Original Research Article

Early Methylphenidate Intervention and Behavioral Outcomes in ADHD: A Systematic Review

Hannah Chaze

Department of Integrative Biology, College of Public Health, University of South Florida, Tampa, FL, United States

ABSTRACT

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder characterized by patterns of inattentiveness, hyperactivity, and impulsivity that impact individuals' daily functioning. Individuals with ADHD typically struggle with focusing on tasks, controlling impulsivity, maintaining high self-esteem, doing well in school, and maintaining social relationships. Methylphenidate (MPH) is used to treat ADHD by working in the central nervous system with neurotransmitters to reduce the symptoms that cause inattentiveness, hyperactivity, and impulsivity. To evaluate its effectiveness, we conducted a PRISMA-guided systematic review, covering 9 studies with a total of 823 patients treated with methylphenidate and 827 age-matched controls, employing data collection of phenotypic description, noticeable drug-related improvements, and behavioral modifications. Treatment with methylphenidate was associated with increased attention and processing speed, along with decreased behavioral issues, inattention, and impulsivity, increased quality of life, and increased processing speed with methylphenidate treatment. Additionally, MPH treatment resolved behavioral issues in all studies with behavioral testing, but there were differences in the behavioral tests performed. A limitation highlighted in the review is that studies evaluating MPH in patient populations demonstrate a sex imbalance in ADHD treatment cohorts, potentially limiting generalizability. These findings suggest that ADHD treatment with MPH decreases impulsive behaviors and increases attention and quality of life in a mostly male patient population.

Keywords: ADHD; methylphenidate; early intervention; behavior tests; impulsivity

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is a common mental disorder impacting an individual's ability to focus, increasing excessive movement (hyperactivity), and increasing impulsivity (1). In children, ADHD additionally impacts interpersonal relationships, leading to misunderstandings, conflict, and social skill deficits (2). Individuals with ADHD may struggle with communication, social cue interpretation, and stable relationships, impacting school and home life. Understanding how ADHD presents itself in its various forms is important, as symptoms vary depending on the type of ADHD an individual has. There are three variations of ADHD, which include predominantly inattentive, predominantly hyperactive and impulsive, or a combination of both (2). Predominantly inattentive ADHD is characterized by difficulty focusing, while predominantly hyperactive and impulsive ADHD involves excessive activity and impulsive decision-making (2). The combined type includes symptoms of both inattentive and hyperactive-impulsive presentations (2).

Corresponding author: Hannah Chaze, E-mail: chazehec@gmail.com.

Accepted July 8, 2026
https://doi.org/10.70251/HYJR2348.44221230

The diagnosis of ADHD is critical to ensure higher levels of educational attainment (3). When ADHD is left untreated, it can create a psychological, financial, social, and academic burden (3). Untreated ADHD during childhood poses a risk for mental health issues during adulthood, extending educational impairment, and increasing the risk for comorbid disorders such as anxiety, depression, antisocial disorders, and personality disorders (3). According to the DSM-5, ADHD is diagnosed as "A persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development."

Rates of ADHD differ across sex, race, and ethnicity. CDC findings from 2024 demonstrate that biological boys are 7% more likely to be diagnosed with ADHD than biological girls. The data also shows that Black and White children are diagnosed 8% more often than Asian children, and American Indian and Alaska Native children are diagnosed 6% more often than Asian children. A 2022 parent survey reported that approximately 7 million U.S. children aged 3-17-about 11.4%- have received an ADHD diagnosis (4). Additionally, annual medical costs for children taking ADHD medication were found to range from $503 to $1,343 (5). Beyond the high cost, ADHD is often complicated by comorbid conditions.

ADHD often coexists with conditions such as behavioral or conduct problems, depression, anxiety, other learning disabilities, developmental delay, speech/language disorder, autism spectrum disorder, and intellectual disability. As children with ADHD become adolescents, the rates of anxiety and depression experience an increase, while behavioral and developmental delays experience a decrease as time goes on. As a result of comorbidities changing over time, treating multiple co-occurring disorders can be particularly challenging.

Treatment for ADHD involves a combination of medical intervention and behavioral interventions. The pharmacological treatments available are non-stimulant and stimulant medications. Stimulants, such as methylphenidate, work to block the reuptake of the neurotransmitter's dopamine and norepinephrine, allowing for the chemicals to linger in the synapse to prolong the effects (6). Non-stimulant medications are used to target the chemicals of norepinephrine and dopamine to improve attention while reducing hyperactivity. Non-stimulant medications are prescribed as a second-line treatment, while the stimulant medication is prescribed initially. Non-stimulants are also more reliable when it comes to a patient having underlying health conditions; the stimulant medication may exacerbate the underlying health condition. (7).

The medications differ in formulation, with one key distinction being the difference between immediate-release (IR) and extended-release (ER) tablets. Immediate-release tablets provide the full dose of the medication immediately after it is ingested; most IR tablets require multiple doses throughout the day to reach full effectiveness. Extended-release tablets prolong the medicine's effect in the body, ultimately reducing the number of daily doses (8).

