CME

Attention-Deficit/Hyperactivity Disorder in Adults

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Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder involving functionally disruptive inattentive and/or hyperactive/impulsive behaviors, such as being easily distracted, regularly failing to follow through on tasks, being restless, or often interrupting others. ADHD diagnosed in childhood often persists into adulthood, with 14.6% of U.S. adults meeting the *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed., criteria for ADHD. When evaluating for adult ADHD, other mental disorders should be included in the differential diagnosis due to the substantial overlap of symptoms and ADHD concurrence with anxiety/stress, mood, personality, impulse control, and substance use disorders. An ADHD diagnosis requires a comprehensive clinical history and evaluation, patient symptom and function assessment (e.g., Adult ADHD Self-Report Scale, Conners Adult ADHD Rating Scales), and gathering of collateral information. Clinical guidelines recommend a subset of amphetamine and methylphenidate stimulants as first-line pharmacotherapy, which may be more effective when combined with psychotherapy. For adults unable to take stimulants or with concurrent anxiety/depression, options include atomoxetine, viloxazine, and bupropion. To monitor for patient misuse or diversion of stimulants, physicians should consider employing controlled substance agreements and prescription drug monitoring programs.

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Adult attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder of executive function associated with inattention, disorganization, and/or hyperactive/impulsive behaviors occurring in people 17 years or older.[1] Adult ADHD is a continuance of childhood symptoms, with 29% of cases persisting into adulthood.[2-4] Although some studies have suggested that a late-onset ADHD subtype can occur that is not a continuance from childhood, more data are needed, and this theory is not considered in the current diagnostic criteria.[5,6] Adults with ADHD are at higher risk of unemployment, educational underachievement, financial difficulties, substance misuse, criminality, divorce, motor vehicle crashes, workplace accidents, and overall mortality compared with the general population.[2,7,8]

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Research suggests that there is a genetic component to ADHD. Family, twin, and adoption studies have shown a heritability rate of 74%.[9] More recently, ADHD has been linked with dozens of genetic mutations that do not cause ADHD in isolation, but as mutations increase so does risk of ADHD, disease severity, and manifestation of comorbid conditions with genetic overlap (e.g., depression, autism).[10] This polygenicity is driving the development of polygenic risk scoring methods that would help with early disease identification.[11]

WHAT'S NEW ON THIS TOPIC

Adult Attention-Deficit/Hyperactivity Disorder

The prevalence of attention-deficit/hyperactivity disorder in U.S. adults rose from 4.4% in 2006 to 14.6% in 2022.

In 2021, more than 3.4 million people 18 years and older in the United States misused prescription stimulants, most commonly amphetamines. An estimated 66% of people who misuse prescription stimulants get the medications from family or friends with prescriptions, and 20% obtain prescriptions themselves by presenting to clinicians with exaggerated or fabricated symptoms.

Rates of overdose deaths from noncocaine stimulants have been exponentially increasing in the United States since 2012, with more than 32,500 deaths in 2021.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	Comments
Validated diagnostic tools and history should be used to confirm DSM-5 criteria for ADHD in adults.[1,19]	C	Expert opinion and consensus guideline in the absence of clinical trials
Neuropsychological testing may increase diagnostic accuracy for adult ADHD when collateral information such as childhood history and observer reports is lacking, malingering is suspected, or confounding mental comorbidities are present.[29,30]	C	Expert opinion and consensus guideline in the absence of clinical trials
Nonpharmacologic therapies recommended for adult ADHD include cognitive behavior therapy, mindfulness, dialectical behavior therapy, and hypnotherapy.[35]	B	Systematic review of studies with inconsistent evidence, which was weakest for dialectical behavior therapy and hypnotherapy
Stimulants are first-line pharmacologic therapy for adult ADHD.[37]	A	Systematic review with consistent evidence from RCTs showing improved executive functioning
Nonstimulant medications (e.g., atomoxetine, viloxazine [Qelbree], bupropion) are indicated for adult ADHD when stimulants are contraindicated, not tolerated, or ineffective.[37,38]	B	Systematic review and small RCTs; bupropion is not approved by the U.S. Food and Drug Administration for ADHD

ADHD = attention-deficit/hyperactivity disorder; DSM-5 = *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed.; RCT = randomized controlled trial.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afpsort.

In 2006, an estimated 4.4% of U.S. adults had ADHD.[12] The prevalence has increased to at least 14.6% based on 2022 data and affects adults across demographics.[13] The increasing prevalence of adult ADHD may be due to a true increase or to an increase in diagnosis as more patients and clinicians become knowledgeable about the disorder. When ADHD was first described in 1902, it was believed to affect only children. The persistence of ADHD into adulthood was not recognized until the early 1990s.[8] In 2013, the *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed., (DSM-5) relaxed diagnostic criteria from symptom onset before 7 years of age to before 12 years. Diagnostic criteria for ADHD did not substantially change with the 2022 release of the DSM-5 text revision (DSM-5-TR).[1]

DIAGNOSIS

Differential Diagnosis

To diagnose adult ADHD, clinicians must rule out other medical and psychiatric conditions that could account for the patient's symptoms. Emotional dysregulation is common in ADHD, but there is substantial overlap with symptoms of other mental disorders. Because other mental disorders commonly co-occur with ADHD, it is important to screen patients for multiple mental health issues (Table 1). The DSM-5-TR Self Rated Level 1 Cross-Cutting Symptom Measure—Adult is a 23-item measure that assesses for signs of depression, anxiety/stress, mania, somatization, self-harm, psychosis, sleep issues, memory issues, personality disorders, and substance misuse.[1] It is available at https://www.psychiatry.org/getmedia/e0b4b299-95b3-407b-b8c2-caa871ca218d/APA-DSM5TR-Level1MeasureAdult.pdf. Other conditions that may have symptom overlap with ADHD include prior traumatic brain injury, thyroid dysfunction, medication adverse effects, organizational skill deficits, environmental factors, and malingering.[1,8,12,14]

