

CASE REPORT

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Gender disparities in ADHD medication efficacy: investigating treatment outcomes for females compared to males

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Abstract

Background ADHD manifests differently across genders, with females often underdiagnosed due to more internalizing symptoms such as inattention, emotional dysregulation, and anxiety. Males, in contrast, tend to display externalizing behaviors such as hyperactivity and impulsivity, leading to earlier and more frequent diagnoses. These diagnostic disparities significantly influence the efficacy and adherence to ADHD treatments across genders.

Objective This narrative review investigates gender disparities in ADHD medication efficacy, focusing on the hormonal, biological, neurophysiological, and sociocultural factors influencing treatment outcomes for females compared to males.

Methods Findings from 35 validated studies were synthesized, including randomized controlled trials (RCTs), observational studies, longitudinal research, systematic reviews, neuroimaging analyses, and qualitative data. Emphasis was placed on gender-specific trends in medication efficacy, adherence, side effects, and long-term outcomes.

Results Hormonal fluctuations in females, such as changes in estrogen levels, influence ADHD symptom severity and medication efficacy. Evidence suggests that females may benefit more from non-stimulant treatments like atomoxetine, while stimulant medications yield more significant improvements in externalizing behaviors for boys. Gender-specific differences in treatment adherence and long-term functional outcomes are highlighted, underscoring the challenges faced by females with ADHD.

Conclusion The underrepresentation of females in ADHD research skews current treatment guidelines. Addressing these gaps requires gender-inclusive studies and personalized treatment approaches that consider both biological and sociocultural differences in ADHD manifestations and treatment responses.

Keywords ADHD, Gender disparities, Pharmacological treatment, Treatment outcomes, Hormonal influence, Medication adherence

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a chronic neurodevelopmental disorder affecting approximately 3% of adults worldwide, significantly impairing functional capacities, quality of life, and socioeconomic outcomes [1, 2]. Over the last decade, the prevalence of ADHD diagnoses has increased substantially, paralleling a rise in prescriptions for ADHD medications, which has placed a significant financial burden on healthcare systems globally [3]. Current clinical guidelines recommend

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a multimodal treatment strategy that integrates pharmacological therapies with psychosocial interventions and long-term follow-up care to address the complex spectrum of ADHD symptoms [4].

Pharmacological treatments for ADHD fall into two primary categories: psychostimulants—including methylphenidate- and amphetamine-based medications—and non-stimulants, such as atomoxetine and guanfacine [5]. However, the availability, accessibility, and regulatory status of these medications vary significantly across countries. For example, in Canada, long-acting amphetamine mixtures, methylphenidate, and lisdexamfetamine are prioritized as first-line treatments. In contrast, the UK primarily recommends psychostimulants, reserving non-stimulant medications such as atomoxetine for cases involving contraindications or comorbid substance use disorders [6].

While effective pharmacological options exist, gender disparities in ADHD diagnosis, symptomatology, and treatment outcomes remain underexplored. ADHD is more frequently diagnosed in males due to their pronounced externalizing symptoms, such as hyperactivity and impulsivity, which are more disruptive and easily recognized. In contrast, females often present with subtler internalizing symptoms, including inattention, emotional dysregulation, and anxiety, which are less overt and frequently misattributed to other conditions, such as mood or anxiety disorders [7]. These diagnostic disparities contribute to delayed treatment initiation in females, exacerbating long-term functional impairments in academic, occupational, and interpersonal domains.

Biological and hormonal differences further complicate ADHD symptomatology and treatment responses between genders. Hormonal fluctuations, such as those associated with puberty, menstruation, pregnancy, and menopause, influence ADHD symptom severity and medication efficacy in females [8, 9]. For instance, elevated estrogen levels during puberty enhance dopamine receptor sensitivity, potentially modulating attention regulation. Conversely, declining estrogen levels during menopause exacerbate ADHD symptoms, often reducing medication effectiveness. Archer and Garcia [10] emphasized the importance of understanding emotional and cognitive dysfunctions in ADHD, particularly in females, to achieve optimal treatment outcomes.

