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# Comprehensive management of attention deficit hyperactivity disorder with comorbidity in children and adolescents: pharmacological and non-pharmacological strategies

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## ABSTRACT

Attention Deficit Hyperactivity Disorder (ADHD) is a reasonably common developmental disorder that affects neurodevelopment. It often occurs alongside other psychiatric and transitional conditions, such as depression, anxiety, and oppositional disorder. This mix of conditions makes it harder to diagnose ADHD correctly and manage it effectively. Coexisting issues can hide the main symptoms of ADHD and require complicated treatment plans. This integrated review combines current pharmacologic and non-pharmacologic strategies. Pharmacological medications, including efficacy and safety profiles, such as stimulants and non-stimulants, offer crucial symptomatic relief. Their efficacy and safety profiles are often discussed, as well as their subtle use in different comorbid situations. The primary non-pharmacological strategies are Cognitive-Behavioral Therapy, primarily for learning emotional regulation and healthy coping mechanisms, and Parent Management Training, which teaches how to strengthen and manage various problem behaviors. Effective management should be implemented using multidisciplinary models that involve various professionals, with psychiatrists as the primary caregivers. It will also investigate how to use artificial intelligence and big data for better care. Finally, a combined treatment supported by research has great potential to improve the quality of life for children and adolescents with ADHD and other conditions, as well as their overall academic and work performance. Although some progress has been made, challenges in diagnosis and therapy still exist. Further studies are needed to investigate the effects of this approach.

**Keywords:** ADHD, comorbidity, child and adolescent psychiatry, medication, therapy

# 1. INTRODUCTION

**Epidemiology and burden**

ADHD usually starts in childhood, but it often carries on into the teenage years and adulthood (Polańczyk et al., 2015). Its continued presence in children, teenagers, and adults creates a significant challenge for individuals, their families, and society. It often affects academic performance, makes social interactions more challenging, and strains family relationships. Besides its noticeable symptoms, this condition also carries a higher risk of long-term adverse effects. These include lower educational achievement, work-related issues, and more use of healthcare services.

**Comorbidity – a key aspect**

A critical and often the most problematic characteristic of ADHD is the high rate of comorbidity, where it very frequently coexists with other psychiatric (and somatic) disorders (especially other developmental defects). Common co-occurring conditions include: anxiety, depression, oppositional defiant disorder (ODD), conduct disorder, autism spectrum disorder (ASD), sleep disorders, and substance use disorders (SUDs), including addictions (Njardvik et al., 2025). This high comorbidity presents an enormous challenge in diagnosis and treatment. Co-occurring conditions can hide very core ADHD symptoms, leading to inappropriate diagnosis or delayed intervention. Also, the presence of various disorders in one patient can extend a patient's suffering and create the need for polypharmacy, complicating treatment regimens and increasing the risk of side effects because of interactions between numerous medications used.

**Purpose of this article**

As ADHD is multifactorial, primarily when comorbidity is involved, this article aims to contribute to a comprehensive overview of contemporary pharmacological and non-pharmacological interventions for the treatment of ADHD with comorbid conditions. We will focus on the necessity of an integrated, multidisciplinary treatment to optimize outcomes for patients presenting with such interconnected problems (De Crescenzo et al., 2012).

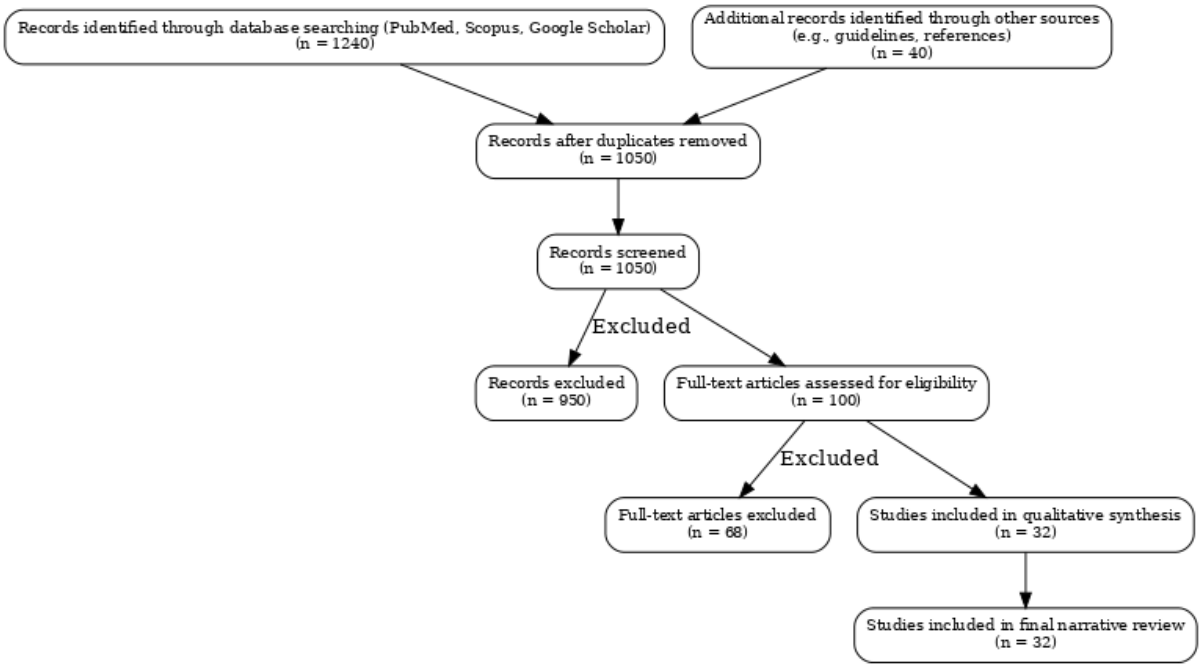


**Figure 1**: PRISMA diagram - literature search and study selection process

# 2. REVIEW METHODS

A broad part of the literature search was identified for this review. The primary electronic databases used were PubMed, Scopus, and Google Scholar. The search strategy focused on gathering high-quality evidence (Figure 1). The research was conducted from February 2025 to June 2025.

