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A Review of Treatment Methods and Available Therapies for Individuals with ADHD

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Abstract

This review explores treatment approaches and therapies for Attention Deficit Hyperactivity Disorder (ADHD), a neurodevelopmental condition affecting adults, with symptoms often persisting from childhood into adulthood. The research examines the efficacy, tolerability, and accessibility of pharmacological and psychosocial interventions. ADHD management necessitates a multimodal approach combining medications, behavioral therapies, and educational interventions tailored to individual needs.

The analysis focuses on stimulant and non-stimulant medications, including methylphenidate, amphetamines, atomoxetine, and alpha - 2 agonists, with regional variations in treatment guidelines. Stimulants, primarily methylphenidate and amphetamine formulations, demonstrate robust efficacy in symptom reduction for patients. Non-stimulant options like atomoxetine are recommended for patients with contraindications to stimulants. Emerging formulations, such as extended-release medications, address tolerance and adherence challenges.

Psychosocial interventions, particularly cognitive behavioral therapy (CBT), complement pharmacological treatments by targeting organizational skills, emotional regulation, and comorbidities like anxiety and depression. Evidence suggests that combined approaches improve long-term functional outcomes, such as academic performance and interpersonal relationships.

Despite advances, gaps in treatment access and the need for individualized care remain significant challenges. This review underscores the importance of ongoing research to optimize ADHD management strategies and ensure equitable access to effective therapies worldwide.

Review Methods

The review is grounded in findings from 44 recent studies sourced through a systematic search of open - access databases, including PubMed and Google Scholar, focusing on literature published between 1990 and 2024.

Abbreviated description of the state of knowledge:

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder affecting approximately 3% of adults, often persisting from childhood. Characterized by inattention, hyperactivity, and impulsivity, the condition significantly impacts social, academic, and occupational functioning. Diagnostic criteria vary between DSM-5 and ICD-11, emphasizing symptom duration, severity, and cross-situational presence. Comorbidity with other mental health disorders is common, complicating diagnosis and treatment.

Management of ADHD employs a multimodal approach, integrating pharmacological and psychosocial therapies. Stimulants like methylphenidate and amphetamines remain first-line treatments, with robust evidence supporting their efficacy. Non-stimulant options, including atomoxetine and alpha-2 agonists, provide alternatives for those unable to tolerate stimulants. Behavioral therapies, particularly cognitive behavioral therapy (CBT), address functional impairments and comorbid conditions.

Regional guidelines influence treatment strategies, with variability in medication availability and recommendations. Despite significant advances, challenges persist in ensuring access to comprehensive care, addressing unmet clinical needs, and tailoring interventions to individual patient profiles.

Conclusion
ADHD is a complex disorder requiring a multimodal treatment approach. Stimulants like methylphenidate and amphetamines are highly effective, with non-stimulants offering alternatives for specific cases. Psychosocial therapies, such as cognitive behavioral therapy, complement pharmacological treatments by addressing functional impairments and comorbidities. Despite progress, challenges remain in ensuring equitable access and optimizing long-term outcomes. A focus on individualized care and integrated strategies is essential to improve the quality of life for individuals with ADHD.

Keywords
Attention Deficit Hyperactivity Disorder, ADHD, neurodevelopmental disorder, pharmacological treatment, stimulants, non-stimulants, cognitive behavioral therapy (CBT), psychosocial interventions, functional impairments.

Introduction

ADHD is a chronic condition affecting about 3% of adults [1], causing significant impairments in function and quality of life [2][3]. Over the past decade, the prescription of ADHD medications has steadily increased [4]. A multimodal approach, including psychosocial and pharmacological treatments, is recommended by guidelines, with ongoing support and follow - up. The choice of pharmacological treatments should take into account factors such as efficacy, tolerability, treatment duration, affordability, and compatibility with other medications [2].

Pharmacologic treatment options for ADHD in adults include both stimulants (such as methylphenidate and amphetamines) and non - stimulant medications (such as atomoxetine and guanfacine). The availability and guidelines for these treatments vary by region [2][5]. Canadian guidelines recommend long - acting amphetamines, methylphenidate, or lisdexamfetamine as first-line options, with atomoxetine or short-acting dextroamphetamine/methylphenidate as second-line [6]. In the UK, psychostimulants are preferred as first-line treatment, though atomoxetine is considered in certain cases, such as with substance use disorders or contraindications to stimulants [5].