Sociocultural factors also play a critical role in shaping diagnostic and treatment disparities. Societal norms often trivialize or normalize ADHD symptoms in females, perceiving behaviors such as talkativeness or emotional sensitivity as personality traits rather than clinical symptoms [11]. This misperception delays diagnosis and contributes to stigma, impacting adherence to treatment and long-term outcomes.

Despite the growing recognition of these gender-specific challenges, there remains a significant underrepresentation of females in ADHD research, leading to a male-centric understanding of the disorder and its treatment [6]. Biederman et al. [3] highlighted the need to address gender-specific differences in ADHD diagnosis, symptomatology, and comorbidities to develop equitable and effective interventions.

This narrative review seeks to bridge these gaps by synthesizing findings from 35 peer-reviewed studies, encompassing a range of methodologies, including randomized controlled trials (RCTs), longitudinal studies, neuroimaging research, and systematic reviews. The review focuses on gender disparities in ADHD diagnosis, medication efficacy, treatment adherence, and long-term outcomes, with particular emphasis on hormonal, biological, and sociocultural factors. By addressing these critical disparities, this study aims to inform personalized and gender-sensitive approaches to ADHD management, ensuring more equitable care for males and females alike.

Methods

Study selection and search strategy

A comprehensive systematic search was conducted across PubMed, PsycINFO, and Scopus databases to identify relevant peer-reviewed studies published between 2000 and 2023. The search included studies providing explicit data on gender-specific differences in ADHD treatment efficacy or outcomes, such as those reviewing female-specific concerns [7], highlighting research gaps in adult ADHD populations [6], and examining emotional dysregulation in ADHD [10].

Inclusion and exclusion criteria

Inclusion criteria

Studies providing explicit data on gender-specific differences in ADHD treatment efficacy or outcomes

Research focusing on pharmacological treatments for ADHD, including stimulants (e.g., methylphenidate, amphetamines) and non-stimulants (e.g., atomoxetine, guanfacine)

Inclusion criteria encompassed studies addressing gender-specific differences in ADHD treatment outcomes, such as those focusing on internalizing symptoms like emotional dysregulation in females [7, 10].

Studies involving children, adolescents, and adults to capture gender-based treatment responses across different life stages.

Research employing robust methodologies, such as the following:

- Randomized controlled trials (RCTs)
- Longitudinal cohort studies

- Case-control analyses
- Systematic reviews and meta-analyses
- Neuroimaging studies using advanced techniques like functional MRI (fMRI) and positron emission tomography (PET)

Exclusion criteria

1. Studies lacking explicit gender-specific data or presenting aggregated outcomes without differentiation by sex
2. Research exclusively focused on non-pharmacological interventions, such as cognitive-behavioral therapy (CBT) or psychoeducation, without pharmacological comparisons.
3. Studies with methodological limitations, such as small sample sizes, inadequate reporting, or insufficient statistical validation

Definition of key terms

- *Validated studies*: Peer-reviewed studies meeting rigorous quality standards, including transparent methodologies, robust statistical analyses, and clear reporting of outcomes
- *Reliability*: Refers to the consistency of findings across the included studies, including reproducibility of outcomes, coherence of results, and methodological transparency.

Study characteristics

The review synthesized findings from 35 peer-reviewed studies, encompassing a range of study designs to ensure a comprehensive understanding of ADHD pharmacotherapy across genders.

Sample sizes

Studies ranged from large-scale population research involving over a million participants to smaller, well-controlled trials with fewer than 200 participants.

Population diversity

Efforts were made to include studies that represent diverse populations, accounting for variability in age, socioeconomic status, and cultural contexts.

Types of ADHD medications examined

1. **Stimulants**: Medications such as methylphenidate and amphetamines were evaluated for their efficacy

in managing core ADHD symptoms, including inattention, hyperactivity, and impulsivity [5]. This meta-regression analysis provided robust evidence on the effectiveness of methylphenidate for adults with ADHD, highlighting its role in symptom management across genders.

2. **Non-stimulants**: Non-stimulants such as atomoxetine and guanfacine were frequently assessed for their effectiveness in addressing internalizing symptoms and emotional regulation, particularly in females [10].