The search was conducted in English, Polish, Spanish, and on a smaller scale in German and Italian (the languages that authors can use at the communication level). The primary focus was placed on the last decade of research in this topic, with a particular emphasis on studies published since 2010. We sincerely acknowledge the evidence base, including systematic reviews, meta-analyses, randomized controlled trials, and significant clinical guidelines or consensus statements, that involved human subjects in the trials. We rejected articles older than 25 years (we primarily used sources from the last 5-10 years) and ultimately included 32 articles to prepare this review.

## 3. RESULTS & DISCUSSION

**Pharmacological interventions: stimulant medications**

Stimulant medications are the first choice for most people with attention-deficit hyperactivity disorder (ADHD). They form the foundation of pharmacological treatment. Their efficacy in typical ADHD symptoms is very well-known and well-tolerated, mainly by patients.

**Mechanism of action and efficacy in core ADHD symptoms**

The primary mechanism of action for classical stimulant medications, such as methylphenidate and amphetamines, involves altering the reuptake and release of primary neurotransmitters in the brain, primarily dopamine and norepinephrine (also known as noradrenaline) (Faraone et al., 2015). Methylphenidate mainly stops the reuptake of these two monoamines, increasing the concentrations in synaptic clefts, especially in the cortex (prefrontal) and striatum. Amphetamines not only inhibit reuptake but also directly promote the release of dopamine, noradrenaline, and other mediators from presynaptic terminals. These two actions help explain why they have a slightly more substantial effect for some patients. By improving the transmission of dopamine and norepinephrine in brain areas important for executive function, attention, and impulse control, stimulants reduce the three main symptoms of ADHD: inattention, hyperactivity, and impulsivity effectively.

Broad research, including many meta-analyses and reviews, consistently shows the superior efficacy of stimulants over placebo in both improving attention and reducing hyperactive/impulsive behaviors. It also enhances executive functions in both children and adolescents with that disorder (Cortese et al., 2018). Patients often see significant improvements in academic performance, social interactions, and family relationships. The quick onset of action, typically within 25 to 60 minutes for immediate-release formulations, along with a high response rate—approximately 70 to 80% of individuals respond positively to at least one stimulant—supports their everyday use in clinical settings. Various forms of stimulants (including immediate-release and extended-release formulations, as well as transdermal patches) offer flexibility in dosing schedules and duration of effect, allowing for tailored treatment plans that suit the individual needs and lifestyles of every patient.

**Safety profile and potential side effects in children and adolescents**

The stimulants are, in general, well-tolerated but are associated with specific safety challenges that require careful monitoring - especially in children and adolescents. The most common side effects are usually dose-dependent and include, among others, weight loss, low appetite, insomnia, headaches, and stomachaches. These are often only temporary and can be frequently managed by adjusting (lowering) the dose, setting the timing of medication, or changing some of the dietary habits.

More serious, but much rarer, concerns include cardiovascular problems, such as an increase in heart rate or blood pressure (Dalsgaard et al., 2014). Based on this, a detailed cardiovascular history and a baseline vital sign assessment are necessary before starting this treatment. Long-term effects on growth have raised significant concerns in the past. However, current evidence suggests that any growth disorder is usually minor and often resolves on its own over time. Such a growth disorder typically does not affect final adult height. The mental adverse effects are uncommon but can include the emergence/exacerbation of anxiety, general irritability, or, in sporadic cases, psychotic symptoms (Chang et al., 2014). Clinical vigilance is crucial in such scenarios, allowing us to detect any occurrences early. The risk of substance use disorder development is a widespread misconception: research consistently shows that treating ADHD with stimulants in childhood actually lowers the long-term risk of developing substance use disorders, likely due to improved impulse control and reduced self-medication behaviors.

**Application in comorbidity**

The presence of other disorders/diseases significantly complicates the treatment of ADHD. Different ways to treat the patients when the stimulants are administered are needed in such scenarios.

**ADHD, anxiety, and/or depression**

When ADHD is accompanied by anxiety disorders or depression, the use of stimulants requires careful consideration. Stimulants can be safe and effective in this population, as successful ADHD treatment often leads to "side improvements" in mood and anxiety symptoms, as it often reduces functional impairments and increases self-esteem. It should be noted, nevertheless, that some individual stimulants (notably higher doses or immediate-release formulations) can actually worsen anxiety or create a sense of agitation. If anxiety is severe or long-lasting, or if it worsens with stimulant monotherapy, the concurrent use of selective serotonin reuptake inhibitors (SSRIs) or serotonin-noradrenalin reuptake inhibitors (SNRIs) becomes a very appropriate strategy that should be considered (Kutcher et al., 2004). Such a connecting point of view makes it possible to target both ADHD and the mood and/or anxiety disorder. Often, it offers much better overall outcomes than treating either condition alone. Careful dose adjustment and a thorough clinical interview (accompanied by a proper examination) are essential to find a suitable compromise between efficacy and tolerability.

