CME

Adult attention deficit/hyperactivity disorder in the ambulatory care setting

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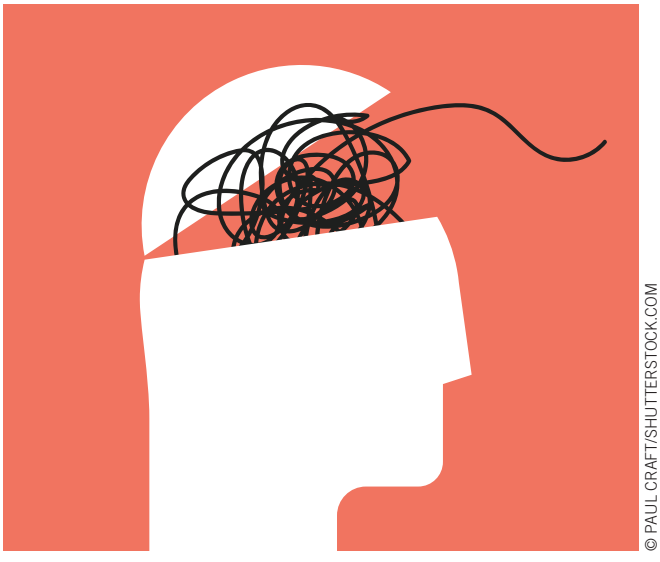
ABSTRACT

Adult attention deficit/hyperactivity disorder (ADHD) is a significant and prevalent disorder. ADHD can impair adults' quality of life, so clinicians in multiple specialties should be able to recognize and treat the disorder. Much of the current literature has focused on childhood ADHD. However, adult ADHD is a common comorbidity in patients with mental illness, and it is essential that patients diagnosed with the disorder are treated appropriately, which can significantly improve outcomes. Adults with untreated ADHD are more likely to have substance dependence, job instability, and an overall poorer quality of life. This article reviews the screening and assessment for adult ADHD along with pharmacologic and nonpharmacologic recommendations for the management of the disorder.

Keywords: ADHD, attention deficit/hyperactivity disorder, adult, persistent ADHD, psychostimulant, inattention



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Learning objectives

- Understand the prevalence of adult ADHD.
- Explain the pathophysiology and clinical features of adult ADHD.
- Describe the first- and second-line treatments for adult ADHD.

Attention deficit/hyperactivity disorder (ADHD) is a neurobehavioral disorder commonly affecting children ages 6 to 17 years. However, ADHD does not always resolve after adolescence; about 4% to 4.5% of adults in the United States have ADHD.[1] Longitudinal studies with a combination of parent, self-reporting, and structured interviews found that 60% of children with ADHD continued to have persistent symptoms into young adulthood and 41.1% met adulthood criteria for persistent symptoms and impairment.[2] In the national comorbidity survey for patients with adult ADHD, the prevalence was higher in men, non-Hispanic whites, and the unemployed.[3] Risk factors for ADHD include genetic mutation and variants, family history of ADHD, comorbid psychiatric conditions, brain injuries, and exposure to cigarette smoke and alcohol in utero.[4]

Psychiatric comorbidities such as anxiety and mood disorders, substance use disorders, and suicidality have been associated with adult ADHD.[3,4] A longitudinal study has shown that adults with persistent ADHD have a significant risk for developing psychiatric comorbidities.[5] Adults with persistent ADHD were eight times more likely to develop a psychiatric comorbidity compared with adults without a history of childhood ADHD.[5] Additionally, adults with persistent ADHD were five times more likely to have a psychiatric comorbidity compared with adults with childhood ADHD not persisting into adulthood.[5]

Adult ADHD and mortality are correlated.[6] A prospective cohort study in Denmark found a twofold increased

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Key points

- An estimated 4% to 4.5% of adults in the United States have ADHD, many adults with this condition are undiagnosed or misdiagnosed.
- About 60% of children with ADHD continue to have persistent symptoms into adulthood.
- Adults with ADHD have a high prevalence of psychiatric comorbidities.
- Psychostimulants are first-line treatments for ADHD.
- For maximal efficacy, patients should be treated with pharmacotherapy and psychosocial therapy.