Review methods

The article utilizes a comprehensive literature review to examine ADHD treatment approaches and therapies. It synthesizes data from clinical guidelines, systematic reviews, meta-analyses, and randomized controlled trials, focusing on both pharmacological and psychosocial interventions. The review compares regional treatment recommendations, evaluates the efficacy and tolerability of stimulant and non-stimulant medications, and explores the role of behavioral therapies such as cognitive behavioral therapy (CBT). Emphasis is placed on evidence-based practices and addressing unmet clinical needs.

Attention Deficit Hyperactivity Disorder

ADHD is recognized as a neurodevelopmental disorder, with its diagnostic criteria relying on observed behavioral symptoms. According to the DSM-5, ADHD remains a diagnosis of exclusion, meaning it should not be diagnosed if the behavioral symptoms are more accurately attributed to other mental disorders, such as psychotic disorders, mood or anxiety disorders, personality disorders, or substance - related intoxication or withdrawal. [7]

Comorbidity with other mental disorders is frequently observed. In the DSM-5, ADHD is characterized by two categories of symptoms: inattention, comprising 11 symptoms, and hyperactivity/impulsivity, which includes 9 symptoms. [7] The previous classification of ADHD into subtypes in the DSM-IV was found to be inconsistent, as it varied depending on situational factors, the informant providing information, or the individual's stage of development. Consequently, this system was replaced in the DSM-5 with the concept of "presentations." [8]

The DSM-5 categorizes ADHD into different presentations: predominantly inattentive (requiring 6 or more of the 11 symptoms), predominantly hyperactive/impulsive (6 or more of the 9 symptoms), and combined presentation (meeting criteria for both). Additionally, it includes a partial remission category. For a diagnosis, symptoms must be present in at least two settings, persist for at least 6 months, begin before the age of 12, and cause significant impairment in social, academic, or occupational functioning. In individuals aged 17 or older, only five symptoms per category are needed for diagnosis. [7] For adults, it is recommended to use validated tools such as the Wender Utah Rating Scale to aid in diagnosis. [9]

In contrast, attention deficit hyperactivity disorder (ADHD) in ICD-11 is defined by a persistent pattern (lasting at least 6 months) of inattention and/or hyperactivity-impulsivity that significantly impairs academic, occupational, or social functioning. Symptoms of inattention and/or hyperactivity - impulsivity are evident before age 12, usually emerging in early to mid-childhood, though clinical recognition may occur later for some individuals. The severity of symptoms exceeds the normal range expected for age and intellectual capacity. [10]

Inattention involves difficulty maintaining focus on tasks lacking high stimulation or frequent rewards, a tendency toward distractibility, and challenges with organization. Hyperactivity refers to excessive motor activity and an inability to remain still, particularly in structured settings requiring self-regulation. Impulsivity is characterized by actions driven by immediate stimuli without adequate deliberation or regard for risks and consequences. [10] The balance and specific expressions of inattentive and hyperactive - impulsive traits differ among individuals and can evolve over time. Diagnosis requires that symptoms are observable across multiple settings (e.g., home, school, workplace, social environments), although their expression may vary depending on the structure and demands of each environment. Symptoms must not be better explained by another mental, behavioral, or neurodevelopmental disorder and should not result from substance use or medication effects. [10]

Treatment

ADHD rarely affects just one area of functioning; instead, it significantly impacts various aspects of an individual's well - being, including academic performance, physical health, occupational functioning and social relationships.

Although it often manifests in childhood, ADHD is frequently chronic, persisting into adolescence and adulthood, often resulting in ongoing impairments. [11] Evaluation of treatment outcomes should, therefore, encompass multiple components, including academic and learning support, psychoeducation, school accommodations, parenting practices, symptom management interventions and the assessment and treatment of comorbid disorders. Additionally, treatment approaches are expected to adapt as the patient progresses through different stages of maturity. [11] For instance, parental practices play a significant role in managing ADHD in children aged 6 - 12 years, whereas psychoeducation focusing on risks such as substance abuse and motor vehicle accidents becomes more relevant during adolescence. In our subsequent discussion of various approaches to ADHD management, it is essential to recognize the significant unmet clinical need in many countries, where only a small proportion of individuals with the condition receive any form of treatment. [12] Regarding the management of ADHD symptoms, medical organizations in the US [13], Canada [14], Latin America [15], and Europe [16] all recommend the use of psychostimulant medications. However, the majority of these organizations recommend starting with psychoeducation and behavioral management, especially for individuals presenting with mild symptoms and impairments. [13][17] U.S. guidelines differ, recommending that medication be considered as part of the initial treatment approach. [13] For children under 6 years old, there is a consensus that treatment should begin with behavioral management through parent training, with medication reserved for severe or unresponsive cases. For example, the National Institute for Health and Care Excellence (NICE) guidelines [16] recommend that medication management for children younger than 5 years be considered only after parent training has been attempted and a second opinion has been obtained from a specialist with expertise in ADHD in young children.