ADHD and conduct disorder (with or without aggression)

For patients with ADHD and underlying conduct disorder (CD) or aggression, stimulants can be more than helpful. Improving impulse control and reducing main ADHD symptoms leads (in a not direct way) to lower impulsive aggression and disruptive behaviors. In cases where aggression significantly affects society or does not respond to stimulants and other medications, as well as when there are underlying mood issues, the patients may need extra medication (Kutcher et al., 2004). This usually involves carefully adding atypical antipsychotics, like risperidone and aripiprazole, at low doses to manage severe aggression, mood changes, or irritability. Mood stabilizers can also be helpful, but it is important to consider their benefits alongside possible side effects. The primary goal is to enhance overall functioning and reduce the risk to the patient and their surroundings.

**ADHD and autism spectrum disorder (ASD)**

The presentation of ADHD symptoms within the context of Autism Spectrum Disorder (ASD) can be very diverse and can show up as many (very different) clinical manifestations. Stimulants can indeed be very effective in reducing ADHD symptoms in individuals with ASD, but their response can vary (depending on the specific set of symptoms from both disorders) and may be associated with a higher risk of adverse effects like getting annoyed easily, or (OCD-like) increased repetitive behaviors, or even conflicts in social life (Rodrigues et al., 2021). Again, it is essential to start with lower doses and increase them slowly, while closely monitoring the patient's reaction to the drug. The benefits must be assessed against potential problems (compliance, side effects, etc.). Non-pharmacological interventions are sometimes even more helpful to such patients and should never be omitted; it is especially crucial to focus on behavioral and social training when such a comorbidity occurs.

**Table 1**. Overview of Pharmacological Interventions for ADHD

| Medication class | Examples | Mechanism of action | Common side effects | Application in comorbidity |
|---|---|---|---|---|
| **Stimulants** | Methylphenidate, Amphetamines | Increase synaptic dopamine and noradrenalin levels. | Lower appetite, weight loss, insomnia, headaches | Can improve mood/anxiety |
| **Non-stimulants** | Atomoxetine, Guanfacine | Selective nonorepinephrine uptake inhibitor (atomoxetine); Alpha-2A adrenergic receptor agonist (guanfacine) | Nausea, decreased appetite (atomoxetine); sedation, fatigue, dizziness (guanfacine) | Preferred for anxiety, tics, or when stimulants are contraindicated |
| **Additional medications** | SSRIs, antipsychotics (atpical), mood stabilizers | Increase serotonin or noradrenalin levels (SSRIs/SNRIs); modulate dopamine/serotonin levels(antipsychotics) | Gastrointestinal issues for SSRIs, metabolic changes for antipsychotics) | Treating co-ocurring disorders |

**ADHD and tics**

The presence of tics (in such clinical manifestations as Tourette's Syndrome or chronic tic disorder) as a comorbidity is especially challenging, as it requires even more delicacy when choosing particular ADHD medications. Historically, it was suggested that stimulants could worsen tics. Still, more recent evidence indicates that for many individuals, stimulants do not actually worsen tics and, in some studies, even report slight improvement in tic severity (primarily because of reduced ADHD symptoms and lower stress levels). If tics are especially severe or consistently worsen while taking stimulants (according to some: also if the patient expresses a strong preference), non-stimulant medications such as atomoxetine, guanfacine (more rarely clonidine) are often preferred as first-line agents (Pringsheim et al., 2019). These drugs have different mechanisms that are not as likely to affect motor functions in a way that would trigger or worsen tics, and provide effective ADHD symptom control without compromising tic management (Table 1).

**Non-stimulant drugs: atomoxetine and guanfacine**

Non-stimulant medications provide another key option for treating ADHD. They have a unique medication profile and clinical usefulness. The most common and effective drugs in this group are atomoxetine and guanfacine, particularly in their extended-release form.

Atomoxetine is a selective norepinephrine reuptake inhibitor. Unlike traditional stimulants, it does not quickly or directly affect dopamine reuptake. Typical adverse effects include gastrointestinal problems: reduced appetite, nausea, abdominal pain, and insomnia or other sleeping disorders, particularly in the early stages of treatment. More serious but less common side effects might include a slight increase in heart rate and blood pressure (Fu et al., 2022). It can also lead to suicidal thoughts or liver failure, which requires close monitoring.

Extended-release guanfacine (and its short-acting sibling, clonidine) is a highly selective alpha-2A adrenergic receptor agonist (Yu et al., 2023). It mainly works on postsynaptic alpha-2A receptors in the prefrontal cortex, which boosts the existing noradrenergic transmission. This effect decreases distractibility, enhances working memory, and regulates impulsivity or hyperactivity, especially in cases of emotional dysregulation. Guanfacine's onset of action (just like atomoxetine) is also gradual, typically taking many weeks (or even months) for full therapeutic effects. The side effect profile differs considerably from stimulants and atomoxetine, commonly including sedation, fatigue, dizziness, and, more rarely, a decrease in blood pressure and heart rate. These last two effects often necessitate careful titration, especially when the first regimen is administered.

