Review

Attention-Deficit/Hyperactivity Disorder Management: Current Therapeutic Approaches and Future Directions

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Abstract

Attention-deficit/hyperactivity disorder (ADHD) negatively impacts both individual and social development, functional outcomes, and quality of life. Despite extensive research on the topic, this psychiatric disorder continues raising significant considerations regarding its optimal management. The present review provides an overview of recent evidence on standard clinical approaches, including pharmacological and behavioral interventions, as well as complementary approaches, including interventions based on physical activity, dietary modifications, microbiota-targeted treatments, digital tools, music therapy, and neurostimulation techniques. ADHD management might rely on a combination of pharmacological and non-pharmacological strategies, with standard treatments showing the most consistent clinical utility. Across therapeutic modalities, most interventions appear to show more consistent effects in pediatric populations, but remain limited regarding generalizability across developmental stages. Moreover, the optimal integration and comparative effectiveness of different interventions remain insufficiently established. Given the multifactorial etiology of ADHD, current therapeutic options may therefore be considered within a personalized framework to better align interventions with individual patient profiles and needs.

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Keywords

attention-deficit/hyperactivity disorder; therapeutic tools; pharmacological treatment; non-pharmacological interventions; emerging approaches

Introduction

Attention-deficit/hyperactivity disorder (ADHD) symptomatology has been associated with deficits in executive functioning, encompassing domains such as inhibitory control, working memory, cognitive flexibility (e.g., set-shifting), as well as planning and organizational abilities [1]. The fifth edition, Text Revision of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5-TR) organizes ADHD symptoms into two core domains: inattention and hyperactivity/impulsivity, each comprising nine criteria [2]. Based on the relative predominance of symptoms, the DSM-5-TR distinguishes predominantly inattentive, predominantly hyperactive/impulsive, and combined presentations, with an additional specifier for partial remission. Diagnostic criteria require symptom presence in at least two settings for a minimum duration of six months, with onset prior to the age of 12 years and clinically significant impairment in social, academic, or occupational functioning. For adolescents aged 17 years and older and adults, the diagnostic parameter is reduced to at least five symptoms within each domain [2].

In the context of ADHD symptom management, behavioral interventions are typically considered the first-line treatment approach for children younger than six years of age [3]. These interventions encompass a range of strategies, including parent-focused programs, cognitive-behavioral therapy (CBT), and skills training [3]. In children aged six years and older, pharmacological treatment is commonly recommended as the initial therapeutic option

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[4]. Nevertheless, the potential adverse effects associated with medication must be carefully considered, including insomnia, decreased appetite, gastrointestinal discomfort such as nausea, and emotional dysregulation [5]. Furthermore, the emergence of tolerance over time may contribute to diminished therapeutic adherence and reduced long-term effectiveness [6]. Current treatment strategies may be particularly relevant regarding ADHD heterogeneity, including subpopulations characterized by distinct comorbid profiles and emerging biomarker-based and neuroanatomical signatures. In fact, these advances in stratification may support the development of more individualized therapeutic approaches [7].

Building on the aforementioned insights and considering the limitations associated with pharmacological management of ADHD, there remains a need to further examine both established and emerging therapeutic strategies across childhood, adolescence, and adulthood. Accordingly, this review provides an overview of recent evidence on standard clinical approaches, including pharmacological and behavioral interventions, as well as complementary approaches, including interventions based on physical activity, dietary modifications, microbiota-targeted treatments, digital tools, music therapy, and neurostimulation techniques. Ultimately, this review offers a psychiatric perspective on the current therapeutic landscape in ADHD, aiming to guide future research directions and inform the development of multimodal treatment strategies.

Methods

A non-systematic, narrative approach was adopted to conduct this review, with the objective of synthesizing recent evidence on both conventional and alternative interventions for ADHD. Due to the heterogeneous nature of ADHD management, which encompasses multiple therapeutic domains, intervention types, and clinical populations, a narrative review was deemed the most appropriate methodology to integrate evidence from diverse sources. In this respect, narrative reviews are particularly suitable when the literature includes substantial variation in therapeutic approaches, as their methodological flexibility allows for the synthesis and interpretation of findings across different areas while facilitating the identification of future research priorities [8]. Thus, this approach was considered preferable to systematic review methodologies, which are generally designed to address more narrowly defined research questions through structured evidence synthesis. A comprehensive search of the literature was performed between April and May 2026 across the PubMed, Scopus, and Web of Science databases. The search strategy included combinations of keywords and related terms associated with ADHD and its therapeutic management, covering different domains such as pharmacological approaches (e.g., stimulant medication, psychotropic agents), behavioral approaches (e.g., cognitive behavioral therapy, mindfulness), lifestyle-based approaches (e.g., physical activity, dietary intervention), as well as alternative and complementary approaches (e.g., gut microbiota, music therapy, digital therapy, neurostimulation). Search terms were adapted according to the specific database requirements and combined using relevant Boolean operators to optimize the identification of studies addressing ADHD treatment and management. In addition, the reference lists of eligible publications were manually screened to identify further relevant studies, along with the incorporation of previously identified literature deemed pertinent to the topic of interest. No language restrictions were applied. However, only studies published between 2016 and 2026 were included in order to prioritize recent evidence. The search strategy followed an iterative process, and study selection was carried out in two sequential stages. First, titles and abstracts were screened, and records deemed irrelevant, as well as duplicates, were excluded. Subsequently, full-text articles that met the initial screening criteria were assessed in detail, with those failing to satisfy the eligibility criteria being removed. Inclusion criteria comprised studies evaluating the effects of therapeutic interventions on ADHD symptoms or related clinical outcomes (e.g., cognitive functioning, executive function, quality of life, functional impairment) in individuals with ADHD. All study designs were considered eligible, including randomized controlled trials (RCTs), observational studies, and review articles. No specific restrictions were applied regarding population characteristics (e.g., age groups, gender, clinical features) or outcome measures. Exclusion criteria were applied only to studies that met the inclusion criteria and included those in which the therapeutic intervention could not be distinguished from co-interventions or other concurrent treatments, studies in which ADHD outcomes could not be separately identified from those of other clinical populations, and studies in which the reported outcomes were not sufficiently relevant in relation to the objectives of the review. Moreover, theses, conference abstracts, and letters to the editor were excluded. Data extracted from the selected studies were synthesized and organized into thematic categories. Given the narrative and descriptive nature of this review, no formal quality assessment of the examined literature was performed.