Starting Medication

ADHD medications should only be prescribed by healthcare professionals who are trained and experienced in diagnosing and managing the disorder. These specialists must have a thorough understanding of the pharmacokinetics and bioavailability of both short - acting and long - acting ADHD medications. Prior to initiating treatment, several factors need to be assessed, including the patient's medical history (and possibly that of the parents), current medications, height, weight, baseline pulse, blood pressure, and cardiovascular health. An electrocardiogram should be performed if the medication could impact the QT interval. Consultation with a cardiologist is essential before starting treatment in cases of congenital heart disease, a history of cardiac surgery, sudden death of a first - degree relative under 40 years of age, or consistently elevated blood pressure exceeding the 95th percentile for the patient's age and height. [18]

Medications

Medications for ADHD are classified into stimulants (or psychostimulants) and non-stimulants, with a range of formulations, delivery systems, and pharmacokinetic profiles available (see table 1). Notably, the availability of these medications varies significantly across the globe, with only limited options accessible in certain countries. [11] Psychostimulants, first introduced for use in children in the 1930s, remain the first-line medications for managing ADHD symptoms.

These include formulations of methylphenidate and amphetamine, which have similar mechanisms of action. Methylphenidate works by blocking presynaptic dopamine and norepinephrine transporters, thereby enhancing catecholamine transmission. Amphetamine also inhibits these transporters but further increases the presynaptic release of dopamine. [19]

Table 1 Medications for attension-deficit hyperativity disorder [11]

	Dose range (mg)	Delivery
Non-stimulants (duration of action 24 h)		
Clonidine, extended release	0,1 – 0,4	Tablet
Guanfacine, extended release	1–4	Tablet
Atomoxetine	0,5 – 1,4 mg/kg; maximum 100 mg	Capsule
Stimulants		
Amphetamine (short; duration of action 4–6 h)		
Dextroamphetamine	5 – 40	Tablet and liquid
Dextroamphetamine-amphetamine	5 – 30	Tablet
Amphetamine (long; duration of action 8–12 h)		
Dextroamphetamine-amphetamine, extended release	5 – 30	Capsule; contents can be sprinkled onto soft food
Dextroamphetamine, sustained release	5 – 40	Capsule
Lisdexamfetamine	10 – 70	Capsule; contents can be dissolved in liquid
Methylphenidate (short; duration of 4 h)		
Methylphenidate, immediate release	10 – 60	Tablet
Methylphenidate, oral solution	10 – 60	Liquid
Dexmethylphenidate, immediate release	2,5 – 20	Tablet
Methylphenidate (intermediate; duration of 6–8 h)		
Methylphenidate hydrochloride, sustained release	10 – 60	Tablet
Methylphenidate, long-acting	10 – 60	Capsule; contents can be sprinkled onto soft food
Methylphenidate (long; duration of 8–12 h)		
Dexmethylphenidate, extended release	5 – 30	Capsule; contents can be sprinkled onto soft food
Methylphenidate, oral solution, extended release	20 – 60	Liquid or chewable tablet
Methylphenidate, osmotic release	18 – 54 for children; 18 – 72 for adults	Tablet; osmotic-release oral system

Methylphenidate, transdermal	10 – 30	Patch
Methylphenidate hydrochloride, extended release	10 – 60	Capsule; contents can be sprinkled onto soft food

In Europe, the first - line treatment for ADHD across all age groups is methylphenidate, available in both short - acting and long - acting formulations. Second - line options include lisdexamfetamine, atomoxetine, and guanfacine. Transitioning to lisdexamfetamine is advised only after a minimum six- week trial of methylphenidate at an appropriate dosage has failed to provide sufficient symptom relief or has caused intolerable side effects. [20] As outlined in the NICE guidelines, atomoxetine and guanfacine are recommended only for patients who cannot tolerate methylphenidate or lisdexamfetamine, or for those whose symptoms have not improved after separate six-week trials of methylphenidate and lisdexamfetamine. This recommendation takes into account the consideration of alternative formulations and appropriate dosing. [16]