**Application in comorbidity**

Non-stimulants are preferred in specific clinical situations, such as first-line treatments or as additional agents. They are favored especially when coexisting anxiety occurs and hinders the patient's life strongly, even if they typically do not worsen anxiety and may even offer an anxiolytic effect in some clinical situations. Similarly, patients with tics (e.g., Tourette's Syndrome), non-stimulant medications like guanfacine are preferred because they are much less likely to worsen tics (and may sometimes reduce their severity, unlike stimulants). Also, in cases where there is a risk of substance abuse or when stimulants are contraindicated due to existing cardiovascular conditions, non-stimulants are a safe alternative (Wolraich et al., 2019). Individuals who experience an unexpected response to stimulants or unacceptable side effects, non-stimulants are also a valid alternative to be the second-line monotherapy options. They can also be effectively used as additional therapy alongside stimulants to target residual symptoms or lower/stop some of the side effects of other medications.

**Pharmacological treatment of underlying disorders**

Effective treatment of ADHD should involve all the health factors of a specific patient - that means also treatment of other comorbid (underlying) conditions. This is often achieved through the use of additional medications that target other problems.

**SSRI/SNRI for depression and anxiety**

Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin-Noradrenalin Reuptake Inhibitors (SNRIs) are the main medications used to treat depression and anxiety in patients with ADHD (Katzman et al., 2017). They work by increasing serotonin levels in the nervous system. SNRIs also boost noradrenaline levels. This helps to improve mood and reduce anxiety. It is essential to be aware of potential drug interactions with atypical antipsychotics for severe behavioral disorders, aggression, and/or psychosis. For severe behavior disorder, aggression, or psychotic episodes in people with ADHD, doctors may suggest atypical antipsychotics such as

aripiprazole or risperidone (Katzman et al., 2017). These medications influence dopamine and serotonin systems. They can effectively lessen severe aggression, impulsivity, irritability, and psychotic symptoms. Doctors typically prescribe them when other treatments have failed or when the symptoms pose a significant safety risk to the patient or others nearby. Dosing is often initiated at low levels with slow dosage changes, due to a greater risk of adverse effects compared to stimulants or non-stimulants. Monitoring must be extensive and include metabolic parameters (weight gain, dyslipidemia, hyperglycemia, and other relevant factors), extrapyramidal symptoms, and, as always in such treatment regimens, prolactin levels.

**Mood stabilizers for bipolar disorder**

For patients with ADHD and coexisting bipolar disorder, particularly if mood lability is imposing problems on patients' performance in society or if ADHD symptoms are made worse by mood instability, in such scenarios, mood stabilizers (e.g., lithium, valproate, lamotrigine, etc.) are absolutely critical (Youngstrom et al., 2009). Treating bipolar disorder is difficult, as an unstable mood can significantly worsen ADHD symptom presentation as well as the treatment response itself. The choice of mood stabilizer depends on the specific presentation of bipolar disorder (mania, depression, mixed features). Monitoring involves regular blood tests for therapeutic drug levels and side effects (renal function for lithium, liver enzymes for valproate).

**Medications for sleep disorders**

Sleep problems are highly prevalent in ADHD and often get worse with symptoms (e.g., difficulty calming down due to hyperactivity) or medication side effects (insomnia from stimulants). Non-pharmacological sleep hygiene strategies are the first-line treatment; however, medications can also be considered when these strategies are insufficient (Wajsziber et al., 2018). These may include short-term use of melatonin (especially for sleep onset insomnia), alpha-2 agonists (like guanfacine or clonidine at bedtime, which also offer ADHD benefits), or, less commonly, very low doses of sedating antidepressants or antihistamines. The goal is to improve sleep quality without excessive morning sedation, thereby indirectly enhancing ADHD management and the overall well-being and health condition of the patient.

**Challenges of polypharmacy**

The need to treat many coexisting conditions at once often leads to polypharmacy, which means the use of multiple medications by one patient (some definitions say at least five drugs used by one patient). Clinically, it is usually beneficial and should not be omitted at all costs; however, polypharmacy also presents several challenges. The primary concern is the potential for interactions between specific drugs, which can significantly reduce medication efficacy and increase the risk of side effects. The doctors must get a very detailed interview from the patients, including all their coexisting disorders and medications (and supplements) used by them, so that we can assess potential pharmacokinetic (a very textbook example: metabolism via cytochrome P450 enzymes) and pharmacodynamic (like sedative effects of two or more drugs) interactions.

Monitoring side effects can become even more complicated because differentiating between the side effects of individual drugs and the adverse reactions of multiple medications used simultaneously is challenging, as research on such complex scenarios is scarce, and it is also problematic to conduct such an experiment independently. This requires detailed follow-up with patients, clear symptom checklists, and laboratory monitoring when needed, such as checking kidney function while giving lithium. Optimizing doses for each medication and considering the overall treatment plan helps prevent over-sedation or excessive stimulation. It is vital to have an apparent reason for using each medication. Regularly reviewing the need for each medication and teaching patients about possible benefits and risks are essential for managing the challenges of taking multiple medications. This approach ensures safe and effective treatment.

**Non-drug and psychosocial strategies**

While medication is the main way to treat ADHD symptoms, a good treatment plan should also include non-drug and psychosocial strategies (Table 2). These methods not only focus on the main symptoms of ADHD but also address related issues, other challenges, and the complex interactions in family life, school, work, and various social settings.

For patients with additional disorders, these interventions are often essential as they offer tools for self-control, emotional strength, and positive behavior that medication alone cannot fully provide.