Established Therapeutic Strategies

Pharmacological Interventions

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In contemporary clinical guidelines, pharmacological treatment represents a central component in the management of individuals diagnosed with ADHD. For instance, the 2019 National Institute for Health and Care Excellence (NICE) guideline advises that medication should be considered following the implementation of environmental adjustments (e.g., reducing noise levels or minimizing distracting stimuli) when ADHD symptoms continue to significantly interfere with functioning [9]. Pharmacological approaches for ADHD are commonly classified into two broad categories: stimulant medications and non-stimulant agents [10]. Stimulants include compounds that enhance catecholaminergic transmission, primarily through dopamine (DA) and norepinephrine (NE) reuptake inhibition or increased synaptic availability, such as methylphenidate (MPH) and amphetamine-based formulations. Non-stimulant options comprise α2-adrenergic receptor agonists (e.g., guanfacine and clonidine), selective NE reuptake inhibitors (e.g., atomoxetine and viloxazine), as well as other psychotropic agents including certain antidepressants (e.g., bupropion, venlafaxine, and desipramine) and antipsychotics (e.g., risperidone, aripiprazole, and olanzapine) [10]. Table 1 summarizes the mechanisms of action, main adverse effects, and potential advantages of several stimulant and non-stimulant compounds used in the treatment of ADHD.

The prevailing neurobiological hypothesis posits that the core clinical manifestations of ADHD (i.e., inattention, hyperactivity, and impulsivity) may be linked to dysfunction within cortico-striato-thalamo-cortical (CSTC) circuits [11]. In this context, evidence indicates that stimulant medications exert their therapeutic effects primarily by inhibiting presynaptic DA and NE transporters, thereby increasing catecholaminergic neurotransmission. In addition, amphetamine-based compounds have been shown to enhance presynaptic DA release. Regarding lisdexamfetamine (LDX), its mechanism of action is proposed to involve the blockade of DA and NE reuptake into the presynaptic neuron, resulting in increased extracellular concentrations of these monoamines [12]. LDX has been reported to modulate a range of protein targets: it acts as an activator of trace amine-associated receptor 1 (encoded by the *TAAR1* gene) and inhibits several presynaptic proteins, including the vesicular monoamine transporter (encoded by the *SLC18A2* gene), the sodium-dependent DA transporter (encoded by the *SLC6A3* gene), the NE transporter (encoded by the *SLC6A2* gene), the serotonin transporter (encoded by the *SLC6A4* gene), and monoamine oxidases A and B (encoded by the *MAOA* and *MAOB* genes) [12]. MPH, in turn, has been reported to interact with multiple molecular targets, primarily acting as an inhibitor of the DA transporter and of the NE transporter. Importantly, both proteins are responsible for DA and NE reuptake, respectively. In addition, MPH has been described as a 5-hydroxytryptamine (i.e., serotonin) receptor 1A (*HTR1A* gene) agonist [12]. Considering that these targets are involved in presynaptic monoaminergic signaling, LDX and MPH contribute to the modulation of DA, NE, and serotonin pathways.

Stimulant medications continue to represent the most effective first-line pharmacological treatment for ADHD. Nevertheless, the evidence regarding adjunctive non-pharmacological interventions, such as behavioral approaches, remains mixed, with research suggesting potential benefits when combined with stimulants compared to pharmacotherapy alone [13]. Despite their potential efficacy, stimulants are generally not recommended for children aged five years and younger, and approximately 30% of patients with ADHD exhibit insufficient response to these agents. Moreover, progress in the development of pharmacological strategies extending beyond dopaminergic and noradrenergic targets (e.g., GABAergic targets) has remained limited [14,15]. On the other hand, non-stimulant medications, including α2-adrenergic receptor agonists such as guanfacine and clonidine, as well as the selective NE reuptake inhibitor atomoxetine, are typically indicated for individuals who show inadequate response to stimulant therapy or who experience adverse effects that limit tolerability [15,16]. Although the precise mechanisms underlying the therapeutic effects of non-stimulant medications are not yet fully understood, several hypotheses have been proposed [17]. For instance, atomoxetine is primarily considered to exert its effects through selective inhibition of presynaptic NE reuptake within the prefrontal cortex (PFC). As a highly selective NE reuptake inhibitor, it binds with high affinity to the NE transporter located on presynaptic membranes, thereby blocking NE reuptake and increasing synaptic noradrenaline availability in the central nervous system [17]. In addition, preclinical evidence from animal models suggests that atomoxetine may indirectly enhance cortical DA transmission through mechanisms mediated by the NE transporter within the PFC, leading to regionally specific increases in DA levels without significantly affecting striatal motor or reward circuits [18]. These neurochemical effects are thought to contribute to improvements in attention and core ADHD symptomatology. Guanfacine, in contrast, acts as an agonist at postsynaptic α2A-adrenergic receptors, reducing cyclic adenosine monophosphate (cAMP) signaling and closing hyperpolarization-activated cyclic nucleotide-gated (HCN) channels. This mechanism strengthens the functional connectivity of pyramidal neurons in the PFC,

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Table 1. Summary of pharmacological substances utilized in the treatment of ADHD.

Substance	Mode of action	Main adverse effects	Potential advantages
Stimulant medications: MPH, dexmethylphenidate, LDX, dextroamphetamine.	Reuptake inhibition and increased release of DA and NE.	Decreased appetite, sleep disturbances, increased blood pressure and pulse, headaches, irritability, stomach pain, and potential effects on growth trajectories.	Large effect sizes for reducing ADHD core symptoms, rapid onset of action, available in short-acting and various long-acting formulations, positive effects on comorbid conduct disorder and oppositional defiant disorder.
Non-stimulant medications: atomoxetine, viloxazine.	Selective NE transporter inhibition by atomoxetine and NE transporter modulation by viloxazine.	Decreased appetite, sleep disturbances, increased blood pressure and pulse, headaches, stomach pain, nausea, vomiting.	"Around-the-clock" effects, non-controlled substances, augmentation to stimulant treatment, potential first-line option in comorbid substance use disorder, disruptive behavior disorder, or tic disorder.
Non-stimulant medications: clonidine, guanfacine.	α2-adrenergic receptor agonism (enhanced noradrenergic neurotransmission).	Somnolence/sedation, fatigue, hypotension, bradycardia, irritability, insomnia.	"Around-the-clock" effects, non-controlled substances, augmentation to stimulant treatment, useful in comorbid substance use disorder, disruptive behavior disorder, and tic disorder.
Other pharmacological agents: antidepressants (bupropion, venlafaxine, desipramine).	Monoamine reuptake inhibition.	Convulsions, psychosis, agitation, insomnia, suicidal thoughts, increased blood pressure, severe allergic reactions.	Broad spectrum of action across comorbid psychiatric conditions, improved tolerability profile, useful in neuropathic pain management.
Other pharmacological agents: antipsychotics (risperidone, aripiprazole, olanzapine).	D2 DA receptor and H1 histaminergic antagonism.	Metabolic and endocrine effects (diabetes, hyperglycemia, weight gain, dyslipidemia), movement disorders, orthostatic hypotension and increased risk of stroke, increased risk of thrombosis or pulmonary embolism.	Effective in reducing both "positive" and "negative" psychiatric symptoms, lower risk of severe movement disorder, versatility across different age groups.

