

REVIEW ARTICLE

# ADHD IN THE FAMILY MEDICINE SETTING: ETIOLOGY, PRESENTATION, AND DIAGNOSIS

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**KEYWORDS**  
  
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**ABSTRACT**  
  
Attention-deficit hyperactivity disorder (ADHD) is a neurodevelopmental phenomenon commonly presented to the primary care physician for diagnosis and treatment. The primary care physician has the capability to diagnose ADHD and should remain well-informed in the current body of literature regarding ADHD. The diagnosis of ADHD is complicated because it presents with significant heterogeneity throughout development and among individuals. Understanding the neurodevelopmental etiology associated with ADHD helps to contextualize the behavioral, emotional, and cognitive deficits with which these patients struggle. Through a more in-depth understanding of ADHD, the primary care physician is more informed and better able to care for patients. As presented in this article, a literature review on the underlying etiology, clinical presentation, and clinical diagnosis of ADHD, this article helps the primary care physician stay up to date on ADHD.

## INTRODUCTION

Attention-deficit hyperactivity disorder (ADHD) has been known under various names since 1775.<sup>1</sup> It is a neurodevelopmental syndrome caused by the cumulative effects of various genetic and environmental risk factors.<sup>1</sup> ADHD manifests as lifelong patterns of inattentiveness, hyperactivity, and impulsivity that are severe enough to impair daily functioning.<sup>1</sup> People with ADHD have been found to be at an increased risk for behavioral health issues such as substance use disorders, unemployment, educational underachievement, delinquency, gambling, depression, relationship difficulties, and teenage pregnancy.<sup>1-4</sup> Correlation with a significantly heightened risk of unnatural causes of death resulting from suicide, unintentional injury, and fatal accidents, such as motor vehicle accidents, has also been identified.<sup>1</sup> There is an upward trend of patients seeking ADHD diagnosis and treatment in the primary care setting.<sup>5</sup> Sixty-five to eighty-five percent of ADHD patients are diagnosed in the primary care setting, and an even larger proportion will seek prescriptions from primary care providers for management of this condition.<sup>6-9</sup> Therefore, it is essential for the primary care provider to be comfortable recognizing, assessing, and treating ADHD to prevent unnatural causes of death and decreased quality of life in these patients.<sup>1-4</sup>

## ETIOLOGY

The etiology of ADHD is a complex interaction of genetic, social, and environmental factors. There is evidence that the genes responsible for ADHD development work through a complex polygenic mechanism. Despite this, ADHD has a 74% heritability from parent to offspring.<sup>1</sup>

In addition to genetics, prenatal factors appear to determine the development of ADHD. The greater the number of prenatal risk factors appears to correlate with an increasing severity of symptoms that develop later in life.<sup>10</sup> Children born preterm are diagnosed with ADHD twice as often as full-term children.<sup>1</sup> Maternal smoking and hypertension also correlate with ADHD development.<sup>1</sup> Early pregnancy vitamin D levels have been inversely correlated with the manifestation of ADHD.<sup>11</sup> This is explained by vitamin D playing a critical neuroprotective and neurodevelopmental role in the embryo during early brain development.<sup>11</sup> Maternal penicillin use also appears to correlate with ADHD development, but it is unclear whether this association exists as a result of the drug or because of the presence of an infection.<sup>12</sup> For example, maternal inflammation, measured by C-reactive protein level, is also associated with ADHD symptom load.<sup>13</sup>

The core etiology of ADHD is impaired neurodevelopment resulting in arousal dysregulation in the brain.<sup>14,15</sup> Recent data show that ADHD correlates with biomarkers on electroencephalogram (EEG), functional magnetic resonance imaging (fMRI), hemodynamics, and genetics.<sup>16</sup> Biomarkers typically show significant differences in the anatomy and physiology of cerebral structures such as the

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prefrontal cortex and amygdala.<sup>16</sup> Future research is working to develop strategies to utilize biologic correlates for diagnosis in the clinical setting.