**Cognitive-behavioral therapy (CBT)**

Cognitive-Behavioral Therapy (CBT) is a psychosocial intervention (scientifically proven and also highly effective as it adapts easily to specific patients' problems) that targets adaptive thought patterns and behaviors that lead to mental pain, suffering, and inappropriate adjustment of the patients in their environment. Historically, it was designed to treat mood and anxiety disorders, but its rules have been effectively tailored for ADHD and its common comorbidities (as well as other disorders).

For children and teens with ADHD, CBT is typically delivered in a modified way that focuses mainly on practical skill acquisition (unlike classical CBT, which focuses on abstract cognitive restructuring). The main components include social skills training (which helps children understand and practice appropriate social principles), as well as communication and conflict resolution (which lead to improving peer relationships often tense due to impulsive or inattentive behaviors). Executive function training aims to enhance organizational skills, planning, time management, and other essential characteristics that are often weak in individuals with ADHD. This can also involve teaching specific strategies on how to initiate a task, complete it, and maintain the effort. CBT often includes straightforward methods for managing impulsivity. These include "stop-think-do" techniques, self-monitoring, and consequence mapping. These approaches encourage children to pause and think about the results before acting (Evans et al., 2014). These skills form the basis for navigating academic and social challenges more effectively.

When underlying anxiety disorders and depression are present, then the CBT's utility is significantly better. The reason behind that is CBT's ability to help individuals identify and challenge anxious thoughts, to teach the patients some relaxation techniques (like diaphragmatic breathing, progressive muscle relaxation), and engage in exposure therapy for phobias or social anxiety. In depressive episodes, CBT focuses primarily on behavioral activation (increasing engagement in activities that lead to pleasure and satisfaction), addressing and deconstructing negative thought patterns, and problem-solving abilities to fight the stressors. In this context, CBT for ADHD complements the treatment of mood and anxiety by improving highly needed skills and reducing functional impairments that often lead eventually to low self-worth. The integration of ADHD-specific strategies within a CBT framework appears to be crucial for changing the complex needs of these patients (Kendall et al, 2008).

**Parent management training (PMT)**

Parent Management Training (PMT) is one of the most effective non-drug treatments for managing ADHD (especially for children and adolescents). Its effectiveness is higher when the patient has more challenging behaviors. PMT does more than help control a child's actions but it teaches parents the skills that are crucial to maintain a structured and predictable home environment. The main goal of PMT is to show practical methods for discipline, establish clear communication, and explain how to set boundaries. This approach results in noticeable improvements in children's behavior (Costin et al., 2007).

**Table 2**. Basic Non-Pharmacological Strategies for ADHD

| Strategy | Main goal | Main components | Use in co-disease (comorbidity) |
|---|---|---|---|
| **Cognitive-Behavioral Therapy (CBT)** | To teach patients healthy coping mechanisms and emotional self-regulation | Training in the fields of social skills, executive function, and tempering impulsivity | Also helps with anxiety and depressive episodes. |
| **Parent Management Training (PMT)** | To educate parents, help them control their child's behavior properly, and establish an organization in the home environment | Clear communication with the child, consistent and predictable discipline, and positive reinforcement | Especially helpful with co-existing ODD |
| **School-Based Interventions** | To fulfill the child's special needs in the educational field | Strategies like extended time for assignments, preferential seating, and organizational techniques | Supports particularly academic success and social relations |

**School-based interventions and educational accommodations**

Provided that ADHD has a visible impact on functioning (in school, at the university, etc.), interventions in the educational environment are crucial factors that should be considered in an effective and complete treatment plan. Appropriate collaboration between parents, teachers, and the clinical team is basically the best way to ensure consistency (which patients with ADHD need so badly as we mentioned before) and discover the total child's potential.

The best strategies include, among others, the development of Individualized Education Programs (IEPs) as well = 504 Plans in the United States (or any similar support webs in other countries). These plans focus on specific accommodations and services that can be adjusted to the particular child's needs. Typical adaptations of this type include preferential seating (away from distractions, near the teacher), extended time for assignments and tests, a reduced workload whenever possible, frequent breaks, and the use of organizational aids (such as planners, checklists, and similar tools). The topography of the classroom and related strategies are also crucial, involving clear rules, consistent routines, immediate and frequent positive reinforcement (such as awards and praise), as well as consistent and effective use of consequences when disruptive behavior occurs.

Collaboration is the basis of any successful school-based intervention (Power et al., 2009). Regular communication between parents, teachers, and doctors ensures that strategies are consistent across settings and that any emerging challenges are addressed effectively. The multidisciplinary approach ensures that the school environment is modified correctly to support the child's individual learning style, significantly lowering the impact of ADHD symptoms on academic achievement and social relations within the school.

**Occupational therapy and physical therapy**

Occupational therapy (OT) and physical therapy (PT) can play an essential role in fighting specific motor or sensory challenges that sometimes coexist with ADHD. Children with ADHD may exhibit difficulties with so-called fine motor skills (like handwriting), gross motor coordination (clumsiness, balance issues), or sensory processing difficulties (Power et al., 2009) (like hypersensitivity to stimuli, seeking sensory input). These types of therapies are, unfortunately, often omitted or forgotten.

Occupational therapy aims to improve everyday living skills (by improving motor coordination and sensory integration). An occupational therapist might work on handwriting skills, strategies for using the patient's own belongings (such as reducing the frequency of losing things), or developing coping mechanisms for sensory sensitivities. Physical therapy focuses more on improving so-called gross motor coordination, balance, and overall physical fitness. That can indirectly improve self-regulation. While these are not primary treatments for basic ADHD symptoms, these therapies can be factors that contribute to a child's overall functional improvement and focus on specific areas of impairment, leading to better participation in school and other activities.