Stimulant medications included MPH, dexmethylphenidate, LDX, and dextroamphetamine. Non-stimulant medications included atomoxetine, viloxazine, clonidine, and guanfacine. Other pharmacological agents used in selected patients or for the management of comorbid conditions rather than as primary treatments for core ADHD symptoms included: antidepressants and antipsychotics. ADHD, attention-deficit/hyperactivity disorder; DA, dopamine; NE, norepinephrine; LDX, lisdexamfetamine; MPH, methylphenidate.

thereby enhancing working memory and attentional control [19]. Furthermore, α2A-receptor activation has been associated with increased dendritic spine maturation and synaptic stabilization in pyramidal neurons of the medial PFC, structures implicated in higher-order cognitive processes such as learning and memory [19,20]. Unlike psychostimulants and atomoxetine, guanfacine does not primarily increase monoaminergic transmission via reuptake inhibition. Instead, it modulates noradrenergic signaling through direct postsynaptic receptor activation in the PFC [19]. Overall, evidence supports pharmacological treatment as an established strategy for improving core ADHD symptoms, with stimulants representing a primary option and non-stimulants providing alternatives when response or tolerability is inadequate. In this respect, treatment selection should consider individual response, adverse effects, and clinical characteristics.

Behavioral Interventions

Initial management of ADHD in preschool-aged children, particularly those between four and five years of age, is grounded in evidence-based behavioral interventions. First-line treatment typically involves parent-training programs focused on behavior management strategies, often complemented by behavioral interventions implemented in educational settings by teachers. Within this non-pharmacological framework, CBT has emerged as an effective approach for managing ADHD, particularly in relation to specific psychosocial difficulties [21]. CBT integrates cognitive and behavioral techniques to help individuals modify maladaptive patterns arising in anxiety-provoking situations, thereby developing more adaptive coping strategies and ultimately improving both functional outcomes and symptom control [22]. In addition to standard CBT approaches, several related interventions have been applied in the context of ADHD management, including mindfulness-

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based therapy (MBT), goal management training (GMT), and dialectical behavior therapy (DBT) [23–25]. Evidence suggests that CBT may be effective in reducing internalizing symptoms associated with ADHD, particularly those that interfere with emotional regulation, while also supporting the development of compensatory coping strategies for core symptom management [26]. In adolescent populations, research has reported secondary improvements in ADHD symptomatology based on parental assessments following CBT interventions. Nevertheless, the overall evidence base provides limited support for significant effects of CBT on functional impairment in this age group [22].

Recent meta-analyses suggest that MBT might offer potential benefits for ADHD-related outcomes, reductions in parenting stress, and improvements in emotional well-being in children and adolescents [27,28]. However, these meta-analyses are largely based on a limited number of RCTs, often characterized by small sample sizes and the use of active comparator conditions. In turn, GMT has been evaluated in adults with ADHD, suggesting potential benefits in executive functioning and symptom reduction, as well as in the management of comorbid conditions when compared with standard treatment approaches [24]. Importantly, a significant reduction in anxiety symptoms was observed in the intervention group relative to controls, but no statistically significant between-group differences were found in daily executive functioning or in the severity of core ADHD symptoms. Similarly, DBT has been investigated in adults with ADHD. In a multicenter RCT including 121 adults with ADHD, Halmøy *et al.* [23] compared the effects of DBT with the control condition over a 14-week period. DBT was assessed in relation to executive functioning and emotional regulation. Although no significant group differences were observed in emotional regulation, improvements in executive functioning were reported in the intervention group. Compared with controls, participants receiving DBT also showed significant improvements in core ADHD symptoms, depressive symptomatology, and quality of life. Nevertheless, no superiority of the intervention over control conditions was observed in relation to anxiety symptom reduction.

When combined with nutritional supplementation, CBT may exert synergistic effects, potentially through complementary mechanisms involving enhanced neurotransmitter synthesis and improved cognitive functioning, in which multi-micronutrient formulations support neural pathways while CBT targets behavioral regulation and cognitive control processes [29]. In addition, a RCT conducted by Wong *et al.* [30] compared a MBT for youth (MYmind) with group CBT in elementary school children diagnosed with ADHD in Hong Kong, assessing outcomes related to attention, behavior, executive functioning, mindfulness, and overall well-being. Secondary outcomes included parental measures such as parenting stress, ADHD symptom severity, rumination, and overall psychological well-being. Results indicated that both MBT and CBT were associated with significant improvements in children's attention at six-month follow-up, along with within-group improvements across most secondary outcomes. However, no statistically significant between-group differences were observed for either primary or secondary outcomes at any assessed time point. Based on the aforementioned, it can be asserted that evidence for behavioral interventions is heterogeneous, with the most consistent support observed for CBT and emerging benefits reported for MBT. In turn, findings for GMT and DBT remain more limited. Although these approaches may provide valuable clinical gains regarding ADHD symptoms and subsequent psychosocial or functional outcomes, it is important to note that their effects could largely vary across interventions and populations.

Emerging Therapeutic Strategies

Physical Activity

Regular physical activity has increasingly been proposed as a promising non-pharmacological intervention for ADHD [31,32]. Children diagnosed with ADHD are more likely to present difficulties in the development of motor coordination, particularly in tasks requiring the planning and execution of complex, sequential, and novel goal-directed actions [33]. Such motor impairments may interfere with academic and daily activities that depend on fine motor precision (e.g., handwriting and typing) and are often linked to slower motor responses and reduced perceptual processing speed within this population [34]. In this context, Chang *et al.* [35] examined whether training involving coordinated head-eye-arm movements, together with sustained visual attention as required in table tennis practice, could enhance executive functioning and school-based handwriting performance in children with ADHD. For this purpose, the authors designed a RCT to investigate the therapeutic efficacy of table tennis training and recruited 48 children with ADHD, who were randomly assigned to one of three equal-sized groups: (i) actual table tennis training, (ii) simulated table tennis training (i.e., exergame), or (iii) a control group receiving no additional training. The intervention lasted 12 weeks, during which both table tennis training modalities (i.e., actual and simulated) were delivered in three one-hour sessions per week. Participants undergoing table tennis training showed significant improvements in handwriting quality, response time, and the time required