mortality rate ratio (MRR) in children, adolescents, and adults diagnosed with ADHD compared with those without ADHD.[6] Of those with ADHD who died, 25 were from natural causes with an MRR of 1.87 and 54 were from unnatural causes or accidental deaths, with an MRR of 3.03 compared with those without ADHD.[6] Adults diagnosed with ADHD had the greatest likelihood of death with an MRR of 4.25 compared with patients diagnosed with ADHD in childhood and adolescence.[6]

PATHOPHYSIOLOGY

The exact pathophysiology of ADHD is not completely understood. However, studies have shown evidence of a genetic basis with serotonin and dopamine variants, as well as evidence of neuropathophysiology.[1,7] Neuroimaging and neuropsychologic studies have shown a correlation between executive function and ADHD.[7] Executive function is responsible for higher cognitive processes that are predominantly in the prefrontal cortex. These cognitive processes include inhibitory control, planning, organizational strategies, emotion, behavior, working memory, flexible thinking, self-control over irrelevant information, and initiating tasks. MRIs of adults with ADHD show a reduction in the gray matter of the frontal cortices and decreased activity in the prefrontal cortex.[1,8]

Dopamine and noradrenaline are heavily concentrated in the prefrontal cortex and are the two main neurotransmitters implicated in adult ADHD. Dopamine is responsible for attention, memory, mood, problem solving, emotional decision-making, and motor activity.[9] Noradrenaline also plays a role in motivation and executive function, specifically working memory and inhibitory control.[10] Dopamine receptors and activity are decreased in patients with ADHD.[1,11] Dysregulation of noradrenaline can cause ADHD symptoms, but the mechanism of noradrenaline in ADHD remains elusive.

CLINICAL PRESENTATION AND DIAGNOSIS

ADHD is commonly diagnosed during a patient's primary school years because order and attentiveness are necessities in school. Therefore, children with excessive impulsiveness, hyperactivity, and irritability become more obvious because their behaviors can disturb the classroom.[12] Conversely, a clear diagnosis is not common for adults presenting with ADHD because the signs and symptoms of ADHD can become clouded; as patients mature and learn how to manage their symptoms, the clinical manifestations of ADHD change.[13] In many of these high-functioning patients, a diagnosis of adult ADHD may be more easily overlooked, which can lead to poor social outcomes.[13] This points to the importance of clinicians knowing how to recognize and diagnose ADHD in adults.

Adults with symptoms of ADHD classically present with educational underachievement, relationship difficulties, sleep disturbances, engaging in risky behaviors, emotional lability, and employment difficulties due to developmentally inappropriate levels of hyperactive, impulsive, and inattentive behaviors.[14] When impulsivity and hyperactivity continue into adulthood, they can be impairing, and often are seen in the lives of adults who engage in high-risk behavior and those with substance abuse disorders.[15] Hyperactivity and impulsivity in adults typically manifest as overtalkativeness, fidgeting, restlessness, difficulty sitting still or relaxing, often feeling impatient, and finding it hard to wait one's turn without becoming angry or short-tempered.[14]

Although hyperactivity and impulsivity are core characteristic traits in childhood, these fundamental symptoms tend to decline during the transition from childhood to young adulthood, while inattention typically persists.[13]

> Many adults with ADHD have comorbid illnesses, and clinicians should treat the most debilitating illness first.