The major symptoms of ADHD: inattention, hyperactivity, and impulsivity are primarily attributed to abnormalities of the prefrontal cortex principally involving the neurotransmitters dopamine and norepinephrine.<sup>18</sup>

ADHD is associated with different etiologies and variable changes in brain development, leading to a spectrum of symptomatology.<sup>18</sup> Dopamine and norepinephrine neurotransmission play key roles in the underpinnings of this disorder.<sup>18</sup> Medical literature typically describes ADHD through the lens of the “dopamine hypothesis,” which attributes symptoms to dysregulation of dopaminergic pathways.<sup>18</sup> To understand the complete spectrum of ADHD symptoms, it is important to recognize the role of norepinephrine, too. Further evidence from genetic studies suggests that variation in genes that are responsible for norepinephrine production can disrupt the prefrontal cortex and disrupt the regulation of attention and behavior. It is likely that a combination of both dopaminergic and noradrenergic disruptions explains the heterogeneity of ADHD among different individuals.<sup>18</sup> Alpha-2 adrenergic agonists are effective pharmacotherapies for ADHD and are believed to modulate both dopaminergic and noradrenergic neurotransmission to alleviate ADHD symptoms.<sup>18</sup>

## PRESENTATION

### Childhood Presentation

The average age of ADHD diagnosis is 7 years.<sup>4</sup> The child shows a pattern of inattentiveness, hyperactivity, and/or impulsivity, which is detrimental to his or her daily functioning and school participation.<sup>4</sup> Hyperactive children with ADHD may run and climb excessively or have difficulty playing quietly.<sup>20</sup> Girls may have fewer externalizing problems than boys and are more likely to present with fatigue and inattention.<sup>20</sup> Boys may present as more hyperactive or aggressive and as a result are more likely to draw the attention of parents and teachers.<sup>20</sup>

### Adolescent Presentation

Identifying ADHD is more difficult in undiagnosed adolescents and adults. This age bracket will often display less hyperactivity.<sup>4</sup> Despite this, the underlying etiology of ADHD persists, and affected adults will often display similar pitfalls as younger people with untreated ADHD.<sup>4</sup> As children grow older, their impulsive behaviors conform less to typical social norms, possibly resulting in adolescents with ADHD being rejected by their peers.<sup>22</sup> Other individuals with ADHD make conscious efforts to mask their symptoms around their peers. This can result in an adolescent who presents with drastically different levels of hyperactivity with peers than at home with family.<sup>22</sup>

### Adult Presentation

Approximately one-third of children in the United States diagnosed with ADHD will continue to struggle with symptoms into adulthood.<sup>6</sup> However, these symptoms do not present the same in adulthood as they did in childhood.<sup>4,6</sup> Adults with

ADHD are more likely to experience hyperactivity in the form of restless energy, an inability to relax, persistent talkativeness, and difficulty engaging in sedentary activities.<sup>20</sup> Hyperactivity in adults may also be expressed as excessive fidgeting, the inability to sit still, or being “on the go” all the time.<sup>6,20</sup> Inattentive ADHD symptoms tend to predominate over hyperactive symptoms in adults.<sup>6</sup> Inattentiveness manifests as a difficulty sustaining attention, disdain towards tasks involving sustained attention, and distractibility.<sup>2,4,6</sup> Inattentiveness can also manifest in the form of disorganization, tardiness, boredom, indecisiveness, and carelessness, which are detrimental to employment and productivity.<sup>20</sup> Emotional dysregulation may present in adulthood as irritability, emotional lability, and emotional reactivity.<sup>6</sup> Adult patients may also report developmentally attenuated emotional symptoms such as mood swings and various difficulties with social, family, and romantic relationships.<sup>2</sup> Adults with ADHD often experience lifetime mood lability with frequent highs and lows, and short-fuse temper outbursts.<sup>20</sup> ADHD partners add strain to their romantic relationships by being inattentive to the needs of their partner or operating on a “short fuse.”<sup>20</sup> Impulsivity may be expressed as persistent impatience, acting carelessly, spending irresponsibly, rapidly moving between jobs and relationships, and sensation-seeking behaviors.<sup>20</sup>

## DIAGNOSTIC CRITERIA

The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)* determines the ADHD diagnostic criteria in the United States. The *DSM-5* characterizes ADHD as a detrimental pattern of inattention and hyperactivity that has persisted since childhood. Symptoms must be robust across different environments, scenarios, and settings. An adult ADHD diagnosis requires at least five inattention symptoms or five hyperactive/impulsive symptoms since childhood. A childhood diagnosis requires six or more for either inattention or hyperactive/impulsive symptoms impairing quality of life. Symptoms must be severe, present before 12 years of age, and inappropriate for the patient’s current age and developmental level.<sup>21</sup> *DSM-5* ADHD symptoms are listed in Table 1.

