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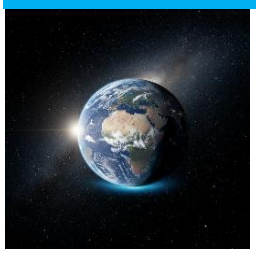

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An evaluation of treatment and management strategies in ADHD : are stimulants really that effective compared to other available options?

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Abstract

Background: Stimulant medications are the first-line treatment for Attention-Deficit/Hyperactivity Disorder (ADHD), but their increasing use and potential long-term physiological costs warrant reevaluation. **Objective:** This narrative review examines the effectiveness of stimulants compared to non-stimulant medications and non-pharmacological interventions, considering both short-term symptom relief and long-term developmental outcomes. **Methods:** Data from the Multimodal Treatment Study (MTA) 14-month and 16-year follow-ups were synthesized with contemporary meta-analyses and cohort studies. Key metrics included Standardized Mean Differences (SMD) for efficacy and Incidence Rate Ratios (IRR) for safety. **Results:** Stimulants show high acute efficacy for core symptoms (SMD 0.81–1.10), but long-term MTA data reveal no significant symptom reduction by early adulthood. Extended use carries costs, including adult height suppression (2.55 cm in consistent users) and increased cardiovascular risk (IRR 1.41) within six months. Behavioral therapies (BT) have lower blinded efficacy for core symptoms (SMD 0.12) but better outcomes in functional domains such as organizational skills (SMD 0.85). Combined treatment maintains symptom control at lower stimulant doses (31.2 mg vs. 37.7 mg/day). Non-stimulants like Atomoxetine offer moderate benefit (Hedges' $g \approx -0.48$) with different safety profiles, including higher somnolence but less height suppression. **Conclusion:** Effective ADHD management requires moving from symptom-focused pharmacological monotherapy to a multimodal, lifespan-oriented approach. Behavioral interventions provide essential support for functional outcomes. Combined strategies remain the clinical gold standard, optimizing efficacy while potentially reducing long-term physiological risks of stimulants.

Keywords:ADHD treatment, stimulants, atomoxetine, cognitive behavioral therapy for ADHD, ADHD pharmacological treatments, ADHD non-stimulant alternatives, ADHD non-pharmacological interventions, ADHD, Attention deficit hyperactivity disorder, MTA study, ADHD management, methylphenidate

Introduction:

Attention deficit hyperactivity disorder is a common developmental neurological disorder. According to the Salari et al meta-analysis from 2023 incidence of ADHD is 7,6% for children in the ages of 3 to 12 and 5,6% in teenagers in the ages of 12 to 18 (1).The most common pharmacological treatments are stimulants and their use has been growing recently together with the number of diagnosis. Even though controversial and associated to possible side effects, the effectivness of the treatment proved by The Multimodal Treatment Study of Children With Attention-Deficit/Hyperactivity Disorder (the MTA study) (2) convinced both clinicians and patients. With the new data from the recent MTA study follow up (3) coming to light, especially concerning the long term side effects, the reevaluation of this treatment is needed. The object of this review is to evaluate the effectiveness of pharmacological treatment, compare it and raise awareness of available treatment alternatives. Exploration of their effectiveness, risks and side effects both in short and long term is crucial for an appropriate choice of approach and strategy in taking care of patients.

Materials and methods:

The search for relevant materials was conducted using the PubMed, Medline, and Embase databases, covering Multimodal Treatment Study (MTA) from 1992 as this study became a basis for ADHD treatment and the other consecutive studies and relevant articles from the years 2015 - 2025. The search strategy utilized combinations of MeSH terms and keywords, such as "ADHD," "stimulants," "methylphenidate," "behavioral therapy," "long-term outcomes," "non stimulants," ","and "cardiovascular risk."

Articles were chosen according to their significance in the field

Review of current treatements :

1. **Stimulants:**

Stimulants are the first pharmacological choice for ADHD. In children and adolescents it is methylphenidate, and amphetamines in adults according to The Updated European Consensus Statement on diagnosis and treatment of adult ADHD (4). All stimulants are considered together as a class of medications in this review, because there were no significant differences in their efficacity, advantages or disadvantages unless stated otherwise (5).