Study designs and methodological scope

1. *Randomized controlled trials (RCTs)*: Meta-regression analyses provide robust efficacy data by aggregating findings from multiple RCTs [1, 2, 5].
2. *Longitudinal studies*: Research tracking participants over extended periods to identify changes in symptomatology and treatment responses, providing insights into long-term outcomes [12, 13].
3. *Observational studies*: These studies offered real-world perspectives on treatment patterns and adherence, as well as underrepresentation in adult populations, including females [6].
4. *Neuroimaging studies*: Functional MRI (fMRI) and PET studies evaluated brain function and treatment responses across genders, with a focus on dopamine receptor activity and fronto-striatal pathways [10]. This research highlights neurobiological disruptions in females with ADHD, which contribute to their unique symptomatology and treatment challenges.
5. *Systematic reviews and meta-analyses*: Comprehensive reviews provided aggregated insights into treatment efficacy and tolerability across gender groups [8, 9]. These reviews also explore the hormonal and developmental differences influencing ADHD in females.
6. *Case-control studies*: These studies focused on comorbidities and clinical presentations, highlighting how gender influences ADHD manifestations and treatment responses [14].

Quality and bias assessment

To ensure the robustness and reliability of conclusions, the following strategies were employed to minimize bias:

1. *Advanced statistical analyses*: Multivariate regression models were used to control for confounding variables such as age, socioeconomic status, and comorbid conditions [15, 16].

2. *Structured data synthesis protocols:* Consistent protocols were followed to ensure methodological rigor in data extraction and synthesis, enhancing reliability and coherence across studies [4].
3. *Addressing underrepresentation:* Studies that explicitly addressed underrepresentation in ADHD research, particularly in female populations, were prioritized for inclusion to ensure gender-balanced insights [6] (Table 1).

Results

Prevalence and symptomatology

Multiple large-scale studies have demonstrated that ADHD is more commonly diagnosed in males, with a male-to-female ratio of approximately 2.5:1, as observed in the CATSS sample [22]. This gender discrepancy aligns with existing literature indicating that boys are more frequently diagnosed with ADHD during childhood. However, evidence suggests that symptomatic prevalence in females is higher than formal diagnostic rates indicate, as their symptoms are often overlooked. For instance, Mowlem et al. [15] reported parent-reported ADHD

symptoms with a symptomatic prevalence of 12.9%, substantially exceeding the rate of formal diagnoses in females. This highlights the tendency for ADHD to be underdiagnosed in females.

Males with ADHD tend to display overt behaviors, such as hyperactivity and conduct problems, which often draw attention from parents, teachers, and clinicians, leading to more frequent diagnoses. In contrast, females with ADHD often exhibit subtler symptoms, such as inattentiveness and emotional dysregulation. These symptoms are less disruptive and are often misattributed, resulting in underdiagnosis. Studies further demonstrate that hyperactivity and conduct problems are stronger predictors of diagnosis and medication prescriptions in females [23]. This reinforces the notion that externalizing behaviors are more likely to trigger clinical intervention.

Despite differences in diagnostic rates, the severity of ADHD symptoms is generally comparable across genders once a diagnosis is established. However, in undiagnosed populations, females typically exhibit lower symptom severity scores than males. These findings underscore the importance of improved diagnostic criteria and clinician training to recognize the subtler presentation of ADHD in females.

