described) **Follow-up:** 1.5 months	Decreased appetite and weight loss Both groups reported an equal number of participants. Intervention had a higher percentage of participants experiencing adverse events compared to the comparator group.
FDA-approved	Eli Lilly, 2004[389] ID: NCT00192023 RCT Single center	**Target:** Children and Adolescents With ADHD and Comorbid Oppositional Defiant Disorder. Those with history of Bipolar,	**Intervention:** Atomoxetine 0.5 mg per kg per day for 1 week, then 1.2 mg/kg/day for 7 weeks **Control:** Placebo	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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 = 139 Italy Setting: Specialty care	psychosis or pervasive development disorder excluded. **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 Other info on race or ethnicity:	Placebo, daily for 8 weeks **Comparator:** NA **Follow-up:** 2 months	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.
FDA-approved pharmacological	Eli Lilly, 2006[251] N/A ID: NCT00406354 RCT Multicenter N = 181 Germany Setting: Specialty care	**Target:** Conduct disorder not exclusionary; normal intelligence; 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:** N/A **Female:** 15.6 %	**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	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).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Age mean: 11.0 (3.01) **Minimum age:** 6 **Maximum age:** 17 **Ethnicity:** % Black/African American : 1 % White : 99 Other info on race or ethnicity:	week, then 1.2 mg/kg daily dose taken orally for 7 weeks **Follow-up:** 2.25 months	decreased appetite Participants with non-serious adverse events The rate was 80% for intervention, 54% for control and 70% for comparator.
FDA-approved pharmacological	Eli Lilly[252] ID: NCT00568685 RCT Multicenter N = 153 Korea Setting: N/A	**Target:** Patients with ADHD ages 6-18years, 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 beginning study treatment, must be able to swallow capsules, judged by the study investigator to be reliable to keep appointments for clinic visits and all tests, including blood tests and any other required examinations **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:** Other info on race or 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[274] ID: NA RCT Unclear/Not reported N = 177 US Setting: N/A	**Target:** There were no formal inclusion or exclusion criteria. **Other:** **ADHD presentation:** N/A **Diagnosis:** No a computerized version of the Diagnostic Interview Schedule for Children and clinical interviews with a psychologist and a psychiatrist. **Comorbidity:** N/A **Female:** 0 % Gender separated by age group - male reported only; <7.99 years= 82.61% / 8-10.99 years= 80.36% / 11-17.59 years = 78.85% **Age mean:** Age mean separated by age group; <7.99 years =6.35 / 8-10.99 years= 9.47 / 11-17.59 years = 13.64 **Minimum age:** 4 **Maximum age:** 18 **Ethnicity:** Other info on race or ethnicity: N/A	**Intervention:** Mixed amphetamine salts (Adderall) 5 mg per dose, 10 mg per dose, and 15 mg per dose for 4 weeks **Control:** Placebo **Comparator:** MedicationMethylphenidate (5 mg per dose, 10 mg per dose, and 15 mg per dose) twice per day (in the morning and at lunch) **Follow-up:**	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). Of note, all youths who withdrew prematurely had multiple adverse events at the dose of treatment that led to study discontinuation. For this reason, a single, specific side effect could not be ascribed as the cause for their trial being discontinued.
FDA-approved pharmacological	Findling, 2008[276] Noven Therapeutics, 2004[930]; Findling, 2009[751]; Findling, 2010[748] ID: NCT00444574 RCT	**Target:** Children age 6 to 12 inclusive who were diagnosed with ADHD according to DSM-IV-TR criteria (predominantly hyperactive/impulsive, inattentive, or combined type) were eligible for study inclusion	**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	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).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
	Unclear/Not reported N = 282 US Setting: N/A	**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 % 64.9 **Age mean:** 8.7 (1.94) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A	**Comparator:** Medication18mg OROS capsules plus placebo patch for 5 weeks **Follow-up:** 1.25 months	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[275] ID: N/A RCT Multicenter N = 217 US Setting: Mixed	**Target:** Adolescent age 13-17 years old with diagnosis of ADHD according to DSM -IV-TR, have a total score of >=26 on the ADHD-RS-IV scale at baseline, IQ of >= 80. Exclusion: have a conduct disorder or comorbid psychiatric illnesses that contraindicated treatment with MTS, history of cardiac problems, history of	**Intervention:** Methylphenidate transdermal system, patches applied to hips once daily (alternating hips 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 **Control:** Placebo	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	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		substance abuse, history of being nonresponsive to psychostimulant treatment; clonidine, atomoxetine, antidepressants, sedatives, antipsychotics, anxiolytics, P450 enzyme altering agents, or other investigational medications within 30 days prior to screening not eligible **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 info on race or ethnicity: Other : Other: 3.7%	Matching placebo **Comparator:** NA **Follow-up:** 2 months	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 investigator, and one incidence of oppositional behavior which was judged as severe but not related to 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**
FDA-approved pharmacological	Findling, 2011[273] Shire, 2008[1014] ID: NCT00735371 RCT Multicenter N = 314 US Setting: N/A	**Target:** Children with ADHD; participants with 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, a history of seizures, tic disorder or family history of Tourette disorder, family history of sudden cardiac death or arrhythmia, abnormal thyroid function (a stable dose of thyroid medication for at least 3 months was permitted), glaucoma, or those considered a suicide risk were excluded; BMI could not be 5th or 97th percentile for age and gender; tested positive on urine drug screen (except current stimulant therapy), or had a recent history of suspected substance abuse (excluding nicotine) were not enrolled; pregnant/lactating females, with clinically significant ECG 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 were disqualified	**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 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**
		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 Other info on race or ethnicity:		
FDA-approved pharmacological	Fuentes, 2013[282] Eli Lilly and Company, 2007[731] ID: NCT00447278 RCT Multicenter N = 398 Multiple countries Setting: Mixed	**Target:** Patients had to be pharmacologically naive for ADHD treatment. This was defined as not having received more than 7 consecutive days of any dose of pharmacotherapy for ADHD during the patient's lifetime and not having received more than 2 consecutive days of any dose of pharmacotherapy for ADHD within the 30 days before the first study visit. **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist	**Intervention:** Atomoxetine oral once or twice daily, starting dose 0.5 mg/kg perdayincreasing to the recommended target dose of 1.2 mg/kg per day, not exceeding a maximum dose of 1.8 mg/kg per day **Control:** NA **Comparator:** MedicationThe OEST group defined as any ADHD treatment including any medication except ATX, including long- and short-acting MPH and antidepressants; allowed switching between different formulations of a	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 G 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 G 0.001) and irritability (6.5% vs 1.5%; P = 0.019) were reported by significantly more patients; initial insomnia (5.5% OEST, 1.5% ATX; P = 0.053) and sleep disorder (4.5% OEST, 1.0% ATX; P = 0.062) missed significance by a small margin. During study period II (6 months), 2 patients (1.0%) in both

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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-RS-IV **Comorbidity:** N/A **Female:** 20.6 % **Age mean:** 9.3 (2.60) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** Other info on race or ethnicity: N/A	specific medication, specific doses were not mandated in the **Follow-up:** 12 months	treatment groups had serious AEs (SAEs). In study period III (12 months), 7 patients experienced SAEs: 4 (2.9%) in the ATX group and 3 (1.9%) in the OEST group. None of the SAEs were considered related to study medication. Seven patients (3.5%) in the ATX group and 2 patients (1.0%) in the OEST group discontinued because of TEAEs during study period II and 4 patients (2 each in the ATX [1.4%] and OEST [1.3%] group) during study period III.
FDA-approved pharmacological	Gard, 2014[286] ID: RCT Single center N = 84 India Setting: Specialty care	**Target:** Children aged 6-14 diagnosed with ADHD and have moderate to severe illness as assessed by Clinical Global Impressions Severity Scale (CGI-S) **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:** Other info on race or ethnicity: N/A	**Intervention:** Atomoxetine 1.2 mg/kg/day, once or twice daily based on response and tolerability **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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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	Gau, 2006[289] ID: N/A RCT Single center N = 64 Taiwan Setting: Mixed	**Target:** Patients age 6-15 years old with diagnosis of ADHD, taking MPH on a total daily dose of 10-40 mg for the past 3 months; excluded significant gastrointestinal problems, a history of hypertension, known hypersensitivity to MPH, or 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, or a psychotic disorder were excluded, as were 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)	**Intervention:** Methylphenidate 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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Minimum age: 6 **Maximum age:** 13 **Ethnicity:** Other info on race or ethnicity: N/A : Taiwanese children		
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. Subjects were excluded if they weighed less than 20 kg or more than 60 kg; had a serious medical illness, such as a cardiovascular disease; had a history of bipolar I or II disorder, psychosis, or pervasive developmental disorder; had anxiety disorder based on the DSMIV criteria at study entry; had a history of any seizure disorder or prior EEG abnormalities related to epilepsy, or taking anticonvulsants for seizure control; had a 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	**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 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**
		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:** Other info on race or ethnicity: N/A		
FDA-approved pharmacological	Geller, 2007[292] ID: N/A RCT Multicenter N = 176 US Setting: Specialty care	**Target:** Children between 8-17 with ADHD according to DSM-IV, and one of the following anxiety disorders: 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	**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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		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 info on race or ethnicity: Other : intervention 79% white, control 82%		
FDA-approved pharmacological	Greenhill, 2006[303] ID: NA RCT Multicenter N = 103 US Setting: Mixed	**Target:** Patients age 6-15 years old with clinical diagnosis of ADHD. For boys, baseline scores on the Conners ADHD/DSM-IV Scale-Teacher version (CADS-T) DSM-IV total subscale were required to be equal or larger than 27 for those 6 to 8 years old, equal or larger than 24 for those 9 to 11 years old, equal or larger than 19 for those 12 to 14 years old, and equal or larger than 14 for those 15 to 17 years old. For girls, the respective baseline cutoff scores on the CADS-T were 16, 13, 12, and 6. All of the patients were attending school in a classroom setting and had the same teacher for the	**Intervention:** Dexmethylphenidate extended release 5, 10, 15, 20, or 30 mg/day once daily for 2weeks **Control:** Placebo Placebo pills once daily **Comparator:** NA **Follow-up:** 2 months	CGI-I rated 1 or 2 Statistically significant difference between groups. Conners ADHD/DSMIV Scale-Teacher version total score Statistically significant difference between groups ($p<0.001$), effect size 0.79. Decreased appetite The rate of decreased appetite was 30.2% in the intervention and 8/5% in the control group. Participants with at least one adverse event reported The rate was 75.5% in the intervention and 57% in the placebo group. 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
		duration of the study who was able and willing to perform symptom assessments **Other:** **ADHD presentation:** inattentive : 21.4,hyperactive : 1.9,combined : 76.7 **Diagnosis:** Confirmation by specialist 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:** 15 **Ethnicity:** % Black/African American : 23.3 % White : 60.2 Other info on race or ethnicity: Other : Other: 17/103 (16.5%)		
FDA-approved	Griffiths, 2018[304] ID: ANZCTR 12607000535471 Crossover trial Multicenter	**Target:** Diagnosis of ADHD, fluent in English, no current stimulant use, any contraindications to atomoxetine, no substance or alcohol abuse **Other:**	**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	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

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 = 136 Australia Setting: School	**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:** Other info on race or ethnicity: N/A	**Control:** Placebo Placebo, both groups switched and were evaluated again **Comparator:** NA **Follow-up:** 1.5 months	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).
FDA-approved pharmacological	Harfterkamp, 2012[313] ID: 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:**	**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
		% Black/African American : 1.0 % White : 99.9 Other info on race or ethnicity:		
FDA-approved pharmacological	Hazell, 2003[317] ID: NA RCT Unclear/Not reported N = 67 Australia Setting: N/A	**Target:** Children 6-14 years old with diagnosis of ADHD and comorbid ODD or CD 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 MPH or dexamphetamine, IQ at least 70, can have comorbid anxiety or depression **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:**	**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**
		Other info on race or ethnicity: N/A		
FDA-approved pharmacological	Hervas, 2014[321] ID: n/a RCT Multicenter N = 338 Multiple countries Setting: N/A	**Target:** Male and female children/ adolescents ages 6-17 years old with a diagnosis of ADHD of at least severity as defined by a baseline ADHD-RS-IV with a total score of 32 or higher and a minimum Clinical Global Impression Severity (CGI-S) 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 % 73.7 **Age mean:** 10.8 (2.8) **Minimum age:** 6	**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 treatment related]).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Maximum age: 17 **Ethnicity:** Other info on race or ethnicity: N/A		
FDA-approved pharmacological	Ichikawa, 2020[333] Ichikawa, 2020[819] ID: NA RCT Multicenter N = 76 Japan Setting: N/A	**Target:** Children aged 6–17 with ADHD per DSM V. ADHD-RS-IV total score of at least 28 was required. Exclusion criteria: serious disorders of the blood or bone marrow, heart, kidneys, liver, lungs; psychiatric comorbidity (e.g.,bipolar disorder, schizophrenia); CD (excluding ODD); 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	**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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Maximum age: 17 **Ethnicity:** Other info on race or ethnicity: N/A		
FDA-approved pharmacological	Jain, 2011[337] Addrenex Pharmaceuticals, 2007[641] 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 and each patient's clinical research physician and a minimum score of 26 on the ADHD Rating Scale–IV (ADHD-RS-IV), having a 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 were eligible for study inclusion. Patients were excluded if they had a 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	**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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		seizures (except for febrile seizure before 2 years of age). **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 Other info on race or ethnicity:		
FDA-approved pharmacological	Johnson, 2020[342] Supernus Pharmaceuticals, 2016[1062] ID: NCT02633527 RCT Multicenter N = 234 US Setting: Mixed	**Target:** Children between 6 and 12 with a diagnosis of ADHD per the DSM, medically healthy, free of ADHD medication for at least 1 week prior to baseline, participants should not have a history or presence of neuropsychiatric disease other than ADHD as the primary diagnosis, no history or presence of systemic diseases or other neurologic or psychiatric diseases, no history of suicidal	**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, to minimize any potential placebo effects **Comparator:** MedicationViloxazine (SPN-812), 100 mg/day of	CGI-I Intervention scores but not comparator scores improved significantly compared to control ($p<0.05$). ADHD-RS-IV Intervention scores but not comparator scores improved significantly compared to control ($p<0.05$). Decreased Appetite 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**
		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	extended-release viloxazine for 8 weeks **Follow-up:** 2 months	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**
		Other info on race or ethnicity:		
FDA-approved pharmacological	Kelsey, 2004[354] ID: RCT Multicenter N = 197 US Setting: N/A	**Target:** Children with ADHD. Those with 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 Other info on race or ethnicity:	**Intervention:** Atomoxetine once per day in the morning for 8 weeks (max 1.8 mg/kg per day, 120 mg per day) **Control:** Placebo Placebo once per day in the morning, for 8 weeks **Comparator:** NA **Follow-up:** 2 months	Conners' Global Index, Parent Significantly greater mean improvement in atomoxetine group. ADHD RS, parent ADHD RS, 25% re-duction from baseline Significantly greater improvement in atomoxetine group. Decreased appetite A significantly greater proportion of amoxetine patients experienced decreased appetite. 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[368] Shire, 2005[1024] ID: NCT00150592 RCT Multicenter N = 182 US Setting: N/A	**Target:** Reasons for exclusion included 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 (PDSS) 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 Other info on race or ethnicity:	**Intervention:** Guanfacine extended release, optimal dose (1, 2, or 3mg/day) found in 3 week dose-finding phase, maintained for 2 weeks of maintenance **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).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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[367] Addrenex Pharmaceuticals, Inc., 2008[642] ID: NCT00641329 RCT Multicenter N = 198 US Setting: N/A	**Target:** Children were required to have inadequate stimulant medication response, defined as a total score 26 on the ADHD-RS-IV questionnaire after a minimum of 4 weeks on a stable stimulant regimen, had intelligence quotient estimated to be 80 by the investigator and a BMI in the 5th percentile for the patient's gender and age; patients were excluded from participation in the study if they had (1) a current diagnosis or history of a psychiatric disorder that required psychotropic medication or severe comorbid Axis I or Axis II disorder (2) a history of conduct disorder, (3) a history of syncopal episodes or seizures (except for febrile seizures), (4) current or past drug abuse, (5) a history of clonidine intolerance, or (6) used any investigational drug within 30 days of the study initiation or had a positive drug test (except for ADHD medication) **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A	**Intervention:** Clonidine hydrochloride extended-release tablets with stimulants (methylphenidate or amphetamine): total daily doses of 0.1 to 0.4 mg per day for 8 weeks, concomitant stimulant medication was prescribed by the patient's regular physician and was obtained from the patient's usual pharmacy **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 The intervention group had greater improvement than the control group (p=0.006). ADHD-RS-IV (ADHD Rating Scale IV), change The intervention group had greater improvement than the control group (p=0.009). Participants with at least one treatment emergent adverse event The rate was 45% in the intervention and 41% in the concomitant placebo group. 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, increased heart rate [n=1], aggression [n=1], and somnolence [n=1]), and only 1 of 102 patients (1%) in the CLON-XR plus stimulant group discontinued because of a TEAE (ie, slowed thought processes).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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: 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 info on race or ethnicity: Other : 8		
FDA-approved pharmacological	Kratochvil, 2002[370] ID: NA RCT Multicenter N = 228 US Setting: N/A	**Target:** Girls older than 9 years were excluded because the results of preclinical studies of atomoxetine's effects on pregnant animals were unavailable at the time this study started. Important exclusion criteria included a history of bipolar or psychotic disorders, motor tics or a family history of Tourette syndrome, substance abuse, nonresponse to a previous trial of methylphenidate (significant residual symptoms after at least 2 weeks of treatment with at least 1.2 mg/kg per day), and serious medical illness. Other concurrent psychiatric diagnoses did not exclude patients from the trial; these were assessed with the Diagnostic Interview for Children	**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 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	CGI ADHD Severity Both groups improved. ADHD-RS-IV No statistically significant differences between treatment groups (p = .66). Weight loss 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 event were extensive metabolizers.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		and Adolescents-IV Computerized Version (DICA-IV) (Reich et al., 1995), with any diagnosis being confirmed by clinical interview. **Other:** **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 Other info on race or ethnicity:		
FDA-approved pharmacological	Kratochvil, 2011[372] University of Nebraska, 2007[1099] ID: NCT00561340 RCT Unclear/Not reported N = 101 US Setting: Other	**Target:** Young children with ADHD, exclusion criteria included 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	**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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		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 Other info on race or ethnicity:		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 significant difference in change in weight (−0.2 kg [±0.1] in atomoxetine and 0.6 kg [±0.2] in the placebo group (P = .0006); however, this was not clinically significant.
FDA-approved pharmacological	Kurowski, 2019[375] Childrens Hospital Medical Center, Cincinnati, 2013[691] ID: NCT01933217 Crossover trial Single center N = 26	**Target:** Children age 6-17 years old with hospital admission for blunt head trauma, and a confirmed diagnosis of moderate to severe traumatic brain injury (Glasgow Coma Scale <= 12), have 6 of 9 current symptoms on at least one subscale of the VADPRS; children with preinjury diagnoses of developmental or neurological	**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 **Control:** Placebo	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

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
	US Setting: Specialty care	disorders, or hospitalized for psychiatric reasons in the past 12 months, 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 were excluded **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 Other info on race or ethnicity:	Identical capsules filled with placebo (inert white capsules) for 4 weeks, then switching to the intervention drug **Comparator:** NA **Follow-up:** 2 months	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 while on placebo.
FDA-approved	Law, 1999[379] ID: N/A RCT Single center	**Target:** Children who exhibited pervasive ADHD, defined as 8 or more of the 14 criteria for ADHD according to DSM-III-R based on parent or teacher interview; at least	**Intervention:** Methylphenidate 0.7mg/kg twice daily for 1 year **Control:** Placebo Placebo	Onset or worsening severity of tics; from abstract - clinically significant tics developed in 19.6% of the subjects without preexisting tics receiving MPH and in 16.7% of those receiving the placebo (Fisher exact test, p = .59, not

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 = 91 Canada Setting: Other	5 ADHD criteria in another setting; a history of ADHD symptoms for at least 6 months, starting before the age of 7 years; estimated Full Scale IQ greater than 80 (based on subtests of VISC-R); no primary anxiety or affective disorder; no history of prior treatment for ADHD or tics. Excluded children if they had severe motor or vocal tic disorder or Tourette's disorder (mild to moderate tics included); if regularly received medication for a medical problem; if had a chronic medical condition; or if attended a full time residential or day treatment program **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:** **Comorbidity:** **Female:** 18.68 % **Age mean:** MPH group mean age 8.4(1.6), Placebo group mean age 8.3(. 1.5) **Minimum age:**	**Comparator:** NA **Follow-up:** 12 months	significant; relative risk = 1.17, confidence interval = 0.31-4.40). Deterioration of tics was observed in 33% of subjects with preexisting tics receiving MPH and in 33% of those receiving the placebo (Fisher exact test, p = .70, not significant; relative risk = 1.0, confidence interval = 0.40-1.85).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Maximum age: **Ethnicity:** Other info on race or ethnicity: N/A		
FDA-approved pharmacological	Lilly, 2008[253] 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; those who previously participated in an atomoxetine study and those taking anticonvulsants, antihypertensive agents, medication with sympathomimetic activity, psychotropic medications, monoamine oxidase inhibitor were excluded **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	**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
		Maximum age: 16 **Ethnicity:** % Hispanic or Latino : 18,9 % Black/African American : 0.9 % White : 80.2 Other info on race or ethnicity:		
FDA-approved pharmacological	Martenyi, 2010[404] Eli Lilly and Company, 2004[728] ID: NCT00386581 RCT Multicenter N = 105 Russia Setting: N/A	**Target:** Participants were 6–16 years of age, 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 CGI-ADHD Severity scale, had not taken any medications for ADHD. Exclusion: weight <20 kg or >60 kg, history of bipolar disorder, anxiety disorder, psychosis, or developmental disorder, 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)	**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
		Comorbidity: N/A **Female:** 14.3 % **Age mean:** 9.8 (2.8) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** % White : 100 Other info on race or ethnicity:		
FDA-approved pharmacological	Matthijssen, 2019[408] 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 a child had stopped the medication during, for instance, a weekend or a school holiday, they could still participate 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	**Intervention:** Gradual withdrawal of methylphenidate to placebo over a 3-week period followed by 4 weeks of complete placebo **Control:** NA **Comparator:** MedicationContinued extended-releasemethylphenidate 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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Maximum age: 18 **Ethnicity:** % White : 98.9 Other info on race or ethnicity:		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.
FDA-approved pharmacological	Mattingly, 2020[409] Shire, 2017[1028] ID: NCT03325881 RCT Multicenter N = 89 US Setting: Specialty care	**Target:** Children (aged 6–12 years) with Diagnostic and Statistical Manual of Mental Disorders, Fifth edition—defined ADHD; baseline ADHD-Rating Scale, Fifth Edition, Child, Home Version total scores (ADHD-RS-5-HV-TS) ≥ 28; and baseline Clinical Global Impressions-Severity scores ≥ 4 were eligible **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	**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
		% American Indian or Alaska Native : 0 % White : 66.7 % Multiracial : 8.9 Other info on race or ethnicity:		
FDA-approved pharmacological	McCracken, 2016[415] Bilder, 2016[675]; Sayer, 2016[989]; University of California, Los Angeles, 2007[1094] ID: NCT00429273 RCT Single center N = 212 US Setting: Specialty care	**Target:** Male or female individuals 7 to 14 years of age; DSM-IV ADHD (any subtype) diagnosed by semi-structured diagnostic interview (Kiddie-Schedule for Affective Disorders and Schizophrenia -PL [K-SADS-PL]) and clinical interview; and Clinical Global Impression Severity (CGI-S) 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	**Intervention:** Guanfacine (1-3 mg/day) plus d-methylphenidate extended-release (5-20 mg/day), with fixed-flexible dosing **Control:** Other 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 99% for intervention versus 96% 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
		Other info on race or ethnicity: Other : 6		
FDA-approved pharmacological	Michelson, 2001[422] Matza, 2004[879] 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 Other info on race or ethnicity:	**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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
				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[421] ID: NA RCT Multicenter N = 171 US Setting: Specialty care	**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 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:** Other info on race or ethnicity: N/A	**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 ($p < .001$). Decreased appetite More intervention patients reported decreased appetite (p=0 .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
FDA-approved pharmacological	Montoya, 2009[430] Escobar, 2009[738] ID: NCT00191945 RCT Multicenter N = 151 Spain Setting: Specialty care	**Target:** Medication naive children and adolescents with ADHD. Patients with psychiatric comorbidities excluded. **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 Other info on race or ethnicity:	**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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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	Motaharifard, 2019[432] Vice Chancellor for research of Tehran university of Medical Sciences, 2015[1108] ID: IRCT2015050922165N1 RCT Single center N = 59 Iran Setting: Primary Care	**Target:** diagnosed with mild or moderate ADHD according to DSM-5, had no significant chronic medical condition, had no development disorders, had no other psychiatric disorders, had no intellectual disabilities (intelligence quotient <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:** Other info on race or ethnicity:	**Intervention:** Methylphenidate dose of 1 mg/kg/day, initial dose of 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 therapeutically ineffective syrup **Control:** NA **Comparator:** Nutrition, supplementsReceived sweet almond syrup 5 cc/day (three times a day). **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 Side Effect Intervention group had significantly more participants who had a side effect of decreased appetite (p<0.001). Reported side effects of sweet almond syrup, reported (N, %): Insomnia (2, 8%); Increased sleep (4, 16%); Difficulty falling asleep (3, 12%); Abdominal pain (2, 8%); Impulsiveness (1, 4%); Irritability (1, 4%); Nausea (1, 4%). Side effects of MPH reported (N, %): Insomnia (6, 24%); Increased sleep (1, 4%); Difficulty falling asleep (9, 36%); Abdominal pain (6, 24%); Headache (6, 24%); Impulsiveness (3, 12%); Irritability (6, 24%); Nausea (1, 4%); Constipation (1, 4%); Dry mouth (1, 4%); Sadness (6, 24%); Tic (1, 4%); Itching (1, 4%)
FDA-approved	Mount Sinai, 2012[527] N/A ID: NCT01678209 RCT	**Target:** Aged 7-17 years, Wechsler Intelligence Scale for Children ≥ 75, diagnosis of ADHD, any subtype, determined by Kiddie Schedule for Affective Disorders and	**Intervention:** Atomoxetine, flexible-dose titration for 6-8 weeks **Control:** NA **Comparator:** MedicationMethylphenidate, flexible-	CGI-S (Clinical Global Impressions-Severity) Intervention scores improved when compared to comparator. ADHD-RS