Other non-pharmacological interventions, such as behavioral therapy, psychotherapy, social skills training, and support groups, are used to treat ADHD. Behavior therapy teaches the parents/guardians skills to manage the child's behavior, while psychotherapy focuses on play and talk therapy for younger children to process emotions, social skills training to teach children with ADHD how to act in social settings to control their compulsions and impulsiveness, and support groups to provide a community that shares experience and advice (9).

Methyl α-phenyl-α-(2-piperidyl) acetate (methylphenidate) is a medication used to treat ADHD and belongs to the drug classification of central nervous system stimulants (10) (Figure 2A). Methylphenidate increases attention span and decreases restlessness in ADHD patients who can't concentrate for long periods of time, are overactive, and get distracted easily (10). Early intervention with methylphenidate helps children manage symptoms, leading to improved family life, higher self-esteem, and better academic performance (11). Methylphenidate is also involved in a series of metabolic pathways to produce ritalinic acid and methylphenidate, which is created when methylphenidate has been metabolized in the body (Figure 2B). Support for early intervention is strengthened by evidence demonstrating that among children aged 3 to 17, 44.1% experienced behavioral or conduct problems and 21.7% exhibited early developmental delays (Figure 1).

Methylphenidate serves to effectively block the reuptake of the neurotransmitter's norepinephrine and dopamine in the presynaptic neurons to inhibit these neurotransmitters by increasing the concentration of norepinephrine in the synaptic cleft (12). This then leads to the prefrontal cortex receiving a larger stimulant activation (12). In children, the bioavailability for extended-release tablets is 105% (12). Suggesting that the methylphenidate being administered to children is being fully absorbed and utilized by the child.

Understanding ADHD in children is important for

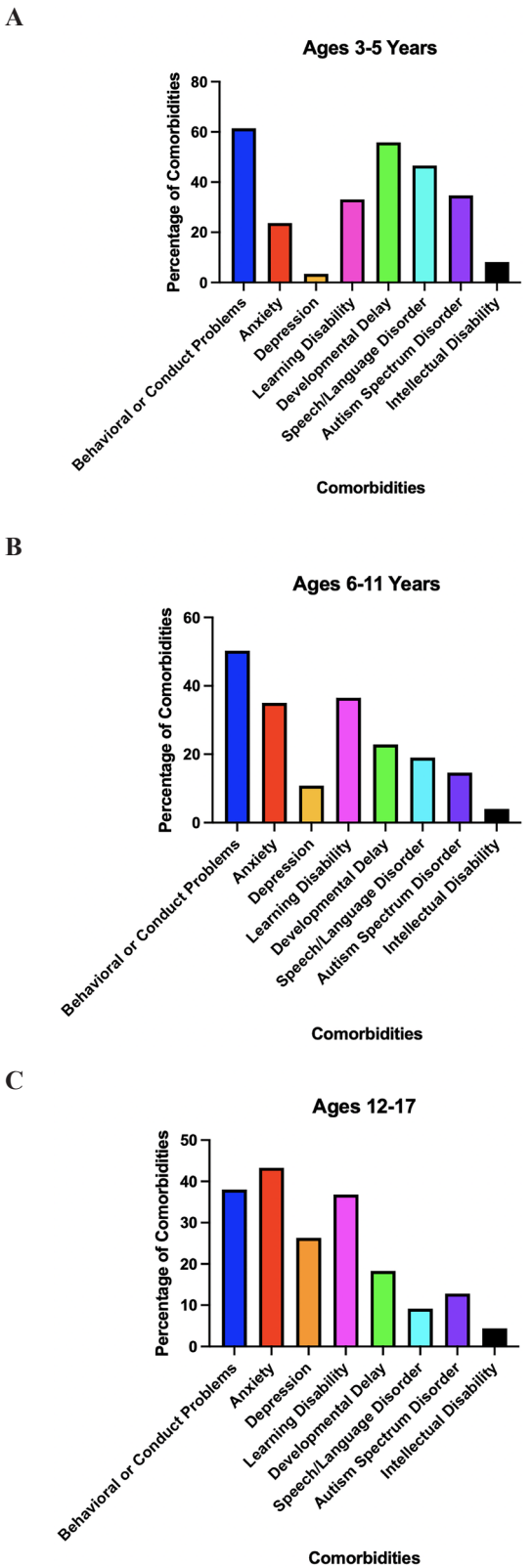

Figure 1. Comorbidities of ADHD. *Bar chart depicting co-occurring conditions with ADHD in adolescents (4).*