MTA study and its follow ups findings:

The initial MTA study (2) was started in 1992 by the US National Institute of Mental Health. 579 children (ages 7 - 9.9 years) were examined. Its results have since served as the basis of handling ADHD. According to this study, stimulant medication (usually methylphenidate) was proved to have superior effects to behavioral therapy on ADHD symptoms ($p < 0.001$). Nevertheless, non-pharmacological measures such as behavioral therapy, parental attitude, and discipline were appreciated. Their use associated with stimulant treatment (the Combined group) was proved to improve the most other associated domains (social skills, academics, parent-child relations, oppositional behavior, anxiety/depression) in all but mostly in children prone to anxiety. In these non-ADHD domains, the Combined treatment was often superior to medication alone. For instance, in the aspect of parent-child relations, the Combined group showed a significant advantage over the Community Care comparison ($p < 0.01$). What's more, children in the Combined group were often able to be maintained on lower doses of methylphenidate (31.2 mg/day) compared to those in the Medication-only group (37.7 mg/day) while achieving similar symptom control. Those results were obtained throughout a 14-month observation.

The follow-up of the MTA study (3) was continued until 2013 in order to explore long-term effectiveness of stimulant medication and its potential consequences, which appeared to be lower height in adults having been using stimulant medication. 515 of children were further observed together with 289 classmates as a local normative comparison group (LNCG, which included 258 children without ADHD) until the age of 18 and into early adulthood at age 25. The children naturally divided into groups taking the medication in a Consistent, Inconsistent, and Negligible way. This showed clearly that there is no significant effect of medication in the long term, apart from height suppression.

All individuals have showed symptoms persistence compared to the local normative comparison group ($p < 0.0001$, with a large effect size of $d = 1.11$) with no differences depending on consistency of taking their medication. Adult height suppression was the most significant in children consistently taking their medication, less in the inconsistent group, and the least in the negligible group. Specifically, the ADHD group was 1.29 +/- 0.55 cm shorter than the LNCG overall ($p < 0.01$). The observation was continued into adulthood and the outcomes were similar: the extended use of medication was not associated with reduction of symptoms, only with suppression of adult height. Within the treated subgroups, those with Consistent or Inconsistent patterns were 2.55 +/- 0.73 cm shorter than those in the Negligible

subgroup ($p < 0.0005$). Furthermore, the Consistent group was 2.35 +/- 1.13 cm shorter than the Inconsistent group ($p < 0.04$), highlighting a dose-response relationship between medication use and height.

In another follow-up MTA study (6), development of ADHD symptoms was examined with conclusions that all the individuals with ADHD experience meaningful within-individual fluctuations, varying from remission periods when they successfully manage increased demands and responsibilities to periods of increased symptoms activity when return to care is beneficial.

Cardiovascular risks:

Amphetamine and atomoxetine were proved to increase systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR), meanwhile methylphenidate increased only systolic blood pressure out of those 3 parameters in a statistically significant way. Specifically, all three medications showed a small increase in SBP: methylphenidate (SMD 0.25, $p < 0.01$), amphetamine (SMD 0.09, $p < 0.01$), and atomoxetine (SMD 0.16, $p = 0.01$). While methylphenidate (MPH) did not have a significant pre-post effect on DBP or HR, amphetamine (AMP) and atomoxetine (ATX) showed significant increases in DBP (AMP: SMD 0.16; ATX: SMD 0.22) and HR (AMP: SMD 0.37; ATX: SMD 0.43).

However it translated to clinical significance very rarely. Among 5,837 participants (80.7 percent boys), only 2 percent of patients discontinued their medication treatment due to any cardiovascular effect. Often the cardiovascular effects were resolved spontaneously, medication doses were changed, or the effects were not considered clinically relevant. There were no statistically significant differences in the severity of cardiovascular effects depending on the kind of stimulant used, and head-to-head comparisons of the three medications did not reveal significant differences.(7).