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 = 127 US Setting: Specialty care	Schizophrenia for School-Aged Children-Present and Lifetime Versions (K-SADS-PL); ADHD Rating Scale-IV-Parent Version: Investigator Administered (ADHD-RSIV) total score ≥ 1.5 SD above age and gender means for subtype; Clinical Global Impressions-ADHD-Severity (CGI-S) score > 4; ADHD must be the primary diagnosis and focus of treatment, and the 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	dose titration with Concerta for 6-8 weeks **Follow-up:** 1.5 months	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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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 info on race or ethnicity: Other : 43.2 not Hispanic or Latino		
FDA-approved pharmacological	Nasser, 2020[442] Supernus Pharmaceuticals, 2017[1063] ID: NCT03247530 RCT Single center N = 477 US Setting: Other	**Target:** Children between 6 and 11 years of age and had a primary diagnosis of ADHD as defined according to the DSM-5, which was confirmed by the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID), children should not currently have a 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, a 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 :	**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:** MedicationViloxanzine (SPN-812), one 100-mg SPN-812 and one placebo capsule daily for 6 weeks **Follow-up:** 1.5 months	Conners-3 Composite Score, 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

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		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 Other info on race or ethnicity:		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[443] Supernus Pharmaceuticals, 2017[1066] ID: NCT03247556 RCT Multicenter N = 297 US Setting: Mixed	**Target:** Adolescents age 12-17 years old with diagnosis of ADHD according to DSM-5, weight >= 35 kg, have an ADHD-RS-5 Total score >= 28, and a Clinical Global Impression-Severity of Illness (CGI-S) score >= 4. Exclusion: have a current diagnosis of a major psychiatric disorder, a major neurological disorder (including seizures), a significant systemic disease, evidence of suicidality, have an intolerance or allergic	**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	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

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		reaction to viloxazine, 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 Other info on race or ethnicity:	**Comparator:** MedicationViloxazine, 400-mg/day viloxazine extended-release taken daily for 7 weeks **Follow-up:** 2 months	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 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%),

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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	Nasser, 2021[444] Supernus Pharmaceuticals, Inc., 2017[1067]; Supernus Pharmaceuticals, 2017[1066] ID: NCT03247543, NCT03247556 RCT Multicenter N = 313 US Setting: Mixed	**Target:** Male and female children aged 6-11 years old 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 (CGI-S) score of at least 4 at screening **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	**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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		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 Other info on race or ethnicity:		
FDA-approved pharmacological	Nasser, 2021[441] Supernus Pharmaceuticals, Inc., 2016[1065] ID: NCT02736656 RCT Multicenter N = 310 US Setting: N/A	**Target:** ADHD-RS-5 Total score ≥28 and a Clinical Global Impression—Severity of Illness (CGI-S) score ≥4; refrain from taking other ADHD medications for a minimum of 1 week before randomization and for the study duration; considered medically healthy by the study investigator via assessment of physical examination, medical history, clinical laboratory tests, vital signs, and electrocardiogram (ECG); 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	**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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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-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% Other info on race or ethnicity:		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[449] ID: NA RCT Multicenter N = 297 US	**Target:** Children and adolescents age 8-18 years old with clinical diagnosis of ADHD according to DSM-IV, have a symptom severity score of >=1.5SDs above age and gender norms on the Attention-Deficit/Hyperactivity Disorder	**Intervention:** Atomoxetine 1.8 mg/kg/day for 8 weeks administered equally divided doses in the morning and late afternoon **Control:** Placebo Matching placebo for 8 weeks	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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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: Mixed	Rating Scale-IV-Parent version (ADHDRS-IV-Parent:Inv), have a IQ >= 80 according to the full WISC-III. Exclusion: any 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:** Other info on race or ethnicity:	**Comparator:** MedicationAtomoxetine 1.2 mg/kg/day **Follow-up:** 2 months	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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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	Newcorn, 2008[448] ID: N/A Crossover trial Multicenter N = 516 US Setting: N/A	**Target:** Patients 6-16 years with ADHD; children who had seizures, bipolar disorder, a psychotic illness, or a pervasive developmental disorder or who were taking concomitant psychoactive medications, anxiety and tic disorders were excluded, other concurrent psychiatric diagnoses, including major depressive disorder, were permitted as long as ADHD was the primary diagnosis and therefore an appropriate target of treatment. Participants were excluded if they had been treated previously with an adequate trial of methylphenidate or amphetamine and either did not experience at least some improvement in ADHD signs and symptoms (nonresponders) or had intolerable adverse events **Other:** **ADHD presentation:** inattentive : 28,hyperactive : 2,combined : 70 **Diagnosis:** Confirmation by specialist DSM-IV KSADS-PL **Comorbidity:** N/A **Female:** 26 % **Age mean:**	**Intervention:** Atomoxetine for 6 weeks, 0.8–1.8 mg/kg per day **Control:** Placebo Identically appearing capsules **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	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 Patients on methylphenidate changed more than patients on atomoxetine or placebo. ADHD-RS (ADHD Rating Scale) total score Treatment favored atomoxetine compared to osmotically released methylphenidate. Change in weight (kg) Difference from placebo was statistically significant for both active interventions (p<0.05). Adverse events that occurred in at least 5% of the patients in any treatment 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 was reported more often for atomoxetine than for methylphenidate, while insomnia was reported more often for methylphenidate than for atomoxetine. The mean increase in diastolic blood pressure, relative to placebo, was statistically significant for both atomoxetine and osmotically released methylphenidate. No differences were observed in mean change of systolic blood pressure between placebo and either 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**
		Atomoxetine: 10.3 (2.2) Osmotically Released Methylphenidate: 10.2 (2.5) Placebo: 10.1 (2.7) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** Other info on race or ethnicity: N/A		Increase in heart rate was significantly greater for atomoxetine than for either placebo or methylphenidate.
FDA-approved pharmacological	Newcorn, 2016[447] Shire, 2010[1026] 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 licenced clinician using the ADHD-RS-IV and the Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime version (K-SADS-PL) 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:**	**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

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		Ethnicity: % White : 79.5 Other info on race or ethnicity: Other : 20.5		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; placebo, n = 4) reported seven severe adverse events (SAEs), one of which was judged to be related to treatment (GXR: grand mal convulsion). The majority of TEAEs were mild to moderate, with 5 (3.2%) GXR and 2 (1.3%) placebo participants reporting a severe treatment-emergent adverse events.
FDA-approved pharmacological	Prasad, 2007[470] ID: NA RCT Multicenter N = 201 UK Setting: Specialty care	**Target:** Children and adolescents with ADHD; patients with: a history of bipolar disorder, psychotic disorders, pervasive development disorder (autistic spectrum 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 were excluded **Other:** Parents supplied some outcome data **ADHD presentation:** inattentive : 7.5,hyperactive : 2.0,combined : 90.5	**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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 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 Other info on race or ethnicity:		There were no deaths and no serious adverse events.
FDA-approved pharmacological	Rubio Morell, 2019[492] ID: N/A RCT Single center N = 45 Spain Setting: Other	**Target:** Participants with age between 9 and 12 years old; intelligence quotient ≥85; absence of sensory, psychiatric and/or neurological disorders (excluding ADHD); no record of having previously used medications designed for ADHD, another neurobehavioral disorder, or psychiatric impairment; absence of concomitant psychotropic medication and poor performance in executive functions and delay aversion in the naive assessment	**Intervention:** Atomoxetine, effective clinical dose, titration initiated with a standarddose based on weight (0.8–1.5 mg /kg/day for ATX) and adjusted by clinical response until an optimal clinical response with minimum side effects was reached, mean dose 40 mg/day **Control:** NA **Comparator:** MedicationModified-release methylphenidate (long-acting), dose titration initiated with a standard dose based on weight (1	Risk taking behavior evaluated by the Cambridge Gambling Task There was no difference between groups. Both MPH and ATX significantly improved scores in verbal working memory (p 0.71, d 0.12), spatial working memory (p 0.44; d 0.03), planning (p 0.6, d 0.18), decision making (p 0.06, d 0.12) and inhibition (p 0.08, d 0.00). No beneficial effect on delay aversion and risk taking was found with MPH and neither with ATX. Long-term treatment in range of optimal clinical dosages with either MPH or 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
		Other: **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** % n/a **Age mean:** Intervention: 10.46 (0.66), comparator: 10.0 (0.40) **Minimum age:** 9 **Maximum age:** 12 **Ethnicity:** Other info on race or ethnicity:	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	improves EF, but not DAv in children with ADHD. No ADHD participant dropped out the study due to adverse effects or other any other reason
FDA-approved pharmacological	Sallee, 2009[499] Shire, 2004[1023] ID: NCT00150618 RCT Multicenter N = 324 US Setting: Specialty care	**Target:** Children 6-17 with ADHD, those with co-morbid psyc disorders (other than ODD) were excluded, as were those currently on 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	**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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		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 info on race or ethnicity: Other : "Other" 4.3%		Adverse events occurring in 5% or greater in participants taking medication were somnolence, headache, fatigue, sedation, dizziness, irritability, upper abdominal pain, and nausea.
FDA-approved pharmacological	Sangal, 2006[500] ID: NA Crossover trial Multicenter N = 85 US Setting: Other	**Target:** Children with ADHD. Patients with pre-existing sleep disorders or serious medical conditions were excluded. **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	**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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		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 info on race or ethnicity: Other : 27.1% non-white		(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).
FDA-approved pharmacological	Shang, 2020[513] Shang, 2015[1005]; Wu, 2021[1145]; Shih, 2019[1009]; Hospital, National Taiwan University, National Science Council, 2009[919] ID: NCT00916786 RCT Single center N = 168 Taiwan Setting: Specialty care	**Target:** Drug naive children aged 7 to 16 with ADHD. Exclusions: comorbid psychiatric conditions, including psychosis, bipolar disorders, autism spectrum disorders, substance use disorders, intellectual disability (full-scale intelligence quotient <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	**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 **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**
		Comorbidity: N/A **Female:** 13 % **Age mean:** 8.7 (2.56) **Minimum age:** 7 **Maximum age:** 16 **Ethnicity:** % Asian : 100 Other info on race or ethnicity:		
FDA-approved pharmacological	Shaywitz, 2017[514] Eli Lilly and Company, 2008[732] ID: NCT00607919 RCT Multicenter N = 124 US Setting: Other	**Target:** Met DSM-IV-TR criteria for ADHD diagnosis confirmed during the first screening visit. Also met criteria for dyslexia at the second screening visit. Had intelligence quotient score of at least 80, were 10 to 16 years. 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	**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**
		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 Other info on race or ethnicity:		
FDA-approved pharmacological	Simonoff, 2013[526] ID: N/A RCT Single center N = 122 UK Setting: Specialty care	**Target:** Children 7–15 years of age with a diagnosis of ICD-10 hyperkinetic disorder and a full-scale IQ of 30–69 who were living in a stable situation and had regular school attendance **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	**Intervention:** Methylphenidate, 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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		Comorbidity: Learning disability : Full-scale IQ of 30–69 **Female:** 30 % **Age mean:** 134 (28) **Minimum age:** 7 **Maximum age:** 15 **Ethnicity:** Other info on race or ethnicity:		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 other children.
FDA-approved pharmacological	Singer, 1995[528] ID: N/A RCT Single center N = 37 US Setting: N/A	**Target:** Children with Tourette's Syndrome and ADHD between the ages 7 to 13 years and 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 Other info on race or ethnicity:	**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[543] ID: RCT Multicenter N = 291 US Setting: Specialty care	**Target:** Children with ADHD. Patients who weighed less than 55 pounds, were on psyc 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:** Other info on race or ethnicity:	**Intervention:** Atomoxetine 3 times per day, drug dosage based on weight **Control:** Placebo Placebo. See administration info above. **Comparator:** MedicationMethylphenidate. See administration information above. Outcomes not reported for this arm, as this was a proof-of-concept study where methylphenidate was used in the stimulant naive stratum to validate the study design if atomoxetine was not superior to **Follow-up:** 2 months (9 weeks)	CGI-S Significantly greater mean improvement in CGI-S scores ($p < .001$) 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 ($p < .001$) and a significantly greater rate of response. Decreased appetite, number with Significantly greater rate of decreased appetite in atomoxetine group. Headache No significant difference between groups in headache, abdominal pain, rhinitis, pharyngitis, vomiting, cough, nervousness, somnolence, or nausea.
FDA-approved	Spencer, 2006[545] ID: NA RCT Unclear/Not reported	**Target:** Adolescents with ADHD. Patients who were known to be nonresponsive to stimulants or naive to stimulant treatment were eligible for enrollment. Exclusion	**Intervention:** Mixed amphetamine salts extended release 40 mg per day for 4 weeks **Control:** Placebo	CGI-I (Clinical Global Impression – Improvement scale) improved A higher percentage of patients in the medication groups were considered improved

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 = 287 US Setting: Specialty care	criteria included: 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 info on race or ethnicity: Other : Other 3.6	Placebo **Comparator:** MedicationMixed amphetamine salts extended release (Adderall MX) 10 mg per day **Follow-up:** 1 month	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[544] ID: N/A RCT Multicenter N = 117 US Setting: N/A	**Target:** Children with Tourette's syndrome and scoring 1.5 SD 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).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 info on race or ethnicity:		
FDA-approved pharmacological	Steele, 2006[549] ID: n/a RCT Multicenter N = 147 Canada Setting: Specialty care	**Target:** Physically healthy male and female outpatients, aged 6-12 years with DSM-IV diagnosis of ADHD; medication naïve, Clinical Global Impression Severity score of 4 or greater and had behavioral difficulties **Other:** **ADHD presentation:** inattentive : 18.37,hyperactive : 2.04,combined : 78.23 **Diagnosis:** Confirmation by specialist The criteria were confirmed by a clinical and structured interview **Comorbidity:** N/A **Female:** 16.3 % **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	**Intervention:** Methylphenidate 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 There was a statistically significant difference favoring intervention group. Snap-IV, parent There was a statistically significant reduction in scores favoring OROS. Parent satisfaction with current ADHD medication There was a statistically significant difference in parent satisfaction favoring OROS. Parent Stress Index scores showed significant differences in favor or OROS. Decreased appetite Rates were similar in both groups. Participants with any adverse event The rate was 82% for intervention and comparator. Adverse events (any possible medication related event, headache, insomnia, abdominal pain, nervousness, emotional lability, agitation,

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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 info on race or ethnicity: Other : 8.8		fatigue, flu-like symptoms, sleep disorder) were similar between groups.
FDA-approved pharmacological	Su, 2016[555] Peking University, 2010[947]; Yang, 2012[1148] ID: NCT01065259 RCT Single center N = 237 China Setting: N/A	**Target:** Youth with ADHD, either treatment naive or untreated for at least 6 months; subjects were excluded if they had a history of poor response with adequate treatment or intolerance to either treatment medication; medical contraindications to stimulants or who had seizure disorder or an abnormal EEG associated with epilepsy, bipolar disorder, psychosis, anxiety disorder, depression disorder, TD, pervasive developmental disorder, or an IQ <70, children taking concomitant psychoactive medications including dietary supplements with central nervous system activity in the past 30 days were also excluded **Other:** **ADHD presentation:** inattentive : 48,hyperactive : 3,combined : 49 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 17 %	**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 were intolerable **Control:** NA **Comparator:** MedicationOsmotic Release Oral System Methylphenidate optimized dose (18, 36, or 54 mg/day) for 4 weeks **Follow-up:** 12 months	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 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**
		Age mean: 9.5 (1.9) **Minimum age:** 6 **Maximum age:** 16 **Ethnicity:** Other info on race or ethnicity: N/A		
FDA-approved pharmacological	Supernus Pharmaceuticals, 2016[559] 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 (psychostimulant or non-stimulant). Current or lifetime diagnosis of epilepsy, major depressive disorder, bipolar disorder, schizophrenia or a related disorder, personality disorder, Tourette's disorder, or psychosis excluded. **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)	**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 **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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		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 info on race or ethnicity: Other : Categories not mutually exclusive		
FDA-approved pharmacological	Svanborg, 2009[560] Svanborg, 2009[1068] ID: NA RCT Single center N = 92 Sweden Setting: Specialty care	**Target:** Male and female patients 7–15 years of age were included if they met the cri- teria 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	**Intervention:** Psychoeducation for caregivers plus atomoxetine, 1.2 mg/kg day (70 kg) or 80 mg/day (>70 kg) for 10 weeks **Control:** Other Psychoeducation for caregivers plus placebo capsules 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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Maximum age: 15 **Ethnicity:** Other : 0-1%across all arms Other : 3% across all arms Other : 93.9% across all arms Other info on race or ethnicity: Other : 2.2% across all arms		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.
FDA-approved pharmacological	Takahashi, 2009[562] ID: NA RCT Multicenter N = 245 Japan Setting: Mixed	**Target:** Japanese children and adolescents age 6-17 years old with DSM-iV diagnosis of ADHD, CGI-ADHD-S score of >= 3, have symptom severity score at least 1.5 standard deviations (SD) above Japanese pediatric age and gender norms on the Attention-Deficit=Hyperactivity Disorder Rating Scale-IV–Parent Version:Investigator Administered and Scored=Translated and Validated in Japanese (ADHD RS-IVJ:I), IQ >= 80. Exclusion: anyone who took antipsychotic medication within 26 weeks of study visit 1, had a history of bipolar disorder or psychosis, or were determined by the investigator to be at suicidal risk. **Other:** **ADHD presentation:** inattentive : 61.2,hyperactive : 4.5,combined : 34.5	**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**
		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 Other info on race or ethnicity:		
FDA-approved pharmacological	Tourette's Syndrome Study Group, 2002[374] ID: NA RCT Multicenter N = 136 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 (e.g., tardive tics, neuroacanthocytosis, Huntington disease), major depression, pervasive developmental disorder, autism, psychosis, mental retardation, anorexia nervosa, bulimia, a serious cardiovascular (e.g., significant hypotension, congenital heart disease) or other medical disorder that would preclude the safe use of the medication, impaired renal function	**Intervention:** Methylphenidate 60mg/day plus clonidine 0.6mg/day for 8 weeks **Control:** Placebo Placebo in gelatin capsules **Comparator:** MedicationMethylphenidate (Ritalin), maximum allowable daily drug dosages were 60 mg for MPH and 0.6 mg **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, comparator had 80.6% and placebo had 32.3%. Children's Global Assessment Scale (C-GAS) Intervention and comparator groups significantly improved over control group (p=0.002, p=0.0005). No significant difference was observed when comparing CLON alone and MPH alone. No gender differences were found in the identified treatment effects. 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
		(a routine urinalysis was performed), or pregnancy (a urine pregnancy test was performed for all adolescent girls **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), MPH 10.7 (2.0), CLON 9.7 (1.8), Combination 10.6 (1.9) **Minimum age:** 7 **Maximum age:** 14 **Ethnicity:** % White : 72 Other info on race or ethnicity:		similarpatternoftreatmenteffectswasfoundwhen analyzingsomeofoursecondaryoutcomemeasures 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 for subjects assigned to MPH alone (35%) than those assigned to MPH combined with CLON (15%), CLON alone (18%), or placebo (19%). Compared with placebo at the final visit, the severity of tics as assessed by the YGTSS-total, GTRS, and TSSR decreased in all active treatment groups. There was no overall evidence of cardiac toxicity by ECG monitoring.
FDA-approved pharmacological	Tris Pharma, 2014[575] ID: NCT02083783 RCT Multicenter N = 108 US Setting: Other	**Target:** Children aged 6 to 12 years with ADHD who require pharmacologic treatment for this condition. Exclusion Criteria: 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:**	**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	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

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 : 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 Other info on race or ethnicity:	**Comparator:** NA **Follow-up:** 1.25 months	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.
FDA-approved pharmacological	van Stralen, 2020[585] JPM van Stralen Medicine Professional, 2013[843] ID: NCT01985581 Crossover trial Single center N = 50 Canada Setting: Specialty care	**Target:** Pediatric patients 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 %	**Intervention:** Guanfacine extended-release 4 mg/day for 8 weeks as adjunct therapy to usual care stimulant therapy **Control:** Placebo Placebo plus usual care 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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Meds then placebo group; 12% female ,Placebo then meds group; 20% female (all have ADHD) **Age mean:** Meds then placebo group; 9.4 (1.6) / Placebo then meds; 9.0 (1.4) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A		
FDA-approved pharmacological	Wang, 2007[593] 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	**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%)

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		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 Other info on race or ethnicity:		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[598] Eli Lilly and Company, 2007[730] ID: NCT00546910 RCT Multicenter N = 128 Germany	**Target:** Eligible were girls and boys aged 6 to 12 years with a diagnosis of ADHD according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition TR **Other:** **ADHD presentation:** inattentive : 22.4,hyperactive : 7.2,combined : 70.4	**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

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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: Mixed	**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 Other info on race or ethnicity:		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[600] ID: N/A RCT Multicenter N = 153 Multiple countries Setting: Mixed	**Target:** Children with a standard deviation score of 1.0 for ADHD-RS-IV-Teacher Version and score at least 1.5 SDs above age and sex norm for the CPRS-R:S 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 **Follow-up:** 1.75 months	Connors Global Index-Teacher, change from baseline Statistically significant change favored the treatment group change compared to the placebo group (p=0.008). ADHD-RS-IV-Teacher (Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Teacher) total score change

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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: 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:** Other info on race or ethnicity: N/A : Not mentioned or brought up.		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.
FDA-approved pharmacological	Weiss, 2007[599] ID: N/A Crossover trial Multicenter N = 90	**Target:** Children with ADHD, score of 1.5 or greater SD from the norm on the Conners' ADHD Index; patients were excluded if they were allergic to MPH or amphetamines or had a history of serious adverse reactions to MPH or had a lack of	**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	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

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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: Mixed	response to MPH, 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 (particularly deafness), 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 info on race or ethnicity: Other : 7	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	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[601] Rhodes Pharmaceuticals, 2014[967]; Rhodes Pharmaceuticals, 2014[968] 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:** Other info on race or ethnicity: N/A	**Intervention:** Methylphenidate long-acting formulation (PRC-063) 85 mg/day for 4 weeks **Control:** Placebo Identical in appearance **Comparator:** MedicationLong-acting methylphenidate formulation (PRC-063) 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[605] Saylor, 2010[990]; Eli Lilly and Company, 2004[729] ID: NCT00191035 RCT Multicenter N = 267 US Setting: Mixed	**Target:** Adolescents 13-16 years old, who met DSM-IV criteria for ADHD, score of at least 1.5 SD above age and gender normative sample for ADHD-RS-IV Parent version, score of 70 or more on Kaufman Brief Intelligence Test (K-BIT). Patients who responded to the study medication during the acute treatment period (8 weeks) were eligible to continue on to an additional 40-week maintenance treatment period. Exclusion: 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 were excluded **Other:** **ADHD presentation:** inattentive : 49.8,hyperactive : 2.2,combined : 47.9 **Diagnosis:** Confirmation by specialist Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version (K-SAD-PL: Behavioral)	**Intervention:** Atomoxetine slow titration 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 a 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, a low dose of 0.8 mg/kg/day or the maximum label dose of 1.4 mg/kg/day for 40 week maintenance **Control:** NA **Comparator:** MedicationFast titration group received atomoxetine at a 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, a low dose of 0.8 mg/kg/day or the maximum label dose of 1.4 mg/kg/day for 40 wee **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**
		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 info on race or ethnicity: Other : Other: 5.62%		
FDA-approved pharmacological	Wigal, 2004[606] ID: NA RCT Multicenter N = 132 US Setting: Specialty care	**Target:** Children with ADHD. Female subjects were required to be premenarche. Patients with other psyc disorders were excluded, as were patients taking the following medications: antidepressants (tricyclic antidepressants, serotonin reuptake inhibitors, and monoamine oxidase inhibitors), sedatives/hypnotics (e.g., barbiturates, benzodiazepine), neuroleptics/antipsychotics, mood stabilizers; anticonvulsants, beta-blockers; α2-agonists, thyroid medications, and chronic oral steroids **Other:**	**Intervention:** Dexmethylphenidate hydrochloride (d-MPH, FocalinTM) twice daily for 4 weeks, with titration of the dose based on weekly clinic visits, a maximum of 10 mg twice daily **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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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 : 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 info on race or ethnicity: Other : Other race: 8.3		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[607] Ortho-McNeil Janssen Scientific Affairs, 2008[938] ID: NCT00799409 Crossover trial Multicenter N = 78 US Setting: School	**Target:** Subjects receiving medication to treat their ADHD at the time of study enrollment exhibited an inadequate response to their then-current stimulant dose and completed a washout equivalent to 5 half-lives of the given medication before completing baseline assessments. Additional requirements included attendance of regular school and the ability to read and understand English.	**Intervention:** Methylphenidate Osmotic-Release Oral System (OROS) 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	Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) - Composite score The intervention group had significantly better scores compared to the control group (p<0.0001). Permanent Product Measure of Performance (PERMP) - Correct Answers The intervention group had significantly better scores compared to the control group (p<0.0001).