**Dietary interventions and supplementation**

The role of diet and supplementation in managing ADHD is a controversial but important topic. The critical analysis of the scientific evidence reveals delicate circumstances characterized by the lack of specific evidence to support whether a particular intervention is efficient.

The most common dietary methods for ADHD are elimination diets. These diets often limit artificial food colorings, preservatives, or specific allergens, such as dairy or gluten. There are also specialized diets, with the Feingold diet being the most recognized. Only small studies and some personal accounts suggest that these diets might help, particularly for individuals with specific food sensitivities. However, we do not have large-scale, well-controlled studies that reliably show their effectiveness as a primary treatment for ADHD symptoms (Nigg et al., 2012). The placebo effect is also essential to consider. Parents' active involvement in their children's diets can lead to noticeable improvements in their children's eating habits.

Nutritional supplementation, especially with omega-3 fatty acids (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]), has gained attention. Omega-3s are essential for brain development and function. Some studies indicate that children with ADHD may have lower levels of Omega-3s. Meta-analyses and systematic reviews have shown modest (but inconsistent) benefits in reducing some ADHD symptoms (particularly inattention), but with a much smaller effect than with scientifically proven pharmacological treatments (Bloch et al., 2011). Omega-3 supplementation is generally considered safe and primarily viewed as a potential additional help (and not really as a primary monotherapy). Other supplements (zinc, iron, various vitamins) lack appropriate research or evidence to support their routine use for ADHD. Doctors should educate patients that changes in diet or supplementation should never replace research-proven pharmacological or non-pharmacological treatments.

**Neurofeedback and other alternative therapies**

The landscape of ADHD interventions also includes various alternative therapies, like neurofeedback. Neurofeedback involves training individuals to self-regulate their brainwaves (e.g., increasing beta waves, decreasing theta waves) using real-time information from an electroencephalogram (EEG). The aim is that by changing specific brainwave patterns associated with attention and executive function, symptoms of ADHD should improve.

The current situation around research and recommendations for neurofeedback is quite mixed. Some studies, often smaller or not well-controlled, report positive outcomes. However, larger trials have shown inconsistent results. Many professional guidelines (both European and American) say that neurofeedback is a "possibly effective" or "experimental" treatment for ADHD. This means there is not enough substantial evidence to recommend it as a standard first-line option (Westwood et al., 2025). Its high cost, time commitment, and variability also create challenges.

**Integrated and individualized care models and treatment**

Effectively treating ADHD along with other conditions requires moving from treatments for each single issue to a more integrated (holistic) approach. This method understands that the effects of ADHD extend beyond basic symptoms. ADHD interacts in complex ways with other conditions, influencing various aspects of a person's life. The best results usually do not come from a single treatment method, but they come from a carefully planned strategy that considers the detailed interactions of biological, psychological, and social factors (Table 3).

**The holistic care concept**

Holistic care in ADHD treatment emphasizes the importance of understanding each patient's unique needs, challenges, and environmental factors. It shifts the focus from individual symptoms to the overall improvement in quality of life. This approach involves recognizing the connection between ADHD symptoms and specific related conditions. A holistic view should include long-term assessment of academic performance, social and family relationships, and self-esteem (not only the clinical symptoms). It means treating the whole person and considering their environment. Effective intervention at one level, such as with medication, can lead to positive effects in other areas, like reducing family conflict (Weissenberger et al., 2017).

**Table 3**. Roles within a Multidisciplinary Integrated Care Team

| **Type of professional** | **Roles in ADHD management/treatment** | **Main responsibilities** |
|---|---|---|
| **Child and adolescent psychiatrist** | Overall diagnostic and treatment planning | Prescribes and manages medications. Coordination. |
| **Psychologist** | Psychosocial interventions | Evidence-based therapies like CBT |
| **Educators (including school psychologists)** | Implements school-based strategies | Ensures classroom accommodations are in place and monitors academic progress. |
| **General practitioners, pediatricians, and other doctors** | First point of contact with the healthcare system | Provides initial screening, monitors general health, and coordinates with specialists. |
| **Family therapists** | Addresses family dynamics and provides training | Delivers Parent Management Training (PMT) and helps improve family relationships. |

**The interdisciplinary team**

To invest deeply in integrated care, it is necessary to commit to a fully interdisciplinary team approach. Every expert in the team is indispensable to the success of the mission of getting through the stormy sea of ADHD with the burden of comorbidity: Child and Adolescent Psychiatrists play the main role in decision-making regarding the correct diagnosis, psychopharmacological treatment, and the overall treatment plan.

Educators and School Psychologists cannot be omitted from the list of necessary individuals to implement school-based interventions and ensure that classroom accommodations are appropriate. Family Therapists are professionals who deal with family situations and implement Parent Management Training (PMT), thus playing a vital role. General Practitioners (Family Doctors) and Pediatricians are indeed the individuals who, without any doubt, are the primary point of contact, providing initial screening, primary care oversight, and coordinating care with specialists. Nurses continuously provide education on medications, inform patients about the symptoms of their disease, and serve as the key liaisons between families, schools, and the rest of the clinical team (Coghill et al., 2016).