ADHD is exclusively a clinical diagnosis.<sup>23</sup> But other diagnostic tools such as neuroimaging and EEG have been used in the diagnosis of ADHD. The Neuropsychiatric EEG-Based Assessment Aid (NEBA) is FDA approved but should only be used as a complementary tool.<sup>24</sup> Rating scales are available to help the physician determine that the *DSM-5* criteria have been met. Most ADHD rating scales are accessible via computer and are practical enough to be completed within a few minutes in the office. A nonexhaustive list of validated ADHD rating scales available to the primary care physician is listed in Table 2.<sup>8,25</sup>

While specialists are valuable in diagnosing ADHD patients through neuropsychiatric batteries, primary care physicians can diagnose and treat ADHD. Since the primary care physician can diagnose ADHD in the clinic, it may be more cost-effective and practical to do so rather than referring patients to a specialist for diagnosis. The physician should determine that the *DSM-5* criteria have been met, through acquiring documentation of symptoms occurring in more than one setting and from at least two credible

TABLE 1:

DSM-5 ADHD symptoms

Inattentive Symptoms	Hyperactive Symptoms	Impulsive Symptoms
Poor listening skills	Squirms or fidgets	Difficulty waiting turn
Loses or misplaces items	Marked restlessness that is difficult to control	Interrupts or intrudes into conversations and activities of others
Sidetracked by external or unimportant stimuli	Appears to be driven by “a motor” or is often “on the go”	Impulsively blurts out answers before questions are completed
Forgets daily activities	Lacks ability to engage in leisure activities in a quiet manner	
Diminished attention span	Incapable of staying seated in class	
Lacks ability to complete work or to follow instructions	Overly talkative	
Aversion to tasks requiring concentration		
Fails to focus on details and/or makes thoughtless mistakes		

sources, including but not limited to impairment in school from a teacher and documentation of symptoms at home from parents.<sup>4</sup>

To make a diagnosis in preschool-aged children, clinicians should conduct a clinical interview with parents, examine the child, and also ask parents and teachers to complete standardized ADHD rating scales.<sup>4</sup> The physician should be reminded that since boys are typically more hyperactive in their symptom presentations, girls are less likely to receive treatment than boys for their ADHD because they primarily experience inattentive symptoms.<sup>20</sup>

Obtaining teacher and parent accounts for adolescents is often more challenging than for younger children. Adolescents are less likely to exhibit overt hyperactive behavior, and self-reports of their own symptoms often differ from other observers.<sup>26</sup> Despite this challenge, physicians should obtain information from at least two adults who interact with the adolescent regularly. Reliable informants include parents, teachers, and youths themselves. No single informant in a single setting is a gold-standard for diagnosis.<sup>26</sup> Additionally, the adolescent patient must actively participate in the evaluation for it to be reliable.<sup>4,26</sup>

TABLE 2:

ADHD rating scales available to the primary care physician

Age Range	Narrowband/ADHD Specific Scales	Broadband/Global Behavioral Scales
All ages	Brown attention/executive function scale function scales	
Pediatrics	Comprehensive Executive Function Inventory (CEFI)	Behavior Assessment System for Children (BASC-3)
	Behavior Rating Inventory of Executive Function 2 (BRIEF-2)	Child Behavior Checklist (CBCL)
		Conners Comprehensive Behavior Scale (CBRS)
Adults	Barkley Adult ADHD Rating Scale-IV (BAARS-IV)	
	Conners Adult ADHD Rating Scales (Conners-3, CAARS)	
	Wender Utah Rating Scale	

Diagnosis of ADHD in adults is also made clinically, after excluding other possible causes of inattention, hyperactivity, and impulsivity.<sup>8</sup> In addition to the clinical evaluation in adults is the reliance on self-report assessments rather than informant accounts by parents and teachers. Structured self-report rating scales and instruments are available to assist physicians in the diagnosis of ADHD.<sup>8</sup> The instruments take less than 20 minutes to complete and assess the diagnostic criteria for ADHD. While there is still limited data estimating the sensitivity and specificity for all scales, they are still the most practical method to quantify ADHD symptoms in the clinic.<sup>8</sup>

There are two important criteria to assess adults. First, that the symptoms of adult ADHD have persisted since childhood. Second, the symptoms impair their quality of life.<sup>9</sup> The reliability of self-reported assessments depends on the accurate recall of the patients for their childhood symptoms. However, adults with ADHD frequently struggle to accurately recall the onset and severity of their symptoms. While a diagnosis based only on self-report is possible, further corroborating information from a family member or parent is recommended.<sup>20</sup> Self-reporting of symptoms may be less reliable to objective reports from outside observers.<sup>9</sup> Adults with higher IQ may also have more effective compensatory strategies to mask their symptoms from others, which further complicates the ability to obtain an accurate diagnosis.<sup>20</sup> Future research aims to develop biologic correlates to diagnose ADHD in the clinical setting through EEG, fMRI, hemodynamics, or genetics.<sup>16</sup> For now, standardized reports from the patients and observers are the mainstay of diagnosis in the primary care setting.<sup>8,9</sup>