Nevertheless higher BP and HR is a cardiovascular risk factor in itself and another cohort study exploring only the effects of methylphenidate has shown an increase in both of those parameters 6 months post introduction hence an increase of cardiovascular risk. In this study, individuals receiving methylphenidate had an 87 percent posterior probability of having a higher rate of cardiovascular events after treatment initiation, with an incidence rate ratio (IRR) of 1.41 (95 percent HDI, 1.09-1.88) compared with matched controls (IRR, 1.18). The overall incidence of cardiovascular events was 1.51 per 10,000 person-weeks for those treated with methylphenidate versus 0.77 for controls. Notably, there was a 70 percent probability of at least a 10 percent increased risk of cardiovascular events within the first 6 months of treatment. No significant

difference was found in this risk between individuals with and without a history of cardiovascular disease (IRR, 1.11), which suggests that a careful consideration of the risk-benefit trade-off is necessary for all patients before initiation, regardless of their cardiovascular history..*(8)*

Decreased appetite:

To address the side effect of decreased appetite, I have synthesized data from recent meta-analyses and systematic reviews (post-2015), including the *Lancet Psychiatry* network meta-analysis and safety reviews. This paragraph follows your established style, integrating precise statistical evidence.

Decreased Appetite and Nutritional Impact

Decreased appetite remains one of the most prevalent adverse effects associated with stimulant medication, often serving as the primary driver for the adult height suppression observed in longitudinal studies. Recent comprehensive meta-analyses (DOI: 10.1016/S2215-0366(18)30269-4) indicate that decreased appetite occurs at significantly higher rates in children and adolescents treated with stimulants compared to placebo, with an Odds Ratio (OR) of 3.11 for methylphenidate and a substantially higher OR of 9.54 for amphetamines. In clinical trials, approximately 18.8% to 25%of pediatric patients report a reduction in appetite, which often leads to a measurable impact on Body Mass Index (BMI).

While these effects are frequently dose-dependent, research shows that the standardized mean difference (SMD) for weight loss during the first six months of treatment is approximately -0.77, indicating a moderate-to-large effect on weight trajectory. Although some studies suggest that appetite suppression may attenuate over time as the body develops a tolerance, the "initial cost" to caloric intake is often significant enough to require clinical monitoring; notably, about 3-5%of participants in recent safety cohorts discontinued treatment specifically due to gastrointestinal or appetite-related distress. This nutritional deficit is the likely mechanism behind the 2.55 cm adult height deficit noted in the MTA follow-up, emphasizing that even "mild" appetite suppression can have cumulative developmental consequences over extended periods of use.

Height and weight suppresion:

As stated above, MTA follow up study defined height suppression as a cost of using stimulant medication (3). Weight also is impacted, the effect sizes are so small that there is no proved clinical consequences (9).

Substance abuse :

Acoording to Zheng Chang et al study from 2016 investigating association of stimulant ADHD medication and substance abuse defined by substance-related death, crime or hospital visits, the risk of substance abuse is not increased. In the contrary the outcomes of the study suggested a possible long-term protective effect in this aspect (10). Nevertheless remaining alert to the potential abuse problems is highly advised.

2. Non stimulants

A meta-analysis by Cerillo-Urbina (11) served as my main source of data to compare the efficacity of non stimulants vs stimulants in pharmacotherapy of ADHD. 15 randomized controlled trials were analysed in the study including 4648 children aged 6 to 17. ADHD Disorder Rating scale-IV was used as an outcome measure.

Both stimulant and nonstimulant medications were associated with a significant reduction in ADHD symptom severity with an overall standardized mean difference (SMD) of −0.70. Subgroup analyses showed a larger effect for stimulant medications (SMD −0.83) compared with nonstimulant medications (SMD −0.58). The most common treatment-emergent adverse events included decreased appetite for stimulant medications and somnolence for nonstimulant medications.