**Algorithmic decision-making**

Making decisions about therapy for ADHD is often not a simple path. It is usually a non-linear process, particularly when there are other conditions involved. It is frequently analogous to the principles of algorithmic decision-making, where clinicians are led along a structured yet flexible path, depending on the patient's characteristics. The main factors considered when making these decisions are:

- Dominant Symptoms: One way to identify the symptoms that are most disabling is to focus on tismost effective treatments.
- Comorbidity Profile: When selecting medication and psychosocial intervention strategies, the pattern of co-occurring disorders and their severity are of significant importance.
- Patient Age: Treatment approaches typically vary by age.
- Family Preferences and Values: Providing families with the appropriate information (taking into account their cultural background, the will to engage in therapy, and their preferences for medications).

The holistic care in ADHD treatment highlights the need to understand each patient's specific needs, challenges, and surroundings. It shifts the focus to the overall improvement of the quality of life. This approach recognizes the link between ADHD symptoms and specific related conditions. A holistic view should include ongoing assessment of symptom severity, academic performance, social and family relationships, and self-esteem. It means treating the whole person and considering their environment. Effective intervention at one level, such as with medication, can lead to positive effects in other areas, like reducing family conflict (Weissenberger et al., 2017).

*Efficacy: Are the core symptoms of ADHD less severe? Are functional goals being met?*
*Safety: Are there any new side effects from the medication? Are vital signs, growth, and metabolic parameters on track?*
*Quality of Life: Is the patient's overall condition improving?*

Functioning Across Environments: Assessment must be thorough. It should go beyond clinic visits to show a complete picture of how the patient functions in different settings, including home, school, and interactions with peers. Using rating scales completed by various informants helps create a detailed view (Cedergren et al., 2022). Telemedicine and digital tools allow us to access and deliver ADHD care in a different way: this is especially important for long-distance relationships or when local resources are not available nearby. These devices could be helpful in many ways to help children, teens, and adults with ADHD:

- Enhanced Accessibility
- Treatment Delivery
- Continuous Monitoring
- Patient Engagement (Gabarron et al., 2025).

The good thing is that the downside does come with some issues about privacy, digital literacy, and the regulations of different countries. Nevertheless, their ability to organize integrated and individual ADHD care for a vast population is so high, which in turn brings them closer to their continuance and quality of life regardless of locality.

**Challenges, barriers, and future directions**

Although there is much progress in understanding and managing ADHD and its comorbidities, the field is still facing major issues and barriers. It is essential to find effective ways to address these challenges. This will help provide the best care, improve long-term outcomes, and guide future research.

**Diagnostic challenges**

Distinguishing symptoms of ADHD from those of coexisting disorders is one of the most challenging problems that has been persisting in clinical practice. Several psychiatric and developmental disorders, like anxiety, depression, ASD, or even sleep disorders, can produce symptoms that resemble or overlap with the main features of ADHD, which are inattention, hyperactivity, and impulsivity. Let us take an instance; in depression, loss of concentration may be misinterpreted as ADHD-related inattention, and restlessness in anxiety may be taken as hyperactivity. The overlap in symptoms can result in patients receiving incorrect diagnoses, being intervened late, or some comorbidities not being recognized. This, in turn, will lead to treatment efficacy being compromised and to patients being in a worse condition. To complete the differential diagnosis, multi-informant assessments, as well as clinical judgment, continue to be a challenging task, especially if there are no clear biological markers (Dreschler et al., 2020).

**Barriers to accessing care**

In addition to diagnostic challenges, vast challenges in the healthcare system and society at large prevent quick and effective access to ADHD care. Stigma is prevalent throughout the world, and it has been most contagious. When families decide to seek help for a diagnosis or treatment, they are often scared of being judged or discriminated against, so they hide. Another issue that is worsening the above is the shortage of specialized professionals, such as child and adolescent psychiatrists, psychologists, and therapists, who are especially missing in underserved or rural areas. The problem of money (for example, not good insurance coverage, high out-of-pocket payments for diagnosis, and therapy) and the factor of distance (travel to specialized clinics) further deepen the discrepancies in care reaching different groups of people. Those, along with a few other factors, are the reasons why a big treatment gap exists, resulting in the situation where many people with ADHD and other comorbidities are left without the support they need (Drechsler et al., 2020).

**Long-term effects of treatment**

The role of pharmacological therapy in the management of ADHD during the short to medium time period in terms of efficacy and safety is well documented; however, the extent to which it is maintained in the long term needs further study. In particular, issues about the extended impact of pharmacotherapy on brain development, cognitive functions, and overall functional outcomes remain into adulthood. These studies are necessary if we are to understand how medication influences both positively and negatively on brain neural pathways and whether its effects are genuinely beneficial for children in practical life, such as school, job, social activities, or improved mental health, including problem-solving over the long term. Research is a fundamental tool for determining appropriate treatment directions and adequately informing patients and their families about the available care options.

**Pharmacogenomics and personalized medicine**

The promise of pharmacogenomics is the door through which personalized medicine can come for the treatment of ADHD. Researching genetic differences that affect drug metabolism (pharmacokinetics) or receptor sensitivity (pharmacodynamics) gives enormous power. It is believed that the detecting of specific genetic markers will make it possible for physicians to guess a person's response to the different drugs (e.g., whether they will respond better to methylphenidate or amphetamines, or if they are prone to specific side effects) and also to go along with less adverse reactions by picking out the numbers of the doses exactly from the beginning (Coghill et al., 2017). As a research subject, this area may open new possibilities in selecting the most appropriate treatment, making it more straightforward and more effective.