In adulthood, inattention typically presents as forgetfulness, unfocused thoughts, poor self-organization, difficulty in planning, and chronic lateness. Inattention also can present as difficulty in preparing, starting, and finishing tasks.[14]

When formulating a diagnosis of ADHD in adults, consider a wide differential diagnosis, because the symptoms of adult ADHD are so commonly overlooked. Substance use disorders, mood and anxiety disorders, and certain medical conditions all have symptoms that overlap with adult ADHD.[15] Screening should be the first method used in identifying and ultimately diagnosing the disorder.[15] When done properly, screening helps the initiation of prompt and appropriate diagnostic and treatment interventions, preventing further major impairments in life activities for patients.[15] Screening also helps reduce treat-

ment costs that can arise from underdiagnosis of the disorder. Costs also can be elevated due to treatment of other psychiatric disorders, such as substance use disorder, that can otherwise be alleviated with proper treatment of the patient's ADHD.[15]

The World Health Organization (WHO) has a validated Adult ADHD Self-Report Scale version 1.1 (ASRS-V1.1, **Table 1**) that is a standardized tool used for assessing ADHD symptoms in patients age 18 years and older.[16] The tool has two versions—one with six questions and one with 18. The six-question version is widely used because it has a greater sensitivity, specificity, and classification accuracy when assessing adults with ADHD.[16] Although these tools are both sensitive and specific, clinicians should still have a high awareness for bias that may occur when patients are self-reporting their symptoms, as most tend to underreport or underestimate their symptoms.[15]

> Atomoxetine is considered first-line nonstimulant therapy for adults with ADHD.

According to the *DSM-5* diagnostic criteria, patients with adult ADHD may exhibit 18 possible symptoms—nine of hyperactivity-impulsivity, and nine for inattention.[17] To meet the diagnostic criteria, patients older than age 17 years should exhibit five or more symptoms in either sphere. The symptoms also must be inappropriate with the patient's presumed developmental level.

TREATMENT

Treatments for adult ADHD include psychostimulants, psychotherapy, and nonstimulants (**Table 2**).[1,18] Clinicians should be aware of the pharmacokinetic profiles of the different medications to ensure that the treatment is effective for the patient.[19] Medication adverse reactions should be closely monitored in the patient's notes and if adverse reactions become intolerable, consider reducing the dosage.[19] Many adults with ADHD have comorbid illnesses, and clinicians should treat the most debilitating illness first.[20]

The first-line treatment for adult ADHD are psychostimulants, which typically are safe and well tolerated.[1,21] To improve adherence, start low and quickly titrate up to the target dose.[21] Long-acting formulations of stimulant therapies generally are preferred because they are less prone to abuse or diversion and allow once-daily treatment, resulting in greater medication adherence.[18] Recent inclusive studies have found that amphetamines are the most efficacious pharmacologic treatment for adult ADHD as reported by clinicians and by patient self-report.[22]

Nonstimulants generally are considered second-line therapy, and are used for patients with contraindications to stimulants or comorbid depression and/or anxiety.[12,18] Atomoxetine is considered the first-line nonstimulant treatment for adults with ADHD.[21] Patients on medications such as methylphenidate and atomoxetine generally showed marked improvement with their symptoms during weeks 4 to 5 and 8 to 10 of use.[21,23]

Selected antidepressants, including bupropion, tricyclic antidepressants, and selective norepinephrine reuptake inhibitors, have a much smaller evidence base as ADHD therapy.[24] These antidepressants promote noradrenergic and dopami-

TABLE 1. ASRS-V1.1 screener from WHO composite international diagnostic interview

Have the patient check the box that best describes how he or she felt and has conducted himself or herself over the past 6 months. Four or more checkmarks in the shaded area indicate that symptoms may be consistent with adult ADHD.

	Never	Rarely	Sometimes	Often	Very often
How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?					
How often do you have difficulty getting things in order when you have a task that requires organization?					
How often do you have problems remembering appointments or obligations?					
When you have a task that requires a lot of thought, how often do you avoid or delay getting started?					
How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?					
How often do you feel overly active and compelled to do things, like you were driven by a motor?					

Reprinted with permission from Kessler RC, Adler L, Ames M, et al. The World Health Organization adult ADHD self-report scale (ASRS): a short screening scale for use in the general population. *Psychol Med.* 2005;35(2):245-256.