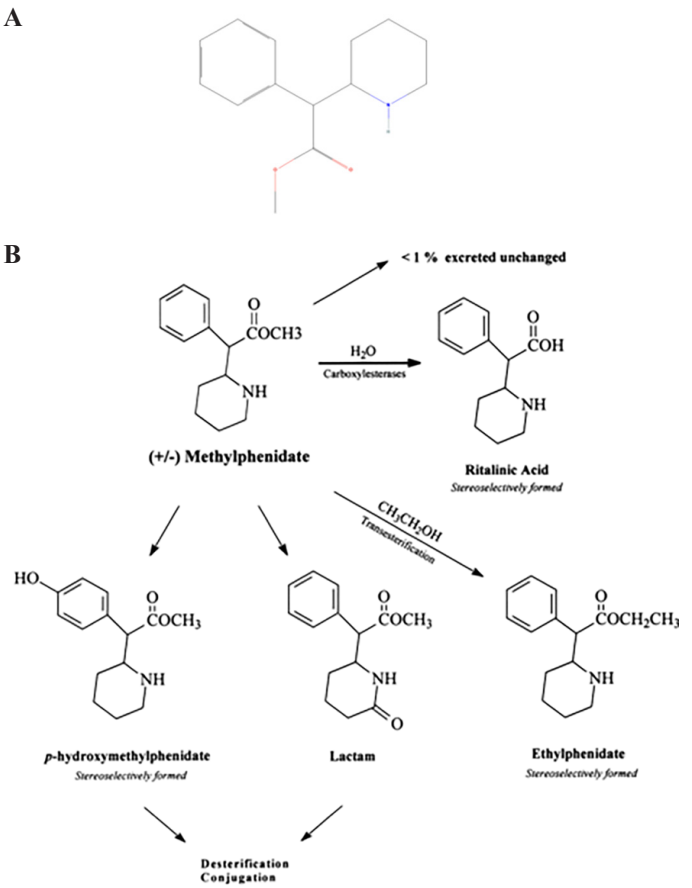

Figure 2. Chemical structure and metabolic pathways of methylphenidate. *(A) Chemical structure of methylphenidate, methyl α-phenyl-α-(2-piperidyl)acetate ($C_{14}H_{19}NO_2$). (B) Major metabolic pathways of methylphenidate in humans (32).*

improving early diagnosis. Medication management through Methylphenidate is important to the treatment of ADHD in adolescents. This systematic review investigates the clinical relevance of methylphenidate clinical trials performed in children, investigating the efficacy of early intervention.

METHODS AND MATERIALS

A systematic review was performed according to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (13). Our research exclusively utilized anonymized data, with no collection of personal information or involvement of human subjects. The study protocol was not registered. Standard protocol approvals, registration, and patient consents do not apply to this review.

Data sources and search strategy

A data search was performed, a thorough search for relevant articles using specific search terms related to ADHD and Early intervention treatment with methylphenidate. The search was conducted utilizing (PUBMED) and covered articles published from the inception of the database until September 1, 2025. The search terms we used included combinations of "methylphenidate" and "ADHD" and ("early intervention" OR "first treatment" or "Early treatment"). A manual examination of the reference lists of eligible studies was conducted through literature reviews to identify suitable studies for inclusion. Any discrepancies in the selection of articles were resolved through discussions. The comprehensive search strategy can be accessed in Figure 3.

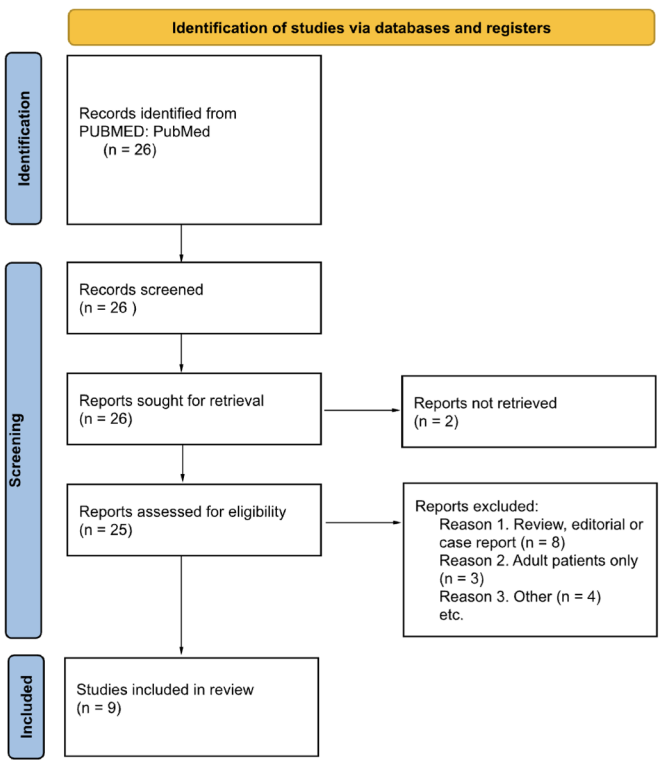

Figure 3. *PRISMA flow diagram showing the study selection process. A total of 26 records were identified through database searches. After searching for duplicates, 26 records were screened, and 25 records were assessed for eligibility. Studies were excluded based on the predefined inclusion and exclusion criteria, including a review, editorial, case report, adult patients only, and others. Ultimately, 9 studies were included in the systematic review.*

Eligibility criteria

The eligible studies included in our analysis focused on ADHD diagnosis and early treatment with methylphenidate. To be included in the review, the studies must have included children who were treated with methylphenidate for ADHD-based symptoms (Table 1, 2). Articles not evaluating methylphenidate were excluded (reason 1). Articles not investigating early intervention with children were also excluded (reason 2). Review articles or articles that did not present novel information were also excluded (reason 3).