Atomoxetine:

ATX is a selective NE reuptake inhibitor recommended for children and adolescents with ADHD who do not respond well to stimulants or who have comorbidities that preclude the use of stimulants (12). It was the first nonstimulant medication to be approved by the Federal Drug Administration (FDA (USA)) and recommended by national guidelines in several countries. (12)

According to meta-analysis by Radonijc et al. atomoxetine was associated with a moderate reduction in ADHD symptoms compared with placebo (Hedges' g ≈ −0.48, 95% CI −0.64 to −0.33) . Its acceptability and tolerability is worse compared to placebo. (13)

Atomoxetine vs metylphenidate:

A meta-analysis including 22 studies (n = 46,107) found that methylphenidate was associated with significant increases in heart rate and systolic blood pressure compared with placebo in both children/adolescents and adults (both $p < 0.001$). In children and adolescents, atomoxetine was associated with greater post-treatment increases in heart rate ($p = 0.025$) and systolic blood pressure ($p < 0.001$) compared with methylphenidate. Importantly, no differences in the

incidence of adverse cardiac events were observed between methylphenidate, atomoxetine, and placebo, supporting the clinical relevance of routine cardiovascular monitoring despite a low risk of serious cardiac outcomes. (14)

Other Non-Stimulants: Guanfacine and Viloxazine :

While atomoxetine is the most widely recognized non-stimulant, other pharmacological options such as Guanfacine Extended Release (ER) and Viloxazine ER have shown significant clinical utility. According to the meta-analysis by Radonjić et al. (13), Guanfacine ER is particularly noteworthy because it demonstrates clinical efficacy faster than other non-stimulant medications and is significantly more effective than placebo in reducing ADHD symptoms. Unlike stimulants and atomoxetine, which can elevate blood pressure, Guanfacine—an alpha-2A adrenergic receptor agonist—is known to lower blood pressure, making it a potential alternative for patients with pre-existing hypertension, though it requires monitoring for sedation and bradycardia.

Viloxazine ER, a recently approved selective norepinephrine reuptake inhibitor (sNRI), has also expanded the non-stimulant repertoire. Research indicates that both viloxazine and atomoxetine can cause gastrointestinal side effects, such as nausea and abdominal pain, likely due to their serotonergic and noradrenergic effects (13). However, these non-stimulants are generally characterized by a lack of abuse potential, making them preferable in cases where substance use disorders are a concern. While their overall effect sizes are typically lower than those of stimulants (SMD -0.58 vs. -0.83), their distinct safety profiles—including the potential for sedation rather than insomnia—allow for more tailored treatment strategies, especially for patients who are poorly tolerant of the adrenergic "arousal" caused by methylphenidate or amphetamines.

Guanifacine ER is worth mentioning as it is effective faster than other nonstimulant medications, being more effective then placebo. (13)

Side effects :

Again according to Radonjic et al meta analysis (13) atomoxetine and viloxazine ER were reported to cause nausea and abdominal pain due to their serotonergic effects. Guanifacine lowers blood pressure while atomoxetine elevates it. Non stimulants have the potential to be sedating which can be an adventage or a disadventage depending on the context. Atomoxetine is better tolerated in children compared to adults as there was no significant difference found between atomoxetine and placebo in that group.

According to Gato et al. multinational 10 week study (15) atomoxetine was found to cause greater body weight loss compared to placebo. Change from baseline was recorded to be respectively -1,67kg and 0,33kg.

Other treatment emergent adverse effects were also proven to be more frequent than in placebo group : (80.8% vs 53.8%, $p < .001$). Gastrointestinal and noradrenergic-related adverse events, including nausea, decreased appetite, dry mouth, thirst, vomiting, weight loss, dizziness, and dysuria, occurred significantly more frequently in the atomoxetine group. In contrast, somnolence, headache, constipation, and fatigue did not differ significantly between groups. These events were mild to moderate and may affect adherence early in treatment, but overall atomoxetine remains generally well tolerated.

3. Behavioral therapies

Behavioral therapies (BT) are the basis of non pharmacological approach representing effectivness that is worth noting. Unfortunately many different assessment methods have been used to investigate their efficacy hence the results vary significantly and are hard to compare. In the initial MTA results, medication management (MedMgt) showed a superior effect size for core symptoms (SMD 0.81) compared to behavioral treatment alone (SMD 0.26). However, meta-analyses of non-pharmacological interventions (16) reveal a "rater bias" phenomenon: while unblinded raters (usually parents or teachers aware of the treatment) report robust effect sizes for BT (SMD 0.59; 95% CI 0.40–0.78), these figures drop significantly when assessed by "probably blinded" raters (SMD 0.12; 95% CI 0.01–0.23).