## Differential Diagnoses

Some neuropsychiatric conditions are commonly misdiagnosed as ADHD including but not limited to learning disorders, sleep disorders, oppositional defiant disorder, anxiety disorder, intellectual disability, language disorder, mood disorders, tic disorders, conduct disorder, and autism spectrum disorder.<sup>27</sup> Oppositional defiant disorder can be mistaken for hyperactivity or impulsive reactivity.<sup>27</sup> Generalized anxiety disorder and major depressive disorder may be mistaken for inattentive presentation, and bipolar disorder may mimic the emotional lability of ADHD.<sup>27</sup> However, daily mood changes in ADHD represent a poorly regulated but normal range of moods, rather than the more severe extremes associated with bipolar disorder.<sup>20</sup> Social disinhibition, resulting from adjustment disorders and posttraumatic stress disorder (PTSD), may resemble the impulsivity and social isolation seen in ADHD.<sup>27</sup> However, many children with ADHD can make initial social overtures but have difficulty maintaining long-term relationships.<sup>27</sup> Children who function at extremes of cognitive development may be disconnected, inattentive, or disruptive in class if the content is perceived as too easy or too difficult.<sup>27</sup> The movements associated with autism spectrum disorders and other neurodevelopmental disorders may be mistaken for hyperactivity. Social deficits and lack of social engagement can help identify autism spectrum disorder, and movement qualities help identify tic disorders.<sup>27</sup> Personality disorders, psychosis, and substance abuse disorders should be considered when assessing adolescents and adults, as these conditions may present as inattention, impulsivity, and academic problems.<sup>27</sup> In the ADHD patient, impulsivity and anger are usually short-lived and thoughtless, rather than intentionally theatrical or manipulative as seen in personality disorders.<sup>20</sup>

Medical conditions can mimic the inattentive signs of ADHD including conditions causing fatigue, pain, sensory impairments, and neurologic conditions that affect attention and arousal.<sup>27</sup> Common somatic diseases that contribute to inattention include obstructive sleep apnea, inflammatory bowel disease, epilepsy, and postconcussion status.<sup>27</sup> The primary care physician needs to recognize the utility of acquiring thorough medical and family histories and physical examination to effectively diagnose ADHD and rule out mimics of the disorder.<sup>27</sup> Laboratory tests, such as thyroid studies, liver function tests, and lead levels, may be helpful for ruling out pathologies mimicking ADHD.<sup>8</sup> Of particular note, adults presenting with new-onset symptoms are not likely to have ADHD.<sup>9</sup> False positive late-onset ADHD cases are common without careful assessment, and clinicians should screen for impairment, psychiatric history, and substance use.<sup>9</sup>

## Challenges to Diagnosis

There is an upward trend of ADHD diagnoses and treatments in recent years, especially in the primary care setting.<sup>5,28,29</sup> Evidence suggests an overdiagnosis of ADHD in youth.<sup>29,30</sup> In 1994 and 2013, the *DSM-4* and *DSM-5* expanded the criteria for ADHD diagnosis, and the prevalence of the diagnosed individuals naturally increased in the United States.<sup>29</sup> The current *DSM-5*

guidelines have expanded the diagnostic criteria to include more mild ADHD symptoms, which correlates with the rising proportion of people treated for ADHD in recent years.<sup>29</sup>

## CONCLUSION

Naturally, primary care physicians will be presented with opportunities and challenges of diagnosing ADHD within their patient population. As this disorder presents significant heterogeneity throughout development and among individuals, the physician should equip himself or herself with the tools to properly diagnose these individuals. Understanding the neurodevelopmental etiology associated with ADHD will help to contextualize the behavioral, emotional, and cognitive deficits with which these patients struggle. Accurately recognizing ADHD and its diverse spectrum of presentations is the first step in providing sufficient care to patients affected with the disorder. While there is debate that ADHD is overdiagnosed in patients with milder symptoms, the family physician is in the first-line position to prevent milder ADHD symptoms from becoming overtreated with pharmacotherapies as well. Therefore, with continued study and analysis of new developments and up-to-date treatments, the physician can more fully, completely, and accurately treat patients.

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