**Development of new drugs and therapies**

The licensing of new, innovative, and different from existing drugs is one of the most critical directions of future work. This comprises several things: Novel Pharmacological Agents: An investigation is underway for new compounds with different modes of action that may offer the following advantages: improved efficacy, tolerance, and a more favorable side effect profile, as well as more precise targeting of a specific symptom cluster or comorbid condition(s). This could include either drugs that operate on different neurotransmitter systems or the provision of drugs through a new kind of delivery.

*Non-Pharmacological Interventions*: In addition to traditional CBT and PMT, technology-assisted therapies have become more popular. These include virtual reality treatments that aim to improve executive functions and digital programs for mindfulness or self-regulation. These approaches seek to increase engagement and access. Combined Modalities: More research is needed to improve the integration and combination of different treatment methods. This is especially important for cases with complex comorbidities.

**Research on the effectiveness of integrated interventions**

The idea of integrated care is well-established, but we still need to examine and compare different care models and their effects on long-term results. We need studies that thoroughly evaluate how effective various multidisciplinary team structures, care coordination strategies, and stepped-care models are in different clinical settings. This includes looking at their impact on reducing symptoms, improving function, increasing patient satisfaction, being cost-effective, and preventing adverse outcomes. Identifying which integrated intervention models work best for specific patient profiles will be key in developing evidence-based service delivery frameworks (Bellato et al., 2025).

**The use of artificial intelligence (AI) and big data**

These tools provide chances to gain a deeper understanding of the complexities of ADHD and its related condition s. Modern analytical methods can process large datasets from electronic health records, neuroimaging studies, genetic databases, and monitoring devices to:

- Find new biomarkers:AI algorithms can find subtle patterns in neuroimaging, genetic, or behavioral data that may serve as diagnostic or predictive indicators for ADHD and its subtypes.
- Predict treatment response: Machine learning models can analyze patient makeup to predict which individuals are most likely to respond to specific treatments.
- Research on the Value of Integrated Interventions

Although the concept of integrated care has been widely accepted, there are still insufficient studies comparing different medical care models and their impact on long-term outcomes. The primary objective of this research is to conduct a methodical examination of how various multidisciplinary team structures, care coordination plans, and stepped-care models function in different clinical settings. This includes their impact on patient happiness, cost-effectiveness, symptom reduction, prevention of adverse outcomes, and improvement of function. Identifying the most suitable integrated intervention models for specific patient profiles will lay the groundwork for service delivery plans grounded in evidence.

**The Use of Artificial Intelligence and Big Data**

Artificial intelligence (AI) and big data offer an opportunity to explore the complexities of ADHD and its comorbidities. Analytical methods can manage massive data pools from electronic health records, neuroimaging, genetic, and monitoring devices to:

- Discover new biomarkers: AI software will aid in identifying very subtle differences in neuroimaging and genPredict treatment response. Experiments using machine learning models will provide data that can help identify therapy options suited to specific individuals.
- Find complicated interactions.
- Improve care pathways. AI can be a tool to create treatment algorithms that guide doctors in their decision-making.
- Make research easier. AI can speed up the discovery of new drugs.
- Discover complex interactions. Big data analytics can show connections between ADHD, different comorbidities, and environmental factors.
- Improve care pathways. AI can assist in developing treatment algorithms that help doctors with complex decision-making processes.
- Make research easier. AI can speed up drug discovery.
- Using these tools will be crucial in overcoming limitations and establishing clearer, more accessible ADHD care for everyone.

## 4. CONCLUSION

The complex nature of ADHD, mainly when it occurs with other disorders, needs a personalized and thoughtful approach to care. This review found that both stimulant and non-stimulant medications can be a massive help for the patients. At the same time, various non-medical and psychosocial methods, such as cognitive-behavioral therapy, parent management training, and school-based interventions, address broader functional issues and improve adaptive skills. The close relationship between ADHD and related conditions (autism spectrum disorder, anxiety, depression, oppositional behaviors) emphasizes the importance of a treatment plan that considers more than just the individual symptoms. Although ADHD and its related conditions can present significant challenges, current evidence and ongoing innovations offer hope and many opportunities to enhance patients' quality of life. With appropriate, evidence-based treatments delivered within a coordinated care system, patients can experience fundamental changes. These changes can result in better

academic performance, stronger social ties, and improved overall well-being. The best care for individuals with ADHD comes from a team of specialists that includes psychiatrists—primarily adolescent psychiatrists—psychologists, therapists, and primary care doctors. This collaboration, along with regular monitoring and adjustments, ensures that treatments meet each patient's changing needs.

**List of abbreviations**
ADHD: Attention-Deficit/Hyperactivity Disorder
AI: Artificial Intelligence
ASD: Autism Spectrum Disorder
CBT: Cognitive-Behavioral Therapy
CD: Conduct Disorder
DHA: Docosahexaenoic Acid
EEG: Electroencephalogram
EPA: Eicosapentaenoic Acid
IEP: Individualized Education Program
ODD: Oppositional Defiant Disorder
OT: Occupational Therapy
PMT: Parent Management Training
PT: Physical Therapy
SNRI: Serotonin-Norepinephrine Reuptake Inhibitor
SSRI: Selective Serotonin Reuptake Inhibitor
SUD: Substance Use Disorder

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**Data and materials availability**

All data sets collected during this study are available upon reasonable request from the corresponding author.

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