Risk of bias assessment

The quality and risk of bias of all eligible studies were evaluated using the Quality Assessment for Diagnostic Accuracy Studies (QUADAS-2) criteria (8). The assessment was carried out by HC, and any disagreements were resolved through discussion with AB (acknowledgements) until a consensus was reached.

RESULTS

Methylphenidate intervention increases quality of life

Children currently undergoing MPH supplementation across all studies noted improvements with treatment. Within studies, there are improvements in the quality of life and functioning levels (15), positive behavioral changes (16), increased processing speed and sustained attention, and executive function (17), increased attention at school, and the development of individual education plans at school (27). These reported improvements extend beyond quality of life and demonstrate a potential MPH-neuronal plasticity pathway through improvements in functioning levels, executive function, and attention.

Study and Patient Characteristics

Data presented are summarized from nine studies reporting patient demographics, co-occurring conditions, clinical outcomes, side effects, and dosing for pediatric patients treated with MPH versus untreated controls (Table 1). The age of intervention ranged from 6 to 14 years old. Co-occurring conditions include autism, tic disorders, learning disorders, TBI, depression, and precocious puberty. MPH was generally associated with improvements in ADHD symptom scores, attention, behavior, and quality of life. Side effects include appetite loss, hypotension, and digestive symptoms. Values are reported as mean ± SD where available; n/a indicates data not reported. Variables include study design, sample

Table 1. *Characteristics and clinical outcomes of pediatric studies evaluating methylphenidate treatment for ADHD. Abbreviations: MPH, methylphenidate; ADHD-RS, ADHD Rating Scale; CGI-S, Clinical Global Impressions-Severity; TBI, traumatic brain injury; n/a, not available; Rx, prescription*

Study	Number of Patients with and without MPH and Percent Female	Average Age of Intervention	Co-Occurring Conditions	Alterations with Rx	Side Effects of Rx
Kawasaki *et al*. (22)	Without MPH: 57 Without MPH % Female: 26.3% With MPH: 68 With MPH % Female: 18%	Group 1: 8.1 ± 1.6	N/a	Significant improvement in ADHD-RS scores and symptom improvement with MPH	hypotension, appetite loss, bitter taste, skin rash, digestive symptoms
De Rossi *et al*. (15)	Without MPH: 444 Without MPH % Female: 18.47% With MPH: 268 With MPH % Female: 9.3%	9 ± 2.9	N/a	Improved the quality of life and functioning levels	N/a
Kaalund-Brok *et al*. (23)	Without MPH: n/a Without MPH % Female: n/a With MPH: 207 With MPH % Female: 24.6%	9.6 ± 1.5	N/a	N/a	Significant decrease in appetite (P value <.001). No change in blood pressure or heart rate
Crippa *et al*., n.d.(24)	Without MPH: 326 Without MPH % Female: 15.3% With MPH: 105 With MPH % Female: 20.9%	9.7 ± 2.7	Autism, tic disorders, and learning disorders	CGI-S (severity) score decreased after 12 weeks	Patients presenting side effects were excluded.
Pai *et al*., 2022 (25)	N/a	N/a	Precocious puberty	ADHD medication does not affect precocious puberty	N/a
Cubero-Millán *et al*., 2014 (26)	N/a	N/a	N/a	Positive behavioral change after the first dose.	N/a
Houmann *et al*. (16)	Without MPH: n/a Without MPH % Female: n/a With MPH: 148 With MPH % Female: 23%	9.61 ± 2.54	Depression and high melatonin levels	Decrease of serum melatonin after Rx p<0.001.	Restored neuroendocrine melatonin balance
LeBlond *et al*. (17)	N/a	6.3 ± 4.1 and 11.5 ± 2.8	Patients selected with TBI head trauma	Increased processing speed Sustained attention Executive function	N/a
Muhammad *et al*. (27)	Without MPH: n/a Without MPH % Female: n/a With MPH: 1 With MPH % Female: 0%	14	Imaginary friends, provisional diagnosis of major depressive disorder, and oppositional defiant disorder	Increased attention at school, Individual education plan	N/a

size, age, sex distribution, co-occurring conditions, MPH dosing, clinical outcomes, and side effects.