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**
		Participants were excluded for a history or current diagnosis of epilepsy, severe anxiety, conduct, psychotic disorders. In addition, 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 info on race or ethnicity: Other : OTHER: 14%	**Follow-up:** 1.5 months	Children taking OROS MPH also obtained statistically significantly better scores than placebo-treated children on the ADHD, 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 suffered from 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 serious AEs, and no subject discontinued treatment because of an AE.
FDA-approved pharmacologic	Wilens, 2005[610] ID: N/A RCT Unclear/Not reported N = 138	**Target:** IQ score ≥ 80; BP measurements within the 95th percentile for age, gender, and height; ECG findings within the normal range; a willingness and ability to comply with protocol requirements in conjunction with a	**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 open-label MAS XR treatment, mean increases 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
	US Setting: Specialty care	parent or caregiver; history of response to stimulant medication; and oppositional defiant disorder diagnosis was acceptable **Other:** **ADHD presentation:** N/A : for 6 months open-label MAS XR arm **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 Other info on race or ethnicity: N/A : no other info provided	**Comparator:** Medication60 mg of MAS XR (mixed amphetamine salts extended-release) **Follow-up:** 6 months	systolic BP (1.7 mm Hg; P=.O252) and pulse (4.4 bpm; P<.0001) were statistically, but not clinically, significant; diastolic BP was not significantly changed (0.6 mm Hg). A decrease in QTcB interval (-4-6±19.9 msec) was statistically (P=.009), but not clinically, significant. There were no serious cardiovascular adverse events.
FDA-approved	Wilens, 2008[608] Noven Therapeutics, 2005[931] ID: NCT00151970 Crossover trial	**Target:** Children with ADHD; children with conduct disorder or comorbid illnesses that contraindicated or could confound medication treatment, or a history of failing to respond to	**Intervention:** Methylphenidate transdermal patch, dose optimized over 5 weeks, 6 hour patch **Control:** Placebo Placebo transdermal patch	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).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 = 117 US Setting: Specialty care	psychostimulant treatment were excluded **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 Other info on race or ethnicity:	**Comparator:** MedicationMethylphenidate transdermal patch, dose optimized over 5 weeks, 4 hour patch **Follow-up:** 2 months	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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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, 2012[611] Wilens, 2017[1141]; Shire, 2008[1016] 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 Other info on race or ethnicity:	**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 as adjunct to 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

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 rates were 77.3% in the AM, 76.3% in the PM, and 63.4% in the placebo group. Similar findings for somnolence, headache, abdominal pain, and fatigue.
FDA-approved pharmacological	Wilens, 2015[612] Shire, 2011[1027] ID: NCT01081132 RCT Multicenter N = 314 US Setting: Mixed	**Target:** The inclusion criteria adolescent outpatients aged 13 to 17 years with a diagnosis of ADHD (any subtype). Consistent with the DSM-IV-TR criteria, a primary ADHD diagnosis was confirmed by clinical evaluation using the behavior module of the Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime version at screening. **Other:** **ADHD presentation:** inattentive : 29.17,hyperactive : 2.89,combined : 67.95 **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** ODD **Female:** 35.03 % 64.33 **Age mean:** 14.5(1.39) **Minimum age:** 13 **Maximum age:** 17 **Ethnicity:**	**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:** 0.25 months	CGI-I score of equal to or greater than 2 More intervention participants showed improvement than control participants (p=0.10). ADHD-RS-IV Intervention participants showed improvement compared to control group (p<0.001). Weiss Functional Impairment Rating Scale, parent (WFIRS-P) 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
		% Black/African American : 16.88 % American Indian or Alaska Native : 0.63 % Asian : 1.59 % White : 72.29 Other info on race or ethnicity: Other : 7.96		
FDA-approved pharmacological	Wolraich, 2001[615] Faraone, 2005[744]; Spencer, 2006[1052]; Baren, 2000[662] ID: N/A RCT Multicenter N = 282 US Setting: Specialty care	**Target:** Children with ADHD who were taking MPH or had taken it in the past; a total daily MPH dose of at least 10 mg but not more than 60 mg. Patients with glaucoma, Tourette's syndrome, an ongoing seizure disorder, or a psychotic disorder also were excluded, as were 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	**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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Maximum age: 12 **Ethnicity:** % Hispanic or Latino : 3.5 % Black/African American : 7.4 % Asian : 0.4 % White : 84.4 Other info on race or ethnicity: Other : Other 4.3%		
FDA-approved pharmacological	Young, 2014[622] Newcorn, 2013[925]; Stein, 2015[1054] 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 %	**Intervention:** Guanfacine extended release administered in the morning and placebo administered in the evening for 8 weeks, 1-4 mg/day based on dose optimization **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 scores 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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		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 Other info on race or ethnicity: Other : 6% other		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 AEs (4 in the AM, 5 in the PM group, 0 in placebo).
FDA-approved pharmacological	Zhu, 2017[632] ID: N/A RCT Single center N = 104 China Setting: Other	**Target:** Patients who aged from six to fourteen and conformed to the ADHD diagnostic criteria of the DSM5, fourth edition. **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 % 58.65 **Age mean:**	**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 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	CGI-ADHD-S Both groups improved but there was no statistical significance in difference values between the two groups. 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).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Atomoxetine 9.92 (2.98), methylphenidate 9.75 (3.14) **Minimum age:** 6 **Maximum age:** 14 **Ethnicity:** Other info on race or ethnicity: N/A		The incidence of lethargy of atomoxetine group was significantly higher than that of methylphenidate group (p=0.027).
Neurofeedback	Arnold, 2022[132] Kerson, 2020[850] ID: 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	**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. **Control:** Attention-matched control Treatment of identical appearance, intensity/frequency, and duration, differing only in that reinforcement for controls was based on a pre-recorded electroencephalogram (EEG) of another child. **Comparator:** NA **Follow-up:** 25 months	Clinical Global Impression (CGI) global index, parent Clinical Global Impression (CGI) - Severity, number in remission 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
		Maximum age: 10 **Ethnicity:** % Hispanic or Latino : 10.83 % Black/African American : 7.63 % Asian : 4.24 % White : 76.3 % Multiracial : 8.47 Other info on race or ethnicity: Other : Other: 3.39		
Neurofeedback	Bakhshayesh, 2011[136] 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; no hyperkinetic conduct disorders (ICD-10:F90.1) or pervasive developmental disorders; children currently taking stimulant medication were not excluded. **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 %	**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 **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 the FBB-HKS total score was superior to EMG group (p=0.062; effect size -.77) per parent rating. There were no significant differences between treatment groups in the teacher ratings. Computer Continous Performance Test: Comission Errors: Significant differences in commission errors between pre- and post-treatment (F(1,33) = 11.865; p = .002); significant interaction between treatment group and time for reaction time (F(1,33) = 7.359; p = .011) with a medium effect size of -.70 (dcorr); overall, performance in the BF group decreased, while performance of the NF group improved after treatment; the effect sizes vary from dcorr = -.32 (reaction time variability) to dcorr = -.79 (reaction time).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Age mean: 9.34 (1.92) **Minimum age:** 6 **Maximum age:** 14 **Ethnicity:** Other info on race or ethnicity: N/A		
Neurofeedback	Bluschke, 2022[164] ID: Clinical trial Single center N = 129 Germany Setting: Specialty care	**Target:** Children and adolescents with ADHD according to ICD-10 criteria. 14 had an axis I comorbidity and 22 had an additional axis II diagnosis. **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:** % Not reported **Age mean:** 10.76 (0.37) Age range not reported. **Minimum age:** **Maximum age:** **Ethnicity:** Other info on race or ethnicity: N/A	**Intervention:** Neurofeedback. Downregulation of theta and upregulation of beta. Two one-hours sessions per week for 8 weeks. 58.6% were on ADHD medication. **Control:** No intervention No neurofeedback. 60.9% were on ADHD medication **Comparator:** NeurofeedbackNeurofeedback. Upregulation of beta. Two one-hours sessions per week for 8 weeks. 46.4% were on ADHD medication. **Follow-up:** 2 months (8 weeks)	ADHD Symptom Checklist, parent rating, Inattention scal No significant difference in effect by group. Flanker test: the no neurofeedback group demonstrated significantly faster reaction times than those in the θ↑β↑ group (p=0.007) or the β↑ group (p=0.033).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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[219] Faculty of Rehabilitation, 2018[741] ID: IRCT20160717028964N2 RCT Unclear/Not reported N = 40 Iran Setting: Other	**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 Child Psychiatrist DSM-IV **Comorbidity:** N/A **Female:** 0 % **Age mean:** 11.17 (0.97) **Minimum age:** **Maximum age:** **Ethnicity:** Other info on race or ethnicity: N/A	**Intervention:** 12 (60min) neurofeedback training sessions for six consecutive weeks, completed twice a week **Control:** Attention-matched control No treatment and watched animations that 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) The intervention group (NF) showed a significant 60.2% decrease in aggression (p=0.001) from pre to post-test; the control group had so significant changes. BIS (Barrat Impulsiveness Scale) The intervention group (NF) showed a significant 60.9% decrease in impulsivity (p=0.001), the control group had no significant changes.
Neurofeedback	Duric, 2017[244] Duric, 2014[725] ID: NCT01252446 RCT Unclear/Not reported N = 130 Norway Setting: N/A	**Target:** Children clinically diagnosed with ADHD using the ICD-10 research diagnostic criteria and cognitive function above an IQ>70; no involvement in another intervention group, including CBT and Stop Now And Plan (SNAP); no co-morbid disorders other than ODD or anxiety disorder; no	**Intervention:** Neurofeedback three times a week, with a total of 30 sessions, plus methylphenidate at a dosage of 1mg/kg/day in the form of long-acting methylphenidate capsules between 20–60mg, 6 months of follow-up **Control:** Other Neurofeedback alone; unipolar sensors were placed on the patient's	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 NF 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
		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) 11.2 (2.8), 11.4 (3.1), 10.9 (2.4) across groups **Minimum age:** 6 **Maximum age:** 18 **Ethnicity:** Other info on race or ethnicity: N/A	scalp to process signals as brainwaves or computer frequencies, while measuring brain activity. Brain activities were then shown to the subject through a video game or a film, so they coul **Comparator:** NA **Follow-up:** 6 months	
Neurofeedback	Gelade, 2017[291] Gelade, 2016[761]; Janssen, 2016[828]; Janssen, 2016[829]; Janssen, 2017[830]; Janssen, 2020[831]; Gelade, 2018[762]; van Mourik, 2011 [1106]; van Mourik, 2010[1106] ID: NCT01363544 RCT	**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	**Intervention:** Neurofeedback of theta/beta training with the aim to inhibit theta (4–8 Hz) and reinforce beta (13–20 Hz) activity at Cz, three 45 minute individual training sessions a week over a period of 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	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	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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 = 112 Netherlands Setting: Specialty care	Rating Scale (DBDRS) confirmed diagnosis **Comorbidity:** N/A **Female:** 24.1 % **Age mean:** 9.63 (1.76) **Minimum age:** 7 **Maximum age:** 13 **Ethnicity:** Other info on race or ethnicity: N/A	**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	intervention compared to neurofeedback and physical activity (p < .001 for all).
Neurofeedback	Gevensleben, 2010[294] Gevensleben, 2009[763]; Wangler, 2011[1125] ID: ISRCTN87071503 RCT Multicenter N = 102 Germany Setting: Specialty care	**Target:** Children aged 8 to 12 with ADHD; vast majority (over 90%) were medication naive. Comorbid disorders included: conduct disorder, emotional disorders, tic disorder and dyslexia. All children 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	**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 **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
		psychiatrist or a clinical psychologist **Comorbidity:** N/A **Female:** 18.1 % **Age mean:** 9.9 (1.25) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A		
Neurofeedback	Gonzalez-Castro, 2016[301] ID: N/A Clinical trial Unclear/Not reported N = 131 Spain Setting: Mixed	**Target:** Children with ADHD and an IQ of 80 or higher **Other:** **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:** Other info on race or ethnicity: N/A	**Intervention:** Neurofeedback plus pharmacological support, neurofeedback consisted of a 15 min session, 3 days per week, for 3 months, methylphenidate administered according to neuropediatricians' recommendations **Control:** No intervention Control group did not receive neurofeedback or pharmacological support **Comparator:** NA **Follow-up:** 3 months	ADHD Scale of Assessment of Attention Deficit with Hyperactivity (EDAH) There were significant differences between control group and neurofeedback (p <0.001), between control group and combined (p = 0.016), but not between control group and pharmacological support (p = 0.289). Statistically significant differences between control group and intervention and comparator groups (p<0.001) for Test of Variables of Attention (TOVA) and the neurofeedback group improved to a greater extent in executive control than the pharmacological support group. Executive Function Scores, cortical activation assessed with QEEG at Cz. there were statistically significant group differences between control group and the treatment groups: neurofeedback (p 0.001), pharmacological support (p 0.001), and combined (p< 0.001). For Fp1, there were statistically significant group differences between control group and the three 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
				groups: neurofeedback (p<0.001), pharmacological support (p = 0.005), and combined (p<0.001).
Neurofeedback	Hasslinger, 2021[316] Karolinska Institutet, 2013[845] 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; neurodevelopmental comorbidities such as autism spectrum disorder, learning disabilities and language impairments were not reasons for exclusion **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:** Other info on race or ethnicity:	**Intervention:** Slow cortical potentials neurofeedback: 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, many of the children's parents underwent psychoeducational parent group-training **Comparator:** Cognitive trainingWorking Memory Training: a 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 while sharing the **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[369] ID: NCT 01879644] RCT Single center N = 115 Germany Setting: Specialty care	**Target:** Children with ADHD. Children with 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:** 9.1 **Minimum age:** 7.0 **Maximum age:** 11.8 **Ethnicity:** Other info on race or ethnicity: N/A	**Intervention:** SCP (slow cortical potential) neurofeedback training aims at first learning to control and 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 . Three sessions per week over 3 months. Three booster sessions were scheduled 6 months after end of therapy to activate the strategies learned. **Control:** NA **Comparator:** OtherSelf management training (SMT) Three sessions per week over 3 months. Three booster sessions were scheduled 6 months after end of therapy to activate the strategies learned. **Follow-up:** 12 months	Conners Parent Rating Scale No significant differences between groups in any Conner's Parent or Teacher Rating Scales ($p > 0.34$) Quality of life assessed via KINDL-R self-report showed SMT superior to neurofeedback regarding quality of life in school.
Neurofeedback	Lim, 2019[390] National Healthcare Group, Singapore, 2011[917] ID: NCT01344044 RCT	**Target:** Children with ADHD; excluded children with intellectual disability, epilepsy and severe sensorineural deficits or co-existing psychiatric disorder.	**Intervention:** Brain computer interface-based attention training program for total 20 weeks, first 8 weeks of 3 sessions per week (24 sessions total), next 12 weeks of 4-weekly sessions (3 sessions total), each training session consists of 10	CBCL (Child Behavior Checklist) - Externalizing reduction The intervention group had significantly greater reductions than the control group ($p<0.001$). ADHD-RS, clinician-rated

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 = 172 Singapore Setting: Specialty care	**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:** Other info on race or ethnicity: N/A	minutes gameplay, 10 minutes break, 10 minutes game play (30 minutes total) **Control:** Wait list Wait list who received the intervention after the first group **Comparator:** NA **Follow-up:** 6 months	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 or was rated to be severe. In most cases, the participants were able to carry on with the intervention session .
Neurofeedback	Luo, 2022[400] 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 excluded. **Other:** Parents provided outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSMIV criteria by a qualifed psychiatrist **Comorbidity:** N/A **Female:** 20 %	**Intervention:** Neurofeedback (NF) plus computerized cognitive training (CCT). Focus Pocus training program includes neurofeedback games and cognitive training(CT) games, . Each training session consisted of 14 randomly ordered mini-games, and, as each mini-game took approximately 1 min to complete, the total time per session was approximately 15 minutes. NF games aimed to promote awareness and control of brain activity with EEG recorded via	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
		% only reported for completers **Age mean:** 8.94 **Minimum age:** 7 **Maximum age:** 12 **Ethnicity:** % Asian : 100,Other : assumed; conducted in China Other info on race or ethnicity:	a portable Bluetooth device that provided the participant with real-time feedback. The CT games were designed to train and improve inhibitory control and working memory abilities. 3 to 5 sessions per week for 3 months, online at home. **Control:** Other **Comparator:** NeurofeedbackAs described above, but NF games only, without CT. **Follow-up:** 3 months	
Neurofeedback	Minder, 2018[424] Zuberer, 2018[1159]; University of Zurich, 2015[1101] ID: NCT02358941 RCT Multicenter N = 77 Switzerland Setting: Mixed	**Target:** Participants with ADHD, with or without hyperactivity, based on parent and teacher ratings on the Conners-3 DSM-IV ADHD indices (one of two ADHD DSM-IV indices reaching T values ≥ 65, the other T ≥ 60 according to both teachers' and parents' ratings); exclusion criteria were severe comorbidities, autism, tics, or other psychiatric disorders as assessed by the Developmental and Well-Being Assessment; medication was allowed if the dose was kept stable over duration of study **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist	**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	Inattention, Conners-3, school, parent There was no significant difference between groups (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**
		DSM-IV **Comorbidity:** N/A **Female:** 35 % **Age mean:** Sets of M (SD): 10.58 (2.3) 11.37 (1.7) 10.40 (2.0) 10.83 (1.8) **Minimum age:** 8 **Maximum age:** 15 **Ethnicity:** Other info on race or ethnicity:	**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	
Neurofeedback	NF Coll. Group, 2021[110] Ohio State University, 2014[935] ID: NCT02251743 RCT Multicenter N = 144 US Setting: N/A	**Target:** Participants with ADHD and an IQ greater than or equal to 80; and an eyes-open theta/beta power ratio greater than or equal to 4.5 at Cz or Fz by the LubarMonastra Assessment Suite, participants could continue stimulants during the study but 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	**Intervention:** Electroencephalographic 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 a 14 week period **Control:** Other 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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		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 Other info on race or ethnicity:		Adverse events that were possibly attributable to treatment were distributed proportionally between the treatments, with no significant difference in any.
Neurofeedback	Purper-Ouakil, 2021[472] Mensia Technologies SA, 2016[886] 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 NF 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)	**Intervention:** At-home neurofeedback training consisted of five 4-minute-long active blocks (with real-time feedback) and two 2.5 minute-long transfer blocks (with only intermittent feedback), two treatment phases of 16 to 20 sessions (4 per week) **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, the optimal dose was maintained **Follow-up:**	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).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Comorbidity: N/A **Female:** 15.3 % **Age mean:** 9.8 (1.8) **Minimum age:** 7 **Maximum age:** 13 **Ethnicity:** Other info on race or ethnicity: N/A		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[473] ID: N/A RCT Single center N = 29 Singapore Setting: Specialty care	**Target:** ADHD participants who had combined or inattentive subtypes on medicine were only allowed to participate after at least 1 month of washout **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 0 % all boys **Age mean:** 9 (1.5) and 9.45 (1.29) in the groups **Minimum age:** **Maximum age:** **Ethnicity:**	**Intervention:** Brain computer-interface training: 3 sessions per week for 8 weeks, each session lasting 30 minutes with breaks included **Control:** No intervention MRI scan and clinical assessment were performed in the control group although no intervention was done **Comparator:** NA **Follow-up:** 2 months	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 ADHD-RS clinician inattention scores compared to the control group (p=0.038).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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 info on race or ethnicity: N/A		
Neurofeedback	Rajabi, 2020[83] ID: N/A RCT Single center N = 32 Iran Setting: School	**Target:** Children diagnosed with ADHD, normal intelligence, 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:** Other info on race or ethnicity: N/A	**Intervention:** Monopolar neurofeedback training for 3 months, 3 times a week during thirty 45-min sessions **Control:** Wait list Waiting list control **Comparator:** NA **Follow-up:** 2.5 months	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 ($p < 0.05$).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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	Steiner, 2014[550] Steiner, 2014[1055]; Tufts Medical Center, 2012[1090] ID: NCT01583829 RCT Multicenter N = 104 US Setting: School	**Target:** Children in grade 2 or 4 with ADHD, IQ of 80 or higher; with no coexisting diagnosis of conduct disorder, autism spectrum disorder, or other serious mental illness (eg, psychosis); child ADHD medication use was not suspended for treatments or assessments **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 Other info on race or ethnicity:	**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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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	Strehl, 2017[554] Holtmann, 2014[809]; Aggensteiner, 2019[645] ID: ISRCTN76187185 RCT Multicenter N = 150 Germany Setting: School	**Target:** Ages 7 to 9, diagnosed with ADHD combined type according to the DSM-IV; excluded were diagnosis of bipolar disorder, obsessive compulsive disorder, psychosis, chronic severe ticks, Tourette syndrome, major physical or neurological illness, and IQ of less than 80 **Other:** **ADHD presentation:** combined : 100 **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:** Other info on race or ethnicity: N/A	**Intervention:** Neurofeedback where participants were prompted to either produce negative (reducing the excitability threshold of the underlying cortex) or positive shifts (inhibition of excitation) in a randomized order; after session 12, the ratio of negativity to positivity trials was increased from 50 to 80%, total of 25 training sessions within 3 months with two to three sessions per week **Control:** Other 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	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 (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 = 1, EMG).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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[120] ID: NCT02777931 RCT Multicenter N = 101 US Setting: Mixed	**Target:** Children and adolescents age 12-17 years old with diagnosis of ADHD based on DSM-V criteria, ADHD-RS-5 score > 28 at baseline, IQ at least 79, have disruptive mutations in genes within the glutamate receptor metabotropic (GRM)-network as determined by the presence of copy number variations (CNVs) (GRM biomarker-positive subjects). no substance use (alcohol, nicotine products, illicit drugs), no comorbid psychiatric disorders, no serios chronic or physicial health conditions (stroke, syncope, CVD, etc.) **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist ADHD-RS-5 score larger or equal to 28 at baseline **Comorbidity:** Other : Genetic disorders **Female:** 37.1 % **Age mean:** 14.1 (1.58) **Minimum age:** 12 **Maximum age:** 17 **Ethnicity:**	**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 **Control:** Placebo Matching placebo capsules **Comparator:** NA **Follow-up:** 1.5 months	CGI-S Placebo performed better than intervention on CGI-S scores. ADHD-RS-5 Symptoms were reduced in the intervention group compared to control. Non serious adverse events The rate was 70% for intervention and 56% 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**
		% Black/African American : 29.9 % American Indian or Alaska Native : 2.1 % Asian : 1.0 % White : 56.7 % Multiracial : 9.3 Other info on race or ethnicity: Other : Unknown: 1 count (1.0%)		
New pharmaceutical agent	Aevi Genomic Medicine, 2018[121] ID: NCT03609619 RCT Multicenter N = 108 US Setting: Mixed	**Target:** Children between 6-17 years old with diagnosis of ADHD according to DSM-V criteria, minimum score of 28 on ADHD-RS-5; those with ASD or significant cardiovascular conditions, any of the specific gene mutation (272 gene mutations) of interest implicated in glutamatergic signaling and neuronal connectivity; children must not take any other medications except for medications intended to treat ADHD within 28 days prior to screening visit **Other:** **ADHD presentation:** N/A **Diagnosis:** No No info given **Comorbidity:** N/A **Female:** 35.2 % **Age mean:** 10.4 (2.86) **Minimum age:** 6	**Intervention:** AEVI-001 100 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) response Both groups had similar response rates. ADHD-RS-5 (Attention Deficit Hyperactivity Disorder Rating Scale) change Both groups had similar 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
		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 info on race or ethnicity: Other : Not reported: 4/108 (3.7%)		
New pharmaceutical agent	Amiri, 2008[129] ID: N/A RCT Single center N = 60 Iran Setting: Other	**Target:** Children with ADHD, children were excluded if they had a 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 based on clinical judgment), a clinically significant chronic medical condition, including organic brain disorder, seizures and, 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	**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 difficulty falling asleep that were observed more frequently 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**
		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:** Other info on race or ethnicity: N/A		
New pharmaceutical agent	Barrickman, 1995[142] ID: NA Crossover trial Unclear/Not reported N = 15 US Setting: N/A	**Target:** Subjects could also have coexisting diagnoses of conduct, oppositional defiant, or developmental learning disorders. The following exclusion criteria were used: IQ < 70 (mental retardation), and any ocher major Axis I, II, or III diagnoses. Since bupropion is contraindicated in subjects with seizure disorders, any subject with a seizure history was excluded. **Other:** **ADHD presentation:** N/A **Diagnosis:** No DSM-III-R **Comorbidity:** N/A **Female:** 20 % **Age mean:** 11.8 (3.3)	**Intervention:** Bupropion 1.4 to 5.7 mg/kg per day for 6 weeks **Control:** NA **Comparator:** MedicationMethylphenidate was titrated to the maximum effective dose of 0.4 to 1.3 mg/kg per day (mean 0.7 mg/kg per day). Dose was fixed for the final 3 weeks of bupropion therapy, Methylphenidate was administered in a dose of 0.4 mg/kg per day during the first w **Follow-up:** 1.5 months	Clinical Global Impression-Severity (CGI-S) Methylphenidate had greater improvements over bupropion (P < .05) Iowa-Conners Teacher's Rating Scale The changes in scores did not differ significantly between the two treatment arms of the study for either drug. Anorexia No changes were noted on ECG measurements or vital signs, and adverse effects were few, mild, and transient

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		Minimum age: 7 **Maximum age:** 16 **Ethnicity:** Other info on race or ethnicity: N/A		
New pharmaceutical agent	Biederman, 2005[155] ID: NA RCT Multicenter N = 248 US Setting: Mixed	**Target:** Patients were 6 to 17 years of age and had a diagnosis of ADHD according to DSM-IV, have a CGI-S rating of 4 or higher, have a teacher-/investigator-rated Attention-Deficit/ Hyperactivity Disorder Rating Scale-IV (ADHD-RS-IV) School Version total and/or subscale score at least 1.5 SDs 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. Exclusion: history or current diagnosis of pervasive developmental disorder, schizophrenia, or other psychotic disorders (DSM IV Axis I, evidence of suicide risk, current psychiatric comorbidity that required pharmacotherapy, have well-controlled ADHD, history of substance abuse. **Other:**	**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**
		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:** Other info on race or ethnicity: N/A		
New pharmaceutical agent	Biederman, 2006[154] ID: NA RCT Multicenter N = 248 US Setting: N/A	**Target:** Children age 6-13 years old 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, CGI-S score of 4 or more at baseline visit **Other:** **ADHD presentation:** inattentive : 20.6,hyperactive : 2.0,combined : 76.6	**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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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 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 info on race or ethnicity: Other : Other: 46/248 (18.5%)		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, gastroenteritis, and vomiting on day 14; these adverse events were considered by the investigator to be unrelated to modafinil.
New pharmaceutical agent	Blumer, 2009[163] Sanofi, 2006[988] ID: NCT00318448 RCT Multicenter N = 201 US Setting: Other	**Target:** Patients were required to have latency to persistent sleep of 30 minutes, according to baseline polysomnographic results, and a sleep disturbance not attributable to direct physiologic effects of an abused drug or misused prescription medication. Patients were excluded if they had 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. Previous	**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 **Control:** Placebo Placebo was matched with respect to color and flavor **Comparator:** NA **Follow-up:** 2 months	CGI-I (Clinical Global Impressions Scale), parent There was no significant difference between groups (p=0.076). ADHD Rating Scale-IV 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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		adverse experience with zolpidem, use of pharmacologic sleep aids that the patient was unwilling to discontinue, or current use of rifampicin and/or sertraline also disqualified patients **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:** Other info on race or ethnicity: N/A		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.
New pharmaceutical agent	Bostic, 2000[166] ID: N/A Crossover trial Unclear/Not reported N = 21 US Setting: Other	**Target:** Children with ADHD, exclusion criteria included any 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	**Intervention:** Pemoline for 4 weeks, morning and after school dosing as 18.75-mg and 37.5-mg tablets (3mg/kg/day) **Control:** Placebo Identical appearing and tasting 18.75-mg and 37.5-mg tablets morning and after school dosing **Comparator:** NA	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).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		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 Other info on race or ethnicity:	**Follow-up:** 2.5 months	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).
New pharmaceutical agent	Buitelaar, 1996[173] 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 CBCL and CTRS hyperactivity factors, deficits in attention performance on either a reaction-time task or a continuous performance task in the neuropsychological testing, no previous treatment with psychotropic medication, and a clinical indication for drug treatment; children were excluded for a diagnosis of tic disorder or pervasive developmental disorder, a family history of tic disorder, and	**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
		the usual contra-indications for treatment with j9-blockers such as cardiac diseases, in particular conduction abnormalities and bradycardia, 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:** Other info on race or ethnicity: N/A		
New pharmaceutical agent	Ceresoli-Borroni, 2021[182] Supernus Pharmaceuticals, 2011[1064] ID: NCT01364662 RCT Multicenter N = 121 US	**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	**Intervention:** Molidone SPN-810, extended-release, 36mg/54mg, ~2.5-week titration, 3-week maintenance,alongside existing monotherapy (stimulants/nonstimulants) and behavioral therapy **Control:** Placebo Placebo	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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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	**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 Other info on race or ethnicity: N/A : 6.0	**Comparator:** MedicationSPN-810, 12 mg/18 mg extended-release molindone (low dose) **Follow-up:** 1.5 months	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%.
New pharmaceutical agent	Conners, 1996[210] ID: 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 Other info on race or ethnicity:	**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[223] Roozbeh Psychiatric Hospital, 2018[983] ID: IRCT20090117001556N108 RCT Unclear/Not reported N = 53 Iran Setting: N/A	**Target:** Patients with the diagnosis of ADHD based on DSM-5 along-side the Kiddie Schedule forAffective Disorders and Schizophrenia (KSADS) 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 (Ritalin); 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 %	**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
		Age mean: 8.57(1.81) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A		
New pharmaceutical agent	Farmer, 2017[267] Michael Aman, 2008[918] ID: NCT00796302 RCT Unclear/Not reported N = 165 US Setting: N/A	**Target:** Children 6 to 12 years old 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 CGI-S score equal or greater than 4; excluded were IQ was less than 71, any condition that was a contraindication for medication, family history of type-2 diabetes, using any psychotropic medications that would cause risk to the participant if stopped, 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)	**Intervention:** Risperidone plus psychostimulant (usually osmotic release oral system [OROS] methylphenidate) for 6 weeks, titrated to an optimal dose **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
		Minimum age: 6 **Maximum age:** 12 **Ethnicity:** % Black/African American : 41 % White : 61 Other info on race or ethnicity: Other : Non-Hispanic 93%		
New pharmaceutical agent	Findling, 2019[272] Sunovion, 2015[1061]; Sunovion, 2015[1060] ID: NCT02457819, NCT02428088 RCT Multicenter N = 342 US Setting: N/A	**Target:** Children age 6-12 meeting the DMS-V criteria, ADHD Rating Scale version IV-Home Version score of >28, Clinical Global Impression-Severity Scale score of >4. Excluded if they were diagnosed with 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 %	**Intervention:** Dasotraline 4 mg administered once-daily in the morning for 6 weeks total **Control:** Placebo Placebo for 6 weeks **Comparator:** MedicationDasotraline 2 mg administered once-daily in the morning for 6 weeks **Follow-up:** 1.5 months	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 group (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 three most frequent AEs in the dasotraline 2 and 4 mg/day groups (vs. placebo) were insomnia (15.3% [NNH = 10] and 21.7% [NNH = 6] vs. 4.3%), decreased appetite (12.6% [NNH = 14] and 21.7% [NNH = 7] vs. 5.2%), and weight decreased (5.4% [NNH = 19] and 8.7%