TABLE 2. Common medications used to treat ADHD in adults[27-32]

Drug	Mechanism of action	Initial titration	Best taken or absorbed	Common adverse reactions	Monitoring parameters	Contraindications
Methylphenidate HCl extended release (Ritalin LA)	Blocks dopamine and norepinephrine transporters	• 20 to 40 mg daily • Maximum dose, 60 mg	Morning, with or without food	Headache, fatigue, decreased appetite, stomachache	• Heart rate • BP • Bloodwork	• Known hypersensitivity to methylphenidate • Tic disorders • Monoamine oxidase inhibitor (MAOI) use within the past 2 weeks
Methylphenidate (Concerta)	Blocks dopamine and norepinephrine transporters	• 18 to 72 mg daily • Maximum dose, 108 mg	Morning, with or without food	Headache, fatigue, decreased appetite, xerostomia	• Heart rate • BP • Bloodwork	• Known hypersensitivity to methylphenidate • Glaucoma • Tic disorders • MAOI use within the past 2 weeks
Dextroamphetamine extended (Adderall XR)	Not well known. Blocks reuptake of norepinephrine and dopamine	• 10 to 30 mg daily • Maximum dose, 40 mg	Morning, with or without food	Abdominal pain, loss of appetite, nausea, weight loss, insomnia	• BP • Monitor mood for manic symptoms and aggression	• Advanced atherosclerosis • Symptomatic cardiovascular disease • Hyperthyroidism • MAOI use • Glaucoma
Atomoxetine (Strattera)	Selective norepinephrine inhibitor	• 40 mg daily for 7 days, then 80 mg daily • Maximum dose, 100 mg	Morning, with or without food	Constipation, nausea, xerostomia, insomnia	• BP • Heart rate • Liver function • Mood and manic symptoms	• Hypersensitivity to atomoxetine • Concomitant MAOI use • Glaucoma • Pheochromocytoma • Lowers seizure threshold • Suicidal thoughts • Caution in patients with eating disorders
Bupropion (Wellbutrin) *off-label use*	Dopamine and norepinephrine reuptake inhibitor	• 150 mg daily • Extended release, 450 mg daily • 200 mg twice daily	Once daily	Xerostomia, nausea, agitation, insomnia, headache, weight loss, dizziness	• Monitor for exacerbation of mania or psychosis	

nergic actions in the prefrontal cortex, which align with the pathophysiology of ADHD and mirror the studied effects of stimulant therapy.[24] Alpha$_2$ adrenergic agonists such as guanfacine and clonidine have shown some benefit in treating adult ADHD, but typically are only used as adjunctive therapy or to treat ADHD-related sleep disturbance.[17]

Atomoxetine is considered first-line for adults with ADHD and comorbidities such as substance abuse, comorbid tic disorders, and anxiety.[24] For adults with comorbid depression, bupropion is recommended; however, it is not FDA-approved for ADHD.[12,24] Both stimulants and atomoxetine should be considered once the mood disorder is stabilized.[25]

Consider nonpharmacologic treatment for patients who are unable to tolerate medication adverse reactions or those who may be nonadherent due to finances or reluctance to take medications.[12] The goals for psychologic therapies for adult ADHD are to help patients understand the disorder and challenge negative beliefs they may hold that affect their function and self-esteem.[26] Therapies include ADHD-tailored cognitive behavioral therapy, psychoeducation for patients and their families, ADHD coaching, and exercise and conditioning.

CONCLUSION

ADHD is a neurodevelopmental disorder that can affect an adult's employment, relationships, academics, and

social functioning. Most adults suffering from ADHD are undiagnosed or misdiagnosed, which can lead to academic failures, relationship difficulties, employment difficulties, and emotional liabilities.[14] Clinicians, especially those in outpatient settings, must be able to recognize signs and symptoms of adult ADHD and be familiar with its treatments. Screening lets clinicians diagnose the disorder before it causes significant lifestyle impairment. Clinicians may be reluctant to diagnose ADHD in adults because of hesitancy to prescribe stimulants, a fear of misdiagnosing the illness, or worsening the patient's comorbid illness. However, clinicians who can accurately diagnose and treat adults with ADHD can help provide patients with a better quality of life and offer them insight into their condition. **JAAPA**

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