Kawasaki *et al.* further subdivided the methylphenidate-treated group into patients who initiated treatment within 3 months of diagnosis (Group 1A) and to who initiated treatment after 3 months (Group 1B) (22). The mean age of intervention was 8.1 ± 1.6 years, and the subgroup ages were 7.9 ± 1.7 years for Group 1A and 8.2 ± 1.6 years for Group 1B. The baseline ADHD-RS hyperactivity scores showed a significantly higher trend in the treated group as compared to the control group (19.2 ± 5.2 vs. 14.9 ± 6.4, p=0.0002). Post-treatment total scores were not significantly different, but the percent improvement was significantly greater in the MPH-treated group.

The patient population pool does not accurately model the Methylphenidate intervention

All studies examined in this review primarily utilized a male-dominant patient population, with the total number of males to female patients treated with MPH being 673:150 or 4.5:1 and the control population being 680:147 or 4.6:1 (Table 1). The current patient population with ADHD represents a 1.6:1 male-to-female ratio in adults with ADHD (21).

ADHD behavioral tests with Methylphenidate intervention demonstrate efficacy

Across all studies investigated, a total of 5 studies evaluated behavioral tests, while 4 studies did not (Table 2). Among all the studies that assessed behavior,

Table 2. *Behavioral and cognitive outcome measures were used in studies of methylphenidate treatment for pediatric ADHD. Abbreviations: MPH, methylphenidate; ADHD-RS, ADHD Rating Scale; CPRS-R, Conners' Parent Rating Scale–Revised; SNAP-IV, Swanson Nolan Pelham Version IV; TOVA, Test of Variables of Attention; CGI-S/CGI-I, Clinical Global Impressions–Severity/Improvement; CBCL, Child Behavior Checklist; CGAS, Children's Global Assessment Scale; CPT, Continuous Performance Test; WISC-IV-PSI, Wechsler Intelligence Scale for Children Processing Speed Index; D-KEFS, Delis-Kaplan Executive Function System; n/a, not available*

Study	Assessment instrument(s)	Assessment context	Principal finding
Kawasaki *et al*. (22)	ADHD-RS; total score	MPH-treated participants compared with controls and other ADHD medications	Baseline symptom burden was higher in the treated group; percentage improvement was greater after MPH
De Rossi *et al*. (15)	CBCL; Children's Global Assessment Scale	Children with and without MPH prescription at first diagnostic assessment	MPH-treated participants showed improved quality of life and functioning; detailed test differences were incompletely reported
Kaalund-Brok *et al*. (23)	ADHD-RS-C, CPRS-R, SNAP-IV, TOVA, CGI-I, CGI-S	Baseline and 12-week follow-up after first MPH treatment	Parent- and teacher-rated inattention, hyperactivity-impulsivity, and conduct problems decreased significantly
Crippa *et al*., n.d.(24)	N/a	N/a	N/a
Pai *et al*., 2022 (25)	N/a	N/a	N/a
Cubero-Millán *et al*., 2014 (26)	N/a	N/a	N/a
Houmann *et al*. (16)	Continuous Performance Test	Early response and longer-term MPH outcome	Greater baseline inattention and response-time variability were associated with poorer treatment response
LeBlond *et al*. (17)	CPT II, D-KEFS Verbal Fluency, WISC-IV-PSI/WAIS-IV-PSI	Neuropsychological testing before and during MPH treatment after pediatric TBI	MPH improved processing speed, sustained attention, and executive functioning
Muhammad *et al*. (27)	Parent-generated CBCL; Conners Rating Scale	Case report before and after MPH treatment	School attention and behavior improved; quantitative test results were not fully reported

several utilized standardized measures. These included the Rating Scale (RS) is a questionnaire used to assess ADHD symptoms, the Child-Behavior Checklist (CBCL) is a parent-report questionnaire that evaluates a child's behavior; the Children's Global Assessment Scale (CGAS), allows practitioners to rate the child's overall level of functioning; and the Test of Variables of Attention (TOVA) is a computerized performance test used to assess impulsivity and attention. Other forms of measurements include the Clinical Global Impression scale (CGI), clinical-rated assessment of treatment response in ADHD; the Clinical Global Severity test (CGS), which evaluates symptom severity; the Conners Continuous Performance Test (Conners CPT 3) is a neuropsychological test assessing sustained attention, impulsivity, and response inhibition; the Delis-Kaplan Executive Function System (D-KEFS) measures executive functions such as cognitive flexibility; and the Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV) which uses a processing speed index to evaluate the ability to quickly and accurately complete tasks involving visual scanning (28).

Kaalund-Brok *et al*. reported significant improvements in behavioral outcomes after 12 weeks of methylphenidate treatment. Parent ADHD rating scales have demonstrated a significant decrease in inattention ($p<0.001$), hyperactivity-impulsivity ($p<0.001$), and conduct problems ($p<0.001$). Teacher ADHD rating scales also showed a significant decrease in inattention ($p=0.001$), hyperactivity-impulsivity ($p=0.004$), and combined symptom scores ($p<0.001$)

DISCUSSION

The findings of this systematic review are aligned with the clinical treatment of pediatric ADHD with MPH intervention. Findings in this review consistently demonstrated improvements in attention, impulse control, behavioral regulation, and quality of life. The outcomes align with the literature suggesting MPH as an effective first-line pharmacological treatment for major ADHD symptoms in children.