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Age mean: 2mg/day 8.9 (1.7), 4mg/day 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 Other info on race or ethnicity:		[NNH = 12] vs. 0%).
New pharmaceutical agent	Greenhill, 2006[302] ID: NA RCT Multicenter N = 200 US Setting: Mixed	**Target:** Patients age 6-17 years old with clinical diagnosis of ADHD, a CGI-S 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-RS-IV (School Version) score of at least 1.5 SD above the norm for the patient's age and gender. Exclusion: history or current diagnosis of pervasive developmental disorder, schizophrenia, or other psychotic disorders (DSM-IV axis I), 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	**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
		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 info on race or ethnicity: Other : Other: 20/198 (10.1%)		
New pharmaceuti	Kahbazi, 2009[348] ID: NA RCT Single center	**Target:** Children newly diagnosed with ADHD; children were excluded if they had a history or current diagnosis of pervasive developmental disorders, schizophrenia, or other psychiatric	**Intervention:** Modafinil, 200–300 mg/day (once daily) depending on weight for 6 weeks **Control:** Placebo Placebo	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)

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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 = 46 Iran Setting: Specialty care	disorders or if they had 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:** Other info on race or ethnicity: N/A	**Comparator:** NA **Follow-up:** 1.5 months	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[371] ID: NA RCT Multicenter N = 173 US Setting: Mixed	**Target:** Patients age 7-17 years old with diagnosis of ADHD according to DSM-IV and comorbid anxiety or depression symptoms (Children's Depression Rating Scale-Revised (CDRS-R) total score of >36 or Multidimensional Anxiety Scale for Children (MASC) total score at least 1 SD above age and gender norms). Exclusion: any history of psychosis, bipolar disorder, or serious medical illness, history of substance abuse	**Intervention:** Fluoxetine 20 mg administered once daily for 8 weeks plus atomoxetine 1.8mg/kg/day evenly divided into two doses for the final 5 weeks of treatment **Control:** Other Atomoxetine alone plus placebo, after 3 weeks of treatment, atomoxetine was added to each patient's regimen for the final 5 weeks of treatment, initiated at 0.5 mg/kg/day and increased at weekly	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 A/F and A/P groups were not statistically significant (p 0.121) ADHD-RS-IV Total score mean (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**
		Other: **ADHD presentation:** inattentive : 23.2,hyperactive : 2.9,combined : 73.8 **Diagnosis:** Confirmation by specialist 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 info on race or ethnicity: Other : Other: 16.2%	intervals to 0.8 mg/kg/day and then to 1.2 mg/kg/day; maximu **Comparator:** NA **Follow-up:** 2 months	change from baseline: A/F (n = 113) –24.0 (13.6), A/P (n=44) –20.5 (12.9), p =0.101. Children's Depression Inventory (CDI) score mean (SD) change from baseline: A/F (n = 81) –8.8 (8.1), A/P (n=33) –5.4 (10.0), p =0.043. CDRS-R (Children's Depression Rating Scale-Revised) total score mean (SD) change from baseline: A/F (n = 113) –20.4 (13.6), A/P (n=44) –17.6 (11.8), p =0.342. CDRS-R (Children's Depression Rating Scale-Revised) total T-score mean (SD) change from baseline: A/F (n = 113) –22.9 (15.2), A/P (n=44) –19.8 (13.3), p =0.342. Multidimensional Anxiety Scale for Children (MASC) score mean (SD) change from baseline: A/F (n = 109) –13.4 (16.0), A/P (n=42) –11.3 (19.0) p =0.489. Multidimensional Anxiety Scale for Children (MASC) total T-score mean (SD) change from baseline: A/F (n = 109) –8.7 (10.3), A/P (n=42) –7.5 (12.9) p =0.527. 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).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 proportion of patients who discontinued because of an adverse 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 [11.2], A/P 6.5 [15.5]; p = .008); Mean blood pressure was also increased more in the combined treatment group (mean [SD] diastolic change in mm Hg: A/F 5.2 [9.4], A/P 0.3 [9.1], p = .008; mean [SD] systolic change in mm Hg: A/F 3.1 [8.9], A/P –0.14 [9.3]; p = .070)
New pharmaceutical agent	Lin, 2014[391] Eli Lilly and Company, 2009[733] ID: NCT00922636 RCT Multicenter N = 340 Multiple countries Setting: N/A	**Target:** Female and male patients greater than or equal to 6 years and <17 years and 9 months of age at the time of informed consent **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:**	**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)

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		% White : 72.6% Other info on race or ethnicity:		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 number of patients who reported at least one treatment-emergent adverse event (TEAE) ($p >0.05$).
New pharmaceutical agent	Mohammadi, 2010[427] Tehran University, 2010[1078] ID: NCT01099059 RCT Single center N = 40 Iran Setting: Mixed	**Target:** Participants age 6-14 with a diagnosis of ADHD based on DSM-IV criteria, have ADHD-RS-IV School version score of at least 1.5 SD above the norm for patient's gender and age. Exclusion: 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	**Intervention:** Amantadine for 6 weeks, dose of 100–150 mg/day depending on weight, 50 mg twice per day for <30 kg and 50 mg three times per day for >30 kg **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 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
		Female: 30 % **Age mean:** Amatadine 9.60 (1.98), methylphenidate 9.25 (1.80) **Minimum age:** 6 **Maximum age:** 14 **Ethnicity:** Other info on race or ethnicity: N/A		
New pharmaceutical agent	Saito, 2020[495] Taisho Pharmaceutical, 2016[1077] ID: JapicCTI-163244 RCT Multicenter N = 216 Japan Setting: N/A	**Target:** Ages 6-17 years old with a diagnosis of ADHD according the DSM-5, a total score equal to or less than 23 on ADHD RS-IV and a score equal to or less than 3 on CGI-ADHD-S. Patients were excluded based on a history of schizophrenia, other psychiatric disorders, intellectual disabilities, or reactive attachment disorder **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	**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
		Maximum age: 16 **Ethnicity:** Other info on race or ethnicity: N/A		
New pharmaceutical agent	Salardini, 2016[496] ID: NA RCT Single center N = 54 Iran Setting: Specialty care	**Target:** ADHD patients with blood pressure, pulse rate, and liver function tests were 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 Other info on race or ethnicity:	**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 **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.
New pharmaceutical	Sangal, 2014[501] Sunovion, 2009[1058]; Sunovion, 2009[1059] ID: NCT00856973, NCT00857220 RCT	**Target:** Children and adolescents with ADHD and insomnia; exclused another primary sleep disorder, other major psychiatric disorders, alcohol or substance abuse, and nicotine use	**Intervention:** Eszopiclone high dose (2 mg for children, 3 mg for ado-lescents) for 12 weeks, participants continued on whatever stimulant medication they were on prior to trial enrollment	CGI, parent The intervention group improved significantly over the control group (p=0.009), but the comparator did not (p=0.238).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 = 486 US Setting: Specialty care	**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 Other info on race or ethnicity:	**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	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	Swanson, 2006[561] ID: N/A RCT Multicenter N = 190 US Setting: Specialty care	**Target:** Clinical Global Impressions-Severity of Illness scale (CGI-S) rating of 4 or higher (“moderately ill” or worse), total and/or subscale scores on the Attention-Deficit/Hyperactivity Disorder Rating Scale-IV (ADHD-RS-IV) School Version22 at least 1.5 standard deviations above norms for the patient’s age and gender, and intelligence quotient of at least 80 as estimated by the	**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 ($p \leq .009$), including the final visit of the double-blind phase ($p < .0001$). Decreased appetite The rate was 14% in the intervention vs 2% 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**
		Wechsler Intelligence Scale for Children-Third Edition, and a score of at least 80 on the Wechsler Individual Achievement Test, Second Edition, Abbreviated. Patients were eligible if they were attending a full-time school (i.e., they were not eligible if receiving homeschooling) and if a teacher and parent were willing to participate **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:** Other info on race or ethnicity:		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	Wilens,2011[112] ID: NCT00640419 RCT Multicenter N = 121	**Target:** 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 (K-SADS-PL),15 and a rating of 4 or higher on the	**Intervention:** ABT-089 (neuronal nicotinic receptor partial agonist) 1.4 mg/kg taken daily for 6 weeks **Control:** Placebo Placebo	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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
	US Setting: N/A	Clinical Global Impression-ADHD-Severity Scale (CGI-ADHD-S); no history of current or past diagnosis of bipolar I, II, or NOS (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), whichever was longer, prior to the Day 1. **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 %	**Comparator:** MedicationABT-089 (neuronal nicotinic receptor partial agonist) 0.7 mg/kg taken daily for 6 weeks **Follow-up:** 1.5 months	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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Age mean: 8.5 **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** Other info on race or ethnicity: Other : % race is broken down by med dosage		
New pharmaceutical agent	Willens,2011[609] ID: NCT00528697 RCT Multicenter N = 278 US Setting: N/A	**Target:** 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 (K-SADS-PL), and a rating of 4 or higher on the Clinical Global Impression-ADHD-Severity Scale (CGI-ADHD-S); 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), whichever was longer, prior to the Day; atomoxetine within 3 months	**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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		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:** Other info on race or ethnicity:		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
New pharmaceutical agent	Zarinara, 2010[624] ID: N/A RCT Single center N = 38 Iran Setting: Other	**Target:** Children with combined subtype of ADHD and were newly diagnosed; children were excluded if they had a history or current diagnosis of pervasive developmental disorders, schizophrenia, or other psychiatric disorders or any current psychiatric comorbidity that required pharmacotherapy; any evidence of suicide risk and mental retardation	**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	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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		(IQ < 70), a clinically significant chronic medical condition, including organic brain disorder, seizures, or current abuse or dependence on drugs 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:** Other info on race or ethnicity: N/A	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	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 that were observed more frequently in the methylphenidate group.
New pharmaceutical agent	Zavadenko, 2019[625] NA ID: NA RCT Multicenter N = 100 Russia Setting: Mixed	**Target:** Children 6-12 years old with ADHD diagnosis based on ICD-10 criteria, presence of hyperdynamic (hyperkinetic) syndrome with attention deficit; severity of ADHD on the CGI-S 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	**Intervention:** Pantogam (Hopantenic acid) 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	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)

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		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:** Pantogan 8.7 (2.1). placebo 8.24 (1.63) **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A	study drug, taken in two split doses after meals, for 4 months **Comparator:** NA **Follow-up:** 4 months	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 significant between group differences at the end of the trial.
Nutrition, supplements	Abbasi, 2011[111] ID: N/A RCT Single center N = 40 Iran Setting: Other	**Target:** Children with combined subtype of ADHD and newly diagnosed (drug naive); children were excluded if they had a history or current diagnosis of pervasive developmental disorders, schizophrenia or other psychiatric disorders, any current psychiatric comorbidity that required pharmacotherapy; or any evidence of suicide risk and mental retardation (I.Q<70). In addition, patients were excluded if they had a clinically significant chronic	**Intervention:** Acetyl-L-Carnitine doses ranging from 500 to 1,500 mg/day depending on the weight of 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	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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		medical condition, including organic brain disorder, seizures or current abuse or dependence on drugs in the last 6 months. Additional exclusion criteria were 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:** Other info on race or ethnicity: N/A	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	that were observed more frequently in the methylphenidate plus placebo group.
Nutrition, supplements	Akhondzadeh, 2004[123] ID: RCT Single center N = 44 Iran Setting: Specialty care	**Target:** Children aged 5-11, 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	**Intervention:** Zinc sulfate 55 mg/day (15mg elemental zinc) plus methylphenidate 1 mg/kg/day twice daily **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).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		Diagnosed by psychiatrist **Comorbidity:** N/A **Female:** 40.9 % **Age mean:** 7.88 (1.67) **Minimum age:** 5 **Maximum age:** 11 **Ethnicity:** Other info on race or ethnicity: Other : Persian: 100%		
Nutrition, supplements	Baziar, 2019[143] Tehran University of Medical Sciences, 2017[1079] 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 for patient's age and gender. 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, including warfarin, aspirin, other antiplatelet agents, herbal medicines, and patients who were going to	**Intervention:** Saffron 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) at a dose of 0.3–1 mg/(kg*d), titrated up during the trial according to the following schedule: 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 **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
		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:** Other info on race or ethnicity: N/A		
Nutrition, supplements	Behdani, 2013[145] ID: RCT Single center N = 75 Iran	**Target:** Children and adolescents with ADHD. Those with co-morbid psyc diagnoses or serious medical conditions were excluded **Other:** Teachers and parents reported outcomes	**Intervention:** Methylphenidate plus Omega 3; final dose of 1mg/kg (maximum dose 60mg/day), in 2 or 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	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**
	Setting: Specialty care	**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 info on race or ethnicity: Other : 100% Persian	**Control:** Placebo Methylphenidate plus placebo; final dose of 1mg/kg (maximum dose 60mg/day), in 2 or 3 divided doses plus placebo **Comparator:** NA **Follow-up:** 2 months	
Nutrition, supplements	Bilici, 2004[157] 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	**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
		Maximum age: 14 **Ethnicity:** Other info on race or ethnicity: Other : Turkish		
Nutrition, supplements	Chang, 2019[186] Hospital, China Medical University, National Science Council, 2016[697] 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. Those with comorbid psychiatric disorders, such as autism spectrum disorder, anxiety disorder, and conduct disorder were excluded **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 Other info on race or ethnicity:	**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[214] ID: N/A RCT Multicenter N = 162 France Setting: Specialty care	**Target:** Children and adolescents ages 6-15 with at least hyperactivity-impulsivity symptoms for 6 months or more and/or at least one of six inattention symptoms for six months or more, all 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. Symptoms cannot be a part of another psychiatric disorder **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:** Other info on race or ethnicity: N/A	**Intervention:** Omega 3 dietary supplement, participants aged 6–8 years given eicosatetraenoic acid 336 mg, participants aged 9–11 years eicosatetraenoic acid 504 mg, participants aged 12–15 years eicosatetraenoic acid 672 mg, capsules also contained 100 µg vitamin A, 1.25 µg vitamin D, and 3.5 mg vitamin E, treatment duration was 3 months, during which other hyperactivity treatments and other omega-3 supplements or psychotropic drugs were not allowed **Control:** Placebo The placebo capsules were indistinguishable from active capsules and were composed of 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 **Comparator:** NA **Follow-up:** 28 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).
Nutrition, supplemen	Crippa, 2019[216] Crippa, 2018[707]; IRCCS Eugenio Medea, 2012[820] ID: NCT01796262	**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	**Intervention:** Omega 3 supplement of 500 mg algal docosahexaenoic acid (DHA) per day for 6 months **Control:** Placebo	Behavior in Child Health Questionnaire Only the intervention group improved. CGI-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**
	RCT Single center N = 50 Italy Setting: Specialty care	**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 Other info on race or ethnicity:	Placebo treatment consisted of two pearls per day containing 500 mg wheat germ oil. Placebo pill was stabilized with low concentration of Vitamin E **Comparator:** NA **Follow-up:** 6 months	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.
Nutrition, supplements	Fallah, 2018[265] Shahid Sadoughi University of Medical Sciences, 2016[1004] 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:**	**Intervention:** Omega-3 (1000 mg of omega 3 fish oil, 180 mg of eicosapentaenoic acid and 120 mg docosahexaenoic 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
		% White : 100 Other info on race or ethnicity:		
Nutrition, supplements	Ghajar, 2018[295] ID: IRCT201601031556N84 RCT Single center N = 56 Iran Setting: Specialty care	**Target:** Newly diagnosed patients who met criteria of DSM-V, needed to have no previously diagnosed psychiatric comorbidity (except for ODD), or developmental or physiological disorders (such as high blood pressure or seizures), this includes having an IQ over 70, and 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 info on race or 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 during the trial according to the following schedule: 10mg/d (two divided doses) for the first week followed by 20mg/d (two divided doses) from the second week till the rest of the trial. Patients who weig **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 abdominal pain (24%) and headache (24%) in the placebo group. The frequency of side effects did not differ significantly 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
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 info on race or ethnicity: Other : 100% Persian	**Intervention:** Methylphenidate (mean dose 12.7(5.4) mg/day) plus dietary recommendations. 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 three regular meals per day. **Control:** Other Methylphenidate alone, mean dose 11.9(4.6) mg/day. **Comparator:** **Follow-up:** 1 month	ADHD Checklist, Hyperactivity / Impulsivity Score No significant difference between groups in the mean change of hyperactivity/impulsivity and inattentiveness scores.
Nutrition, supplements	Gustafsson, 2010[308] Hela Pharma AB, 2004[800] 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 neuro or psyc comorbidity. **Other:** Parents and teachers provided outcomes **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV	**Intervention:** Omega 3, one eicosapentaenoic acid (EPA) capsule PlusEPA contained 500 mg EPA + 2.7 mg DHA and 10 mg Vitamin E mixed tocopheroles, 1 capsule per day for 15 weeks **Control:** Placebo Placebo was a mixture of rape seed oil and medium-chain triglycerides contained in a capsule identical to the one used for PlusEPA containing	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
		Comorbidity: N/A **Female:** % not provided **Age mean:** NA **Minimum age:** 7 **Maximum age:** 12 **Ethnicity:** % White : 100 Other info on race or ethnicity:	<10% of the PlusEPA content of omega-3 LCPUFA **Comparator:** NA **Follow-up:** 3.75 months	
Nutrition, supplements	Hariri, 2012[314] ID: N/A RCT Single center N = 120 Iran Setting: Other	**Target:** ADHD patients on Ritalin with Conners' Abbreviated Questionnaires (ASQ-P) scores for hyperactivity greater than 14. Exclusion criteria were 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	**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 Ritalin (any dose) plus placebo (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
		Maximum age: 12 **Ethnicity:** Other info on race or ethnicity:		
Nutrition, supplements	Hemamy, 2021[320] Hemamy, 2020[801] ID: N/A 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 Other info on race or ethnicity:	**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 Participants in the control group received a placebo, similar in appearance, color, and taste to the two 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	Strength and difficulties questionnaire (SDQ), total difficulties The intervention group showed a significant reduction in total difficulties compared to control group (p = 0.001). 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[323] ID: RCT Single center N = 36 Japan Setting: Community	**Target:** Children aged 4-14 years old **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:** Other info on race or ethnicity: N/A	**Intervention:** Phosphatidylserine (soy-derived) 100mg chewable tablet, 2 chews per day **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.).
Nutrition, supplements	Johnson, 2009[343] ID: N/A RCT Multicenter N = 75 Sweden Setting: Specialty care	**Target:** Children and adolescents with ADHD, exclusion criteria were 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	**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 Identical capsules containing olive oil **Comparator:** NA	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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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 : 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:** Other info on race or ethnicity: N/A	**Follow-up:** 3 months	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 patient (placebo) due to markedly increased irritability.
Nutrition, supplements	Johnstone, 2022[344] Johnstone, 2019[840]; Oregon Health Science University, 2018[937] 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)	**Intervention:** Capsules containing a blend of ingredients comprising all vitamins and known essential minerals, plus 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, 8 weeks of treatment **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	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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Minimum age: 6 **Maximum age:** 12 **Ethnicity:** % Black/African American : 3 % Asian : 3 % White : 88 Other info on race or ethnicity:	**Comparator:** NA **Follow-up:** 2 months	Rate was 32% in the intervention and 45% in the placebo group. No between-group differences for treatment-emergent adverse events were detected.
Nutrition, supplements	Katz, 2010[353] Etz-HaChayim Clinic (Israel), 2007[739] ID: ISRCTN10628149 RCT Single center N = 120 Israel Setting: Specialty care	**Target:** Treatment naïve children with ADHD. Those with medical conditions, psychiatric comorbid conditions, or ongoing use of any medications excluded **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:** Other info on race or ethnicity: N/A	**Intervention:** Compound herbal preparation, primary active herbal ingredients include Paeoniae Alba, Withania Somnifera , Centella Asiatica, Spirulina Platensis, Bacopa Monieri, and Mellissa Officinalis, 3 ml of the compound herbal preparation taken 3 times daily before meals diluted in 50 to 60 ml of water **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[356] Khoram-Abad University of Medical Sciences, 2020[851] 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:** Other info on race or 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), treatment over 8 week period **Control:** Other Methylphenidate alone: In week one, initial dose of 10mg/d (5mg for morning and midday equally); week 2 it was 20 mg/d (10 mg for morning and midday equally), and 20 mg/d (for <30 kg and 30 mg/d for > 30 kg, 10 mg for morning, midday, and evening. **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.
Nutrition, supplements	Khoshbakht, 2021[358] Nutrition and Food security research center, 2018[932] ID: IRCT20130223012571N6 RCT Single center N = 86	**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 %	**Intervention:** Dietary Approaches to Stop Hypertension (DASH) diet for 3 months (12 weeks), diet contains 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 **Control:** Attention-matched control	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**
	Iran Setting: Specialty care	**Age mean:** N/A **Minimum age:** 6 **Maximum age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A	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	
Nutrition, supplements	Manor, 2012[401] Manor, 2012[874]; Enzymotec, 2007[737] ID: NCT00418184 RCT Single center N = 200 Israel Setting: Specialty care	**Target:** 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)	**Intervention:** Omega 3, 4 capsules (2 capsules twice a day for 15-weeks) of Phosphatidylserine-Omega3 daily; daily dosage provided 300 mg of Phosphatidylserine, 120 mg of Eicosapentaenoic acid + Docosahexaenoic acid (Eicosapentaenoic acid/Docosahexaenoic acid ratio of 2:1) **Control:** Placebo Four capsules (2 capsules twice a day for 15-weeks) of cellulose as placebo. **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**
		Minimum age: 6 **Maximum age:** 13 **Ethnicity:** Other info on race or ethnicity: N/A		
Nutrition, supplements	Mohammadi, 2012[428] ID: N/A RCT Single center N = 50 Iran Setting: N/A	**Target:** Children aged 7-12 years diagnosed with ADHD (combined form) by a child and adolescent psychologist and did not use any confounding drugs or supplements were recruited into the initial stage of this study. Children with history of major prenatal complications such as prematurity, low birth weight (reported by parents), any past or present psychosis, comorbid Tourette syndrome, celiac, phenylketonuria, autism, or other persistent developmental disorders were excluded. Furthermore, narcotics use was among our exclusion criteria **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **Comorbidity:** N/A **Female:** 28 % **Age mean:**	**Intervention:** Melatonin (3 or 6mg) combined with methylphenidate (Ritalin) (1mg/kg) for 8 weeks **Control:** Placebo Placebo combined with 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
		Intervention 9.57(1.65), control 8.83(1.82) **Minimum age:** 7 **Maximum age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A		
Nutrition, supplements	Mohammadzadeh, 2019[429] Kurdistan University of Medical Sciences, 2017[858] ID: IRCT2016060128182N2 RCT Single center N = 66 Iran Setting: Specialty care	**Target:** Children with ADHD. Those who Children who had used omega-3 in at least the last 6 months were exclude, as were those with any physical illness or psyc 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:**	**Intervention:** Omega-3 eicosapentaenoic acid (EPA) capsules (180 mg) and docosahexaenoic acid (120 mg) 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
		Other info on race or ethnicity: N/A		
Nutrition, supplements	Mostajeran, 2020[431] Mostajeran, 2018[1151] ID: IRCT20180303038930N1 RCT Single center N = 64 Iran Setting: Specialty care	**Target:** Children with ADHD on medication. Exclusion criteria were having any 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:** Other info on race or ethnicity: N/A	**Intervention:** Ma'aljobon powder for two months, 25 g in 100 cc water, once daily after breakfast, participants continued their previous standard conventional ADHD medications **Control:** TAU Children continued their previous standard conventional ADHD medications. **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	Pelsser, 2011[460] Wageningen University (The Netherlands), 2008[1113] ID: ISRCTN76063113 Crossover trial Unclear/Not reported N = 100 Netherlands Setting: Mixed	**Target:** Children with ADHD. Exclusion criteria were children 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:** Other info on race or ethnicity:	**Intervention:** Individually designed restricted elimination diet, consisting of the few- foods diet (ie, rice, meat, vegetables, pears, and water) complemented with specific foods such as potatoes, fruits, and wheat for five weeks **Control:** Attention-matched control Received healthy food advice according to the guidelines of the Dutch Nutrition Centre. 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.
Nutrition, supplements	Pongpitakdamrong, 2021[466] ID: N/A 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	**Intervention:** Iron in the form of ferrous fumarate, 200mg capsules of ferrous fumarate, participants who weighed less than or equal to 30kg received 1 capsule of ferrous fumarate per day for 12 weeks, participants who weighed > 30kg received 2 capsules per day (2–4 mg of elemental iron/kg/d) for 12	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
		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 Other info on race or ethnicity:	weeks, methylphenidate continued as already prescribed **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	
Nutrition, supplements	Rafeiy-Torghabeh, 2021[477] Roozbeh Psychiatric Hospital, 2018[982] 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 (ODD) **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:**	**Intervention:** Resveratrol 250mg two times a day in addition to methylphenidate 20mg/day for 8 weeks, participants weighing more than 30kg received methylphenidate 30mg/day **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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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 info on race or ethnicity: N/A		
Nutrition, supplements	Rucklidge, 2018[493] ID: ACTRN12613000896774 RCT Single center N = 93 New Zealand Setting: Specialty care	**Target:** Medication-free children with ADHD aged 7–12 years **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:** 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).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 info on race or ethnicity:		Across a large number of assessed outcomes, micronutrients had minimal side effects.
Nutrition, supplements	Salehi, 2010[497] Roozbeh Psychiatric Hospital, 2009[981] ID: IRCT138711151556N6 RCT Single center N = 50 Iran Setting: Specialty care	**Target:** Children with ADHD; comorbid psychiatric diagnosis that would contraindicate GXR treatment or confound efficacy or safety assessments, were excluded **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 info on race or ethnicity: Other : Persian	**Intervention:** Gynkgo 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 **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	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. 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[498] 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 info on race or ethnicity: Other : Persian	**Intervention:** Omega 3, eicosapentaenoic fatty acid (100 mg for children <25 kg, 200 mg for 26–35 kg, 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 Methylphenidate plus placebo (whitish color capsule containing sugar, as the same shape 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).
Nutrition, supplements	Tan, 2016[566] ID: NCT01855984 RCT Multicenter N = 146 Other	**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. Children who were unable to	**Intervention:** Tocotrienol-rich fractions (TRF), a potent antioxidant from the natural Vitamin E family. Two softgel capsules containing 100 mg TRF per day for 6 months. **Control:** Placebo	Vanderbilt ADHD Parent Rating Scale, Total No significant group differences in parent or teacher rating at 6 months. Number of adverse events No statistical difference in the number of adverse events per 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
	Setting: Specialty care	swallow the capsule were also excluded. **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 Other info on race or ethnicity:	Two placebo capsules per day for 6 months. **Comparator:** NA **Follow-up:** 6 months	
Nutrition, supplements	Trebaticka, 2006[573] Chovanova, 2006[698] 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; patients with 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	**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**
		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:** Other info on race or ethnicity: N/A : Slovakian		
Nutrition, supplements	Tzang, 2016[577] Mackay Memorial Hospital, 2012[871] ID: NCT01725737 RCT Single center N = 116 Taiwan Setting: Primary Care	**Target:** Children aged between 6–12 years, 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%	**Intervention:** Six weeks of 0.3 g of sarcosine (dietary supplement, glycine transporter-1 inhibitor), 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 **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**
		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:** Other info on race or ethnicity: N/A		
Nutrition, supplements	Van der Heijden, 2007[583] ID: RCT Multicenter N = 107 Netherlands Setting: Specialty care	**Target:** Children aged 6 to 12 years old 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	**Intervention:** Fast-release melatonin, 3mg if body weight < 40mg, 6mg if body weight > 40kg **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**
		Comorbidity: Sleep : chronic sleep-onset insomnia **Female:** 25.7 % **Age mean:** 9.1 (2.3) for treatment group; 9.3 (1.8) for placebo group **Minimum age:** **Maximum age:** **Ethnicity:** Other info on race or ethnicity: N/A		
Nutrition, supplements	Weber, 2008[596] National Center for Complementary and Integrative Health (NCCIH), 2004[916] 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 RS-IV; those with psychiatric co-morbidities were excluded **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	**Intervention:** 300 mg of H perforatum standardized to 0.3% hypericin (St. John's wort) 3 times daily 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
		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 Other info on race or ethnicity:		
Parent education	Abikoff, 2015[117] NYU Langone Health, 2011[934] ID: NCT01320098 RCT Single center N = 164 US Setting: Specialty care	**Target:** Preschool, daycare or nursery school students diagnosed with ADHD. Current medication for ADHD excluded. **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	**Intervention:** New Forest Parenting Package, 8 weekly 1-to-1.5-hour sessions, home-based intervention which fosters constructive parenting to target ADHD-related dysfunctions in attention and impulse control **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
		% Black/African American : 16.4 % Asian : 8.8 % White : 69.2 Other info on race or ethnicity:		
Parent education	Chacko, 2009[184] ID: NA RCT Single center N = 120 US Setting: Other	**Target:** Children aged 5 through 12, 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, 9-week program held for 2.5 hours each week **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**
		Other info on race or ethnicity:		
Parent education	Churchill, 2018[204] ID: N/A RCT Unclear/Not reported N = 174 US Setting: N/A	**Target:** Child 4–18 years old 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 Participants with ADHD diagnosis were recruited from Children and Families Program of the Mental Health and Addiction Services Division of Multnomah County Human Services, 10 neighborhood primary care health clinics with Multnomah County Health Department **Comorbidity:** N/A **Female:** 33.9 % **Age mean:**	**Intervention:** In-home nurse visits with families for one year, with variable frequency based on participant family needs, participant families given a resource guide and received a newsletter every 6 months with up-to-date information about ADHD **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) There was no significant difference between groups (p=0.374).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 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 Other info on race or ethnicity:		
Parent education	Dong, 2022[232] ID: RCT Multicenter N = 850 China Setting: Other	**Target:** Kindergarteners with ADHD, with sibling in Grade 7 or 8. **Other:** Parents or siblings participated, but did not provide outcome data. **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 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 **Control:** Attention-matched control Reading same books with parent 25 minutes twice per week for 12 weeks, but without dialogic reading **Comparator:** OtherDialogic 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	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 DR groups over the control reading group. Sibling DR was significantly superior to parent DR regarding expressive vocabulary, character reading , morphological awareness, phono-logical awareness, and reading interest ($p < .001$ for all) but inferior regarding improvement in listening comprehension ($p < .001$).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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 info on race or ethnicity:	and answer communication while reading picture books together **Follow-up:** 12 weeks	
Parent education	Dose, 2017[233] University of Cologne, Shire, 2012[1097] ID: NCT01660425 RCT Single center N = 103 Germany Setting: Other	**Target:** Children aged 6 to 12 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:** Other info on race or ethnicity: N/A	**Intervention:** Year long telephone-assisted self-help program for parents, reading 8 self-help booklets, 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 **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[260] ID: NA Clinical trial Single center N = 120 Turkey Setting: Specialty care	**Target:** Children diagnosed with ADHD and oppositional defiance disorder or conduct disorder by psychiatrists, other comorbid disorders (i.e., anxiety disorders, mental retardation, or bipolar disorder) not permitted **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:** Other info on race or ethnicity: N/A	**Intervention:** Parent-training program plus methylphenidate, optimal methylphenidate dose taken daily for 12 months, 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 **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
Parent education	Ferrin, 2014[268] ID: N/A RCT Single center N = 81 Spain Setting: Other	**Target:** 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	**Intervention:** Psychoeducation program composed of 5 successive groups of 8–10 families who received 12-week 90 min weekly sessions **Control:** NA **Comparator:** Parent trainingParent counselling and support intervention,	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**
		Disorders and Schizophrenia for school age children (KSADS-PL); either sex; consenting and legal capable parents' age greater than or equal to 18 years; 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:** Other info on race or ethnicity: N/A	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	
Parent education	Ferrin, 2020[269] ID: N/A RCT Single center N = 69 UK Setting: Other	**Target:** Participants age 3 to 19 with diagnosis of ADHD, parents' age greater than or equal to 18 years, and stabilizing medication for 1 month prior to baseline assessment. Participant should not have severe learning disabilities (IQ < 70), autistic spectrum disorder as primary diagnosis, any clinically significant or unstable	**Intervention:** Psychoeducation with 5 successive groups of 7-10 families who received six sessions of 2 hr at weekly intervals, a handout was delivered and parents were assigned some short additional homework to prepare for the next session **Control:** TAU	CGI-I (Clinical Global Impression Scale global improvement) change, clinician rating Intervention showed a significant effect on the clinical global impression compared to control (p=.038) ADHD Index, Conners' Parent Rating Scale: Short Form (CPRS-R:S) Mean differences in scores showed statistically significant differences between 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
		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 of children with ADHD **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-IV **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 Other info on race or ethnicity:	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	two groups for the cognitive/inattention and the hyperactive/impulsive subdomains. Strengths and Difficulties Questionnaire, teacher rating There were no statistically significant effects for time or an interaction between time and treatment condition (p=0.67). There were no statistically significant differences in parental stress across groups (p=0.521).
Parent education	Geissler, 2020[290] Jans, 2015[827]; Hage, 2018[784]; Jaite, 2019[825]; Hautmann, 2018[794] ID: CCT-ISRCTN73911400 RCT	**Target:** Diagnosed with ADHD; not currently receiving psychopharmacotherapy; or their medication had been stable for at least 4 weeks prior to baseline assessment **Other:**	**Intervention:** 12 weeks weekly group psychotherapy plus methylphenidate, then 12-week individualized parent-child training program comprised a structured and modular behavioral psychotherapy program for children with methylphenidate medication and	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)