Table 1 Comprehensive table layout

Study ID/author(s) and year	Design	Sample size	Gender distribution (M/F)	Key findings
Castells et al., 2011 [5]	RCT, meta-regression	1200	M: 700, F: 500	Methylphenidate effective across genders, with higher male response rates
Wilens et al., 2002 [1, 2]	RCT	350	M: 180, F: 170	Amphetamines reduced hyperactivity more in males; females showed better improvement in attention
Biederman et al., [12]	Longitudinal	500	M: 250, F: 250	Long-term stimulant efficacy more pronounced in males, females benefited more from non-stimulants
Owens et al., 2017 [13]	Longitudinal	400	M: 180, F: 220	Females exhibited more internalizing symptoms and emotional regulation challenges
Ramos-Quiroga et al., 2014 [6]	Observational	1500	M: 900, F: 600	Females underrepresented in adult ADHD studies, delayed diagnosis common
Manza et al., 2022 [17]	Neuroimaging (PET)	100	M: 50, F: 50	PET studies show sex-specific dopamine receptor activity differences influencing treatment responses
Sobanski et al., 2008 [18]	Case control	300	M: 160, F: 140	Comorbidities more prevalent in females, significant impact on treatment outcomes
Littman & Wagenberg, 2023 [19]	Observational	1200	M: 700, F: 500	ADHD females reported greater social impairments and emotional challenges
De Jong et al., 2024 [20]	Qualitative study	100	M: 0, F: 100	Female-specific ADHD support groups improved coping strategies
Arnett et al., 2015 [16]	Observational	1000	M: 500, F: 500	Gender differences in symptom severity, females reported higher emotional distress
McKechnie et al., 2023 [21]	Observational	2500	M: 1400, F: 1100	ADHD diagnosis and treatment patterns influenced by gender and socioeconomic factors
Archer & Garcia, 2016 [10]	Observational	500	M: 300, F: 200	Emotional dysregulation more common in females, need for tailored treatment approaches

Neurobiological and behavioral differences

Gender disparities in ADHD extend beyond symptom presentation to include significant neurobiological differences. Research by Archer and Garcia [10] and others has shown that females with ADHD experience pronounced disruptions in specific brain regions, particularly the fronto-striatal and parietal areas, which are critical for executive functions such as attention regulation, impulse control, and task management. These neurobiological disruptions may contribute to the unique challenges faced by females in managing ADHD-related behaviors.

Neuroimaging studies have observed differences in dopamine release patterns between genders. For instance, females with ADHD show greater dopamine increases in the nucleus accumbens (NAc), a region linked to reward processing and motivation, when treated with methylphenidate [17]. However, no significant sex differences were noted in dopamine release within the dorsal striatum, which governs motor control and habit formation. These findings highlight the influence of gender-specific neurobiological mechanisms on ADHD symptomatology and treatment responses.

Treatment efficacy and gender differences

The efficacy of ADHD medications varies across genders, as demonstrated by several systematic reviews and meta-analyses. These studies assessed a wide range of pharmacological treatments, including stimulants (e.g., methylphenidate and amphetamines) and non-stimulants (e.g., atomoxetine and guanfacine). The primary focus was to measure changes in ADHD symptoms, brain activation patterns, and overall treatment outcomes.

Males are more likely to be prescribed ADHD medications at all ages, reflecting their higher clinical prevalence and more overt symptoms. However, gender differences in treatment outcomes become more apparent in adulthood. In children, boys typically exhibit more significant improvements in attention tasks following stimulant use. For adults, both genders show similar improvements in symptom severity, though females often report smaller reductions in overall symptoms compared to males [24].

Interestingly, females with ADHD often experience greater improvements in emotional regulation and social functioning, areas where they frequently struggle more than males. This suggests that ADHD treatment may offer unique benefits for women, particularly in emotional and social well-being [25].

Adverse effects and comorbidities

Gender-specific differences in the adverse effects of ADHD medications have been widely reported. For instance, females taking atomoxetine are more likely to

experience somnolence and gastrointestinal symptoms, such as abdominal pain, compared to males. Additionally, females tend to report heightened sensitivity to stimulant-related side effects, such as appetite suppression and mood fluctuations. Additionally, comorbidities associated with ADHD exhibit gender-specific patterns. Males with ADHD are more likely to develop externalizing disorders such as oppositional-defiant disorder (ODD), whereas females are more prone to internalizing disorders such as depression and anxiety [26, 27]. These gender-specific comorbidities complicate the diagnostic process for females, as internalizing disorders can mask ADHD symptoms, leading to misdiagnosis or failure to diagnose ADHD.

Socioeconomic and educational outcomes

Gender differences in outcomes are particularly pronounced in academic settings. Females with ADHD are more likely to experience speech and language impairments, which contribute to poorer academic performance compared to their male counterparts [13]. This disparity often persists into adulthood, with females reporting lower levels of educational attainment and occupational achievement. Conversely, males with ADHD are more likely to engage in risky behaviors and substance use, further complicating their long-term outcomes.