The functional improvements that were shown across studies suggest a potential association between early MPH treatment and outcomes that are consistent with neuronal plasticity, though no neuroimaging studies were included, and direct evidence of neurological changes cannot be established from the current review. Neuronal plasticity is inferred indirectly through functional and behavioral improvements observed across studies. These improvements include quality of life and functional levels (15), positive behavioral changes (16), increased processing speed, sustained attention, executive function (17), and increased attention at school (27). The functional gains may indicate an underlying neuroplastic change, though this interpretation remains speculative in the absence of imaging data. Additionally, findings from a mouse model demonstrated that MPH administration completely restored behavioral impairments with prenatal nicotine exposure (19), potentially offering preliminary mechanistic insight, though caution is warranted in extrapolating these findings to human populations.

The presence of comorbidities across the reviewed studies further complicated the interpretation of MPH outcomes, as conditions such as depression, anxiety, and behavioral disorders may independently influence treatment response (4). Figure 1 demonstrates that the depression rate increases with age, suggesting that a delayed pharmacological intervention may contribute to the emergence of secondary mental health conditions, which reinforces the importance of early intervention.

The patient populations represented in the reviewed studies do not accurately depict the disease demography with respect to gender. Across all studies, the samples collected are predominantly male. In the six studies that reported gender, female participants stayed below 27%. This discrepancy limits the generalizability of the findings and risks of obscuring gender-specific symptoms. Underrepresentation may further complicate the understanding of ADHD symptom expression, treatment efficacy, and behavioral outcomes in females.

According to the findings in Table 1, reported side effects of MPH include hypotension, weight loss, appetite loss, bitter taste, dermatologic symptoms, and digestive issues. Similarly, the National Health Service (NHS) identifies common adverse side effects such as headaches, insomnia, loss of appetite, abdominal pain, dry mouth, and nausea or vomiting (20), (18). These side effects are consistent with the side effects present in Table 1 of the results section.

Future research should investigate a patient population that reflects more on the clinical phenotype of ADHD, including equal testing amongst both genders. The current studies rely on narrow and unbalanced samples, limiting the generalizability of the findings. To improve diagnostic consistency, researchers should work toward developing a universal behavioral assessment for ADHD, similar to the universal test for Autism (Autism Diagnostic Observation Schedule). This tool would allow for the measurement of hyperactivity, inattentiveness,

impulsivity, and attentional control across all populations, encouraging a distinction of ADHD from other neurodevelopmental conditions.

Future research should also investigate the extent to which early intervention influences the performance on universal diagnostic assessments, more specifically, in determining whether early behavioral or pharmacological treatment will yield quantifiable reductions in hyperactivity and measurable improvements in academic performance. Additionally, incorporating biological assessments that show metabolic profiling through blood collection and analysis may identify biomarkers that are associated with ADHD and symptom severity. Conjointly, the collaboration should contribute to the development of a standardized diagnostic and monitoring assessment that includes behavioral, biological, and performance-based indicators, which will further advance the rate of early detection to provide early treatment plans with long-term benefits.

Limitations

Several limitations should be considered when interpreting the findings of this systematic review. The included studies incompletely reported sex-based data (7 reported sex-based data, 2 did not), making the treated population reflect a male-to-female ratio of 4.5:1, which is disproportionate to the clinically observed 1.6:1 ratio (21), further limiting the generalizability of findings to female patients. This limitation obscures sex-specific symptom presentations and treatment responses. Another limitation is the heterogeneity of study designs, which include cohort studies, behavioral assessments, neuropsychological testing studies, case reports, and large observational studies. This methodological variability has many inconsistencies in the measurement of outcomes, which then complicates direct comparison and affects the overall strength of the conclusions drawn. Additionally, the variability in reporting across the nine studies limited the data standardization. Multiple studies incompletely reported variables such as demographic characteristics, dosing information, adverse effects, and outcome measures which results in inconsistencies in data across all nine studies. This limited the overall uniform data extraction, which reduced the ability to directly compare the findings across all nine studies.

CONCLUSION

This systematic review demonstrates that early MPH intervention reduces inattention, hyperactivity, and impulsivity while improving attention, processing speed, and overall quality of life in pediatric ADHD patients. Nonetheless, the heterogeneity of behavioral assessment tools across multiple studies limits direct comparisons. In addition, the patient population is male-skewed (4.5:1 treated ratio versus the clinically observed 1.6:1), which restricts the generalizability of these findings to female patients. Future research should prioritize balanced sex representation, standardized behavioral assessment protocols, and biomarker profiling to develop more equitable and comprehensive diagnostic and treatment plans for children with ADHD.