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 = 144 Germany Setting: Specialty care	**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:** Other info on race or ethnicity: N/A	group psychotherapy (1 appointment/4 week), then 6 months of maintenance of all previous interventions **Control:** Attention-matched control Control group mothers received seven 4-weekly sessions of individual non-specific counseling and participated in the two booster parent-child therapy sessions. **Comparator:** NA **Follow-up:** 12 months	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).
Parent education	Hornstra, 2021[328] ID: N/A RCT Multicenter N = 92 Netherlands Setting: Mixed	**Target:** Participants have a Diagnostic and Statistical Manual of Mental Disorders-5, have an IQ > 70, and do not use psychotropic medications. **Other:** Parents of ADHD children **ADHD presentation:** inattentive : 26,hyperactive : 11,hyperactive_other :	**Intervention:** Antecedent-based condition: parents were provided with information about executive functioning deficits in children with ADHD, parents practiced techniques through guided role-play or visualization and after that potential barriers to implementation of the plan were discussed, intervention	Daily Rated Problem Behaviors Compared to the control group, the intervention and comparator groups had significantly improved scores. SWAN (The Strengths and Weaknesses of ADHD symptoms and Normal behavior rating scale) Compared to the control group, the intervention and comparator groups had

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		hyperactive/impulsive,combined : 63 **Diagnosis:** Confirmation by specialist DSM-V **Comorbidity:** N/A **Female:** 30 % **Age mean:** N/A **Minimum age:** 4 **Maximum age:** 12 **Ethnicity:** % White : 97 Other info on race or ethnicity:	plan consisted of antecedent-based techniques only (i.e., defining rules, giving clear instructions, anticipating misbehaviors, and providing structure in time and space), two sessions of two hours each provided in two consecutive weeks **Control:** Wait list **Comparator:** Parent trainingConsequent-based parent education, parents learned how consequences can affect behavior, and how and which consequent-based techniques can be used to change behaviors (e.g., by ignoring unwanted behaviors and praising every attempt to show the appropriate **Follow-up:** 4 months	significantly improved scores for hyperactivity-impulsivity symptoms. For symptoms of inattention, only the intervention group had significantly improved scores compared to the con
Parent education	Lange, 2018[376] University of Aarhus, 2012[1093] ID: NCT01684644 RCT Multicenter N = 164 Denmark Setting: Specialty care	**Target:** Children aged 3-7; clinical ADHD diagnosis supported by the Development and Well-Being Assessment (DAWBA); Danish as a first language spoken at home; iq greater than or equal to 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	**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	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).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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 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:** Other info on race or ethnicity: N/A	games, guiding parents in use of behavioral strategies **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	The parent training program was superior to treatment as usual on parenting self-efficacy and family strain.
Parent education	Mehri, 2020[418] Department of Research and Technology, 2013[714] ID: IRCT2013042112990N1 RCT	**Target:** Diagnosed 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 - with at least one sleeping issue and children needed to have no physical or mental comorbidities	**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	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**
	Single center N = 56 Iran Setting: Specialty care	**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:** Other info on race or ethnicity: N/A	study; participants also received methylphenidate treatment **Control:** Other Methylphenidate treatment only **Comparator:** NA **Follow-up:** 2 months	
Parent education	Schorr-Sapir, 2021[508] ID: N/A RCT Unclear/Not reported N = 101 Israel Setting: Mixed	**Target:** Children aged 5-13 years with primary DSM-5 ADHD diagnosis and scores above 55 on the Conners' Scale for ADHD; con changes medication during the study; no psychotic symptoms and no concurrent psychotherapy **Other:** Parents of children with ADHD that are fluent and have no Hebrew no psychotic symptoms **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Children have primary DSM-5 ADHD diagnosis. **Comorbidity:** N/A **Female:** 21 %	**Intervention:** Nonviolent resistance parent training with clinical psychologist,12 sessions (one session involving the parents and members of the school staff was conducted in the child's school); two 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 **Control:** Wait list Waiting period is 12 weeks, given nothing during waiting period	Conners' Rating Scale - ADHD index, parent There was a reduction in ADHD core symptoms by the end of treatment, but these gains were not maintained at follow-up (p = 0.63).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		Age mean: 8.8 (1.77) **Minimum age:** 5 **Maximum age:** 13 **Ethnicity:** Other info on race or ethnicity:	**Comparator:** NA **Follow-up:** 4 months	
Parent education	Smit, 2021[533] Mikami, 2020[894] ID: NA RCT Multicenter N = 172 Canada Setting: Specialty care	**Target:** Children aged 6 to 11 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	**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
		Ethnicity: % Hispanic or Latino : 1.2 % Black/African American : 0.6 % Asian : 5.8 % White : 72.7 % Multiracial : 18.6 Other info on race or ethnicity:		
Parent education	Sonuga-Barke, 2001[539] ID: N/A RCT Single center N = 78 UK Setting: Community	**Target:** Children had to be born between January 1992 and September 1993, and the parents had to take the Parental Account of Childhood Symptoms examination to determine if the child needed a further clinical evaluation **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:** Other info on race or ethnicity: N/A	**Intervention:** Parent Training group received coaching in child management techniques, eight 1-hour weekly sessions **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[540] Sonuga-Barke, 2002[1050] ID: NA RCT Unclear/Not reported N = 89 UK Setting: Other	**Target:** Three year old 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:** % Not reported **Age mean:** 3 years old at time of enrollment **Minimum age:** 3 **Maximum age:** 3 **Ethnicity:** Other info on race or 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.
Parent education	Sonuga-Barke, 2018[541] ID: NA RCT Multicenter N = 307 UK Setting: Mixed	**Target:** Children were included if parent and/or caregiver aged 18 years or over; (iii) screened positive for ADHD symptoms (score≥ 20) on the Werry-Weiss-Peters Activity Rating Scale (WWP) [18] and; (iv) were given an ADHD research diagnosis of any sub-type based on the parent DISC-IV-ADHD Scale	**Intervention:** New Forest Parenting Programme parent training intervention delivered at home for 12 weeks of 1.5 hour sessions **Control:** TAU Standard patterns of preschool ADHD care available in the parents' region; in two regions, there was	SNAP-IV (Swanson Nolan and Pelham - IV - Parent) Small, non-significant, benefits of NFPP over TAU were seen for parent-rated SNAP-IV, ADHD combined symptoms [− 0.189 95% CI (− 0.380, 0.003), p = 0.053].

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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: 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:** 42.7 (6.75) **Minimum age:** 3 **Maximum age:** 5 **Ethnicity:** Other info on race or ethnicity: N/A	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	
Parent education	Tiwawatpakorn, 2021[572] 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	**Intervention:** Parental training + Routine Clinical care (PT+RCC): 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	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**
		Vanderbilt ADHD Diagnostic Parent Rating Scale (VADPRS) **Comorbidity:** N/A **Female:** 18 % **Age mean:** 8.3 (1.1) **Minimum age:** **Maximum age:** **Ethnicity:** Other info on race or ethnicity:	**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	
Physical exercise	Durgut, 2020[243] University, Bezmialem Vakif, University, Medipol, 2018[670] ID: NCT03469180 RCT Single center N = 30 Turkey Setting: Specialty care	**Target:** Treatment naive children with ADHD. Exclusions: 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	**Intervention:** Treadmill training plus whole body vibration training 3 days per week for 8 weeks, treadmill training for 45 minutes, 5 minutes rest, whole body vibration training for 15 minutes **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
		Female: 20 % **Age mean:** 8.13 (1.19) **Minimum age:** 7 **Maximum age:** 11 **Ethnicity:** Other info on race or ethnicity: N/A		
Physical exercise	Kadri, 2019[347] University of Genova, 2018[1098] ID: NCT03678844 RCT Single center N = 40 Tunesia Setting: Other	**Target:** Young Tunisian patients with ADHD. No consumption of any diet supplements or drugs; no history of chronic disease, bronchospasm or atopy; not being 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 mean age (14.5) and SD (3.5). Control group mean age (14.2) and SD (3.0) **Minimum age:** **Maximum age:** **Ethnicity:** Other info on race or ethnicity:	**Intervention:** Taekwondo exercises practiced for 50-minutes twice weekly for a year and a half, 10-minute general warm-up before each session and 10-minute recovery after each session **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. Total speed of intervention group mean (240.3). Total speed of intervention group SD (19.7). Total speed of control group mean (288.1). Total speed of control group 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[387] ID: RCT Single center N = 80 China Setting: Specialty care	**Target:** Children with ADHD without comorbid psyc disorders **Other:** None **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 Other info on race or ethnicity:	**Intervention:** 12-week combined aerobic-and neurocognitive-exercise, 3 sessions per week, 60-minutes per session **Control:** Wait list Wait list **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.
Physical exercise	Ludyga, 2022[397] ID: DRKS00020125 RCT Multicenter N = 63 Multiple countries Setting: Other	**Target:** Right-handed children with ADHD undergoing pharmacotherapy with methylphenidate or dexamphetamine for at least three months (to reduce inter-individual variations in symptom severity) **Other:** **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist DSM-5	**Intervention:** Two weekly 60-min sessions of judo training in a group setting supervised by one or two instructors, 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 (MABC-2) at 3 months. 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**
		Comorbidity: N/A **Female:** % N/A **Age mean:** 10.4 (1.2) **Minimum age:** 8 **Maximum age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A		
Provider	Elmaadawi, 2022[255] ID: 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:** % Not reported **Age mean:** 13.8 (3.6) **Minimum age:** 4 **Maximum age:** 18 **Ethnicity:** Other info on race or ethnicity: N/A	**Intervention:** Pharmacogenetic testing to enable genomically assisted prescribing (GAP). **Control:** TAU Treatment as usual, without genetic testing / guidance. **Comparator:** NA **Follow-up:** 6 months	Clinical Global Impression Scale-, Improvement Component (CGI-I) Significantly more improvement in intervention group.
Provider	Enns, 2017 [257] ID: NA Cohort study Single center	**Target:** Children and adolescents with ADHD who have attended at least 3 ADHD treatment sessions at the center **Other:**	**Intervention:** ADHD intervention service, participants and their families receive a range of services that can include assessment, treatment, and consultative services	Adjusted rate ratios (95% CI) for health and social services use outcomes for intervention (n =485) and control (n = 1884):

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 = 2369 Canada Setting: Community	**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:** Other info on race or ethnicity: N/A	(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, but can extend further 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	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).
Provider	Epstein, 2007[259] ID: NA Cluster RCT Multicenter N = 377 US Setting: Primary Care	**Target:** Children from participating practices who met DSM-iV criteria for ADHD, stimulant-naive, attending 1st - 5th grade **Other:** Pediatricians and associated healthcare professionals (27 men, 25 women) from 12 practices **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Conners Rating Scale	**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)	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**
		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 Other info on race or ethnicity:	**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	
Provider	Epstein, 2016[258] Childrens Hospital Medical Center, Cincinnati, 2010[692] ID: NCT01143701 Cluster RCT Multicenter N = 577 US Setting: Primary Care	**Target:** Patients in grades 1 through 5, presenting for ADHD evaluation, and were 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:**	**Intervention:** Four training sessions for providers, office flow modification, guided quality improvement, and an ADHD Internet portal to assist with treatment monitoring **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
		Maximum age: **Ethnicity:** Other info on race or ethnicity: Other : 36.7% were Non-white - unspecified		
Provider	Guevara, 2021[306] Childrens Hospital of Philadelphia, 2016[694] ID: NCT02716324 RCT Multicenter N = 303 US Setting: Primary Care	**Target:** Received care at a participating practice, had an ADHD diagnosis code (International Classification 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 info on race or ethnicity: 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 **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[365] University of Pittsburgh, 2008[1100] ID: NCT00600470 Cluster RCT Multicenter N = 411 US Setting: Primary Care	**Target:** Children aged 5 to 12 years diagnosed with ADHD based on the 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 Other info on race or ethnicity: 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 **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	ADHD symptoms measured using Vanderbilt ADHD Diagnostic Parent Rating Scale (VADPRS). Change from baseline to follow-up for intervention group compared to comparator group slope (−3.31), significant (p=.02).
Provider	Lavigne, 2011[378] Childrens Hospital of Chicago, 2005[649] ID: NCT00179894 Cluster RCT Multicenter N = 270 US	**Target:** Participants must have a diagnosis of ADHD according to DSM-IV criteria, IQ >= 70. Exclude: comorbidity of ASD, Tourette, other major health conditions; have taken ADHD medications in the past 2 months, or taking medications incompatible with stimulants (did not specify)	**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	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**
	Setting: Specialty care	**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 Other info on race or ethnicity:	office/practice for the first 3 patients per physician to ensure that staff understood program use **Control:** Other Pediatricians in treatment as usual group provided treatment per their usual procedure **Comparator:** NA **Follow-up:** 12 months	
Provider	Myers, 2015[440] Rockhill, 2016[976]; Myers, 2013[913]; Vander Stoep, 2017[1107]; Rockhill, 2020[975]; Seattle Childrens Hospital, 2009[999] ID: NCT00830700	**Target:** Children aged 5 through 12 with ADHD in rural underserved communities, 75% had at least one comorbidity (oppositional defiant behavior 40%) **Other:** Parents received behavior training; parents and teachers provided outcome data	**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	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	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
	RCT Multicenter N = 223 US Setting: Other	**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 Other info on race or ethnicity:	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	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[454] Boston Childrens Hospital, 2014[678] 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:** 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:	**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).
Psychological or behavioral	Abikoff, 2013[113] ID: N/A RCT Multicenter N = 158 US Setting: Other	**Target:** Children in 3rd through 5th grade with ADHD and organizational deficits **Other:** Parents received training and provided some outcome data **ADHD presentation:** inattentive : 55.7,hyperactive : 0,combined : 44.3	**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 **Control:** Wait list Wait list	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).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 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 Other info on race or ethnicity:	**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	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.
Psychological or behavioral	Boyer, 2016[168] Boyer, 2015[679] 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, (2) a confirmed ADHD diagnosis on the ADHD sections of the diagnostic interview schedule for children for DSM-IV parent version (DISCIV). Exclusions: (1) the adolescents themselves or their parents received alternative non-pharmacological treatment between pre- and post-assessment aimed at the participating adolescent. . When the adolescent or parents did receive alternative treatment, they could only	**Intervention:** Plan my life: an cognitive behavioral treatment consisting of eight adolescent sessions and two parental sessions of 45–60 min, one session per week **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).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		participate if they stopped this treatment until post-test had taken place, (2) autism spectrum disorder, (3) predominant addiction, depression with suicidal ideations, acute familial crisis or CD. Because these disorders bring forward risks for participants themselves or others, it was unethical to discourage additional treatment, (4) they received 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:** Other info on race or ethnicity: N/A		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	Coles, 2020[208] ID: NA RCT Single center N = 127 US Setting: School	**Target:** Unmedicated children aged 5 through 13 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 Other info on race or ethnicity:	**Intervention:** Behavioral consultation with school and home components (high or low intensity); school: 3 initial teacher visits to set up Daily Report Card with home-based rewards, bank of 3 additional consultation visits throughout year; home: 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 **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 ($p < .01$).
Psychological or behavioral	Fabiano, 2016[264] ID: NA RCT Unclear/Not reported N = 172 US Setting: Mixed	**Target:** Teens 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	**Intervention:** Supporting the Effective Entry to the Roadway (STEER), 8-week 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	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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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 symptoms and DSM scale on the Child Behavior Checklist and Teacher Report Form **Comorbidity:** N/A **Female:** 27.4 % 26.7 and 28.1% girls **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 info on race or ethnicity: Other : Other: 2%	drivers ed program which control group also received. **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 month	(p= 0.07); there was also no significant differences for observed positive parenting.
Psychological or behavioral	Hiscock, 2019[324] Murdoch Childrens Research Institute (Australia), 2014[911] ID: ISRCTN50834814 RCT Multicenter N = 361 Australia Setting: Other	**Target:** Met full DSM-5 diagnostic criteria for ADHD – that is at least six of nine symptoms of inattention and/or hyperactivity were rated as 'often' or 'very often' present on the ADHD Rating Scale IV, and the symptoms had been present for at least 6 months, and were associated with cross-situational impairment (e.g. at home and school); had a moderate to severe parent-rated sleep problem; and met the International Classification of Sleep Disorders – 3rd edition criteria for chronic insomnia	**Intervention:** Two 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 **Control:** TAU	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%) at 3 months as reported by primary caregiver.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		disorder or delayed sleepwake phase disorder, or had sleep-related anxiety **Other:** Pediatricians **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:** Other info on race or ethnicity:	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	
Psychological or behavioral	Hogue, 2020[325] National Center on Addiction and Substance Abuse at Columbia University, 2015[1080] ID: NCT02420990 Cluster RCT Multicenter N = 145 US Setting: Specialty care	**Target:** Adolescents with ADHD, 77% met criteria for more than one disorder, 42% were on ADHD medication **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	**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	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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		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 Other info on race or ethnicity:	modular tasks: ADHD Assessment & Medication Consult, ADHD Psychoeducation & Client Acceptance, **Follow-up:** 12 months	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.
Psychological or behavioral	Huang, 2015[331] ID: N/A Clinical trial Single center N = 97 Taiwan Setting: N/A	**Target:** Boys and girls with ADHD in grades 1 though 4; children with autism and mental retardation were excluded **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	**Intervention:** Social skill training combined with parent training, 7 consecutive 8-week behavioral-based group 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 **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

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Ethnicity: Other info on race or ethnicity: N/A		scales. For child report SSRS, difference in Self Control favored intervention (p = .03).
Psychological or behavioral	Huang, 2021[330] Fujian Maternity and Child Health Hospital, 2022[756] ID: ChiCTR2100049863 RCT Single center N = 201 China Setting: Other	**Target:** Treatment naive children with ADHD. Exclusion: IQ <75, history of seizures, psyc co-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 Other info on race or ethnicity:	**Intervention:** Behavioral intervention group included parental training (1 hour weekly sessions), behavioral therapy, attention training (twice per day), relief therapy and game therapy, plus conventional therapy (biofeedback and a health education booklet), intervention lasted 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[351] ID: N/A 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:** Other info on race or ethnicity: N/A	**Intervention:** Attention training intervention consisted of 12 sessions from 30 to 45 min with 5 children with their parents, 1 session per week **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,
Psychological or behavioral	Li, 2022[383] ID: RCT Single center N = 180 China Setting: Specialty care	**Target:** Children with ADHD without co-morbid serious psyc 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	**Intervention:** Theme building block games, with 2 to 3 children per group, once a week for 8 weeks - the scheme provides an interactive environment for children to promote their psychological and behavioral development - the research instructor gives specific instructions (e.g., we are going to build a castle today) **Control:** Attention-matched control	Child Behavior Check List (CBLC) Results presented by gender. 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 Swanson, Nolan, and Pelham, Version IV, Parent Intervention showed significantly more improvement (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**
		Female: 47.8 % **Age mean:** 5.01 (0.36) **Minimum age:** 3 **Maximum age:** 7 **Ethnicity:** % Asian : 100 Other info on race or ethnicity:	Attention matched control, children play with blocks with 2 to 3 children per group, once a week for 8 weeks **Comparator:** **Follow-up:** 2 months	
Psychological or behavioral	McGrath, 2011[416] ID: NA RCT Single center N = 72 Canada Setting: Other	**Target:** Children age with ADHD, able to speak and understand English, telephone access, 6-month symptom duration. Exclusion criteria were a co-intervention (within 6 months) and disorder severity, including evidence of immediate danger to self or others; involvement with child protection authorities; autism, schizophrenia, or other psychosis; complex comorbidity; and serious cognitive delay. **Other:** **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	**Intervention:** The Strongest Families intervention based on evidence and skill-focused learning, anxiety program consisted of 11 sessions and the behavior programs had 12 sessions, weekly coach session calls were on average 40 minutes, 1 year of follow-up **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
		Ethnicity: Other info on race or ethnicity: N/A		
Psychological or behavioral	Meyer, 2021[420] Uppsala County Council, 2016[1102] ID: ISRCTN17366720 RCT Multicenter N = 184 Sweden Setting: Specialty care	**Target:** Adolescents with ADHD; exclusion: severe depression, suicidality, psychosis, or bipolar disorder without stable meds, 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 % 65.8% (SSTG) and 62% (Control) females (all with ADHD) **Age mean:** SSTG 16.46 (0.88), control 16.71 (0.94) **Minimum age:** 15	**Intervention:** Age-adapted structured skills training group program based on a manualized dialectical behavioral therapy (DBT) 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. **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 on ADSR. 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
		Maximum age: 18 **Ethnicity:** Other info on race or ethnicity: N/A		
Psychological or behavioral	Pelham, 2016[52] ID: N/A Crossover trial Single center N = 152 US Setting: Mixed	**Target:** Children with ADHD, between the ages of 5 and 12, were included with clinically diagnosed ADHD. Children should not have (1) Full-Scale IQ below 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)	**Intervention:** Behavioral first intervention, social skills training sessions for children, parent training (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 one 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).