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to achieve automation of writing skills. These findings suggest that structured interventions integrating motor learning with executive control demands, such as table tennis training, may yield therapeutic benefits for both handwriting performance and executive functioning in children with ADHD. Similarly, Liang *et al.* [36] investigated the effects of aerobic and neurocognitive exercise, incorporating moderate-to-vigorous physical activity, on executive functions and sleep quality in children with ADHD. In a parallel two-group RCT design, 80 children with ADHD aged 6–12 years were assigned to either a 12-week combined aerobic and neurocognitive exercise intervention group or a wait-list control group. In addition, 40 children with typical development aged 6–12 years were recruited as healthy controls. The results showed that the exercise intervention was beneficial for improving three core executive functions (i.e., inhibitory control, working memory, and cognitive flexibility), as well as for reducing sleep latency and sleep disturbances. Nevertheless, despite encouraging findings, evidence regarding the efficacy of structured physical exercise in individuals with ADHD remains limited and has yet to be clearly established [37]. Given that individuals with ADHD experience specific executive function difficulties that can impair goal-directed behavior, the development and systematic evaluation of exercise-based interventions customized to this population might be clinically valuable, as physical activity has been shown to improve attention and cognitive functioning through neurobiological mechanisms involving neurotransmitter systems (e.g., DA, NE). However, it should not be considered a standalone treatment for ADHD. Thus, evidence suggests that physical activity may improve certain functional outcomes in children with ADHD, but its effects might vary according to the type and duration of the exercise as well as the outcomes assessed. Furthermore, several limitations related to this therapeutic approach should be taken into account, such as the relatively transient nature of its effects, challenges related to long-term adherence, limited efficacy in individuals with more severe symptoms, and variability in individual responses.

Dietary Interventions

Dietary approaches investigated in ADHD can be grouped into three main categories: restriction of food additives, supplementation with essential fatty acids, and structured elimination diets [38]. Several studies have focused on interventions involving the removal of artificial food colorings, flavorings, and other additives from the diets of children diagnosed with ADHD [38,39]. In this respect, meta-analytic evidence suggests a small but statistically significant improvement in ADHD symptoms following exclusion of food additives. However, these effects are not consistently robust when analyses are adjusted for publication bias [38]. Among elimination-based approaches, the Few Foods Diet (i.e., the oligoantigenic diet) involves the temporary restriction of a wide range of commonly consumed foods, particularly those suspected of triggering sensitivities or allergic responses [40]. This dietary regimen typically includes controlled supplementation with vitamins and calcium-rich water, along with a limited set of foods such as certain vegetables (e.g., brassicas and carrots), fruits (e.g., banana and apple), carbohydrates (e.g., rice and potatoes), and selected proteins (e.g., quinoa and sunflower seeds) [41]. Evidence suggests that this intervention may yield relatively large effect sizes in reducing ADHD symptom severity compared with other dietary strategies [42]. In addition, various nutrients, including vitamins, minerals, and polyunsaturated fatty acids (PUFAs), as well as specific dietary patterns such as the Mediterranean diet, have been proposed as potentially beneficial in ADHD management [43,44]. The mechanisms underlying the effects of these dietary interventions remain incompletely understood. One proposed pathway suggests that nutritional factors influencing behavioral outcomes in ADHD may also modulate gut microbial composition, including alterations in microbial diversity and species abundance within the gastrointestinal tract [45]. Thus, evidence indicates that dietary interventions may have a modest role in reducing ADHD symptoms, with potentially greater effects reported for structured elimination diets. However, the findings remain inconsistent across dietary approaches, and their clinical application may be limited by two key factors: adherence difficulties and the risk of nutritional deficiencies associated with restrictive regimens.

Microbiota-Based Interventions

Several plausible mechanisms have been proposed to explain how the gut microbiome (GM) may modulate behavioral manifestations in individuals with ADHD [46]. In fact, the potential influence of the GM on immune, neural, and endocrine pathways, including hormone regulation and neurotransmitter signaling, has been extensively documented [47]. These systems are closely involved in the development and functioning of key brain regions such as the amygdala, PFC, and hippocampus, which have been implicated in the pathophysiology of ADHD [45,48]. Evidence further indicates that the GM can affect cognition, emotion, and behavior through modulation of immune responses, neurotransmitter metabolism (e.g., DA, serotonin, and gamma-aminobutyric acid), and regulation of the hypothalamic-pituitary-adrenal (HPA) axis [47,48].

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Several review studies have examined the effects of microbial-based interventions on ADHD symptomatology. For instance, adopting a narrative approach, Checa-Ros *et al*. [45] examined the functioning of the gut-brain axis (GBA) in pediatric ADHD populations, highlighting the role of omega-3 PUFAs and the GM as potential therapeutic targets. Their findings suggest a bidirectional interaction between the GM and omega-3 PUFA metabolism that may influence ADHD-related symptoms. Moreover, an imbalance in the omega-3/omega-6 PUFA ratio has been associated with the induction of neuroinflammatory processes and subsequent dysregulation of dopaminergic signaling, which is considered a key pathway underlying core ADHD symptoms. Probiotic supplementation has been proposed to help restore this balance by enhancing omega-3 PUFA levels and correcting the omega-3/omega-6 ratio, potentially leading to improvements in neuronal membrane stability, dopaminergic neurotransmission, and neuroinflammatory status. In turn, supplementation with eicosapentaenoic acid/docosahexaenoic acid (EPA/DHA) has been shown to induce changes in GM composition, which may be beneficial for individuals with ADHD. These effects are thought to occur, at least in part, through modulation of dopaminergic neurotransmission. In a separate systematic review, Allahyari *et al*. [49] evaluated the effects of probiotics, prebiotics, and synbiotics in children diagnosed with ADHD. Notably, supplementation with *Lacticaseibacillus* (formerly *Lactobacillus*) *rhamnosus* strain GG was associated with improvements in emotional, physical, social, and academic functioning, as well as higher health-related quality of life compared with the placebo group. The review also reported that Synbiotic 2000, which is a formulation combining probiotic strains (e.g., *Pediococcus pentosaceus*, *Lacticaseibacillus casei* subsp. *paracasei*, *Lactiplantibacillus plantarum*, and *Leuconostoc mesenteroides*) with prebiotic compounds such as fermentable fibers (e.g., beta-glucan, inulin, pectin, and resistant starch), was effective in reducing markers of intestinal and vascular inflammation in children with ADHD. These effects were proposed to be mediated, at least in part, through increased production of short-chain fatty acids (SCFAs). Furthermore, a meta-analysis conducted by Liang *et al*. [50] assessed the efficacy of probiotic interventions for ADHD symptomatology and explored potential moderators of treatment response. Overall, the available evidence indicated no statistically significant differences between probiotic supplementation and placebo in improving ADHD symptoms. Nevertheless, although results did not reach statistical significance, the findings suggested a possible trend toward greater efficacy with multi-strain probiotic formulations, highlighting a potential avenue for future investigation.