ACKNOWLEDGEMENTS

Aleksander Bogoniewski assisted in article editing, methodology selection criteria, and risk of bias assessments.

CONFLICT OF INTEREST

The author declares that there are no conflicts of interest related to this work.

REFERENCES

1. Elmaghraby R, Garayalde S. What is ADHD? American Psychiatric Association; 2022. Available from: https://www.psychiatry.org/patients-families/adhd/what-is-adhd#section_4 (accessed on 2026-01-25).
2. Mayo Clinic. Attention-deficit/hyperactivity disorder in children: symptoms and causes. Mayo Clinic; 2025. Available from: https://www.mayoclinic.org/diseases-conditions/adhd/symptoms-causes/syc-20350889 (accessed on 2026-01-25).
3. Hamed AM, Kauer AJ, Stevens HE. Why the diagnosis of attention deficit hyperactivity disorder matters. *Front Psychiatry*. 2015; 6: 168. https://doi.org/10.3389/fpsyt.2015.00168
4. Centers for Disease Control and Prevention. Data and statistics on ADHD. CDC; 2024. Available from: https://www.cdc.gov/adhd/data/index.html (accessed on 2026-01-25).
5. Matza LS, Paramore C, Prasad M. A review of the economic burden of ADHD. *Cost Eff Resour Alloc*. 2005; 3: 5. https://doi.org/10.1186/1478-7547-3-5
6. DrugBank. Methylphenidate. DrugBank; 2005. Available from: https://go.drugbank.com/drugs/DB00422 (accessed on 2026-01-25).
7. Oisin A. Non-stimulant medications for ADHD. News-Medical; 2024. Available from: https://www.news-

medical.net/health/Non-Stimulant-Medications-for-ADHD.aspx (accessed on 2026-01-25).
8. Alto Pharmacy. The difference between extended- and immediate-release medications. Alto Pharmacy; 2022. Available from: https://www.alto.com/blog/post/difference-between-extended-and-immediate-release-medications (accessed on 2026-01-25).
9. Children's Hospital of Philadelphia. Research-based interventions addressing social challenges. Available from: https://www.chop.edu/sites/default/files/adhd-social-7-research-based-interventions-addressing-social-challenges.pdf (accessed on 2026-01-25).
10. Mayo Clinic. Methylphenidate oral route: description and brand names. Mayo Clinic; 2024. Available from: https://www.mayoclinic.org/drugs-supplements/methylphenidate-oral-route/description/drg-20068297 (accessed on 2026-01-25).
11. Storebø OJ, Storm MRO, Pereira Ribeiro J, Skoog M, Groth C, Callesen HE, *et al*. Methylphenidate for children and adolescents with attention deficit hyperactivity disorder. *Cochrane Database Syst Rev*. 2023; 3 (3): CD009885. https://doi.org/10.1002/14651858.CD009885.pub3
12. Verghese C, Abdijadid S. Methylphenidate. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024.
13. PRISMA. Preferred Reporting Items for Systematic Reviews and Meta-Analyses. PRISMA; 2020. Available from: https://www.prisma-statement.org/ (accessed on 2026-01-25).
14. Recarey-Rama S, Conde-Pumpido Zubizarreta S, Brenlla C, Gerpe-Rieiro E, Gil-Rodriguez A, Tubío-Fungueiriño M, *et al*. Exploring the sensory profile and pharmacogenetic biomarkers in child and youth ADHD patients undergoing methylphenidate treatment: a systematic review conducted in European studies. *J Psychiatr Res*. 2025; 190: 512-21. https://doi.org/10.1016/j.jpsychires.2025.09.002
15. De Rossi P, Pretelli I, Menghini D, D'Aiello B, Di Vara S, Vicari S. Clinical characteristics of children and adolescents with ADHD with or without methylphenidate prescription at their first diagnostic assessment. *Eur Arch Psychiatry Clin Neurosci*. 2023; 273: 879-90.
16. Houmann TB, Kaalund-Brok K, Clemmensen LB, Petersen MA, Plessen KJ, Bilenberg N, *et al*. Early treatment response as predictor of long-term outcome in a clinical cohort of children with ADHD. *Eur Child Adolesc Psychiatry*. 2024; 33: 2179-91. https://doi.org/10.1007/s00787-023-02158-z
17. LeBlond E, Smith-Paine J, Riemersma JJ, Horn PS, Wade SL, Kurowski BG. Influence of methylphenidate on long-term neuropsychological and everyday executive functioning after traumatic brain injury in children with secondary attention problems. *J Int Neuropsychol Soc*. 2019; 25 (7): 740-9. https://doi.org/10.1017/S1355617719000444
18. National Health Service. Side effects of methylphenidate for children. NHS; 2025. Available from: https://www.nhs.uk/medicines/methylphenidate-children/side-effects-of-methylphenidate-for-children/ (accessed on 2026-01-25).
19. Contreras D, Piña R, Carvallo C, Godoy F, Ugarte G, Zeise M, *et al*. Methylphenidate restores behavioral and neuroplasticity impairments in the prenatal nicotine exposure mouse model of ADHD: evidence for involvement of AMPA receptor subunit composition and synaptic spine morphology in the hippocampus. *Int J Mol Sci*. 2022; 23 (13): 7099. https://doi.org/10.3390/ijms23137099
20. Khalili H, Mahmoudi-Gharaei J, Mohammadi M, Faghihi T, Karimzadeh I, Khajehpiri Z. Adverse reactions of methylphenidate in children with attention-deficit/hyperactivity disorder: report from a referral center. *J Res Pharm Pract*. 2014; 3 (4): 130-6. https://doi.org/10.4103/2279-042X.145389
21. Stibbe T, Huang J, Paucke M, Ulke C, Strauss M. Gender differences in adult ADHD: cognitive function assessed by the test of attentional performance. *PLoS One*. 2020; 15 (10): e0240810. https://doi.org/10.1371/journal.pone.0240810
22. Kawasaki Y, Suzuki Y, Miyazaki K, Suzuki N, Hoshina M, Kato A, *et al*. A retrospective single-center study on the characteristics of children with attention-deficit hyperactivity disorder requiring early drug therapy from 2013 to 2022 and changes in treatment over time. *Fukushima J Med Sci*. 2025. doi:10.5387/fms.25-00016.
23. Kaalund-Brok K, Houmann TB, Hebsgaard MB, Lauritsen MBG, Lundstrøm LH, Grønning H, *et al*. Outcomes of a 12-week ecologically valid observational study of first treatment with methylphenidate in a representative clinical sample of drug-naïve children with ADHD. *PLoS One*. 2021; 16 (10): e0253727. https://doi.org/10.1371/journal.pone.0253727
24. Crippa A, Rosi E, Mauri V, Valli A, Nobile M, *et al*. Clinical outcomes of a 12-week, first treatment with methylphenidate in an Italian representative sample of children and adolescents with ADHD. *Sci Rep*. 2025; 15: 24787. https://doi.org/10.1038/s41598-025-10684-w
25. Pai LF, Wang DS, Hsu WF, Huang SW, Chung CH, Chen SJ, *et al*. New insights into precocious puberty and ADHD: a nationwide cohort study. *Pediatr Res*. 2023; 93: 1647-54.
26. Cubero-Millán I, Molina-Carballo A, Machado-