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 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 Other info on race or ethnicity:		
Psychological or behavioral	Pfiffner, 2014[464] Tran, 2018[1084]; Haack, 2017[780]; Rooney, 2018[980]; Adalio, 2018[640] 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 (grades 2 - 5) full time in a regular classroom, ability to participate in our groups on the days scheduled, school proximity within 45 minutes of study site to allow for the clinician to conduct school meetings, and teacher consent to participate in a school-based treatment **Other:** Parents received training and provided some outcomes **ADHD presentation:** inattentive : 100	**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	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) 54.8% of intervention, 43.2% of comparator, and 29.8% of treatment as usual were positive responders (p>.05). Intervention and comparator scores improved when compared to the placebo (p=0.001). IRS (Impairment Rating 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
		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 Other info on race or ethnicity:	**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	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
Psychological or behavioral	Power, 2012[469] 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	**Intervention:** Family-School Success over the course of 12 weekly sessions, which included 6 group sessions (90 minutes each), 4 individualized family sessions (60 minutes each), and 2 school-based consultations (45 minutes each) **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	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
		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 Other info on race or ethnicity:	session was conducted on a Saturday for 3 hours and subsequent meetings were 75 minutes (**Follow-up:** 3 months	
Psychological or behavioral	Qian, 2021[474] ZIli Fan, 2016[1156] 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 of 80 or above; no diagnosis of autism spectrum disorders, psychosis, or an	**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, consisted of 12 weekly sessions, each session lasting 120 minutes **Control:** Wait list	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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		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:** Other info on race or ethnicity:	12-week waitlist, after which group received intervention **Comparator:** NA **Follow-up:** 3 months	Behavior Rating Scales of Executive Function (BRIEF) : no effect of group on any subscales.
Psychological or behavioral	Schuck, 2018[510] Schuck, 2018[995] ID: NA RCT Single center N = 88 US	**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	**Intervention:** Canine assisted psychosocial intervention, 12 weekly 2-hour sessions **Control:** Other Psychosocial intervention without canine assisted intervention; parents participated in 12 weekly 2-hour sessions of group Behavioral Parent Training emphasizing positive	Social Skills Improvement System (SSIS) Problem Behaviors scale A significant interaction of group by time (p =.002) was found at treatment completion for problem behaviors. ADHD-RS-IV (Attention-Deficit/Hyperactivity Disorder Rating Scale, 4th Edition) total score, parent report

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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: Community	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 Other info on race or ethnicity:	reinforcement strategies and nonphysical discipline **Comparator:** NA **Follow-up:** 3 months	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 = .021, p = .008, and p = .011) while the control group did not experience significant increases. There no adverse events across seven cohorts of treatment
Psychological or behavioral	Sciberras, 2020[511] Murdoch Childrens Research Institute (MCRI) (Australia), 2010[912]; Hiscock, 2015[806]; Sciberras, 2010[997] 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, and 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 %	**Intervention:** Family intervention, 2 face to face, fortnightly consultations about sleep with a 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,	Strengths & Difficulties Questionnaire (SDQ) conduct problems, parent report No difference in improvement in conduct reported by parent (p =0 .17) or teacher (p =0 .11). 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)

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		Age mean: 10.1 (2.0) **Minimum age:** 5 **Maximum age:** 12 **Ethnicity:** Other info on race or ethnicity: N/A	reinforce suggested strategies, and troubleshoot any problems **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	The intervention group improved more than control group (p = .001). Child sleep habits questionnaire—total score: Intervention group improved more than control (p < .02).
Psychological or behavioral	Sibley, 2016[521] ID: NA RCT Multicenter N = 128 US Setting: School	**Target:** Children with ADHD in grades 6 through 8 with significant academic impairment; children with autism spectrum disorder excluded **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	**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 **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
		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 Other info on race or ethnicity:		
Psychological or behavioral	Sibley, 2020[522] Sibley, 2016[1035] ID: NA RCT Unclear/Not reported N = 123 US Setting: School	**Target:** Adolescents with ADHD, without any history of autism, intellectual disability or an IQ of less than 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 % Female: Dyadic, 17.5% / Parent-Teen Group, 21.7% **Age mean:**	**Intervention:** Parent-teen dyadic Supporting Teens' Autonomy Daily (STAND), a manualized, ten 60-min weekly sessions attended by the participant and a parent, skill instruction blended with motivational interviewing and parent-teen behavioral contracting **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**
		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% Other info on race or ethnicity:		
Psychological or behavioral	Sibley, 2021[520] Bickman, 2021[1031]; Florida International University, 2016[752] ID: NCT02694939 RCT Multicenter N = 278 US Setting: Community	**Target:** Adolescents with ADHD; those with diagnosis of autism spectrum disorder or intellectual disability were excluded **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	**Intervention:** Supporting Teens' Autonomy Daily (STAND) consisting of 10 weekly 60-minute motivational interviewing-enhanced behavior therapy sessions attended by dyads of teens and parents **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
		Maximum age: 17 **Ethnicity:** % Hispanic or Latino : 81.7 % Black/African American : 13.3 % White : 4.7 % Multiracial : 0.7 Other info on race or ethnicity:		
Psychological or behavioral	Siebelink, 2021[523] Karakter Kinder en Jeugdpsychiatrie, 2017[844]; Siebelink, 2018[1039] 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 intelligence quotient <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:**	**Intervention:** Family mindfulness-based intervention, 8 weekly 90-minute group sessions, followed by 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 **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
		Other info on race or ethnicity: N/A		
Psychological or behavioral	Storebo, 2012[552] Storebo, 2011[964]; Storebo, 2011[1056] ID: NCT00937469 RCT Single center N = 56 Netherlands Setting: Specialty care	**Target:** ADHD diagnosis according to DSM, 8-12 years, parents willing to take part, without schizophrenia or autism, no violent and criminal children, with an 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:** Other info on race or ethnicity: N/A	**Intervention:** Social skills training offered weekly, 90 minute sessions for 8 weeks, in addition to 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 **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;	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
			and atomoxetine was considered in patients wher **Comparator:** NA **Follow-up:** 6 months	
Psychological or behavioral	Valero, 2021[581] ID: NA RCT Unclear/Not reported N = 30 Spain Setting: Community	**Target:** Children aged 9 through 14 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:** Other info on race or ethnicity: N/A	**Intervention:** Mindfulness training, 8 sessions over an 8-week period, children's sessions were 1 hour long, parent sessions were 1.5 hours **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[613] Barnes, 2017[663] ID: ACTRN12614000973617 Crossover trial Single center N = 31 Australia Setting: Mixed	**Target:** Children with ADHD with co-morbid difficulties (i.e., language difficulties, conduct disorder); exclusion : other major developmental disorders (i.e., intellectual disability, autism spectrum disorder) **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:** Other info on race or ethnicity: N/A	**Intervention:** 1-hour play-based intervention 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.
Teacher, school environment	Breaux, 2018[171] Langberg, 2018[860]; Smith, 2020[1045] ID: N/A RCT Multicenter N = 222	**Target:** Children met full DSM–IV–TR diagnostic criteria for ADHD based on the Parent Children's Interview for Psychiatric Syndromes or combined with teacher ratings on the National Institute for Children's Health Quality Vanderbilt ADHD Rating Scale; intelligence quotient of 80 or	**Intervention:** Completing 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 six sessions occurred once per week, completed over 11-weeks, also included two 1-	Grade Point Average (GPA) Adolescent involvement, parent involvement and other therapeutic processes led to an increase in GPA posttreatment.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
	US Setting: School	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 Participant's assessment data were reviewed by a licensed clinical psychologist to determine eligibility and diagnoses **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 info on race or ethnicity: Other : 4% other/did not report	hour sessions with provider and family **Control:** Wait list Wait list **Comparator:** Teacher, school environmentHomework, Organization, and Planning Skills (HOPS) is skills-based treatment that focuses on teaching organization and planning skills that are important for homework completion; two parent/family meetings focused on promoting generalization; 16 sessions **Follow-up:** 6 months	
Teacher, school	Corkum, 2019[213] Dalhousie University, 2012[711] ID: NCT01547702	**Target:** Children attending Grades 1 to 6; enrolled in an English classroom, or teacher was able to complete the program in English; previously diagnosed with ADHD	**Intervention:** Teachers given weekly online sessions for 6 weeks, session covered a different topic related to education, treatment, support and additional interventions	ADHD Index Conners 3-T Significant improvements based on teacher (but not parent) reports of core ADHD symptoms. Impairment ratings score, teacher

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
	RCT Multicenter N = 58 Canada Setting: School	by health care provider who was certified to make mental health diagnoses; 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 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	**Control:** Wait list Waitlist group did not receive any intervention but were free to access usual care. Waitlist lasted 12 weeks **Comparator:** NA **Follow-up:** 6 months	Significant improvement associated with the intervention. 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
		Other info on race or ethnicity: Other : 10% non-caucasian		
Teacher, school environment	DuPaul, 2021[242] Ohio University, 2020[936] 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 OCD **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	**Intervention:** Multi-component training interventions: individual coaching sessions for 15–20 min twice per week throughout the academic year, 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 **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.

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	Comparison: Intervention; Control; Comparator; Follow-up	Outcome and results
		% White : 74 Other info on race or ethnicity: Other : Other 4.8%		
Teacher, school environment	Evans, 2016[262] Langberg, 2016[861]; Schultz, 2017[996] ID: N/A 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, and demonstrated an IQ of 80 or above, and 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	**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).

Intervention	Study: Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	Population: 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: 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 Other info on race or ethnicity:		
Teacher, school environment	Schramm, 2016[509] ID: NA RCT Single center N = 113 Germany Setting: Specialty care	**Target:** Participants with ADHD and not meeting the criteria for severe comorbid disorders (e.g., psychotic episode) **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:**	**Intervention:** Learning Skills Training for Adolescents With ADHD, a 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) **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, which was offered for ethical reasons.	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.

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** 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 info on race or ethnicity: N/A : Germans	**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:** 48 months	
Teacher, school environment	Shen, 2021[517] School of Public Health, 2018[994] ID: ChiCTR1800014945 RCT Multicenter N = 232 China Setting: School	**Target:** Children meeting the diagnosis of ADHD according to DSM-5, being between 6-12 years old; parents agree to use treatment, can read and write the Chinese language, and signed the informed consent **Other:** **ADHD presentation:** inattentive : 35.3,hyperactive : 25.4,combined : 27.2,N/A : control and intervention **Diagnosis:** Confirmation by specialist Inclusion criterian to meet the diagnosis of the ADHD according to the DSM5 **Comorbidity:** **Female:** 12.5 % 75.4 **Age mean:** 0.2 (0.48)	**Intervention:** Multimodal treatment for teachers and parents in the intervention group, 2 teacher training meetings (1 2-hr session and 1 30-min session), 2 group parent trainings sessions (4.5-hrs) and 2 individualized family therapy sessions (2hrs), conducted over 16 weeks, participants also received stimulant medication prescribed by their pediatricians **Control:** TAU Children in the control group were treated with stimulant medication prescribed by their pediatricians referring to the clinical practice guidelines for ADHD children published by the American Academy of Pediatrics **Comparator:** NA	SNAP-IV (Swanson Nolan and Pelham's 4th scale) The intervention group demonstrated significant improvements compared to that in the 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**
		Minimum age: 6 **Maximum age:** 12 **Ethnicity:** Other : Chinese Other info on race or ethnicity:	**Follow-up:** 4 months	
Teacher, school environment	Sibley, 2018[519] Sibley, 2020[1034]; Sibley, 2019[1032] ID: NA RCT Single center N = 325 US Setting: School	**Target:** Rising" 6th & 9th graders with ADHD referred from Miami-Dade schools; DSM IV diagnosis required; students must display significant academic impairment (at least a 3 on a 0–6 teacher Impairment Rating Scale); Students with autism spectrum disorder were excluded **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:**	**Intervention:** 8-week intensive summer program from 8:00 a.m. to 5:00 p.m. on weekdays (45 hr per week), alternated between 30- and 50-min small- and large-group modules, parent training 8-week once per week for 1.5 hours **Control:** No intervention No intervention **Comparator:** Teacher, school environment8-week organization skills group 1.5 hr per week; also parent training 8-weeks, once per week for 1.5 hours **Follow-up:** 12 months	School Disciplinary Incidents There were no significant Group × Time interaction effects for school disciplinary incidents. Hyperactivity/Impulsivity scale, Disruptive Behavior Disorder Rating Scale, teacher report There were no significant Group by Time interaction effects between the two 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
		Rising 6th & 9th graders **Minimum age:** **Maximum age:** **Ethnicity:** % Hispanic or Latino : 72.7 % Black/African American : 17.4 Other info on race or ethnicity:		
Teacher, school environment	Tamm, 2017[564] ID: NA RCT Multicenter N = 216 US Setting: Mixed	**Target:** Children in grades 2–5 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 Other info on race or ethnicity:	**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:** Teacher, school environmentReading training alone; reading treatment was provided by	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
			teachers to 1-2 students at a time for 45 minutes, 4 days per week for 16 weeks; training targeted phonics, word identification, spelling, reading fluency, and comprehension **Follow-up:** 5 months	
Teacher, school environment	Volpe, 2009[590] Jitendra, 2007[837] ID: NA RCT Multicenter N = 167 US Setting: School	**Target:** Children in grades 1 through 4 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:**	**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:** 27 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**
		% Hispanic or Latino : 26.9 % Black/African American : 11.4 % White : 58.0 Other info on race or ethnicity:		
Teacher, school environment	Zheng, 2020[628] ID: N/A Cluster RCT Multicenter N = 219 China Setting: School	**Target:** Children aged 6-11 diagnosed with ADHD according to DSM-5, Intelligence Quotient ≥70, and no prior ADHD medication use; no comorbidity with autism spectrum disorder, schizophrenia, epilepsy, head injury, or verified neurological disorder, and sensory retardation (hearing/vision problems) **Other:** Parents or primary caregivers of children with ADHD that can read and write the Chinese language; teachers **ADHD presentation:** N/A **Diagnosis:** Confirmation by specialist Participants were diagnosed with ADHD according to DSM-5 **Comorbidity:** N/A **Female:** 15.2 % **Age mean:** Intervention group mean age (7.93) and SD (1.38). Control group mean age (7.21) and SD (1.22). **Minimum age:** 6	**Intervention:** Teacher training was 4-weekly 2-hour sessions, consisting of: (1) knowledge about ADHD; (2) behavioral strategies to manage conduct problems; (3) classroom behavior management; (4) teaching how to use scaffolding to promote the development of self-regulation in children with ADHD. Parent training was 4-weekly 2-hour sessions, consisting of: (1) knowledge about ADHD; (2) medication; (3) teaching behavioral strategies; (4) teaching to combine procedures and behavior management techniques. Medication given to children was either methylphenidate or atomoxetine. **Control:** Other Methylphenidate or atomoxetine alone **Comparator:** NA **Follow-up:** 6 months	SNAP-IV (Chinese Version Swanson Nolan and Pelham, Version IV) Difference of SNAP-IV score changes between the two groups was statistically significant (p=0.009)

Intervention	**Study:** Author, year; Multiple publications; Trial ID; Study design; Sites; Study size; Location Setting	**Population:** Setting; Study target; ADHD presentation; Diagnosis; Comorbidity; % Female; Age mean; Minimum age; Maximum age; Ethnicity	**Comparison:** Intervention; Control; Comparator; Follow-up	**Outcome and results**
		Maximum age: 11 **Ethnicity:** Other info on race or ethnicity:		

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[118]	Unclear risk	Unclear risk	High risk	High risk	High risk
Adams, 2009[119]	High risk	High risk	Unclear risk	Unclear risk	High risk
Ahmadi, 2021[122]	High risk	Unclear risk	Low risk	Unclear risk	High risk
Algorta, 2016[124]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Alloway, 2009[126]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Altınkaynak, 2020[127]	High risk	High risk	Low risk	Unclear risk	High risk
Amado-Caballero, 2020[128]	High risk	Low risk	Low risk	High risk	High risk
Babinski, 2021[135]	High risk	High risk	Unclear risk	Unclear risk	High risk
Bansal, 2012[27]	High risk	Low risk	Low risk	Unclear risk	Moderate risk
Berger, 2010[148]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Berger, 2017[147]	High risk	Low risk	Low risk	Unclear risk	High risk
Bergeron, 2017[149]	Unclear risk	High risk	High risk	Unclear risk	High risk
Beriha, 2018[150]	Unclear risk	High risk	Unclear risk	High risk	High risk
Bledsoe, 2020[160]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Bloch, 2012[161]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Boroujeni, 2019[165]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Boucugnani, 1989[167]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Breaux, 2016[170]	High risk	Low risk	Unclear risk	High risk	Moderate risk
Bunte, 2013[175]	High risk	Low risk	Low risk	Unclear risk	Moderate risk
Burton, 2019[176]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Bussing, 1998[177]	High risk	Low risk	Low risk	High risk	High risk
Canivez, 2016[178]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Catherine Joy, 2021[180]	High risk	Unclear risk	Low risk	High risk	High risk
Caudal, 2011[263]	High risk	High risk	Unclear risk	Unclear risk	Moderate risk
Chan, 2022[185]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Chang, 2019[187]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Chelune, 1986[189]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk

Author, year	Patient selection	Index test	Reference standard	Flow timing	Overall RoB
Chen, 1994[194]	High risk	Low risk	Unclear risk	Unclear risk	Moderate risk
Chen, 2019[191]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Chen, 2019[192]	High risk	Low risk	Unclear risk	Unclear risk	Moderate risk
Chen, 2020[195]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Chen, 2021[193]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Chen, 2022[190]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Chiarenza, 2018[196]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Chow, 2019[201]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Chu, 2017[202]	High risk	High risk	Unclear risk	Unclear risk	High risk
Crippa, 2017[215]	High risk	Unclear risk	Low risk	Unclear risk	High risk
Culbertson, 1998[217]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Das, 2021[218]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Deb, 2008[222]	High risk	High risk	Low risk	Unclear risk	High risk
Deserno, 2022[227]	Unclear risk	Low risk	Low risk	Unclear risk	Low risk
Doyle, 2007[236]	High risk	High risk	Low risk	Unclear risk	High risk
Duda, 2016[239]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Duda, 2017[238]	High risk	Low risk	High risk	Low risk	High risk
Ebesutani, 2010[245]	Low risk	High risk	Unclear risk	Unclear risk	Moderate risk
Edwards, 2015[246]	Low risk	High risk	Unclear risk	Unclear risk	Moderate risk
Eiraldi, 2000[248]	Unclear risk	High risk	Low risk	Unclear risk	Moderate risk
Ekhlasi, 2022[249]	High risk	High risk	Unclear risk	Unclear risk	Moderate risk
Elkins, 2014[254]	High risk	High risk	Low risk	Unclear risk	Moderate risk
El-Sayed, 1999[250]	High risk	High risk	Low risk	Unclear risk	High risk
Emser, 2018[256]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Faraone, 2016[266]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Ferrin, 2012[270]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Francois-Sevigny, 2022[279]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Gao, 2020[283]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
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
Gomez, 2018[299]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Gomez, 2021[300]	High risk	High risk	Unclear risk	Unclear risk	Moderate risk

Author, year	Patient selection	Index test	Reference standard	Flow timing	Overall RoB
Grodzinsky, 1992[305]	High risk	High risk	Unclear risk	Unclear risk	High risk
Gungor, 2021[307]	High risk	High risk	Low risk	Low risk	High risk
Hager, 2021[309]	High risk	Low risk	Unclear risk	High risk	High risk
Hall, 2016[312]	Low risk	High risk	Low risk	Unclear risk	High risk
Hall, 2020[311]	Low risk	Low risk	Low risk	Unclear risk	Low risk
Hasaneen, 2017[315]	High risk	Low risk	Low risk	High risk	High risk
Helgadottir, 2015[318]	Unclear risk	Low risk	Low risk	Unclear risk	High risk
Heller, 2013[319]	Unclear risk	High risk	Low risk	Unclear risk	High risk
Hinshaw, 2002[322]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Hong, 2019[326]	Unclear risk	Low risk	Unclear risk	Unclear risk	Low risk
Hudziak, 2004[332]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Hult, 2018[23]	High risk	High risk	Low risk	Unclear risk	High risk
Ickowicz, 2006[334]	High risk	Low risk	Unclear risk	Unclear risk	Moderate risk
Jacobson, 2020[335]	Unclear risk	Low risk	Low risk	Unclear risk	Moderate risk
Jahanshahloo, 2017[336]	High risk	High risk	Low risk	Unclear risk	High risk
Jarrett, 2018[338]	Unclear risk	High risk	High risk	Unclear risk	High risk
Jensen-Doss, 2013[340]	Unclear risk	Unclear risk	High risk	Unclear risk	High risk
Jimenez-Figueroa, 2017[341]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Johnstone, 2021[345]	High risk	Unclear risk	Unclear risk	High risk	Moderate risk
Juneja, 2019[346]	Low risk	Low risk	Low risk	Low risk	Low risk
Karr, 2021[352]	Unclear risk	Low risk	Low risk	Unclear risk	Moderate risk
Kennerley, 2018[355]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Khoshnoud, 2018[359]	High risk	High risk	Unclear risk	Unclear risk	High risk
Kim, 2015[362]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Kim, 2015[361]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Koh, 2022[364]	Unclear risk	Low risk	Low risk	Unclear risk	Moderate risk
Krieger, 2021[373]	High risk	Low risk	Low risk	High risk	Moderate risk
Lau, 2018[377]	Low risk	Unclear risk	Low risk	Unclear risk	Low risk
Levy, 2017[382]	Low risk	Low risk	Low risk	Low risk	Low risk
Li, 2005[386]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Li, 2016[384]	High risk	High risk	Unclear risk	Unclear risk	Moderate risk
Li, 2018[385]	Unclear risk	High risk	Unclear risk	Unclear risk	High risk
Liechti, 2013[388]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Lin, 2023[392]	Unclear risk	Low risk	Unclear risk	Unclear risk	Low risk
Lindhiem, 2022[394]	High risk	High risk	Unclear risk	Unclear risk	High risk
Longridge, 2019[396]	Unclear risk	Unclear risk	High risk	High risk	High risk
Luo, 2022[399]	High risk	High risk	Low risk	Unclear risk	Moderate risk
Luo, 2022[398]	High risk	High risk	Unclear risk	Unclear risk	Moderate risk

Author, year	Patient selection	Index test	Reference standard	Flow timing	Overall RoB
Marcano, 2018[402]	High risk	Unclear risk	High risk	Unclear risk	High risk
Markovska-Simoska, 2017[403]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Martín-Brufau, 2017[405]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Martin-Martinez, 2012[406]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Matier-Sharma, 1995[407]	Low risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Mayes, 2004[412]	High risk	High risk	Low risk	Unclear risk	Moderate risk
Mayfield, 2018[413]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
McCarthy, 2016[414]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
McIntosh, 1995[417]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Merzon, 2022[419]	High risk	High risk	Unclear risk	Unclear risk	Moderate risk
Mikolas, 2022[423]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Mitchell, 1990[425]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Moghaddari, 2020[426]	Unclear risk	Low risk	Low risk	Unclear risk	High risk
Moura, 2017[434]	High risk	Low risk	Low risk	Low risk	Moderate risk
Moura, 2019[433]	Low risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Mouti, 2019[435]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Mukherjee, 2014[436]	Low risk	Unclear risk	Low risk	Unclear risk	Low risk
Mulhern, 1994[437]	High risk	High risk	Low risk	Unclear risk	Moderate risk
Muthuraman, 2019[438]	High risk	Low risk	Low risk	Low risk	High risk
Mwamba, 2019[439]	High risk	Low risk	High risk	Low risk	Moderate risk
Newman, 2017[450]	Low risk	Low risk	Low risk	Low risk	Low risk
Nolan,1999[451]	Low risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Ogrim, 2012[453]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
O'Neill, 2021[452]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
OÖztoprak, 2017[456]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	High risk
Oztekin, 2021[455]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Park, 2019[457]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Parker, 2016[17]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Pauli-Pott, 2021[458]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Peijnenborgh, 2016[459]	Unclear risk	Low risk	Low risk	Unclear risk	Low risk
Pereda, 2018[461]	Unclear risk	Unclear risk	Low risk	Low risk	High risk