Long-term outcomes and gender disparities

Longitudinal studies highlight significant gender differences in the long-term trajectories of individuals with ADHD. Females are at higher risk for developing mood disorders, including depression, over their lifetime. Additionally, untreated ADHD in females is associated with poorer occupational performance, increased rates of relationship difficulties, and higher overall functional impairment compared to males [28].

Discussion

Gender bias in diagnosis and research

The underdiagnosis of ADHD in females is rooted in diagnostic frameworks that overlook internalizing symptoms, such as inattention and emotional dysregulation [7]. Further, Hinshaw and Blachman [8, 9] emphasize that societal expectations often mask ADHD symptoms in females, leading to diagnostic delays. Historically, ADHD has been predominantly conceptualized as a male disorder, with diagnostic criteria heavily weighted toward overt externalizing symptoms such as hyperactivity and impulsivity [15]. This focus has led to a systemic failure to recognize the subtler, internalizing symptoms commonly presented by females, such as inattention, emotional dysregulation, and anxiety [4, 23].

Societal expectations further compound these biases. For instance, hyperactive behaviors in females are often mislabeled as talkativeness or social exuberance, delaying clinical recognition and intervention [11]. Similarly, inattentiveness or emotional symptoms in females are frequently attributed to anxiety or mood disorders, overshadowing the possibility of ADHD [16, 29]. These diagnostic disparities highlight the urgent need for gender-sensitive diagnostic tools and revised clinical frameworks that account for the nuanced presentation of ADHD in females.

Tailored treatment strategies

Evidence underscores the importance of adopting gender-sensitive treatment protocols to address the unique challenges faced by females with ADHD. Multimodal treatment approaches that integrate pharmacological therapies with non-pharmacological interventions are particularly effective. Emotional dysregulation, a critical symptom in ADHD, is more pronounced in females and significantly impacts treatment outcomes [10]. Tailored multimodal treatment strategies, as emphasized by Rucklidge [30], should address both biological and sociocultural factors to optimize outcomes. For example, while stimulant medications such as methylphenidate and amphetamines are beneficial across genders, females may derive greater benefit from non-stimulant medications like atomoxetine, especially when internalizing symptoms such as anxiety or depression are present [31]. Furthermore, emotional dysregulation, a critical symptom in ADHD, is more pronounced in females and significantly impacts treatment outcomes, as highlighted by Archer and Garcia [10]. This underscores the need for tailored therapeutic approaches that specifically address emotional and cognitive dysfunctions in females with ADHD.

Non-pharmacological interventions, such as CBT and psychoeducation, are essential components of treatment for females with ADHD. These approaches target areas where females often struggle more significantly, such as emotional regulation, interpersonal difficulties, and academic challenges [32]. Combining these interventions with pharmacotherapy enhances treatment efficacy and improves long-term outcomes, particularly for addressing comorbid conditions like anxiety and depression.

Integrating non-pharmacological interventions

Although pharmacological treatments remain central to ADHD management, non-pharmacological interventions play a pivotal role in addressing the broader impacts of the disorder, particularly in females. For instance, CBT helps individuals develop practical coping mechanisms for inattention, impulsivity, and emotional dysregulation. Psychoeducation empowers patients and their families

with a deeper understanding of the disorder, facilitating better management and reducing stigma.

The integration of non-pharmacological approaches is especially beneficial for managing the emotional and social difficulties disproportionately experienced by females with ADHD. These interventions not only complement pharmacotherapy but also provide essential support for addressing common comorbidities, such as anxiety and mood disorders. Future research should focus on expanding the evidence base for these interventions and exploring their role in comprehensive ADHD care.

Addressing sociocultural factors

Sociocultural influences significantly shape the diagnosis and management of ADHD, particularly in females. Females are often socialized to suppress disruptive behaviors, leading to a misperception of their symptoms as traits like shyness or sensitivity [11]. This cultural conditioning not only delays diagnosis but also contributes to stigma, which can undermine treatment adherence and outcomes.

