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## **Evidence-Based Treatment of ADHD: Pharmacotherapy and Psychosocial Interventions in Current Clinical Guidelines**

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**Abstract**

**Background.** Attention-deficit/hyperactivity disorder (ADHD) is a condition that affects how a person focuses, regulates behavior, and manages impulses. As a result, individuals with ADHD often experience difficulties in everyday life, including at school, at work, and in social relationships. It is characterized by persistent attention deficit, hyperactivity, and impulsivity.

**Aim.** This literature review evaluates current treatments for ADHD, including both medication and non-medication options, and discusses their effectiveness.

**Materials and Methods.** This review summarizes current evidence on medication and psychosocial treatments for attention-deficit/hyperactivity disorder (ADHD). The review included original studies and reviews from the Cochrane, PubMed, and Google Scholar databases. The article selection process ended in February 2026.

**Results.** Medicines that stimulate the brain are the best treatment for ADHD for people of all ages. Non-stimulant medications show moderate effectiveness and may be particularly useful in patients with contraindications to stimulants or comorbid conditions. Pharmacotherapy tends to produce larger effect sizes in children than in adults, although it is effective in both populations.

**Conclusions.** The current evidence shows that a multimodal approach is the best way to treat ADHD. Stimulants are still the best type of drug for this, but doctors need to plan treatments for each patient that take into account their mental and social well-being, any other health problems, their age, and how well they can handle the medication to ensure the best possible care.

**Keywords:** ADHD, treatment, pharmacotherapy, cognitive behavioral therapy

## **Introduction**

Attention-deficit/hyperactivity disorder (ADHD) is a condition that affects how a person focuses, regulates behavior, and manages impulses. As a result, individuals with ADHD often experience difficulties in everyday life, including at school, at work, and in social relationships. It is characterized by persistent attention deficit, hyperactivity, and impulsivity. The disorder begins in childhood and persists into adulthood in many people. According to the DSM-5 criteria, symptoms must be present for at least 6 months for a diagnosis to be made. [1]

Epidemiological studies indicate that ADHD affects 7.6% of children aged 3 to 12 years. It also affects 5.6% of individuals aged 12 to 18. [2] It has been shown that 2.58% of adults have ADHD that was diagnosed in childhood and persisted into adulthood. However, looking at the adult population as a whole, ADHD occurs in 6.76% of people, regardless of whether it was diagnosed in childhood or later in life. [3]

Early diagnosis and appropriate treatment of ADHD are important because this disorder significantly affects the lives of those affected. People with ADHD have been shown to have higher mortality rates and higher rates of intellectual disability than neurotypical people. In addition, people with ADHD earn lower incomes and have higher rates of unemployment. [4]

ADHD is associated with high social costs, including additional healthcare expenses and reduced or lost productivity. The total social cost of ADHD in 2018 and 2019 was as high as US\$14.44 billion. [5]

This paper aims to review current methods of treating ADHD, including pharmacotherapy and non-pharmacological treatments, and to discuss their effectiveness.

### **Characteristics of ADHD**

ADHD has been associated with impaired functionality of neural networks in the prefrontal cortex, a strategic area responsible for maintaining attention and regulating impulses. Research has demonstrated that patients diagnosed with ADHD exhibit reduced dopamine and norepinephrine transmission in the prefrontal cortex. This reduction in transmission results in diminished activity and fewer connections compared to those observed in neurotypical individuals. In adults, the severity of symptoms is associated with the presence and severity of neuroanatomical changes in the brain [6]

The symptoms of ADHD can vary from person to person. The DSM-5 criteria distinguish three types of symptom presentation.

The first type is patients in whom inattention predominates; they mainly experience reduced concentration, easy distraction, forgetting tasks, and problems with work organization. The subsequent category comprises patients in whom symptoms of hyperactivity and impulsivity predominate. These patients tend toward impulsive behavior, talkativeness, difficulty in maintaining seated posture, and impaired self-control. The third category, known as mixed, combines both types of symptoms. [7]

ADHD symptoms vary with age; for instance, in children, hyperactivity and impulsivity play the main role, whereas in adults, problems with organization are more common. [8]

The presence of ADHD is associated with a higher risk of other mental disorders, the most common of which are oppositional defiant disorder (34.7%), anxiety disorders (18.4%), and enuresis (10.8%) [9]. Comorbidity exacerbates patients' functioning and requires a comprehensive therapeutic approach.