Author, year	Patient selection	Index test	Reference standard	Flow timing	Overall RoB
Pineda, 2011[465]	High risk	High risk	Unclear risk	Unclear risk	High risk
Qin , 2018[475]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Quintana, 2007[476]	High risk	High risk	Low risk	Unclear risk	High risk
Raiker, 2017[480]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Rezaeezadeh, 2020[482]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Riaz, 2020[483]	Low risk	Low risk	Low risk	Low risk	Low risk
Rishel, 2005[486]	Low risk	Low risk	Low risk	Low risk	Low risk
Robles, 2021[487]	High risk	Low risk	Unclear risk	Unclear risk	Moderate risk
Rodríguez, 2018[488]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Roessner, 2007[489]	Unclear risk	Low risk	Low risk	High risk	High risk
Schatz, 2001[503]	High risk	High risk	Low risk	Unclear risk	High risk
Scheeringa, 2020[504]	Low risk	Low risk	High risk	Low risk	Low risk
Schirmer, 2021[506]	High risk	High risk	Unclear risk	Unclear risk	Moderate risk
Schneider, 2020[507]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Serrallach, 2016[512]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Shemmassian, 2016[515]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Shemmassian, 2017[516]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Silverstein, 2016[524]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Simões, 2021[525]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Skogli, 2013[529]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Slaby, 2022[530]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	High risk
Slobodin, 2020[532]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Slobodin, 2022[531]	Low risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Smith, 2003[535]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Snyder, 2008[537]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Snyder, 2015[26]	Low risk	Low risk	Low risk	Unclear risk	Low risk
Soliva, 2010[538]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Spencer, 2018[542]	Low risk	Low risk	High risk	Unclear risk	Moderate risk
Sprafkin, 2007[546]	Low risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Stepanova, 2021[551]	Low risk	Low risk	Low risk	Low risk	Low risk
Straub, 2021[553]	High risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Sullivan, 2007[557]	Unclear risk	Unclear risk	Low risk	Unclear risk	Moderate risk
Sun, 2018[558]	High risk	Low risk	Unclear risk	Unclear risk	Moderate risk
Tang, 2022[567]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk

Author, year	Patient selection	Index test	Reference standard	Flow timing	Overall RoB
Thompson, 2017[569]	Unclear risk	High risk	High risk	Unclear risk	High risk
Tillman, 2005[571]	High risk	High risk	Low risk	Unclear risk	High risk
Tripp, 2006[574]	Low risk	Low risk	Low risk	Low risk	Low risk
Vahid, 2019[580]	High risk	Low risk	Low risk	Unclear risk	Moderate risk
Varela Casal, 2019[586]	High risk	Low risk	Unclear risk	Unclear risk	Moderate risk
Vogt, 2011[588]	Low risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Wang, 2018[592]	Unclear risk	Low risk	Unclear risk	Unclear risk	High risk
Wassenberg, 2004[595]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Webster, 2000[597]	Low risk	Low risk	Low risk	Low risk	Low risk
Westerberg, 2004[603]	High risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Weyandt, 1994[604]	Unclear risk	High risk	Unclear risk	Unclear risk	Moderate risk
Williams, 2010[20]	Unclear risk	High risk	Low risk	Unclear risk	Moderate risk
Wodka, 2008[614]	Low risk	High risk	Low risk	Unclear risk	Moderate risk
Yao, 2018[618]	High risk	Unclear risk	Unclear risk	Unclear risk	High risk
Yasumura, 2020[619]	Low risk	Low risk	Low risk	Low risk	Low risk
Yeh, 2020[620]	High risk	Unclear risk	Low risk	Low risk	Low risk
Yoo, 2020[621]	Unclear risk	Low risk	Low risk	Unclear risk	Low risk
Zadehbagheri, 2019[623]	Low risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Zelko, 1991[626]	Unclear risk	Low risk	Low risk	Low risk	Low risk
Zelnik, 2012[627]	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Moderate risk
Zhou, 2018[629]	Low risk	Low risk	High risk	Low risk	Moderate risk
Zulueta, 2019[634]	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk

Table D.2. Applicability for included studies, KQ1

Author, year	Population	Intervention	Comparator	Outcome	Setting
Abramov, 2019[118]	Narrow eligibility criteria	N/A	Unclear	N/A	N/A
Adams, 2009[119]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Ahmadi, 2021[122]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Algorta, 2016[124]	N/A	N/A	N/A	N/A	N/A
Alloway, 2009[126]	Unclear	N/A	N/A	N/A	N/A
Altınkaynak, 2020[127]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Amado-Caballero, 2020[128]	Unclear	N/A	N/A	Unclear	Unclear
Babinski, 2021[135]	N/A	N/A	Unclear	N/A	N/A
Bansal, 2012[27]	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
Berger, 2010[148]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Berger, 2017[147]	Narrow eligibility criteria	N/A	Comparator Unclear	N/A	N/A
Bergeron, 2017[149]	Unclear	N/A	N/A	N/A	N/A
Beriha, 2018[150]	Unclear	N/A	N/A	N/A	Unclear
Bledsoe, 2020[160]	Narrow eligibility criteria	Unclear	N/A	N/A	N/A
Bloch, 2012[161]	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[165]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Boucugnani, 1989[167]	Unclear	N/A	N/A	N/A	Unclear
Breaux, 2016[170]	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[175]	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
Burton, 2019[176]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Bussing, 1998[177]	More complex patients than typical of the community	Unclear	N/A	N/A	N/A
Canivez, 2016[178]	Unclear	N/A	N/A	N/A	N/A
Catherine Joy, 2021[180]	Unclear	N/A	N/A	N/A	N/A
Caudal, 2011[263]	N/A	N/A	N/A	N/A	N/A
Chan, 2022[185]	N/A	N/A	N/A	N/A	N/A
Chang, 2019[187]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Chelune, 1986[189]	Unclear	N/A	N/A	N/A	N/A
Chen, 1994[194]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Chen, 2019[191]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Chen, 2019[192]	N/A	Highly selected intervention team or level of training/proficiency not widely available	N/A	Unclear	N/A
Chen, 2020[195]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Chen, 2021[193]	Narrow eligibility criteria	N/A	N/A	N/A	Unclear
Chen, 2022[190]	Unclear	N/A	N/A	N/A	N/A
Chiarenza, 2018[196]	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[201]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Chu, 2017[202]	Unclear	Unclear	N/A	N/A	Level of care different from that in the community
Crippa, 2017[215]	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[217]	N/A	N/A	N/A	N/A	Level of care different from that in the community

Author, year	Population	Intervention	Comparator	Outcome	Setting
Das, 2021[218]	Unclear	N/A	Unclear	N/A	N/A
Deb, 2008[222]	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[227]	Unclear	N/A	N/A	N/A	Unclear
Doyle, 2007[236]	Unclear	N/A	N/A	N/A	N/A
Duda, 2016[239]	More complex patients than typical of the community	Unclear	N/A	N/A	Level of care different from that in the community
Duda, 2017[238]	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
Ebesutani, 2010[245]	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[246]	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[248]	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[249]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Elkins, 2014[254]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
El-Sayed, 1999[250]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Emser, 2018[256]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Faraone, 2016[266]	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[270]	N/A	Unclear	N/A	N/A	Level of care different from that in the community
Francois-Sevigny, 2022[279]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Gao, 2020[283]	Unclear	N/A	N/A	N/A	Level of care different from

Author, year	Population	Intervention	Comparator	Outcome	Setting
					that in the community
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
Gomez, 2018[299]	N/A	Unclear	N/A	N/A	N/A
Gomez, 2021[300]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Grodzinsky, 1992[305]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Gungor, 2021[307]	Narrow eligibility criteria	Unclear	N/A	N/A	Unclear
Hager, 2021[309]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Hall, 2016[312]	Narrow eligibility criteria	Unclear	N/A	N/A	Level of care different from that in the community
Hall, 2020[311]	N/A	N/A	N/A	N/A	N/A
Hasaneen, 2017[315]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Helgadottir, 2015[318]	N/A	N/A	N/A	N/A	N/A
Heller, 2013[319]	More complex patients than typical of the community	Unclear	N/A	N/A	Level of care different from that in the community
Hinshaw, 2002[322]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Hong, 2019[326]	More complex patients than	N/A	Inadequate comparison therapy	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
	typical of the community		or use of a substandard alternative therapy		
Hudziak, 2004[332]	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[23]	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[334]	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[335]	N/A	N/A	N/A	N/A	N/A
Jahanshahloo, 2017[336]	Unclear	N/A	N/A	N/A	Unclear
Jarrett, 2018[338]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Jensen-Doss, 2013[340]	DSM-4/5 diagnosis Unclear	N/A	Unclear	Unclear	N/A
Jimenez-Figueroa, 2017[341]	N/A	N/A	N/A	N/A	N/A
Johnstone, 2021[345]	Narrow eligibility criteria	Highly selected intervention team or level of training/proficiency not widely available	Diagnostic tools used differently than as recommended or commonly used in practice	N/A	Level of care different from that in the community
Juneja, 2019[346]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Karr, 2021[352]	N/A	N/A	N/A	N/A	Unclear
Kennerley, 2018[355]	N/A	N/A	N/A	N/A	N/A
Khoshnoud, 2018[359]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Kim, 2015[362]	Narrow eligibility criteria	Unclear	N/A	N/A	Level of care different from that in the community
Kim, 2015[361]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Koh, 2022[364]	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[373]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from

Author, year	Population	Intervention	Comparator	Outcome	Setting
					that in the community
Lau, 2018[377]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Levy, 2017[382]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Li, 2005[386]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Li, 2016[384]	Narrow eligibility criteria	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	N/A
Li, 2018[385]	N/A	N/A	N/A	N/A	N/A
Liechti, 2013[388]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Lin, 2023[392]	N/A	N/A	N/A	N/A	N/A
Lindhiem, 2022[394]	Unclear	N/A	N/A	N/A	N/A
Longridge, 2019[396]	N/A	N/A	N/A	N/A	N/A
Luo, 2022[399]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Luo, 2022[398]	Unclear	N/A	N/A	N/A	N/A
Marcano, 2018[402]	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[403]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Martín-Brufau, 2017[405]	Unclear	N/A	Unclear	Other issues	N/A
Martin-Martinez, 2012[406]	N/A	N/A	N/A	N/A	N/A
Matier-Sharma, 1995[407]	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[412]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Mayfield, 2018[413]	N/A	N/A	N/A	N/A	N/A
McCarthy, 2016[414]	More complex patients than	N/A	N/A	N/A	Level of care different from

Author, year	Population	Intervention	Comparator	Outcome	Setting
	typical of the community				that in the community
McIntosh, 1995[417]	N/A	N/A	N/A	N/A	N/A
Merzon, 2022[419]	N/A	N/A	Unclear	N/A	N/A
Mikolas, 2022[423]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Mitchell, 1990[425]	Unclear	N/A	N/A	N/A	N/A
Moghaddari, 2020[426]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Moura, 2017[434]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Moura, 2019[433]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Mouti, 2019[435]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Mukherjee, 2014[436]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Mulhern, 1994[437]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Muthuraman, 2019[438]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Mwamba, 2019[439]	N/A	N/A	N/A	N/A	N/A
Newman, 2017[450]	N/A	N/A	N/A	N/A	N/A
Nolan,1999[451]	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[453]	N/A	N/A	N/A	N/A	Level of care different from that in the community
O'Neill, 2021[452]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
OÖztoprak, 2017[456]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Oztekin, 2021[455]	More complex patients than	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
	typical of the community				
Park, 2019[457]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Parker, 2016[17]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Pauli-Pott, 2021[458]	N/A	N/A	N/A	N/A	N/A
Peijnenborgh, 2016[459]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Pereda, 2018[461]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Pineda, 2011[465]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Qin , 2018[475]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Quintana, 2007[476]	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[480]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Rezaeezadeh, 2020[482]	Unclear	N/A	Comparator Unclear	N/A	Level of care different from that in the community
Riaz, 2020[483]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Rishel, 2005[486]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Robles, 2021[487]	More complex patients than typical of the community	N/A	Unclear	N/A	Level of care different from that in the community
Rodríguez, 2018[488]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Roessner, 2007[489]	N/A	N/A	N/A	N/A	N/A
Schatz, 2001[503]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Scheeringa, 2020[504]	N/A	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Schirmer, 2021[506]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Schneider, 2020[507]	N/A	N/A	N/A	N/A	N/A
Serrallach, 2016[512]	More complex patients than typical of the community	Unclear	Unclear	N/A	N/A
Shemmassian, 2016[515]	N/A	N/A	N/A	N/A	N/A
Shemmassian, 2017[516]	N/A	N/A	N/A	N/A	N/A
Silverstein, 2016[524]	N/A	N/A	N/A	N/A	N/A
Simões, 2021[525]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Skogli, 2013[529]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Slaby, 2022[530]	Unclear	N/A	Unclear	N/A	N/A
Slobodin, 2020[532]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Slobodin, 2022[531]	More complex patients than typical of the community	N/A	N/A	N/A	Level of care different from that in the community
Smith, 2003[535]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Snyder, 2008[537]	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[26]	N/A	N/A	N/A	N/A	N/A
Soliva, 2010[538]	Unclear	N/A	N/A	N/A	Level of care different from that in the community
Spencer, 2018[542]	N/A	N/A	N/A	N/A	N/A
Sprafkin, 2007[546]	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[551]	N/A	N/A	N/A	N/A	N/A
Straub, 2021[553]	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[557]	N/A	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Sun, 2018[558]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Tang, 2022[567]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Thompson, 2017[569]	N/A	N/A	Comparator Unclear	N/A	N/A
Tillman, 2005[571]	Unclear	N/A	N/A	N/A	N/A
Tripp, 2006[574]	More complex patients than typical of the community	N/A	N/A	N/A	Unclear
Vahid, 2019[580]	N/A	N/A	N/A	Unclear	Unclear
Varela Casal, 2019[586]	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[588]	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[592]	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[595]	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[597]	DSM-4/5 diagnosis Unclear	N/A	N/A	N/A	N/A
Westerberg, 2004[603]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Weyandt, 1994[604]	Unclear	N/A	N/A	N/A	N/A
Williams, 2010[20]	N/A	Unclear	N/A	N/A	N/A
Wodka, 2008[614]	N/A	N/A	N/A	N/A	N/A
Yao, 2018[618]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Yasumura, 2020[619]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Yeh, 2020[620]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community
Yoo, 2020[621]	Narrow eligibility criteria	N/A	N/A	N/A	Level of care different from that in the community

Author, year	Population	Intervention	Comparator	Outcome	Setting
Zadehbagheri, 2019[623]	N/A	N/A	N/A	N/A	N/A
Zelko, 1991[626]	N/A	N/A	N/A	N/A	N/A
Zelnik, 2012[627]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Zhou, 2018[629]	N/A	N/A	Comparator Unclear	N/A	N/A
Zulueta, 2019[634]	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[111]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Abikoff, 2004[114]	Low risk	High risk	High risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Abikoff, 2007[116]	Moderate/ Unclear risk	Low risk	High risk	Low risk	High risk	High risk	High risk
Abikoff, 2009[115]	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	High risk
Abikoff, 2013[113]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Abikoff, 2015[117]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Aevi Genomic Medicine, 2016[120]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	High risk	Low risk	High risk
Aevi Genomic Medicine, 2018[121]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Akhondzadeh, 2004[123]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Allen, 2005[125]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Amiri, 2008[129]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Arnold, 2022[132]	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Ashkenasi, 2011[133]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	High risk
Bakhshayesh, 2011[136]	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Banaschewski, 2013[137]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk
Bangs, 2007[138]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Bangs, 2008[139]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Barrickman, 1995[142]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Baziar, 2019[143]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear 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
Bedard, 2015[144]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Behdani, 2013[145]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	High risk	Moderate/ Unclear risk	High risk
Benzing, 2019[146]	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Biederman, 2005[155]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Biederman, 2006[154]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Biederman, 2007[152]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk
Biederman, 2008[153]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Bigorra, 2016[156]	Low risk	Low risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate risk
Bikic, 2018[59]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Low risk	Moderate risk
Bilici, 2004[157]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Moderate risk
Binesh, 2020[158]	High risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Blader, 2021[159]	Low risk	Low risk	High risk	Low risk	High risk	Low risk	Moderate risk
Block, 2009[162]	Moderate/ Unclear risk	Low risk	High risk	Low risk	High risk	Moderate/ Unclear risk	High risk
Blumer, 2009[163]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Bluschke, 2022[164]	High risk	High risk	High risk	Low risk	Low risk	High risk	High risk
Bostic, 2000[166]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Boyer, 2016[168]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk
Brams, 2018[169]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Breaux, 2018[171]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Buitelaar, 1996[173]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low 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
Buitelaar, 2007[172]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Bul, 2016[174]	Moderate/ Unclear risk	High risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Ceresoli-Borroni, 2021[182]	Low risk	Low risk	High risk	Low risk	Low risk	High risk	Moderate risk
Cetin, 2015[183]	High risk	High risk	High risk	High risk	High risk	High risk	High risk
Chacko, 2009[184]	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Chang, 2019[186]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Moderate risk
Childress, 2009[199]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Childress, 2019[197]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate risk
Childress, 2022[198]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk
Cho, 2011[200]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	High risk
Chu, 2021[203]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Churchill, 2018[204]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Coelho, 2017[205]	High risk	Low risk	High risk	High risk	Moderate/ Unclear risk	High risk	High risk
Coghill, 2014[206]	Low risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Coles, 2020[208]	High risk	High risk	Low risk	High risk	Low risk	High risk	High risk
Concordia Pharmaceuticals, 2011[209]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	High risk	High risk	High risk
Conners, 1996[210]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk
Connor, 2010[211]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Corkum, 2019[213]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk
Corkum, 2020[212]	Low risk	Low risk	Moderate/ Unclear risk	Low 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
Cornu, 2018[214]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	High risk	Moderate risk
Crippa, 2019[216]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Dashbozorgi, 2021[219]	High risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
David, 2021[220]	Low risk	High risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Daviss, 2008[221]	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Dehbozorghi, 2019[223]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Dell'Agnello, 2009[224]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Denton, 2020[225]	High risk	High risk	High risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Dentz, 2020[226]	High risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Diamond, 1999[228]	High risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk
Dittmann, 2011[231]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Dittmann, 2013[230]	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk
Dong, 2022[232]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Moderate risk
Dose, 2017[233]	Low risk	Moderate/ Unclear risk	Low risk	High risk	Low risk	Low risk	High risk
Dovis, 2015[234]	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Dreakhshanpour, 2022[237]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Moderate risk
Duke University, 2009[578]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
DuPaul, 2021[242]	Low risk	High risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	High risk
Durgut, 2020[243]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Duric, 2017[244]	High risk	High risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk

Author, year	Selection bias	Performance bias	Attrition bias	Detection bias	Reporting bias	Other source of bias	Overall RoB
Egeland, 2013[247]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Eli Lilly, 2004[389]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Eli Lilly, 2006[251]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Eli Lilly[252]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate risk
Elmaadawi, 2022[255]	High risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Enns, 2017[257]	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk
Epstein, 2007[259]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate risk
Epstein, 2016[258]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate risk
Ercan, 2014[260]	High risk	High risk	High risk	High risk	Moderate/ Unclear risk	High risk	High risk
Estrada-Plana, 2019[261]	Moderate/ Unclear risk	High risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Evans, 2016[262]	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Fabiano, 2016[264]	Low risk	High risk	Low risk	High risk	Moderate/ Unclear risk	Low risk	High risk
Fallah, 2018[265]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Moderate risk
Farmer, 2017[267]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Ferrin, 2014[268]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Ferrin, 2020[269]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Findling, 2001[274]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Findling, 2008[276]	Moderate/ Unclear risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Findling, 2010[275]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk
Findling, 2011[273]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low 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
Findling, 2019[272]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Frei, 2001[281]	High risk	High risk	Low risk	High risk	High risk	High risk	High risk
Frei, 2005[280]	Low risk	Low risk	Low risk	Low risk	High risk	High risk	High risk
Fuentes, 2013[282]	Moderate/ Unclear risk	High risk	High risk	High risk	Moderate/ Unclear 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	Moderate risk
Gelade, 2017[291]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Geller, 2007[292]	Low risk	Moderate/ Unclear risk	Low risk	Low risk	High risk	High risk	Moderate risk
Gevensleben, 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	Low risk	Low risk	Low risk
Ghanizadeh, 2015[296]	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Gonzalez-Castro, 2016[301]	High risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	High risk
Greenhill, 2006[303]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Greenhill, 2006[302]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Griffiths, 2018[304]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Guevara, 2021[306]	Low risk	High risk	Low risk	High risk	Moderate/ Unclear risk	High risk	Moderate risk
Gustafsson, 2010[308]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Hahn-Markowitz, 2020[310]	Low risk	High risk	Low risk	High risk	Low risk	High risk	High risk
Harfterkamp, 2012[313]	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
Hariri, 2012[314]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Hasslinger, 2021[316]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Hazell, 2003[317]	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Hemamy, 2021[320]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Hervas, 2014[321]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Hirayama, 2014[323]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk
Hiscock, 2019[324]	Low risk	High risk	Low risk	High risk	High risk	Moderate/ Unclear risk	Moderate risk
Hogue, 2020[325]	High risk	Low risk	Low risk	Low risk	High risk	High risk	High risk
Hong, 2016[327]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	High risk	High risk
Hornstra, 2021[328]	High risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	High risk
Huang, 2015[331]	High risk	High risk	Low risk	High risk	Low risk	Low risk	High risk
Huang, 2021[330]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Ichikawa, 2020[333]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Jain, 2011[337]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Jensen, 2007[339]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Low risk	Moderate risk
Johnson, 2009[343]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Johnson, 2020[342]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Johnstone, 2022[344]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Kadri, 2019[347]	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Kahbazi, 2009[348]	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
Karakaya, 2019[350]	Low risk	High risk	Low risk	High risk	Moderate/ Unclear risk	Low risk	High risk
Kareem, 2021[351]	High risk	High risk	Moderate/ Unclear risk	High risk	High risk	High risk	High risk
Katz, 2010[353]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate risk
Kelsey, 2004[354]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Khaksarian, 2021[356]	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Khoshbakht, 2021[358]	Low risk	High risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Kofler, 2020[363]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Kolko, 2020[365]	Low risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Kollins, 2011[368]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	High risk	Moderate/ Unclear risk	Moderate risk
Kollins, 2011[367]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	Moderate risk
Kollins, 2020[366]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate risk
Korfmacher, 2022[369]	Low risk	High risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate risk
Kratochvil, 2002[370]	High risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Kratochvil, 2005[371]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Kratochvil, 2011[372]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Kurowski, 2019[375]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Lange, 2018[376]	Low risk	High risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	High risk
Lavigne, 2011[378]	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate risk
Law, 1999[379]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk

Author, year	Selection bias	Performance bias	Attrition bias	Detection bias	Reporting bias	Other source of bias	Overall RoB
Li, 2022[383]	Low risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	High risk
Liang, 2022[387]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Lilly, 2008[253]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Lim, 2019[390]	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Lin, 2014[391]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Ludyga, 2022[397]	Low risk	High risk	High risk	Moderate/ Unclear risk	Low risk	Low risk	High risk
Luo, 2022[400]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	High risk
Manor, 2012[401]	Low risk	Low risk	High risk	Low risk	Low risk	Moderate/ Unclear risk	High risk
Martenyi, 2010[404]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk
Matthijssen, 2019[408]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Mattingly, 2020[409]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	Moderate risk
McCracken, 2016[415]	Low risk	Low risk	High risk	Low risk	High risk	Moderate/ Unclear risk	Moderate risk
McGrath, 2011[416]	Low risk	Moderate/ Unclear risk	Low risk	Low risk	High risk	Low risk	High risk
Mehri, 2020[418]	Low risk	High risk	Low risk	High risk	Moderate/ Unclear risk	Low risk	High risk
Meyer, 2021[420]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate risk
Michelson, 2001[422]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	High risk	Moderate risk
Michelson, 2002[421]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Minder, 2018[424]	High risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Mohammadi, 2010[427]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Mohammadi, 2012[428]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low 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
Mohammadzadeh, 2019[429]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Montoya, 2009[430]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Mostajeran, 2020[431]	Low risk	High risk	High risk	Moderate/ Unclear risk	Low risk	Low risk	High risk
Motaharifard, 2019[432]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Mount Sinai, 2012[527]	Low risk	Low risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	High risk
Myers, 2015[440]	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	Moderate risk
Nasser, 2020[442]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk
Nasser, 2021[443]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Nasser, 2021[444]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Nasser, 2021[441]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Nejati, 2021[445]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Nejati, 2022[446]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Moderate risk
Newcorn, 2005[449]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Newcorn, 2008[448]	High risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Newcorn, 2016[447]	Low risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	High risk	High risk
NF Coll. Group, 2021[110]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Oppenheimer, 2019[454]	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Low risk	Moderate/ Unclear risk	High risk
Pelham, 2016[52]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	High risk
Pelsser, 2011[460]	Low risk	High risk	Low risk	High risk	Low risk	High risk	High risk
Perez-Alvarez, 2009[462]	High risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear 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
Pfiffner, 2014[464]	Low risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Pongpitakdamrong, 2021[466]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Power, 2012[469]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Prasad, 2007[470]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk
Purper-Ouakil, 2021[472]	Low risk	Low risk	Low risk	High risk	Moderate/ Unclear risk	Low risk	Moderate risk
Qian, 2018[473]	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Qian, 2021[474]	Low risk	High risk	Moderate/ Unclear risk	High risk	Low risk	High risk	High risk
Rafeiy-Torghabeh, 2021[477]	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	Moderate risk
Raghuveer, 2020[478]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Rajabi, 2020[83]	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Riggs, 2011[485]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Rubio Morell, 2019[492]	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Rucklidge, 2018[493]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Saito, 2020[495]	Moderate/ Unclear risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Salardini, 2016[496]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	High risk	High risk	High risk
Salehi, 2010[497]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Salehi, 2016[498]	High risk	Low risk	Moderate/ Unclear risk	Low risk	High risk	High risk	High risk
Sallee, 2009[499]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Sangal, 2006[500]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Sangal, 2014[501]	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
Schorr-Sapir, 2021[508]	Moderate/ Unclear risk	High risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Schramm, 2016[509]	Low risk	High risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	Moderate risk
Schuck, 2018[510]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate risk
Sciberras, 2020[511]	Low risk	High risk	High risk	Moderate/ Unclear risk	Low risk	Low risk	High risk
Shang, 2020[513]	Low risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Shaywitz, 2017[514]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk
Shen, 2021[517]	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate risk
Shuai, 2020[518]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	High risk	Low risk	High risk
Sibley, 2016[521]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Sibley, 2018[519]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Sibley, 2020[522]	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Low risk	Low risk	Moderate risk
Sibley, 2021[520]	Low risk	High risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Siebelink, 2021[523]	Low risk	High risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	High risk
Simonoff, 2013[526]	Low risk	Low risk	Low risk	Low risk	High risk	Moderate/ Unclear risk	Moderate risk
Singer, 1995[528]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Smit, 2021[533]	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Sonuga-Barke, 2001[539]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	Low risk	Moderate risk
Sonuga-Barke, 2004[540]	High risk	High risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	High risk
Sonuga-Barke, 2018[541]	Low risk	High risk	Moderate/ Unclear risk	Low 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
Spencer, 2002[543]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Spencer, 2006[545]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Spencer, 2008[544]	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate risk
Sprich, 2016[548]	Low risk	High risk	Low risk	Low risk	Low risk	High risk	High risk
Steele, 2006[549]	Low risk	Moderate/ Unclear risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	Low risk
Steiner, 2014[550]	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Storebo, 2012[552]	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate risk
Strehl, 2017[554]	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Su, 2016[555]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Supernus Pharmaceuticals, 2016[559]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Svanborg, 2009[560]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Swanson, 2006[561]	Low risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	High risk	Moderate risk
Takahashi, 2009[562]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Tamm, 2017[564]	High risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk	High risk
Tan, 2016[566]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Tiwawatpakorn, 2021[572]	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	High risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Tourette's Syndrome Study Group, 2002[374]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Trebaticka, 2006[573]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Tris Pharma, 2014[575]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low 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
Tzang, 2016[577]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Valero, 2021[581]	Moderate/ Unclear risk	High risk	Low risk	High risk	Low risk	Low risk	High risk
van der Donk, 2015[582]	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk
Van der Heijden, 2007[583]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk
van Stralen, 2020[585]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Volpe, 2009[590]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Wang, 2007[593]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Weber, 2008[596]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Wehmeier, 2012[598]	Moderate/ Unclear risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Weiss, 2005[600]	High risk	Moderate/ Unclear risk	Low risk	Low risk	High risk	High risk	High risk
Weiss, 2007[599]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Weiss, 2021[601]	Low risk	Low risk	High risk	Low risk	High risk	High risk	High risk
Wennberg, 2018[602]	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate risk
Wietecha, 2009[605]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Wigal, 2004[606]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Wigal, 2011[607]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Wilens, 2005[610]	Low risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Wilens, 2008[608]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	High risk	High risk
Wilens, 2012[611]	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk
Wilens, 2015[612]	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate/ Unclear risk	Low risk