Casas I, Fernández-López L, Martínez-Serrano S, Tortosa-Pinto P, *et al*. Methylphenidate ameliorates depressive comorbidity in ADHD children without any modification on differences in serum melatonin concentration between ADHD subtypes. *Int J Mol Sci*. 2014; 15 (9): 17115-29. https://doi.org/10.3390/ijms150917115

27. Muhammad NA, Wan Ismail WS, Tan CE, Jaffar A, Sharip S, Omar K. Attention-deficit hyperactive disorder presenting with school truancy in an adolescent: a case report. *Ment Health Fam Med*. 2011; 8 (4): 249-54.
28. Linnenbank M, Feldmann R, Schulte-Körne G, Beimdiek S, Strittmatter E. Children with autism spectrum disorder of all ages, levels of symptom severity and general cognitive ability display low processing speed index scores warranting special educational assistance. *J Autism Dev Disord*. 2022; 52: 3668-77. https://doi.org/10.1007/s10803-021-05249-5
29. Nasser A, Kosheleff AR, Hull JT, Liranso T, Qin P, Busse GD, *et al*. Translating Attention-Deficit/Hyperactivity Disorder Rating Scale-5 and Weiss Functional Impairment Rating Scale-Parent effectiveness scores into Clinical Global Impressions clinical significance levels in four randomized clinical trials of SPN-812 extended-release in children and adolescents with attention-deficit/hyperactivity disorder. *J Child Adolesc Psychopharmacol*. 2021; 31 (3): 214-26. https://doi.org/10.1089/cap.2020.0148
30. Early Intervention Foundation. Child Behaviour Checklist (CBCL/6-18). London: Early Intervention Foundation; 2020. Available from: https://www.eif.org.uk/files/resources/measure-report-child-cbcl.pdf (accessed on 2026-02-20).
31. Multi-Health Systems. Conners Continuous Performance Test, 3rd ed. Toronto: Multi-Health Systems. Available from: https://storefront.mhs.com/collections/conners-cpt-3 (accessed on 2026-02-20).
32. Markowitz JS, Straughn AB, Patrick KS. Advances in the Pharmacotherapy of Attention-Deficit-Hyperactivity Disorder: Focus on Methylphenidate Formulations. *Pharmacotherapy*. 2003 Oct; 23 (10): 1281-99. https://doi.org/10.1592/phco.23.12.1281.32697