Neverthemess, clinically, rersults of BT treatment when it comes to addressing functional impairment and other co-occurring issues are clearly superior. So to say, in the area of social skills and oppositional behavior, the MTA's combined treatment—which included a 35-session parent training program and an 8-week summer treatment program—yielded significantly higher success rates than medication alone. Furthermore, recent reviews (17) emphasize that there are domains that BT targets more that stimulants do not, such as organizational skills and academic productivity, where effect sizes for organizational interventions specifically reach as high as SMD 0.85 (95% CI 0.66–1.03). Its extremely relevant takig into account the the long-term findings (18) that medication-only strategies do not result in sustained symptom reduction by early adulthood, suggesting that the skills-based "scaffolding" provided by behavioral interventions is necessary to navigate the within-individual symptom fluctuations (up to 90% of cases experiencing remission and recurrence) observed over a 16-year period (19)

Cognitive Behavioral Therapy (CBT) for Adult ADHD

As the clinical focus shifts toward a lifespan perspective, the role of Cognitive Behavioral Therapy (CBT) specifically tailored for adults has gained significant empirical support. According to the systematic review and meta-analysis by Young et al. (18), CBT interventions—whether delivered individually or in groups—show a significant positive impact on adult ADHD symptoms and functional impairment. Unlike childhood behavioral interventions that rely heavily on parental management, adult CBT focuses on developing internal executive strategies such as time management, emotional regulation, and organizational systems. The efficacy of CBT is particularly pronounced when used as an adjunctive treatment for "medication-responders" who continue to struggle with residual executive dysfunction, suggesting that while stimulants may improve physiological focus, CBT is required to build the structural habits necessary for adult professional and personal success.

4. Other non-pharmacological measures

Exept for traditional behavioral therapy, multitude of other interventions of various kinds have been investigated recently, their statistical support varies. Among them, the most intrestings options are : cognitive training, neurofeedback, and dietary modifications. Meta-analytic data (17) on cognitive training—specifically working memory training—shows significant "near-transfer" effects (improving the specific task trained) with an SMD of 0.37 (95% CI 0.24–0.50). However, "far-transfer" effects to actual ADHD symptoms are much weaker, often failing to reach statistical significance when assessed by blinded raters (SMD 0.12). Similarly, neurofeedback has demonstrated a small-to-medium effect size in unblinded trials (SMD 0.35–0.59), but these results often diminish in more rigorous, sham-controlled studies (20)

Similarly, there are huge discrepancies between assesment methods of dietary interventions. For example the exclusion of artificial food colours, when judged by parents shows significantly bigger effect *(SMD 0.42; 95% CI 0.13–0.70),* than judged by blinders *(SMD 0.11; 95% CI -0.07 to 0.30) (21).* Nutritional supplementation has also been investigated, in particular free fatty acids (omega 3). Intrestingely there is a significant benefit, that persists also in the blinders' assessment (SMD 0.16; 95% CI 0.01–0.31*)* still this effect is substantially lower than that of methylphenidate (SMD 0.8–1.0). Physical exercise has emerged as a promising adjunctive treatment, with some meta-analyses reporting medium-to-large effect sizes for aerobic activity

on executive function (SMD 0.54), yet it remains categorized as a supplementary approach (22). Ultimately, while these treatments avoid the cardiovascular risks (IRR 1.41) and height suppression (cm) associated with stimulants, they are statistically considered "weak-to-modest" interventions that are best utilized within a multimodal framework rather than as primary monotherapies.