The effectiveness of psychostimulants in alleviating ADHD symptoms during short - term treatment has been demonstrated in numerous clinical trials involving both children and adults with ADHD. For example, a meta - analysis encompassing over 10,000 children and adolescents (with trials lasting approximately three months) revealed that both methylphenidate and amphetamine produced moderate - to - large effect sizes. Clinician ratings indicated effect sizes of 0.78 for methylphenidate and 1.02 for amphetamine, while teacher ratings showed an effect size of 0.82 for methylphenidate (data for amphetamine were unavailable). [21] A meta - analysis of 18 studies suggested that methylphenidate is also effective in adults, with an effect size of 0.6 based on both self - reported and clinician - reported changes in symptoms. [22]

Moreover, another meta - analysis involving over 8,000 adult participants demonstrated moderate effect sizes for both methylphenidate (0.49) and amphetamine (0.79) [21] An additional meta - analysis of 22 trials involving children with ADHD and nine trials involving adolescents with ADHD compared methylphenidate and amphetamine, finding both interventions to be highly effective. Amphetamine showed slightly larger effect sizes (0.99) compared to methylphenidate (0.72). [23] The side - effect profiles of these medications are comparable, with appetite suppression, insomnia, dry mouth, and nausea being the most frequently reported side effects. However, amphetamine may be slightly more likely to cause side effects. [24] Side effects are generally comparable between adults and children but may occur more frequently in younger children (i.e., those aged 5 years and younger). [25]

According to NICE guidelines [16], treatment with medication for children over 5 years old should begin with methylphenidate, with a switch to amphetamine if the response is insufficient. For adults aged 18 years and older, NICE recommends initiating treatment with either methylphenidate or the amphetamine formulation lisdexamfetamine.

Methylphenidate

Methylphenidate is a commonly prescribed first-line medication for ADHD. It functions by targeting dopamine and norepinephrine transporters, leading to an increase in the levels of these neurotransmitters in the prefrontal cortex. [26] There are different formulations of methylphenidate available. Immediate-release versions are typically prescribed for younger or smaller children (weighing less than 16 kg) who are new to psychostimulant treatments.[13] The typical dosing for methylphenidate is twice daily, spaced about 4 hours apart (e.g., before school and at lunchtime), with the option of administering up to three doses per day. Liquid formulations are available for children who cannot swallow tablets. While food doesn't significantly affect the overall effectiveness, a high-fat meal taken with long-acting solid formulations may delay the onset of action. [26] The titration to the maximum effective dose of methylphenidate can occur rapidly, as clinical benefits are often seen within a few days to a week. Doses can be adjusted every 7 days. Once an appropriate dose is reached, clinicians may consider transitioning to once-daily formulations for convenience.

Amphetamine

While the mechanism of action for methylphenidate and amphetamines is believed to be similar, amphetamine products additionally promote the release of dopamine. These products also tend to have a higher potential for causing decreased appetite compared to methylphenidate. [27] There are immediate-release tablets, extended-release capsules, and liquid available.

Atomoxetine

As mentioned earlier, psychostimulants are generally the first-line treatment for ADHD. However, some patients may be unable to tolerate these medications due to side effects or contraindications, such as allergies to psychostimulants or comorbid tic disorders like Tourette's syndrome. Additionally, between 10% and 30% of patients may not respond to psychostimulant treatment. [28] Atomoxetine serves as an alternative treatment for patients who cannot tolerate psychostimulants or have contraindications. It is believed to act as a selective norepinephrine reuptake inhibitor, which helps increase norepinephrine levels in the brain, thus alleviating ADHD symptoms. This makes it an option for patients who do not respond to or cannot use stimulant medications. [29] Atomoxetine increases norepinephrine and dopamine levels in the prefrontal cortex by inhibiting their reuptake. This localized effect is thought to enhance behaviors regulated by this brain region. The focused action in the prefrontal cortex reduces the medication's impact on other areas of the brain, which is likely why atomoxetine does not have abuse potential. [30] As a result, atomoxetine is not classified as a controlled substance, in contrast to psychostimulants.

Alpha$_2$-Agonists

Before atomoxetine was approved by the FDA in 2002, [29] there were no FDA - approved alternatives to psychostimulants for treating ADHD. Alpha2-agonists like immediate-release clonidine and guanfacine, primarily used for controlling blood pressure, were prescribed off-label as second-line treatments for patients who did not respond to two psychostimulants or as adjuncts for those with suboptimal results from psychostimulants alone. [13][31][32]