Research has also evaluated the use of probiotics as an adjunct to pharmacological treatment. For instance, Ghanaatgar *et al*. [51] conducted an eight-week, double-blind, randomized, placebo-controlled trial with a sample of 38 children aged 6–12 years. The participants received a probiotic formulation as an adjunct to MPH for the treatment of ADHD. The probiotic formulation consisted of a multi-strain mixture that included *Bacillus subtilis*, several *Bifidobacterium* species (e.g., *B. bifidum*, *B. breve*, *B. longum* subsp. *infantis*, and *B. longum*), multiple *Lactobacillus* species (e.g., *L. acidophilus*, *L. helveticus*, *L. delbrueckii* subsp. *bulgaricus*, *Lacticaseibacillus casei*, *Lactiplantibacillus plantarum*, *Lacticaseibacillus rhamnosus*, and *Ligilactobacillus salivarius*), as well as *Lactococcus lactis* subsp. *lactis* and *Streptococcus thermophilus*. The probiotic group showed a significant increase in Conners Parent Rating Scale-Revised Short Form (CPRS-R-S) scores at week 4 and week 8 compared with the placebo group. In addition, a statistically significant reduction in Clinical Global Impression (CGI) scores was observed in the probiotic group, with a mean decrease of 0.7 points by week 8 relative to placebo. CGI scores also showed a consistent downward trend across all time points assessed (i.e., week 4 vs. baseline, week 8 vs. week 4, and week 8 vs. baseline). In turn, in a triple-blind RCT involving 60 Iranian patients with ADHD aged 4–16 years, Sangsefidi *et al*. [52] tested the effects of probiotic supplementation as an adjunct to MPH. Participants were randomly allocated to receive either a probiotic formulation containing *Lacticaseibacillus plantarum* strain PTCC 1896 and *Bifidobacterium animalis* subsp. *lactis* strain BB-12, or a placebo, over an eight-week period. The results indicated a significant reduction in ADHD symptoms in the probiotic group after four weeks of intervention. Thus, the findings suggest that incorporating probiotics might offer complementary benefits for specific ADHD symptoms when used along with standard stimulant medication. However, no statistically significant differences were observed at the end of the eight-week treatment period. Notably, a significant improvement in auditory response control was reported in the probiotic group compared with placebo at study completion. Despite these promising findings, the efficacy of microbiota-based interventions for ADHD is limited by several factors. For instance, current evidence remains largely associative rather than causal, making it difficult to determine whether alterations in the GM contribute to ADHD pathophysiology or instead reflect ADHD-related factors. In addition, several challenges currently hinder the implementation and clinical translation of microbiota-based interventions. First, the lack of clinical standardization remains a major limitation, as no specific probiotic strains or standardized dosages have yet been established as effective

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for improving core ADHD symptoms. Second, substantial variability across studies may be explained by several confounding factors, including differences in participant age, gender distribution, dietary patterns, and the use of conventional ADHD medications. In this respect, the bidirectional relationship between medication use and the GM represents an important consideration, as commonly prescribed stimulant medications for ADHD (e.g., MPH) may influence gut motility and microbial composition, complicating the interpretation of whether microbiota alterations represent contributing factors or secondary consequences of treatment. Therefore, microbiota-based interventions should not be considered substitutes for evidence-based ADHD treatments. However, they may represent a potential complementary approach for managing co-occurring gastrointestinal symptoms. In this respect, evidence suggests potential benefits of specific probiotic formulations, but consistent improvements in core ADHD symptoms have not been demonstrated. Moreover, the lack of standardized strains and dosages, as well as the need for further controlled research, mean that their clinical potential remains exploratory to date.

Digital-Based Interventions

Digital therapy, often delivered through video game platforms, refers to evidence-based software interventions that provide medical treatment directly to patients [53]. These interventions are designed for the management a range of conditions and they can be implemented as standalone applications or used in combination with adjunctive approaches such as exercise-based programs, dietary plans, or hardware-supported methods (e.g., neurofeedback training) [53]. Within the context of ADHD, digital therapeutic approaches have been developed to target core deficits in attention regulation and executive functioning (e.g., working memory capacity) [54]. Meta-analytic evidence indicates that such interventions may improve symptoms of inattention, reduce reaction times on continuous performance tasks, and attenuate hyperactivity/impulsivity in individuals diagnosed with ADHD [54]. For instance, Oh *et al*. [55] noted that game-based digital interventions demonstrated greater efficacy than control conditions in reducing inattention and hyperactivity/impulsivity, based on clinician or assessor ratings.

In recent years, a growing number of "serious games" have been developed for the treatment of ADHD and other neurodevelopmental disorders. Unlike commercial video games, "serious games" are specifically designed for therapeutic or educational purposes rather than entertainment. In this respect, a systematic review has reported promising evidence supporting their effectiveness in alleviating ADHD symptoms among children [56]. In turn, another emerging area of research concerns the use of large language models (e.g., OpenAI's ChatGPT), along with robotic systems to support and enhance non-pharmacological interventions for children with ADHD [57]. Findings from a study exploring the integration of large language models, particularly ChatGPT, suggest that this platform may exhibit capabilities in adaptive communication, contextual responsiveness, and emotionally attuned interaction, highlighting its potential utility in ADHD care settings [57]. Thus, such systems could contribute to the personalization and scalability of therapeutic support by complementing existing clinical approaches. However, the study also emphasizes important limitations, particularly regarding data privacy, cultural adaptability, and the inability to interpret non-verbal cues, all of which represent critical challenges for the safe and effective integration of these technologies into healthcare practice [57]. Overall, digital-based interventions show promising potential for improving inattention and certain aspects of executive functioning in individuals with ADHD, particularly through game-based approaches. Nevertheless, the evidence remains insufficient to support their use as established complements to conventional treatments, and further research is needed to clarify their long-term efficacy, safety, and actual applicability across clinical and educational settings.

Music-Based Interventions

Research suggests that music-based interventions, including musical performance and auditory stimulation, may reduce symptom severity across several neurodevelopmental disorders, such as autism spectrum disorder and ADHD [58]. Music therapy is commonly implemented through two main modalities: active music therapy, which involves the production of music through instruments or voice, and passive music therapy, which consists of listening to music performed by others [58]. Engagement in music listening and performance has been shown to recruit bilateral neural networks across sensory, motor, cognitive, linguistic, and affective domains. In fact, neuroanatomical studies of musicians indicate enhanced sensorimotor integration, reflected in increased functional connectivity and structural differences in regions such as the basal ganglia, corpus callosum, and cerebellum [58]. Individuals with ADHD have been reported to present difficulties in temporal processing, a core ability for music perception and rhythm synchronization [59]. In this context, musical training, particularly instrumental practice, has been associated with improvements in timing skills and auditory cortical development among children with ADHD [60]. Thus, these findings suggest

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that structured musical training may represent a potential intervention for addressing certain cognitive and perceptual deficits associated with ADHD.