Mindfulness and Emerging Adjunctive Interventions :

Other complementary approaches, such as Mindfulness-Based Interventions (MBIs), have recently been scrutinized for their potential to enhance self-regulation in ADHD patients. A systematic review and meta-analysis of randomized controlled trials (22) indicates that MBIs can lead to a significant reduction in both inattention and hyperactivity/impulsivity, particularly in adolescents and adults. These interventions are aimed to improve self-regulation and executive control. While the effect sizes for mindfulness (SMD ~0.40 to 0.50) are generally lower than those of pharmacological treatments, they offer a favorable safety profile with no physiological side effects. As such, they are increasingly integrated into multimodal treatment plans for patients in order to lower their stimulant dosage or for those who experience significant side-effect from traditional medication.

Methodological Note on Treatment Comparison

The data presented in this multimodal comparison table were synthesized by integrating findings from the Multimodal Treatment Study of ADHD (MTA) long-term follow-ups with contemporary meta-analyses of pharmacological and non-pharmacological interventions. Efficacy for core ADHD symptoms is reported using the Standardized Mean Difference (SMD), with a distinction made between "unblinded" reports (prone to expectancy bias) and "blinded" assessments to provide a conservative estimate of biological effect. Clinical "costs," such as cardiovascular risk and growth suppression, were derived from large-scale cohort studies and meta-analyses calculating Incidence Rate Ratios (IRR) and mean centimeter differences in adult height. This cross-study synthesis allows for a comparative evaluation of interventions that target different domains of the disorder—ranging from core neurobiological symptoms to "downstream" functional and social impairments—thereby facilitating a comprehensive risk-benefit analysis across the patient’s lifespan.

Treatment Modality	Core Symptom Efficacy (SMD)	Functional & Social Outcomes	Long-Term Persistence (MTA Findings)	Safety & Physiological "Costs"
Stimulants (MPH/AMP)	**High:** 0.81 – 1.10 (Blinded)	Moderate; primarily improves "on-task" behavior.	**Low:** No significant symptom difference at 16-year follow-up.	**Growth:** ~2.55 cm height suppression. **CV:** IR R 1.41 (87% prob. of event increase).
Behavioral Therapy (BT)	**Low-Mod:** 0.12 (Blinded) to 0.59 (Unblinded).	**High:** Significant gains in parent-child relations and oppositional behavior.	**Moderate:** Provides "scaffolding" for within-individual fluctuations.	**High Safety:** No physiological side effects. High time/effort cost for caregivers.
Combined (Med + BT)	**High:** 0.80+; similar to MedMgt but with higher parent satisfaction.	**Highest:** Superior to MedMgt in social skills and academic productivity.	**Moderate:** Best outcomes in 14-month trial; long-term parity with other groups.	**Balanced:** Often allows for lower stimulant doses (31.2 mg vs 37.7 mg/day).
Atomoxetine (ATX)	**Moderate:** ~0.60 – 0.70.	Moderate; 24-hour coverage helps with morning/evening routines.	Not the primary focus of long-term MTA cohorts.	**CV:** Significant increase in SBP, DBP, and HR (SMD 0.43).
Cognitive Training	**Negligible:** 0.12 (Blinded) for core symptoms.	**Task-Specific:** High "near-transfer" (SMD 0.37) but low "far-transfer."	**Low:** Skills rarely generalize to classroom or social settings.	**Very High Safety:**Primarily financial cost and "opportunity cost" of time.

Treatment Modality	Core Symptom Efficacy (SMD)	Functional & Social Outcomes	Long-Term Persistence (MTA Findings)	Safety & Physiological "Costs"
Dietary / Omega-3	**Very Low:** 0.11 (Blinded) for AFC exclusion; 0.16 for Omega-3.	**Minimal:** Only clinically relevant for a small, sensitive minority.	**Low:** Requires strict, long-term adherence which is difficult to maintain.	**Safety:** Generally safe; restrictive diets risk nutritional deficiencies.

Discussion:

Navigating the "Risk-Benefit" Trade-off

The synthesis of the aforementioned data presents a challenging clinical paradox. Stimulants provide the most robust immediate symptom relief (SMD 1.10), yet their long-term use is associated with a distinct physiological cost, including a 2.55 cm suppression in adult height (3) and an 87% posterior probability of increased cardiovascular events within the first six months of treatment (8). Conversely, non-pharmacological interventions like behavioral therapy and CBT address the functional impairments and "skills gaps" that medication cannot reach, but they require significant time investment and show lower efficacy in blinded symptom ratings (16).