These medications were also prescribed when the patient had a comorbid condition, such as Tourette's disorder, that could be worsened by psychostimulant therapy, particularly when tics were a concern. [33] However, these agents were often challenging for patients to tolerate due to their side effects and could lead to rebound hypertension if stopped abruptly. Recently, extended-release formulations of these drugs have been introduced, which reduce the initial blood pressure drop and are generally better tolerated compared to the immediate-release versions. [32] These agents should be considered for patients who have not responded to psychostimulants or atomoxetine alone, or who need treatment for co - occurring psychiatric conditions. Alpha2-agonist therapy may also benefit patients displaying aggression due to its mild sedative effect. [34] Alpha2-agonists can be used either as monotherapy or alongside other treatments for patients who have not responded sufficiently to psychostimulants. [35][36] The exact mechanism of action for alpha2-agonists in ADHD remains unclear, but it is believed that these agents mimic norepinephrine's effects at alpha2A adrenoreceptors in the prefrontal cortex. Guanfacine specifically targets the alpha2A adrenoreceptors, while clonidine affects alpha2A, B, and C receptors. This difference suggests that guanfacine may have a less sedative effect and a smaller impact on blood pressure due to its selective action on the alpha2A receptors. [32]

Behavioral-based therapy

There is ongoing debate regarding the role of behavioral therapy in ADHD treatment. The questions revolve around whether it should be first - line therapy for all patients or just for younger individuals or those with milder symptoms. Additionally, whether a combination of medication and behavioral therapy is ideal for all patients is still unclear. Guidelines from the American Psychiatric Association, American Medical Association, and the American Academy of Child and Adolescent Psychiatry offer differing opinions, with recent studies suggesting that the correct outcomes may not always be identified or monitored. [37] Focusing on functional outcomes rather than just the DSM symptoms may be more beneficial in the long term. These outcomes include daily living activities, relationships with peers and parents, and academic performance. Shifting attention to these areas could provide a more comprehensive understanding of ADHD’s impact and treatment effectiveness. [38][39]

Cognitive Behavioral Therapy (CBT) for ADHD typically focuses on helping individuals identify and modify negative thought patterns and behaviors that interfere with daily functioning, such as time management difficulties, emotional dysregulation, and poor organizational skills. It aims to provide patients with coping mechanisms to improve focus, task completion, and interpersonal skills. For adults with ADHD, CBT has been shown to not only reduce core ADHD symptoms but also alleviate comorbid issues such as anxiety and depression. Studies have found that CBT can lead to significant improvements in functioning, with long-term benefits seen in areas like work productivity and interpersonal relationships. [40] Psychosocial treatments, including psychoeducation, cognitive behavioral therapy (CBT), support groups, skills training, and coaching, are considered to offer additional benefits in managing ADHD. [41][42] However, most studies examining these interventions are small and lack strong design. The effectiveness of these approaches in reducing core ADHD symptoms or primarily improving secondary outcomes like psychosocial functioning and impairments remains unclear.

A randomized study of 419 adults with ADHD, comparing medication with and without group psychotherapy, provides some clarification on the role of psychotherapy in enhancing ADHD management [43] Short-term and 1-year effects on ADHD symptoms were observed with drug treatment, but not with psychotherapy. However, group psychotherapy was associated with better 1-year outcomes in overall clinical improvement, as measured by the Clinical Global Impression, when combined with the trial drug rather than placebo. This supports current guidelines recommending psychological therapies as adjuncts to pharmacological treatments for adult ADHD [44]

Conclusions

ADHD is a complex and chronic neurodevelopmental disorder that affects individuals' academic, occupational, and social functioning throughout their lives. Effective management requires a multimodal treatment approach that integrates pharmacological and psychosocial interventions. Stimulants, such as methylphenidate and amphetamines, remain the first - line pharmacological options due to their well-documented efficacy in symptom reduction across all age groups. Non - stimulant medications, including atomoxetine and alpha-2 agonists, provide viable alternatives for patients who cannot tolerate stimulants or do not respond adequately to them. Recent advancements, such as extended - release formulations, have improved treatment adherence and reduced side effects, further enhancing therapeutic outcomes. Psychosocial therapies, particularly cognitive behavioral therapy (CBT), complement medication by addressing challenges in emotional regulation, organizational skills, and comorbid conditions like anxiety and depression. These approaches help improve long-term functional outcomes, such as academic performance and interpersonal relationships. Evidence supports the combined use of pharmacological and behavioral interventions, especially in cases with complex symptomatology or significant functional impairments.

Despite these advances, several challenges remain. Access to care is uneven globally, and many individuals with ADHD remain undiagnosed or untreated. Moreover, there is a need for further research to optimize treatment strategies, including tailoring interventions to specific patient needs and evaluating long-term outcomes of combined therapies. Addressing these gaps will require collaborative efforts to ensure that evidence - based, individualized treatment is available to all affected by this pervasive disorder.

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