Comparative Effectiveness Review
Number 267

ADHD Diagnosis and Treatment in Children and Adolescents

Executive Summary

Main Points

Diagnosis

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

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Treatment

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

Monitoring

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

Background and Purpose

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

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

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

Methods

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

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

Results

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

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

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

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

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

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

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

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

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

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

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

Strengths and Limitations

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

Implications and Conclusions

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

References

1. Kemper AR, Maslow GR, Hill S, et al. Attention Deficit Hyperactivity Disorder: Diagnosis and Treatment in Children and Adolescents. Comparative Effectiveness Review No. 203. (Prepared by the Duke University Evidence-based Practice Center under Contract No. 290-2015-00004-I.) AHRQ Publication No. 18-EHC005-EF Agency for Healthcare Research and Quality (US). Rockville (MD): 2018. https://www.ncbi.nlm.nih.gov/pubmed/29558081
2. Jadad AR, Boyle M, Cunningham C, et al. Treatment of attention-deficit/hyperactivity disorder. Evid Rep Technol Assess (Summ). 1999 Nov(11):i-viii, 1-341. PMID: 10790990.
3. Charach A, Dashti B, Carson P, et al. Attention Deficit Hyperactivity Disorder: Effectiveness of Treatment in At-Risk Preschoolers; Long-Term Effectiveness in All Ages; and Variability in Prevalence, Diagnosis, and Treatment. Compartative Effectiveness Review No. 44 (Prepared by the McMaster University Evidence-based Practice Center under Contract No. MME2202 290-02-0020.) AHRQ Publication No. 12-EHC003-EF Agency for Healthcare Research and Quality Rockville, MD: Oct Preschoolers; Long-Term Effectiveness in All Ages; and Variability in Prevalence, Diagnosis, and Treatment October 2011. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=22191110
4. Agency for Healthcare Research and Quality. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. Rockville (MD); 2008.

Full Report

Peterson BS, Trampush J, Maglione M, Bolshakova M, Brown M, Rozelle M, Motala A, Yagyu S, Miles J, Pakdaman S, Gastelum M, Nguyen BT, Tokutomi E, Lee E, Belay JZ, Schaefer C, Coughlin B, Celosse K, Molakalapalli S, Shaw B, Sazmin T, Onyekwuluje AN, Tolentino D, Hempel S. ADHD Diagnosis and Treatment in Children and Adolescents. Comparative Effectiveness Review No. 267. (Prepared by the Southern California Evidence-based Practice Center under Contract No. 75Q80120D00009.) AHRQ Publication No. 24-EHC003. PCORI Publication No. 2023-SR-03. Rockville, MD: Agency for Healthcare Research and Quality; March 2024. DOI: https://doi.org/10.23970/AHRQEPCCER267.
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