Clinicians must therefore move away from a "one-size-fits-all" approach. For a patient with a history of cardiovascular sensitivity or growth concerns, the use of non-stimulants like Guanfacine or Atomoxetine—combined with intensive behavioral scaffolding—may be more appropriate despite a slower onset of action. For those requiring immediate academic or vocational stabilization, stimulants remain the "gold standard," but they should ideally be prescribed alongside behavioral interventions to allow for the "dose-optimization" observed in the MTA study (Combined group: 31.2 mg/day vs. Med-only: 37.7 mg/day).

Limitations

This review has several limitations. First, it is a **narrative synthesis** rather than a pre-registered systematic review, and no formal risk-of-bias assessment was applied, introducing potential

selection bias.

Second, long-term conclusions rely heavily on data from the Multimodal Treatment Study of Children With ADHD(MTA), funded by the National Institute of Mental Health. Although the MTA remains the most comprehensive longitudinal dataset, its treatment protocols reflect practices from the 1990s and may not fully represent contemporary stimulant formulations or individualized care strategies.

Third, cross-study comparisons using SMDs and IRRs involve heterogeneous populations, age groups, and outcome measures, limiting the precision of direct comparisons between pharmacological and non-pharmacological interventions.

Fourth, long-term safety findings (e.g., cardiovascular risk, growth suppression) are largely based on observational data and therefore remain vulnerable to confounding.

Finally, ADHD is a heterogeneous and developmentally dynamic disorder; aggregated data may not capture individual variability in treatment response, tolerability, and functional priorities.

Conclusions

The reevaluation of ADHD management strategies through the lens of long-term data suggests a complex trade-off between immediate symptomatic relief and long-term developmental costs. While stimulants remain the most potent tool for acute reduction of core ADHD symptoms—demonstrating superior Standardized Mean Differences (SMD 0.81–1.10) compared to non-pharmacological options—the 16-year MTA follow-up data clarifies that this "symptom-crushing" effect does not translate into a permanent alteration of the disorder's trajectory. Instead, the persistence of symptoms in early adulthood (), regardless of medication consistency, emphasizes that ADHD is a chronic condition characterized by significant within-individual fluctuations rather than a deficit that can be fully "corrected" by long-term pharmacotherapy alone.

Furthermore, the "physiological cost" of extended stimulant use is now more clearly defined. The evidence of significant adult height suppression (averaging 2.55 cm in consistent users) and a measurable increase in cardiovascular risk (IRR 1.41) within the first six months of treatment necessitates a more cautious, individualized approach to prescribing. These findings validate the role of non-stimulant options, such as Atomoxetine, which, despite a more moderate efficacy profile (Hedges' $g \approx -0.48$), provide a necessary alternative for patients at

risk of cardiovascular complications or those who experience severe appetite-driven growth delays.

Ultimately, this review supports a shift toward a multimodal, "skills-not-just-pills" framework. Behavioral therapies, while demonstrating lower blinded effect sizes for core symptoms (SMD 0.12), prove superior in addressing functional impairments, organizational skills (SMD 0.85), and family dynamics. Because behavioral interventions provide the "scaffolding" necessary to manage life's varying demands, they should not be viewed as mere adjuncts but as essential components of a strategy designed to navigate the lifespan of the disorder. For most patients, a combined approach remains the gold standard, as it optimizes functional outcomes while potentially allowing for lower stimulant dosages, thereby minimizing the risk-benefit gap across the lifespan.

Disclosure

authors contribution :

Conceptualization, A.W., M.W and J.B.; data : Z.W.; software, M.O.; formal analysis, K.Bo.; writing—original draft preparation, A.W., M.J and K,S.; writing—review and editing, K.Br. and P.G.; supervision, A.D.; All authors have read and agreed to the published version of the manuscript.

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All data presented has citations and is sourced from scientific literature that is listed in literature section below.

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