## **Pharmacological treatment**

### **Stimulant drugs**

First-line pharmacological treatments include stimulants for children, adolescents, and adults with ADHD. [10]

#### **Metofenidate (MPH)**

The mechanism of action of metofenidate inhibits the reuptake of dopamine (DA) and noradrenaline (NE) by the DAT (dopamine transporter) and NET (norepinephrine transporter), increasing their synaptic concentrations and prolonging postsynaptic membrane stimulation. [11] Compared to other stimulants of this type, it does not cause neurotransmitter release; rather, it acts primarily as a reuptake inhibitor of DA and NE. This action stimulates the anterior cerebral cortex, limbic system, and striatum, relieving symptoms such as difficulty maintaining concentration, difficulty controlling automatic reactions, and improved frustration tolerance. [12]

#### **Amphetamines** (for instance: lisdexemfetamine, dexamfetamine)

The mechanism involves blocking DAT and NET and increasing the release of DA and NE from presynaptic vesicles into synapses. [13] Some of them like lisdexemfetamine (amphetamine combined with lysine), have a longer duration of action and more stable action, different from MPH. [14]

In short, MPH primarily acts by inhibiting neurotransmitter reuptake, whereas amphetamine derivatives both block reuptake and stimulate neurotransmitter release from presynaptic vesicles, leading to a more pronounced effect on the postsynaptic membrane.

In a meta-analysis, Cortese et al. reviewed 133 randomized controlled trials comprising 10,068 children and adolescents and 8,131 adults. A review of existing studies shows a consistent pattern of efficacy for stimulants, including amphetamines and MPH, in reducing ADHD symptoms when compared to placebo, as evaluated by clinical practitioners. [15] In contrast, Grcevich et al. conducted a comparison of amphetamines and MPH in children and found no notable differences in either effectiveness or safety. However, amphetamines were more often associated with the possibility of less frequent dosing. [16]

## **Adverse effects**

Both MPH and amphetamines are associated with decreased appetite, insomnia, anxiety, fear, headache, excessive agitation or irritability, increased blood pressure, heart rate, and heart palpitations.[17] More severe cardiovascular effects are very rare in normal use as directed by a physician, but a few cases have been reported in the literature.[18]

## **Risk of addiction**

Patients diagnosed with substance use disorder (SUD) or a pronounced tendency to lack control over their system are more likely to be concerned about the use of MPH. According to some studies, approximately 30% of patients with SUD may experience this medication if not used correctly. [19] However, when used therapeutically and under medical supervision, MPH and amphetamine preparations are unlikely to lead to psychoactive addiction. [20]

## **Non-stimulant drugs**

**Atomoxetine** acts as a selective inhibitor of the norepinephrine transporter (NET), leading to elevated synaptic norepinephrine levels. Additionally, it raises dopamine concentrations in brain regions with low dopamine transporter (DAT) expression, such as the anterior frontal cortex.[21] Atomoxetine is superior to placebo in alleviating ADHD symptoms, such as inattention and hyperactivity; however, its therapeutic impact is generally less pronounced compared to stimulant medications. [22] Meta-analyses confirm its moderate efficacy in RCTs: it improves symptoms compared to placebo. [23] Common side effects of atomoxetine include headache, reduced appetite, nausea, dry mouth, drowsiness, and sleep disturbances. In children and adolescents, its use has been linked to a slightly elevated risk of suicidal thoughts. [24]

**Bupropion** has been observed to inhibit both the dopamine transporter (DAT) and the norepinephrine transporter (NET), exhibiting a mechanism of action analogous to that of other agents that block these transporters. However, the precise molecular mechanisms through which bupropion exerts its effects remain to be fully examined. [25]

In a 2001 study, Wilens and colleagues evaluated 40 participants: 21 received bupropion and 19 received a placebo. After six weeks, the bupropion group demonstrated a significantly greater reduction in ADHD symptoms compared to the placebo group (42% vs. 24%). Moreover, 76% of individuals taking bupropion achieved a response of 30% or more, whereas this level of response was observed in 37% of those receiving a placebo. [26]

Bupropion may be moderately effective in ADHD, particularly in adults, although its clinical effects are often smaller than those of standard stimulants. [27]

A key adverse effect to keep in mind is its potential to reduce the seizure threshold. Bupropion can elevate the likelihood of seizures, particularly when administered at higher doses or in individuals who are already at increased risk. [28]

**Guanfacine** acts as a selective agonist at postsynaptic  $\alpha_2A$ -adrenergic receptors, the activation of which in the prefrontal cortex has been shown to enhance norepinephrine transmission, thereby improving executive functioning, attentional control, and the regulation of impulsive behavior. [29]

A meta-analysis including 12 randomized controlled trials and a total of 2,653 participants found that guanfacine demonstrated significantly greater efficacy than placebo in reducing ADHD symptoms, with response rates of approximately 58–64% compared to about 30–40% in the placebo groups. [30]

The most commonly observed adverse effects were drowsiness (~38.6%), headache (~20.5%), and fatigue (~15.2%). In total, around 80% of participants in the meta-analysis reported experiencing at least one adverse effect, though serious complications were uncommon. [31]