A systematic review by Martin-Moratinos *et al*. [61] examined the available evidence on the potential of music-based interventions to reduce ADHD symptomatology. The authors reported that active music therapy may improve hemispheric synchrony, social functioning, and reduce levels of aggression and impulsivity. In contrast, passive music therapy was associated with improvements in academic-related skills, including arithmetic performance, drawing ability, and reading comprehension, as well as with enhancements in attention and behavioral regulation. In addition to active (i.e., music production) and passive (i.e., music listening) modalities, music therapy can also be implemented interactively (e.g., music composition with feedback), and all of these formats have been reported to confer potential benefits for individuals with ADHD, particularly in terms of symptom reduction and task performance [61]. Contrary to the assumption that music may act as a distractor, it has been suggested that it can function as a regulatory stimulus, influencing emotional and cognitive states. In this respect, rhythm appears to constitute a particularly relevant component due to its relationship with temporal processing and timing regulation [61]. In a comparable line of work, another systematic review by Saville *et al*. [62] focused on three main areas: (i) music performance and processing in individuals with ADHD, (ii) music listening as a form of cognitive stimulation, and (iii) music-based interventions aimed at reducing ADHD symptoms. The review revealed that individuals with ADHD often experience difficulties in musical tasks requiring precise timing, rhythm perception, and processing of complex auditory information, although these impairments do not necessarily extend to rhythmic improvisation or expressive musical performance. Overall, music listening was generally associated with beneficial effects across multiple domains, and most studies of music therapy reported positive outcomes for individuals with ADHD. Building on these insights, it is plausible that music-based interventions may be highly engaging and capable of modulating dopaminergic pathways and arousal regulation. However, their limitations include inconsistent clinical evidence, the potential for distraction, and the presence of underlying motor and rhythm-related difficulties that may make it challenging for some individuals with ADHD to accurately process timing-related tasks.

Neurostimulation Techniques

Neurostimulation represents another innovative non-pharmacological strategy for the management of ADHD, involving the application of electrical or magnetic stimulation to modulate activity in brain regions implicated in attentional control, particularly the PFC. Although these approaches are generally considered safe, clinical evidence regarding their efficacy remains inconsistent. In this respect, they are typically considered for individuals who show inadequate response to stimulant medications [63]. Among the main neurostimulation modalities, trigeminal nerve stimulation (TNS) involves the use of a wearable device with surface electrodes placed on the forehead during sleep to deliver low-level electrical stimulation to branches of the trigeminal nerve. This technique is intended to influence brainstem activity and, in turn, improve attentional processes [64]. In this context, Conti *et al*. [65] conducted a confirmatory multicenter, double-blind, sham-controlled, parallel-group, phase 2b RCT to investigate the short- and long-term efficacy (six months) of real versus sham TNS in 150 children and adolescents with ADHD. The authors found improvements in scores on the mind-wandering scale (MEWS) after four weeks of TNS treatment among children with ADHD. These results might be attributed to the fact that mind-wandering constitutes a significant cognitive dysfunction in ADHD, potentially contributing to deficits in sustained attention and overall cognitive performance [65].

Another primary neurostimulation modality is transcranial magnetic stimulation (TMS), which consist of a non-invasive clinical procedure that employs focused magnetic fields to modulate neuronal activity in the PFC. A narrative review by Memon [66] examined the application of TMS for the treatment of ADHD among adolescents affected by this condition. The review concluded that there remains a need for large-scale clinical trials with larger and more diverse samples to further evaluate the efficacy and safety of TMS in adolescents with ADHD, particularly those who are non-responders to, or intolerant of, standard pharmacological treatments, as suggested by currently available preliminary evidence. Given the current knowledge regarding the efficacy and safety of TMS in the treatment of ADHD, further large-scale studies are required to investigate its potential application in adolescents with medication-refractory or medication-intolerant ADHD. Moreover, current and future mental healthcare providers should receive formal education and training on the use of TMS as an alternative or complementary intervention to pharmacological and/or behavioral approaches in adolescents with appropriate clinical indications, including but not limited to ADHD.

Finally, transcranial direct current stimulation (tDCS) constitutes another non-invasive neuromodulation technique that delivers a low-intensity electrical current through scalp electrodes in order to modulate cortical excitability

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and promote neuroplastic changes. A recent RCT conducted by Leffa *et al.* [67] showed that, when applied over the PFC, tDCS was associated with improvements in specific domains of higher-order cognition in both healthy individuals and clinical populations, including attentional control and working memory performance. Conversely, a comprehensive RCT investigating tDCS in adolescents with ADHD found no substantial evidence of improvements in ADHD symptoms or cognitive performance following multiple sessions of anodal tDCS targeting the right inferior frontal cortex (rIFC) combined with cognitive training [68]. These findings contribute to the existing literature on cognitive and clinical outcomes of tDCS in ADHD following 1–5 sessions, predominantly involving stimulation of the left dorsolateral PFC. Given the increasing commercial and clinical availability of tDCS, these results are clinically relevant, as they suggest that rIFC stimulation may not be an appropriate neurotherapeutic approach for cognitive or clinical remediation in ADHD [68]. Thus, while research on neurostimulation as a drug-free therapeutic approach for ADHD has expanded, important limitations remain. The main barrier to the clinical integration of these technologies is the lack of robust evidence supporting their efficacy. Indeed, research has raised concerns regarding the effectiveness of techniques such as TNS and tDCS, as these interventions might not demonstrate outcomes superior to those observed with placebo conditions. Taken together, the evidence for neurostimulation techniques remains limited and heterogeneous, with preliminary findings suggesting potential benefits for some modalities but inconsistent effects across interventions and outcomes. Thus, further research is needed to establish their safety and actual clinical applicability before they can be considered an established option for the treatment of ADHD.