To counter these challenges, clinicians must adopt a holistic approach that considers sociocultural contexts when diagnosing and treating ADHD in females. Public awareness campaigns and educational initiatives can play a critical role in challenging stereotypes, promoting accurate understanding, and reducing stigma surrounding ADHD in females.

Gender differences in symptom trajectories and comorbidities

Longitudinal studies have revealed distinct developmental trajectories and comorbidity patterns for males and females with ADHD. Females are more likely to develop internalizing disorders, such as anxiety and depression, which can mask core ADHD symptoms and complicate diagnosis and treatment [13, 33]. These comorbidities exacerbate long-term functional impairments, particularly in academic and occupational domains.

In contrast, males with ADHD are more likely to exhibit externalizing behaviors, such as aggression and conduct problems, which often prompt earlier clinical attention. Understanding these gender-specific patterns is essential for designing tailored interventions that address the unique needs of both sexes [34].

Medication efficacy and adherence

Gender differences in medication efficacy and adherence have been well-documented. Meta-regression analyses, such as Castells et al. [5], provide robust evidence on the efficacy of stimulant medications, particularly methylphenidate, in managing ADHD symptoms. However,

adherence challenges remain higher in females, as highlighted by Wilens et al. [1, 2], necessitating personalized medication plans. While stimulant medications are effective for managing ADHD symptoms across genders, females often report greater improvements in emotional regulation and social functioning, areas where they face more significant challenges compared to males [10]. However, females are also more likely to discontinue treatment due to side effects or a perceived lack of efficacy [6].

Improving adherence among females requires a gender-sensitive approach that addresses these barriers. Clinicians should consider alternative treatments, such as non-stimulant medications, and prioritize proactive management of side effects. Incorporating patient education into treatment plans is another critical step, as it empowers females with ADHD to take an active role in their care and enhances their understanding of long-term benefits.

Neurobiological and hormonal influences

Neurobiological research highlights significant differences in brain structure and function between males and females with ADHD. Neurobiological disruptions in fronto-striatal and parietal regions, as noted by Archer and Garcia [10], contribute to the unique challenges faced by females with ADHD. Hormonal changes during puberty and menopause further exacerbate these symptoms, underscoring the importance of gender-specific interventions [8, 9]. These disruptions can contribute to the distinct emotional and cognitive challenges faced by females with ADHD, emphasizing the importance of gender-specific approaches to treatment [7]. Hormonal fluctuations further complicate ADHD symptomatology in females. Conversely, the drop in estrogen during menopause can exacerbate symptoms, emphasizing the need for age- and gender-specific treatment strategies that address the evolving nature of ADHD across the lifespan.

Additionally, Biederman et al. [3] explored the functional impairments in adults with ADHD and highlighted the gender-based differences in long-term outcomes, reinforcing the importance of recognizing neurobiological and hormonal factors in treatment planning. Moreover, Faraone et al. [35] identified how comorbidities and familial influences affect treatment patterns and outcomes, further underscoring the need for tailored interventions for females with ADHD.

Long-term outcomes and policy implications

The long-term impacts of ADHD are particularly severe for females. Untreated ADHD in females is associated with poorer academic achievement, lower occupational attainment, and higher rates of psychiatric comorbidities,

such as depression and anxiety [28]. These challenges highlight the importance of early diagnosis and intervention to mitigate long-term consequences.

Healthcare policies should prioritize gender-sensitive approaches to ADHD care. This includes revising diagnostic criteria to better capture the unique presentations of ADHD in females, providing enhanced training for clinicians to reduce diagnostic biases, and investing in public health campaigns to increase awareness and reduce stigma.

Future directions

Future research should focus on conducting longitudinal studies to explore gender-specific symptom trajectories and the long-term effects of treatment modalities. Additionally, there is a critical need for studies evaluating the efficacy of non-pharmacological interventions, such as CBT and psychoeducation, for females with ADHD. Expanding research into the neurobiological and hormonal underpinnings of ADHD will also provide valuable insights into gender-specific symptomatology and treatment responses.

Conclusion

This narrative review synthesizes findings from 35 studies, offering critical insights into the gender disparities in ADHD diagnosis, symptomatology, treatment, and long-term outcomes. It underscores the urgent need for reform in diagnostic frameworks, treatment protocols, and research methodologies to address the distinct challenges faced by females with ADHD.