### **Pharmacotherapy in adults vs children**

Treatment selection is contingent on the patient's age. A meta-analysis of 133 randomized controlled trials, including 10,068 children and 8,131 adults, found that stimulants were effective across both age groups, though their impact was notably stronger in children. [32]. In children, stimulants showed an effect size of roughly 0.8–0.9, whereas in adults it was around 0.6, suggesting a comparatively lower treatment response in the adult population.[33]. Consequently, stimulants are considered the first-line therapy in children because of their robust and well-established effectiveness. In adults, stimulants remain a first-line option. Still, the presence of comorbid psychiatric conditions—such as anxiety, depression, or substance use disorders—needs to be taken into account when determining the most appropriate treatment.[34]. Nonetheless, research comparing adolescents and young adults found no meaningful difference in the effectiveness of atomoxetine between the two age groups. [35]. When choosing a treatment, it is also important to account for variations in side effects. Children are more likely to experience decreased appetite and drowsiness, whereas adults are more likely to experience increased heart rate, elevated blood pressure, and insomnia.[36]. In conclusion, children tend to show a more pronounced response to medication, whereas in adults,

treatment choices are often guided more by tolerability and the existence of co-occurring conditions. [37].

### **Non-pharmacological treatment**

While pharmacotherapy is rightly regarded as the primary treatment of patients with ADHD, the effective combating of the condition's effect on daily life function and the psychological deficits left behind by factors such as the impaired ability to maintain focus in comparison to one's peers often requires additional, non-pharmacological interventions.

Psychotherapy is a well-established method of treatment, often used in tandem with the previously mentioned medication. Several schools of psychotherapy exist, of which cognitive-behavioral therapy (CBT) is among the most studied and utilized. A meta-analysis of the effects of CBT on ADHD patients showed its effectiveness in reducing core symptoms (SMD = -0,45), depression (SMD = -0,23), anxiety (SMD = -0,24), and negative effects on executive function (SMD = -0,43) [38]. Positive effects were also shown with dialectical behavior therapy (DBT), which similarly reduced core symptoms (SMD = -0,51) and improved quality of life (SMD = 0,41) compared to control groups [39].

The 1999 MTA study was a landmark trial that demonstrated that, in children aged 7-10, ADHD pharmacotherapy achieved a pronounced short-term effect [40], which was followed by a noticeable fall-off in later follow-ups. Furthermore, it was shown that combination treatments allowed for lower medication dosages without negatively affecting overall function [41]. In children, psychotherapy often additionally targets the patient's environment, i.e., their family unit or school, rather than focusing solely on themselves. A form specific to this age group is parent training, which equips caregivers with tools to better manage a child's ADHD behaviors and improve relationships. A robust meta-analysis of this technique found positive effects on all parental outcomes compared with control groups, and also improved parents' feelings of competence and mental health [42]. A recent study evaluating the effectiveness of psychological interventions found improved functional outcomes in groups receiving medication together with CBT, parent training programmes, or both, compared to those receiving only medication, among whom only a reduction in attention deficit was observed [43].

It is worth noting that a review of social skills training (SST), a method that focuses on teaching patients to understand social cues and recognize emotional expressions, did not find significant improvements in emotional competency, social skills, or overall behavior when assessed by

teachers [44]. As such, it is not possible to conclude whether this form of therapy has any noteworthy benefit for children with ADHD.

Dietary interventions play a supplementary role to standard ADHD treatments; however, their effects should not be overlooked. It has been reported that both children and adults with the condition were more likely to present with key nutrient deficiencies crucial to the maintenance of proper neurotransmitter function, such as omega-3 fatty acids, zinc, group B vitamins, and vitamin D [45]. Therefore, supplementation has the potential to improve treatment outcomes. A review of trials evaluating the effectiveness of omega-3 acid supplementation found a greater reduction in symptom severity, as measured by the Conners Rating Scale, compared with control groups [46]. Multinutrients reduced symptoms in 66% of patients after a 16-week treatment, and additionally increased average height growth during that time period by an average of 0.5cm [47]. A comprehensive dietary intervention was found to achieve significant reductions in carbohydrate intake, reduce obesity, and, perhaps more importantly, reduce symptom severity as measured by the CPR-RS scale [48]. A slight, yet clinically significant, negative effect was observed with artificial food colorings, with their intake leading to a small behavioral decrement that could be additive to already-experienced symptoms [49]. Restriction diets allowed for a similarly partial improvement of functioning [50]. This literature review evaluates current treatments for ADHD, encompassing both pharmacological and non-pharmacological interventions, and assesses their relative effectiveness.

## **Conclusions**

The treatment of ADHD should be personalized and take many factors into account. Medications, especially stimulant ones, are still the best way to reduce the main symptoms. But the best results are seen when these medications are used together with talk therapy. It is very important to consider the patient's age, any other health conditions, and how well they can tolerate treatment. This helps to make sure the therapy works as well as possible and that the patient can function well in the long term.

## **DISCLOSURES**

### **Author's contribution:**

Conceptualization: JM, MC, PG

Methodology: JM, MC, PG

Formal analysis: JM, MC, PG

Investigation: JM, MC, PG

Writing - rough preparation: JM, MC, PG

Writing - review and editing: JM, MC, PG

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