Overview of Findings and Limitations

Evidence indicates that ADHD is a mental health condition that can negatively affect both individual and social development, functional outcomes, and quality of life. Despite extensive research on the topic, this psychiatric disorder continues raising significant considerations regarding its optimal management. The present review has focused on examining a range of therapeutic strategies for ADHD, including both established and emerging approaches, in order to provide a contemporary overview. Based on the evidence synthesized, several general key points can be identified regarding the current landscape. First, stimulant medications represent the primary approach for ADHD. They act through modulation of dopaminergic and noradrenergic neurotransmission within CSTC circuits. In turn, non-stimulant agents are generally reserved as second-line or adjunctive options. In terms of population applicability, stimulants are not recommended for very young children and some patients show suboptimal response. Research should focus on optimizing drug delivery systems and existing stimulant-based options, such as prodrugs of d-amphetamine and d-MPH. Compared to earlier formulations, these prodrugs enable once-daily dosing with prolonged duration of action, improving pharmacokinetic profiles and clinical usability. Second, behavioral interventions represent the primary non-pharmacological option for ADHD, particularly in preschool and school-aged populations. Evidence suggests that CBT can promote benefits in emotional and behavioral domains, but effects on core symptoms are less consistent. The most consistent evidence for CBT appears to be observed in preschool and school-aged children, particularly through parent-training frameworks. However, heterogeneity in intervention components may yield differential effects across children with varying demographic and clinical profiles. Related interventions (e.g., MBT, GMT, and DBT) also show potential benefits, particularly in adults, but findings are heterogeneous or limited to specific domains (e.g., executive functioning, anxiety, quality of life). Third, interventions based in physical activity may have potential benefits for ADHD, particularly in children, with findings suggesting improvements in executive functions, motor coordination, and cognitive control processes. Thus, physical activity programs represent a safe and potentially effective adjunct to standard treatments for young individuals with ADHD. In this respect, it should be underscored that generalizability across the lifespan and among diverse populations for this intervention is largely limited. Fourth, dietary interventions in ADHD can be categorized into food additive exclusion, essential fatty acid supplementation, and structured elimination diets. Overall evidence on these interventions suggest modest and inconsistent improvements in core symptom severity. The more consistent evidence is derived from pediatric samples, while data in adolescents and adults are scarce. In this respect, the restrictive nature of some dietary protocols and variability in individual nutritional and metabolic responses might constrain their feasibility and consistency across different populations. Fifth, research on the relationship between the GM and ADHD suggests that the GBA may influence behavioral and cognitive symptoms through immune, endocrine, and neural pathways, involving key brain regions implicated in ADHD pathophysiology and modulation of neurotransmitter systems. Nevertheless, variability in GM composition across individuals complicates translation into standardized treatment recommendations. Furthermore, lifestyle, dietary, development-related, and neurobiological factors should be considered as relevant

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confounders that may contribute to inter-individual variability in treatment response. Although preliminary findings are promising, current evidence remains insufficient to draw definitive conclusions regarding the clinical efficacy of microbiota-targeted interventions. Sixth, evidence on digital-based interventions for ADHD suggests modest benefits on core symptoms, particularly inattention, reaction time, and hyperactivity/impulsivity. The more consistent evidence stems from pediatric samples, but findings are constrained by heterogeneity in program design, intervention duration, and outcome measures. Although digital-based interventions undoubtedly appear promising in light of potential future technological developments, further research is still needed to optimize such approaches in order to enhance their efficiency and suitability for the target population. Seventh, evidence on music-based interventions, particularly derived from school-aged samples, suggests potential benefits for ADHD symptoms such as inattention, impulsivity, and emotional dysregulation, as well as improvements in select cognitive and academic-related outcomes. However, music therapy is not intended to achieve full symptomatic remission in individuals with ADHD. Therefore, it represents a safe complementary strategy that may offer benefits to specific populations, but that also requires further research in order to provide more evidence regarding its effectiveness and applicability. Finally, neurostimulation techniques, including TNS, TMS, and tDCS, aim to modulate brain networks involved in attentional control. Evidence suggests potential but inconsistent effects on ADHD symptoms, and no clear or uniform clinical efficacy across modalities. In addition, evidence is largely preliminary and developmentally uneven, constraining definitive conclusions across age groups. Thus, although contemporary neurostimulation approaches might result attractive due to their potential to induce neuroplastic alterations, further empirical validation is still required to determine their clinical effectiveness across diverse ADHD populations and individualized treatment frameworks.

Although non-pharmacological interventions generally present a favorable safety profile compared with pharmacological treatments, they are not exempt from potential adverse effects and implementation challenges. For instance, interventions based on physical activity could potentially be associated with physical injuries or fatigue, particularly when exercise intensity is not appropriately adapted to individual capabilities [35,37]. Similarly, dietary interventions might require careful monitoring, as restrictive approaches could potentially increase the risk of nutritional deficiencies and impaired growth, especially in children [38,39]. In turn, microbiota-based interventions appear to be generally well tolerated, although transient gastrointestinal symptoms may occur, while their long-term safety and clinical standardization remain insufficiently established [47]. Digital-based interventions represent a growing area of interest. However, their implementation requires consideration of potential risks related to excessive screen exposure, sleep disruption, problematic use patterns, and emotional dysregulation [54,55]. Furthermore, the incorporation of technologies based on artificial intelligence raises additional concerns regarding data privacy, algorithmic transparency, and clinical oversight [57]. Music-based interventions may also present challenges, including sensory overload or distraction in certain individuals [62]. Neurostimulation approaches, including TNS, TMS, and tDCS, have generally demonstrated acceptable tolerability, although adverse effects such as headaches, fatigue, sleep disturbances, and local skin irritation should not be overlooked, and their long-term safety profiles require further investigation [63,66]. Therefore, while non-pharmacological interventions may provide valuable complementary strategies for ADHD management, their implementation should consider individual characteristics, potential risks, and the need for appropriate supervision to maximize clinical benefits while minimizing adverse outcomes.

This review is subject to several limitations. First, the evidence for non-pharmacological interventions in ADHD is difficult to interpret due to a heterogeneous literature characterized by methodological constraints. For instance, unlike pharmacological interventions, many non-pharmacological approaches cannot be fully blinded (e.g., physical activity, music-based interventions, computer-based programs, neurostimulation techniques). Although sham or placebo-like control conditions are sometimes developed to improve blinding, these controls may still be partially distinguishable from active interventions and can introduce additional sources of bias. Second, some studies rely on performance in laboratory-based cognitive tasks as primary outcomes and these measures may not fully capture real-world functioning and may have limited ecological validity in explaining symptom variability across contexts and over time. In addition, there remains a need for more robust, high-quality evidence on non-pharmacological approaches for ADHD. In particular, adequately powered, well-controlled, parallel-group randomized clinical trials are required for interventions where current evidence is still insufficient. Third, the interpretation of the efficacy of ADHD interventions across the lifespan is limited by the unequal distribution and availability of evidence across age groups, highlighting the need for age-specific therapeutic strategies. In this respect, several limitations in the available adult ADHD literature may have influenced the conclusions of the present review: (i) long-term clinical trials