Addressing gender bias in ADHD diagnosis

The evidence highlights a persistent gender bias in ADHD diagnosis, where externalizing symptoms, such as hyperactivity and impulsivity, dominate diagnostic criteria. These criteria often fail to capture the subtler internalizing symptoms more common in females, such as inattention, emotional dysregulation, and anxiety. This discrepancy has led to significant underdiagnosis and delayed treatment in females [15, 23]. Addressing these biases demands a paradigm shift in clinical practice, with the adoption of gender-sensitive diagnostic tools and enhanced clinician training to recognize ADHD's diverse presentations.

Advancing treatment strategies

Gender-sensitive treatment approaches are crucial to optimizing ADHD management. Tailored treatment strategies must address the distinct needs of females with ADHD. Archer and Garcia [10] highlight the importance of addressing emotional dysregulation, while Rucklidge [30] emphasizes integrating non-pharmacological

interventions to complement medication. While stimulant medications, such as methylphenidate, are effective across genders, females often respond more favorably to non-stimulant options like atomoxetine, especially when comorbid conditions such as anxiety or depression are present [31, 36]. Furthermore, integrating non-pharmacological interventions, such as CBT and psychoeducation, is vital for addressing the emotional, social, and academic challenges disproportionately faced by females [4, 32]. Tailored multimodal treatment strategies provide the most effective pathway for improving long-term outcomes.

Medication adherence and long-term outcomes

Biederman et al. [3] demonstrated the long-term functional impairments associated with untreated ADHD in adults, particularly females. Faraone et al. [35] highlighted the impact of familial and comorbid factors on treatment outcomes, underscoring the need for individualized care. Nonadherence compounds the functional impairments associated with ADHD, particularly in academic, occupational, and interpersonal domains [13]. Improving adherence requires targeted interventions, including patient education, personalized treatment plans, and proactive management of side effects. Early diagnosis and sustained treatment are pivotal to mitigating the long-term impacts of ADHD on females, who are at greater risk of developing comorbid conditions, including anxiety and depression, and experiencing poorer life outcomes [28].

Incorporating sociocultural considerations

Sociocultural factors significantly contribute to the underrecognition and mismanagement of ADHD in females. Societal norms and stereotypes often obscure ADHD symptoms in females, leading to delayed diagnoses and inadequate interventions [11]. Public health initiatives must prioritize awareness campaigns and clinician education to challenge these misconceptions and promote equitable care. By addressing these sociocultural barriers, the accurate diagnosis and effective treatment of ADHD can be ensured for individuals across all genders.

Neurobiological and hormonal influences

Neurobiological and hormonal differences between males and females further contribute to disparities in ADHD symptomatology and treatment responses. Research indicates that hormonal fluctuations, such as those associated with puberty or menopause, significantly influence ADHD symptoms and medication efficacy in females. Ramos-Quiroga et al. [6] stress the underrepresentation of females in ADHD research, calling for inclusive studies that inform equitable healthcare policies). These

findings underscore the need for age- and gender-specific treatment strategies that adapt to the evolving nature of ADHD symptoms across the lifespan.

Policy implications and research directions

The findings of this review have important implications for healthcare policy and clinical practice. Diagnostic criteria must be revised to capture the unique presentations of ADHD in females. Clinician training should be enhanced to reduce diagnostic bias and improve treatment delivery for diverse populations. Public health policies should focus on reducing stigma, promoting awareness, and ensuring equitable access to ADHD care for females.

Future research should prioritize the following:

1. *Longitudinal studies* to explore gender-specific symptom trajectories and treatment outcomes over time
2. *Comparative studies* evaluating the efficacy of pharmacological and non-pharmacological interventions for females with ADHD
3. *Neurobiological research* investigating the hormonal and structural differences that influence ADHD symptomatology and treatment responses in females
4. *Sociocultural studies* to identify and address barriers to diagnosis and treatment in diverse populations

Final thoughts

While considerable progress has been made in understanding ADHD, substantial gaps remain in addressing gender disparities. A holistic approach—encompassing biological, psychological, and sociocultural factors—is essential to ensuring that individuals with ADHD, regardless of gender, receive appropriate, personalized, and effective care. Bridging these gaps will not only improve outcomes for females with ADHD but also advance the broader field of ADHD research and clinical practice.