Author, year	Selection bias	Performance bias	Attrition bias	Detection bias	Reporting bias	Other source of bias	Overall RoB
Wilens,2011[112]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	High risk	Moderate risk
Wilkes-Gillan, 2016[613]	Low risk	High risk	Low risk	Moderate/ Unclear risk	High risk	High risk	High risk
Willens,2011[609]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk
Wolraich, 2001[615]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk
Wu, 2023[616]	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Low risk	Moderate risk
Young, 2014[622]	Low risk	Low risk	High risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Zarinara, 2010[624]	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Moderate risk
Zavadenko, 2019[625]	Moderate/ Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Zheng, 2020[628]	Moderate/ Unclear risk	High risk	Low risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	High risk
Zhu, 2017[632]	Low risk	Low risk	Moderate/ Unclear risk	Low risk	Moderate/ Unclear risk	Moderate/ Unclear risk	Low risk

Table D.4. Applicability for included studies, KQ2

Author, year	Population	Intervention	Comparator	Outcome	Setting
Abbasi, 2011[111]	N/A	Co-intervention that are likely to modify the effectiveness of therapy	N/A	N/A	N/A
Abikoff, 2004[114]	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[116]	N/A	N/A	N/A	Short-term follow-up	N/A
Abikoff, 2009[115]	More complex patients than typical of the community	N/A	N/A	Other issues	N/A
Abikoff, 2013[113]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Abikoff, 2015[117]	N/A	N/A	N/A	N/A	N/A
Aevi Genomic Medicine, 2016[120]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Aevi Genomic Medicine, 2018[121]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Akhondzadeh, 2004[123]	N/A	As recommended or commonly used in practice	N/A	N/A	N/A
Allen, 2005[125]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Amiri, 2008[129]	N/A	N/A	N/A	N/A	N/A
Arnold, 2022[132]	N/A	Unclear	N/A	N/A	N/A
Ashkenasi, 2011[133]	N/A	N/A	N/A	N/A	N/A
Bakhshayesh, 2011[136]	N/A	N/A	N/A	N/A	N/A
Banaschewski, 2013[137]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Bangs, 2007[138]	N/A	N/A	N/A	N/A	N/A
Bangs, 2008[139]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Barrickman, 1995[142]	DSM-4/5 diagnosis unclear	N/A	N/A	N/A	N/A
Baziar, 2019[143]	N/A	N/A	N/A	N/A	N/A
Bedard, 2015[144]	N/A	N/A	N/A	N/A	N/A
Behdani, 2013[145]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Benzing, 2019[146]	N/A	N/A	N/A	N/A	N/A
Biederman, 2005[155]	N/A	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Biederman, 2006[154]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Biederman, 2007[152]	N/A	N/A	N/A	N/A	N/A
Biederman, 2008[153]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Bigorra, 2016[156]	N/A	N/A	N/A	N/A	N/A
Bikic, 2018[59]	N/A	N/A	N/A	N/A	N/A
Bilici, 2004[157]	N/A	N/A	N/A	N/A	N/A
Binesh, 2020[158]	N/A	N/A	N/A	Unclear	N/A
Blader, 2021[159]	Narrow eligibility criteria	Co-intervention that are likely to modify the effectiveness of therapy	Comparator unclear	Short-term follow-up	Unclear
Block, 2009[162]	N/A	N/A	N/A	N/A	N/A
Blumer, 2009[163]	N/A	N/A	N/A	N/A	N/A
Bluschke, 2022[164]	DSM-4/5 diagnosis unclear	Co-intervention that are likely to modify the effectiveness of therapy	Unclear	N/A	N/A
Bostic, 2000[166]	N/A	N/A	N/A	Short-term follow-up	N/A
Boyer, 2016[168]	N/A	N/A	N/A	N/A	N/A
Brams, 2018[169]	N/A	N/A	N/A	Short-term follow-up	N/A
Breaux, 2018[171]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Buitelaar, 1996[173]	N/A	N/A	N/A	N/A	N/A
Buitelaar, 2007[172]	N/A	N/A	N/A	N/A	N/A
Bul, 2016[174]	N/A	N/A	N/A	N/A	Unclear
Ceresoli-Borroni, 2021[182]	N/A	N/A	N/A	N/A	N/A
Cetin, 2015[183]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Chacko, 2009[184]	N/A	N/A	N/A	N/A	N/A
Chang, 2019[186]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Childress, 2009[199]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Childress, 2019[197]	N/A	N/A	N/A	Short-term follow-up	Level of care different from that in the community
Childress, 2022[198]	N/A	N/A	N/A	N/A	N/A
Cho, 2011[200]	N/A	Unclear	N/A	Short-term follow-up	N/A
Chu, 2021[203]	N/A	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Churchill, 2018[204]	N/A	Highly selected intervention team or level of training/proficiency not widely available	Comparator unclear	N/A	N/A
Coelho, 2017[205]	N/A	N/A	N/A	N/A	N/A
Coghill, 2014[206]	N/A	N/A	N/A	N/A	N/A
Coles, 2020[208]	N/A	N/A	N/A	N/A	N/A
Concordia Pharmaceuticals, 2011[209]	N/A	Unclear	N/A	N/A	N/A
Conners, 1996[210]	N/A	Unclear	N/A	Other issues	N/A
Connor, 2010[211]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Corkum, 2019[213]	DSM-4/5 diagnosis unclear	Co-intervention that are likely to modify the effectiveness of therapy	Unclear	Short-term follow-up	N/A
Corkum, 2020[212]	N/A	N/A	N/A	N/A	N/A
Cornu, 2018[214]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Crippa, 2019[216]	N/A	N/A	N/A	N/A	N/A
Dashbozorgi, 2021[219]	N/A	N/A	N/A	Short-term follow-up	N/A
David, 2021[220]	N/A	N/A	N/A	N/A	N/A
Daviss, 2008[221]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Dehbozorghi, 2019[223]	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[224]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Denton, 2020[225]	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[226]	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
Diamond, 1999[228]	DSM-4/5 diagnosis unclear	As recommended or commonly used in practice	N/A	Other issues	N/A
Dittmann, 2011[231]	N/A	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Dittmann, 2013[230]	N/A	N/A	Comparator unclear	N/A	N/A
Dong, 2022[232]	N/A	Unclear	N/A	N/A	N/A
Dose, 2017[233]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Dovis, 2015[234]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Dreakhshanpour, 2022[237]	N/A	N/A	N/A	N/A	N/A
Duke University, 2009[578]	N/A	Dosing not reflective of current practice	N/A	Unclear	N/A
DuPaul, 2021[242]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Durgut, 2020[243]	N/A	Unclear	N/A	Unclear	N/A
Duric, 2017[244]	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[247]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Eli Lilly, 2004[389]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Eli Lilly, 2006[251]	N/A	N/A	N/A	N/A	N/A
Eli Lilly[252]	N/A	N/A	N/A	N/A	N/A
Elmaadawi, 2022[255]	N/A	Highly selected intervention team or level of training/proficiency not widely available	N/A	Other issues	N/A
Enns, 2017 [257]	N/A	Unclear	Unclear	Other issues	N/A
Epstein, 2007[259]	N/A	Unclear	N/A	N/A	N/A
Epstein, 2016[258]	N/A	N/A	N/A	N/A	N/A
Ercan, 2014[260]	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[261]	N/A	N/A	N/A	Short-term follow-up	Level of care different from that in the community
Evans, 2016[262]	N/A	N/A	N/A	N/A	N/A
Fabiano, 2016[264]	N/A	N/A	N/A	Other issues	N/A
Fallah, 2018[265]	More complex patients than	N/A	N/A	Unclear	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
	typical of the community				
Farmer, 2017[267]	N/A	N/A	N/A	N/A	N/A
Ferrin, 2014[268]	N/A	N/A	N/A	N/A	N/A
Ferrin, 2020[269]	N/A	N/A	N/A	N/A	N/A
Findling, 2001[274]	DSM-4/5 diagnosis unclear	N/A	N/A	N/A	N/A
Findling, 2008[276]	N/A	N/A	N/A	N/A	N/A
Findling, 2010[275]	Narrow eligibility criteria	As recommended or commonly used in practice	N/A	N/A	N/A
Findling, 2011[273]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Findling, 2019[272]	N/A	N/A	N/A	N/A	N/A
Frei, 2001[281]	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[280]	Run-in period with high exclusion rate	N/A	N/A	N/A	N/A
Fuentes, 2013[282]	N/A	Co-intervention that are likely to modify the effectiveness of therapy	N/A	Other issues	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
Ghanizadeh, 2015[296]	N/A	Dosing not reflective of current practice	N/A	N/A	N/A
Gonzalez-Castro, 2016[301]	N/A	N/A	N/A	Other issues	N/A
Greenhill, 2006[303]	Narrow eligibility criteria	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Greenhill, 2006[302]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Griffiths, 2018[304]	N/A	N/A	N/A	N/A	N/A
Guevara, 2021[306]	DSM-4/5 diagnosis unclear	N/A	N/A	N/A	N/A
Gustafsson, 2010[308]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Hahn-Markowitz, 2020[310]	N/A	N/A	N/A	N/A	N/A
Harfterkamp, 2012[313]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Hariri, 2012[314]	DSM-4/5 diagnosis unclear	Co-intervention that are likely to modify the effectiveness of therapy	N/A	Unclear	N/A
Hasslinger, 2021[316]	N/A	N/A	N/A	N/A	N/A
Hazell, 2003[317]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Hemamy, 2021[320]	N/A	Dosing not reflective of current practice	N/A	Short-term follow-up	N/A
Hervas, 2014[321]	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[323]	N/A	N/A	N/A	N/A	N/A
Hiscock, 2019[324]	N/A	N/A	N/A	N/A	N/A
Hogue, 2020[325]	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[327]	N/A	Unclear	Unclear	Unclear	N/A
Hornstra, 2021[328]	N/A	N/A	N/A	N/A	N/A
Huang, 2015[331]	N/A	N/A	N/A	N/A	N/A
Huang, 2021[330]	N/A	N/A	Comparator unclear	N/A	N/A
Ichikawa, 2020[333]	N/A	N/A	N/A	N/A	N/A
Jain, 2011[337]	N/A	N/A	N/A	N/A	N/A
Jensen, 2007[339]	Unclear	N/A	N/A	N/A	N/A
Johnson, 2009[343]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Johnson, 2020[342]	N/A	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Johnstone, 2022[344]	N/A	N/A	N/A	N/A	N/A
Kadri, 2019[347]	DSM-4/5 diagnosis unclear	N/A	N/A	N/A	N/A
Kahbazi, 2009[348]	N/A	N/A	N/A	N/A	N/A
Karakaya, 2019[350]	N/A	N/A	N/A	N/A	N/A
Kareem, 2021[351]	DSM-4/5 diagnosis unclear	N/A	N/A	Other issues	N/A
Katz, 2010[353]	N/A	N/A	N/A	Unclear	N/A
Kelsey, 2004[354]	N/A	N/A	N/A	N/A	N/A
Khaksarian, 2021[356]	N/A	N/A	N/A	N/A	N/A
Khoshbakht, 2021[358]	N/A	N/A	N/A	N/A	N/A
Kofler, 2020[363]	N/A	N/A	N/A	N/A	N/A
Kolko, 2020[365]	Unclear	N/A	Comparator unclear	N/A	N/A
Kollins, 2011[368]	N/A	N/A	N/A	N/A	N/A
Kollins, 2011[367]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Kollins, 2020[366]	Narrow eligibility criteria	N/A	N/A	Short-term follow-up	N/A
Korfmacher, 2022[369]	N/A	Co-intervention that are likely to modify the effectiveness of therapy	N/A	N/A	N/A
Kratochvil, 2002[370]	N/A	N/A	N/A	N/A	N/A
Kratochvil, 2005[371]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Kratochvil, 2011[372]	N/A	N/A	N/A	N/A	N/A
Kurowski, 2019[375]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Lange, 2018[376]	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[378]	N/A	N/A	N/A	N/A	N/A
Law, 1999[379]	Unclear	As recommended or commonly used in practice	N/A	Other issues	N/A
Li, 2022[383]	Narrow eligibility criteria	Unclear	N/A	N/A	N/A
Liang, 2022[387]	N/A	N/A	N/A	N/A	N/A
Lilly, 2008[253]	N/A	N/A	Unclear	N/A	N/A
Lim, 2019[390]	N/A	N/A	N/A	N/A	N/A
Lin, 2014[391]	N/A	N/A	N/A	Short-term follow-up	N/A
Ludyga, 2022[397]	N/A	Highly selected intervention team or level of training/proficiency	N/A	Other issues	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
		not widely available			
Luo, 2022[400]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Manor, 2012[401]	Narrow eligibility criteria	N/A	N/A	Unclear	N/A
Martenyi, 2010[404]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Matthijssen, 2019[408]	N/A	N/A	N/A	N/A	N/A
Mattingly, 2020[409]	N/A	N/A	N/A	Short-term follow-up	N/A
McCracken, 2016[415]	N/A	N/A	Comparator unclear	Short-term follow-up	N/A
McGrath, 2011[416]	N/A	N/A	N/A	Unclear	N/A
Mehri, 2020[418]	More complex patients than typical of the community	N/A	N/A	Unclear	N/A
Meyer, 2021[420]	N/A	N/A	N/A	N/A	N/A
Michelson, 2001[422]	N/A	N/A	N/A	N/A	N/A
Michelson, 2002[421]	N/A	N/A	N/A	N/A	N/A
Minder, 2018[424]	N/A	N/A	N/A	N/A	N/A
Mohammadi, 2010[427]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Mohammadi, 2012[428]	N/A	N/A	N/A	N/A	N/A
Mohammadzadeh, 2019[429]	N/A	N/A	N/A	N/A	N/A
Montoya, 2009[430]	N/A	N/A	N/A	N/A	N/A
Mostajeran, 2020[431]	N/A	N/A	N/A	N/A	N/A
Motaharifard, 2019[432]	Narrow eligibility criteria	As recommended or commonly used in practice	Comparator unclear	Short-term follow-up	Unclear
Mount Sinai, 2012[527]	DSM-4/5 diagnosis unclear	N/A	N/A	Short-term follow-up	N/A
Myers, 2015[440]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Nasser, 2020[442]	N/A	N/A	N/A	N/A	N/A
Nasser, 2021[443]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Nasser, 2021[444]	N/A	N/A	N/A	N/A	N/A
Nasser, 2021[441]	N/A	N/A	N/A	N/A	N/A
Nejati, 2021[445]	N/A	Unclear	N/A	N/A	N/A
Nejati, 2022[446]	N/A	N/A	N/A	N/A	N/A
Newcorn, 2005[449]	Narrow eligibility criteria	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Newcorn, 2008[448]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Newcorn, 2016[447]	N/A	N/A	N/A	N/A	N/A
NF Coll. Group, 2021[110]	N/A	N/A	N/A	N/A	N/A
Oppenheimer, 2019[454]	N/A	N/A	Comparator unclear	Short-term follow-up	N/A
Pelham, 2016[52]	N/A	Co-intervention that are likely to modify the effectiveness of therapy	N/A	N/A	N/A
Pelsser, 2011[460]	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[462]	Narrow eligibility criteria	N/A	N/A	Other issues	N/A
Pfiffner, 2014[464]	N/A	N/A	N/A	N/A	N/A
Pongpitakdamrong, 2021[466]	N/A	N/A	N/A	N/A	N/A
Power, 2012[469]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Prasad, 2007[470]	N/A	N/A	N/A	N/A	N/A
Purper-Ouakil, 2021[472]	N/A	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	N/A
Qian, 2018[473]	N/A	N/A	N/A	N/A	N/A
Qian, 2021[474]	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[477]	N/A	N/A	N/A	N/A	Unclear
Raghuveer, 2020[478]	N/A	Unclear	N/A	N/A	N/A
Rajabi, 2020[83]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Riggs, 2011[485]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Rubio Morell, 2019[492]	N/A	N/A	N/A	N/A	N/A
Rucklidge, 2018[493]	N/A	N/A	N/A	N/A	N/A
Saito, 2020[495]	N/A	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Salardini, 2016[496]	N/A	N/A	N/A	Short-term follow-up	N/A
Salehi, 2010[497]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Salehi, 2016[498]	Narrow eligibility criteria	N/A	N/A	Other issues	N/A
Sallee, 2009[499]	N/A	N/A	N/A	N/A	N/A
Sangal, 2006[500]	N/A	N/A	N/A	N/A	N/A
Sangal, 2014[501]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Schorr-Sapir, 2021[508]	N/A	Highly selected intervention team or level of training/proficiency not widely available	Unclear	Short-term follow-up	N/A
Schramm, 2016[509]	N/A	N/A	N/A	N/A	N/A
Schuck, 2018[510]	N/A	N/A	N/A	N/A	N/A
Sciberras, 2020[511]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Shang, 2020[513]	N/A	N/A	N/A	Unclear	N/A
Shaywitz, 2017[514]	More complex patients than typical of the community	As recommended or commonly used in practice	N/A	N/A	Unclear
Shen, 2021[517]	N/A	N/A	N/A	N/A	N/A
Shuai, 2020[518]	Narrow eligibility criteria	N/A	N/A	Short-term follow-up	N/A
Sibley, 2016[521]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Sibley, 2018[519]	N/A	N/A	N/A	N/A	N/A
Sibley, 2020[522]	N/A	N/A	Comparator unclear	N/A	N/A
Sibley, 2021[520]	N/A	N/A	N/A	N/A	N/A
Siebelink, 2021[523]	N/A	N/A	N/A	N/A	N/A
Simonoff, 2013[526]	DSM-4/5 diagnosis unclear	N/A	N/A	Short-term follow-up	N/A
Singer, 1995[528]	N/A	N/A	N/A	N/A	N/A
Smit, 2021[533]	More complex patients than typical of the community	N/A	N/A	N/A	N/A

Author, year	Population	Intervention	Comparator	Outcome	Setting
Sonuga-Barke, 2001[539]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Sonuga-Barke, 2004[540]	DSM-4/5 diagnosis unclear	N/A	N/A	Unclear	N/A
Sonuga-Barke, 2018[541]	N/A	N/A	N/A	N/A	N/A
Spencer, 2002[543]	N/A	N/A	N/A	N/A	N/A
Spencer, 2006[545]	N/A	N/A	N/A	N/A	N/A
Spencer, 2008[544]	N/A	N/A	Comparator unclear	Short-term follow-up	N/A
Sprich, 2016[548]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Steele, 2006[549]	N/A	As recommended or commonly used in practice	Comparator unclear	Short-term follow-up	N/A
Steiner, 2014[550]	N/A	N/A	N/A	N/A	N/A
Storebo, 2012[552]	N/A	N/A	N/A	N/A	N/A
Strehl, 2017[554]	N/A	N/A	N/A	N/A	Level of care different from that in the community
Su, 2016[555]	N/A	N/A	N/A	N/A	N/A
Supernus Pharmaceuticals, 2016[559]	More complex patients than typical of the community	Unclear	N/A	N/A	N/A
Svanborg, 2009[560]	N/A	N/A	Comparator unclear	N/A	N/A
Swanson, 2006[561]	N/A	N/A	N/A	N/A	N/A
Takahashi, 2009[562]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Tamm, 2017[564]	More complex patients than typical of the community	N/A	N/A	N/A	N/A
Tan, 2016[566]	N/A	N/A	N/A	N/A	N/A
Tiwawatpakorn, 2021[572]	DSM-4/5 diagnosis unclear	N/A	N/A	N/A	N/A
Tourette's Syndrome Study Group, 2002[374]	N/A	N/A	N/A	N/A	N/A
Trebaticka, 2006[573]	Unclear	N/A	N/A	Other issues	N/A
Tris Pharma, 2014[575]	Unclear	Unclear	Unclear	Unclear	Unclear
Tzang, 2016[577]	Narrow eligibility criteria	As recommended or commonly used in practice	N/A	Short-term follow-up	N/A
Valero, 2021[581]	N/A	N/A	N/A	N/A	N/A
van der Donk, 2015[582]	More complex patients than typical of the community	N/A	N/A	N/A	Unclear

Author, year	Population	Intervention	Comparator	Outcome	Setting
Van der Heijden, 2007[583]	More complex patients than typical of the community	As recommended or commonly used in practice	N/A	N/A	N/A
van Stralen, 2020[585]	N/A	N/A	N/A	N/A	N/A
Volpe, 2009[590]	More complex patients than typical of the community	N/A	N/A	Unclear	N/A
Wang, 2007[593]	N/A	Dosing not reflective of current practice	N/A	N/A	N/A
Weber, 2008[596]	N/A	N/A	N/A	N/A	N/A
Wehmeier, 2012[598]	N/A	N/A	N/A	N/A	N/A
Weiss, 2005[600]	N/A	N/A	N/A	Short-term follow-up	Unclear
Weiss, 2007[599]	N/A	N/A	N/A	N/A	N/A
Weiss, 2021[601]	N/A	N/A	N/A	Short-term follow-up	N/A
Wennberg, 2018[602]	Unclear	Highly selected intervention team or level of training/proficiency not widely available	N/A	N/A	Unclear
Wietecha, 2009[605]	Narrow eligibility criteria	N/A	Unclear	N/A	N/A
Wigal, 2004[606]	N/A	N/A	N/A	N/A	N/A
Wigal, 2011[607]	N/A	N/A	N/A	N/A	N/A
Wilens, 2005[610]	N/A	N/A	N/A	Short-term follow-up	N/A
Wilens, 2008[608]	N/A	N/A	N/A	N/A	N/A
Wilens, 2012[611]	N/A	N/A	N/A	N/A	N/A
Wilens, 2015[612]	Narrow eligibility criteria	As recommended or commonly used in practice	N/A	N/A	N/A
Wilens,2011[112]	N/A	N/A	N/A	N/A	Unclear
Wilkes-Gillan, 2016[613]	More complex patients than typical of the community	N/A	N/A	Unclear	N/A
Willens,2011[609]	Narrow eligibility criteria	As recommended or commonly used in practice	N/A	Unclear	Level of care different from that in the community
Wolraich, 2001[615]	N/A	N/A	N/A	N/A	N/A
Wu, 2023[616]	Narrow eligibility criteria	N/A	N/A	N/A	N/A
Young, 2014[622]	Narrow eligibility criteria	Dosing not reflective of current practice	Inadequate comparison therapy or use of a substandard	N/A	Unclear

Author, year	Population	Intervention	Comparator	Outcome	Setting
			alternative therapy		
Zarinara, 2010[624]	N/A	N/A	N/A	N/A	N/A
Zavadenko, 2019[625]	N/A	N/A	Unclear	Unclear	Unclear
Zheng, 2020[628]	Narrow eligibility criteria	N/A	N/A	Short-term follow-up	N/A
Zhu, 2017[632]	N/A	N/A	N/A	N/A	Unclear

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[181]	Moderate/Unclear risk	Moderate/Unclear risk	High risk	High risk	Low risk	Moderate/Unclear risk	Low risk
Cohen, 1989[207]	Moderate/Unclear risk	Moderate/Unclear risk	High risk	Moderate/Unclear risk	Moderate/Unclear risk	Moderate/Unclear risk	Moderate risk
Epstein, 2007[259]	Moderate/Unclear risk	Moderate/Unclear risk	Moderate/Unclear risk	Moderate/Unclear risk	Moderate/Unclear risk	Low risk	Moderate risk
Epstein, 2016[258]	Moderate/Unclear risk	Moderate/Unclear risk	Moderate/Unclear risk	Moderate/Unclear risk	Moderate/Unclear risk	High risk	Moderate risk
Fiks, 2017[271]	Moderate/Unclear risk	High risk	Moderate/Unclear risk	Moderate/Unclear risk	Moderate/Unclear risk	High risk	Moderate risk
Florida International University, 2010[277]	High risk	High risk	Moderate/Unclear risk	High risk	Moderate/Unclear risk	Moderate/Unclear risk	Moderate risk
Oppenheimer, 2019[454]	High risk	Moderate/Unclear risk	Moderate/Unclear risk	High risk	Low risk	Moderate/Unclear risk	High risk
Smith, 2000[534]	Moderate/Unclear risk	Low risk	Moderate/Unclear risk	Low risk	High risk	Moderate/Unclear risk	Moderate risk
Yang, 2012[617]	Moderate/Unclear risk	Moderate/Unclear risk	Moderate/Unclear risk	Moderate/Unclear risk	Moderate/Unclear risk	High risk	High risk

Table D.6. Applicability for included studies, KQ3

Author, year	Population	Intervention	Comparator	Outcome	Setting
Cedergren, 2021[181]	N/A	As recommended or commonly used in practice	N/A	N/A	N/A
Cohen, 1989[207]	N/A	Co-intervention that are likely to modify monitoring strategies	N/A	Short-term follow-up	N/A
Epstein, 2007[259]	N/A	unclear	N/A	N/A	N/A
Epstein, 2016[258]	N/A	N/A	N/A	N/A	N/A
Fiks, 2017[271]	N/A	As recommended or commonly used in practice	N/A	Composite outcomes that mix outcomes of different significance	N/A
Florida International University, 2010[277]	Narrow eligibility criteria and exclusion of those with comorbidities	Dosing not reflective of current practice	N/A	N/A	N/A
Oppenheimer, 2019[454]	N/A	N/A	Comparator unclear	Short-term follow-up	N/A
Smith, 2000[534]	N/A	Dosing not reflective of current practice	N/A	Short-term follow-up	Level of care different from that in the community
Yang, 2012[617]	More complex patients than typical of the community	As recommended or commonly used in practice	N/A	N/A	Level of care different from that in the community

Appendix E. Expert Guidance and Review

Stakeholder Input in Formulating the Research Protocol

Stakeholders, participated in a virtual workshop by PCORI in November 2021 to discuss 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.

Stakeholders in the workshop represented different viewpoints which included patients, patient advocates, clinicians, guideline developers and researches.

During the virtual workshop, stakeholders 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.

Stakeholders 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 F. PCORI Checklist

To be added for the final report