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in adults remain limited compared with the extensive pediatric literature; (ii) discontinuation rates for non-stimulant medications may be higher among adults due to adverse effect profiles, complicating comparisons with other pharmacological approaches; and (iii) clinical recommendations emphasize the need to consider psychiatric comorbidities (e.g., anxiety, depression) when evaluating treatment efficacy, as these mental health conditions may influence responses to conventional "treat-to-target" pharmacological approaches. Moreover, direct comparisons of therapeutic efficacy across developmental stages remain challenging due to differences in study methodologies, assessment frameworks, and treatment characteristics, underscoring the need for future age-stratified research to clarify the relative benefits and limitations of each intervention. Finally, this review is descriptive and does not include a formal quality assessment of the included research or a quantitative synthesis of the available evidence. Furthermore, due to the narrative nature of this review, it may be subject to both selection and interpretation bias. Beyond the aforementioned limitations and at a field-wide level, ADHD management research is also constrained by substantial variability in intervention protocols, outcome measures, follow-up periods, and definitions of clinical response across studies, which restricts direct comparisons between therapeutic approaches and contributes to uncertainty regarding their relative effectiveness.

Future Directions

A pharmacological treatment deemed ideal for ADHD management, defined by its clinical, pharmacodynamics, safety, and tolerability profiles, could serve as a benchmark for evaluating currently available medications and guiding future drug development. However, advancing pharmacological options for ADHD requires the identification and investigation of novel therapeutic targets informed by emerging evidence on the biological mechanisms implicated in its pathophysiology [7]. In this context, several investigational compounds have been developed in recent years, although none have yet received regulatory approval for clinical use. These candidate agents include brexpiprazole, carbidopa, centanafadine, dasotraline, mazindol, metadoxine, sativex, serdexmethylphenidate, solriamfetol, tipepidine, and vortioxetine [10,15]. In parallel, the identification of novel therapeutic targets, such as neurosteroid- and cannabinoid-related pathways, reflects an expansion toward alternative neurobiological mechanisms in ADHD treatment research. Although these emerging approaches appear promising, further rigorous investigation is required to establish their safety profile, therapeutic efficacy, and long-term clinical effects [15].

An emerging line of research focuses on the "druggable genome", which is defined as the subset of genes that encode potential targets for pharmacological intervention. Advances within this framework may facilitate the development of more effective and better-tolerated treatments. In this respect, analyses of genome-wide data in ADHD have yielded notable findings. Hegvik *et al*. [69] reported that genes encoding the primary molecular targets of first-line ADHD medications did not show significant associations with the disorder, suggesting that currently approved treatments may act through mechanisms that are not directly aligned with the core genetic architecture of ADHD. In contrast, three loci located on chromosomes 1, 4, and 12 were found to be significantly associated with ADHD and to contain several pharmacologically tractable genes. Among these, a subset has already been identified as drug targets for other conditions, including cancer, autoimmune diseases, and other neurodevelopmental disorders [69].

The future of ADHD management appears to lie in a multidisciplinary framework that integrates pharmacological treatment with behavioral strategies and emerging non-pharmacological interventions. However, although some alternative approaches have shown preliminary efficacy, further research is required to clarify their potential additive or synergistic effects when used in combination. For instance, interventions such as physical activity, mindfulness-based practices, and dietary modifications may produce greater benefits when implemented as integrated components of a combined treatment model rather than as isolated adjuncts to drug administration. Similarly, microbiota-targeted interventions may be integrated within dietary modification programs. In this context, nutritional psychiatry may represent a pivotal clinical avenue in ADHD management, as the combination of dietary modulation with both psychobiotic and nutraceutical supplementation could exert synergistic effects that enhance overall treatment efficacy, including established approaches such as pharmacotherapy and psychotherapy, particularly in light of the heterogeneous clinical presentation and long-term functional impact characteristic of mental disorders [70]. Nevertheless, future studies should also examine the impact of introducing these interventions at earlier developmental stages, including at the time of initial diagnosis or during prodromal or early symptom presentation prior to pharmacological treatment initiation. In addition, such research should prioritize adequately powered sample sizes, strengthened procedures to reduce the risk of bias, and improve the robustness of findings.

Considering the findings of this review, as well as the

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future directions previously outlined, the following key perspectives may be proposed as a concise synthesis of priority areas for future research within the context of ADHD management: (i) optimization of stimulant prodrugs to improve pharmacokinetic profiles and treatment adherence; (ii) elucidation of novel pharmacological targets to expand mechanisms-based drug development; (iii) reassessment of current pharmacotherapy in light of emerging genetic evidence suggesting partial misalignment with molecular configuration; (iv) identification of moderators of response to enable developmentally sensitive non-pharmacological interventions; (v) evaluation of multimodal interventions to clarify potential synergistic effects across treatment strategies; (vi) cautious use of digital tools, especially AI-based, until robust evidence supports their safety and efficacy for clinical application; (vii) strengthening regulatory and public health strategies regarding the neurobehavioral impact of food additives commonly present in widely marketed products for children, particularly in relation to attentional and behavioral outcomes; (viii) promotion of healthier dietary patterns (e.g., plant-based diets) through targeted public health initiatives in key settings (e.g., schools) to support early adoption and long-term behavioral change; (ix) development of awareness campaigns to reduce potential social stigma and to foster more inclusive perceptions of affected individuals; and (x) design of more standardized outcome measures and rigorously controlled trial designs to reduce bias and improve the translational value of non-pharmacological research.

Conclusions

Evidence suggests that ADHD management might rely on a combination of pharmacological and non-pharmacological approaches, with standard treatments showing the most consistent clinical utility. Across therapeutic modalities, most interventions appear to show more consistent effects in pediatric populations, but remain limited regarding generalizability across developmental stages. Although addressing ADHD may require multimodal management, the optimal integration and comparative effectiveness of different interventions remain insufficiently established. Given the multifactorial etiology of ADHD, involving both biological and environmental determinants, current therapeutic options may therefore be considered within a personalized framework to better align interventions with individual patient profiles and needs. In this respect, intervention selection should consider developmental stage and predominant symptom domains. Behavioral approaches may be particularly relevant in younger children, whereas pharmacological treatments combined with psychosocial interventions may represent central components of management in older children, adolescents, and adults with clinically significant symptoms. Complementary approaches may be considered as adjunctive options targeting specific difficulties, such as executive dysfunction, emotional regulation, sleep disturbances, or lifestyle-related factors, although their role in routine clinical practice requires further validation.

Availability of Data and Materials

Not applicable.

Author Contributions

Conceptualization: ABR; Literature search and analysis: ABR and JJB; Original Draft Preparation: ABR and JJB; Review and Editing: ABR; Supervision: ABR. Both authors approved the final version, and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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