Bias and methodological considerations

Publication bias remains a significant concern in systematic reviews and meta-analyses, particularly when examining gender differences in ADHD diagnosis and treatment. Studies reporting significant or positive findings are more likely to be published, potentially skewing the available literature toward emphasizing gender disparities. This bias can obscure a more nuanced and accurate understanding of ADHD's presentation and treatment efficacy across genders.

Although some studies, such as Ginsberg et al. [31], employed rigorous statistical methods, including funnel plots and Egger's tests, to detect and mitigate publication bias, these practices were inconsistently reported across

the reviewed studies. Mitsis et al. [14] shed light on diagnostic complexities, including the lack of agreement between parents and teachers, which disproportionately affects females. Ramos-Quiroga et al. [6] underscore the necessity of addressing publication bias and ensuring gender balance in study populations. As a result, the reliability of conclusions regarding gender-specific trends in ADHD treatment efficacy and outcomes may be compromised. Additionally, smaller studies with statistically significant results are often overrepresented, while null or less impactful findings are underreported.

Addressing bias in future research

To improve the robustness and reliability of ADHD research, several strategies should be prioritized:

1. *Transparent reporting*: Future studies should consistently report methods used to assess and address publication bias, including statistical techniques and data synthesis protocols.
2. *Balanced representation*: Ensuring gender-balanced representation in study populations is essential to accurately capture the experiences and treatment responses of both males and females with AD
3. *Longitudinal designs*: Employing longitudinal study designs will enable researchers to track ADHD symptoms, treatment efficacy, and adherence over time, providing insights into gender-specific trajectories and outcomes.
4. *Accounting for confounding variables*: Researchers should control for potential confounders, such as socioeconomic status, comorbid conditions, and treatment history, to ensure that observed gender differences are not attributable to these factors.

Publication bias and methodological challenges

Publication bias remains a significant concern in systematic reviews and meta-analyses, particularly when examining gender differences in ADHD diagnosis and treatment. Studies with significant or positive findings are more likely to be published, potentially skewing the literature toward emphasizing gender disparities. Although efforts to address publication bias, such as using funnel plots and Egger's tests, are noted in some studies, the application of these methods has not been uniformly reported across the reviewed literature [5, 31, 37]. This inconsistency increases the risk of overrepresenting studies with significant results while underreporting null or

less impactful findings, thereby limiting the generalizability of conclusions.

To improve the robustness and reliability of future ADHD research, it is essential to address these biases by adopting transparent reporting practices. Future studies should employ the following:

- *Longitudinal designs*: Tracking ADHD symptom trajectories and treatment efficacy over time, while considering gender-specific variations, to provide a comprehensive understanding of ADHD outcomes
- *Balanced representation*: Ensuring that study populations include adequate representation of both genders to capture nuanced treatment responses and symptom profiles
- *Controlling for confounding variables*: Accounting for socioeconomic status, comorbid conditions, and prior treatment history to ensure that observed differences are genuinely attributable to gender and not other factors
- Addressing publication bias and methodological inconsistencies will enable a more balanced and accurate understanding of ADHD and its gender-specific manifestations. This, in turn, will contribute to more equitable diagnostic and therapeutic strategies that align with the needs of both males and females.

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Authors' contributions

D.A. (Davoud Amiri) conducted a thorough review and analysis of the selected studies in collaboration with L.B. (Lamberto Briziarelli) and E.T. (Enrico Tempesta). D.A. identified and examined the relevant research, after which L.B. and E.T. reviewed and validated the analysis to ensure accuracy and reliability. D.A. reviewed and analyzed the selected studies. L.B. and E.T. revised and validated the research findings. All authors contributed to and reviewed the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Ethics approval and consent to participate

Not applicable. This study was a meta-analysis of previously published data and did not involve direct interaction with human participants.

Consent for publication

All authors have reviewed and approved the final manuscript and consent to its publication.

Competing interests

The authors declare no competing interests.

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