Diagnostic Recommendations

For suspected cases of ADHD, a three-part approach to the assessment is recommended. First, the assessment findings can be considered negative if the patient reports no symptoms before 12 years of age,[1] although patients may not recall or have insight into symptoms before that age. Second, validated self-report and observer screening measures for ADHD symptoms can be completed and interpreted as positive or negative. One example is the Adult ADHD Self-Report Scale (https://www.myfoothold.org/app/uploads/2022/10/Adult-ADHD-Self-Screening-1.pdf).[15-17] Third, the DSM-5-TR diagnostic criteria require the presence of several inattentive or hyperactive-impulsive symptoms in two or more settings that

TABLE 1

Differential Diagnosis of ADHD

Mental disorder	Symptoms shared with ADHD	Symptoms different than ADHD
Anxiety	Emotional lability, irritability, restlessness	Panic attacks, prominent worrying, can focus when relaxed
Major depression	Difficulty focusing, emotional lability, irritability, procrastination/poor motivation, demoralization	Anhedonia, persistent depressive symptoms
Mania/bipolar depression	Difficulty focusing, emotional lability, restlessness, impulsivity	Manic-depressive cycling, elated mood and grandiosity during manic episodes
Posttraumatic stress disorder	Difficulty focusing, emotional lability, irritability	Linked to trauma, hypervigilance
Substance use disorder	Inattentive, hyperactivity	Symptom onset coincides with substance use, and symptoms substantially improve with sustained abstinence

ADHD = attention-deficit/hyperactivity disorder.

TABLE 2

DSM-5-TR ADHD Diagnostic Criteria and Classifications

A. A persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development, as characterized by (1) and/or (2):

1. **Inattention:** Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities:

   Note: The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or failure to understand tasks or instructions. For older adolescents and adults (age 17 or older), at least five symptoms are required.

   a. Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (e.g., overlooks or misses details, work is inaccurate).

   b. Often has difficulty sustaining attention in tasks or play activities (e.g., has difficulty remaining focused during lectures, conversations, or lengthy reading).

   c. Often does not seem to listen when spoken to directly (e.g., mind seems elsewhere, even in the absence of any obvious distraction).

   d. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., starts tasks but quickly loses focus and is easily sidetracked).

   e. Often has difficulty organizing tasks and activities (e.g., difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganized work; has poor time management; fails to meet deadlines).

   f. Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (e.g., schoolwork or homework; for older adolescents and adults, preparing reports, completing forms, reviewing lengthy papers).

   g. Often loses things necessary for tasks or activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).

   h. Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts).

   i. Is often forgetful in daily activities (e.g., doing chores, running errands; for older adolescents and adults, returning calls, paying bills, and keeping appointments).

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ADHD = attention-deficit/hyperactivity disorder; DSM-5-TR = *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed., text revision.

TABLE 2 (continued)

DSM-5-TR ADHD Diagnostic Criteria and Classifications

2. **Hyperactivity and impulsivity:** Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities:

   Note: The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or a failure to understand tasks or instructions. For older adolescents and adults (age 17 or older), at least five symptoms are required.

   a. Often fidgets with or taps hands or feet or squirms in seat.
   b. Often leaves seat in situations when remaining seated is expected (e.g., leaves his or her place in the classroom, in the office or other workplace, or in other situations that require remaining in place).
   c. Often runs about or climbs in situations where it is inappropriate. (Note: In adolescents or adults, may be limited to feeling restless.)
   d. Often unable to play or engage in leisure activities quietly.
   e. Is often "on the go," acting as if "driven by a motor" (e.g., is unable to be or uncomfortable being still for extended time, as in restaurants, meetings; may be experienced by others as being restless or difficult to keep up with).
   f. Often talks excessively.
   g. Often blurts out an answer before a question has been completed (e.g., completes people's sentences; cannot wait for turn in conversation).
   h. Often has trouble waiting his/her turn (e.g., while waiting in line).
   i. Often interrupts or intrudes on others (e.g., butts into conversations, games, or activities; may start using other people's things without asking or receiving permission; for adolescents and adults, may intrude into or take over what others are doing).

B. Several inattentive or hyperactive-impulsive symptoms were prior to age 12 years.

C. Several inattentive or hyperactive-impulsive symptoms are present in two or more settings, (e.g., at home, school, or work; with friends or relatives; in other activities).

D. There is clear evidence that the symptoms interfere with, or reduce the quality of, social, academic, or occupational functioning.

E. The symptoms do not occur exclusively during the course of schizophrenia or another psychotic disorder and are not better explained by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal).

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ADHD = attention-deficit/hyperactivity disorder; DSM-5-TR = *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed., text revision.

have a major impact on function.[1] Clinicians should be aware that some people with ADHD may appear high performing in one setting but spend a significant amount of time and effort maintaining that level of performance or have reduced performance in other settings. Also, many patients lack insight into their condition and are unable to wholly communicate their symptomatology.[15,18]

If a patient's presentation and screening results are suggestive of ADHD, they must then meet DSM-5-TR criteria for a formal diagnosis (Table 2).[1] There are several validated self-report diagnostic tools that have been derived from DSM-5-TR criteria[8,16,17,19,20] (Table 3).

To avoid an inappropriate diagnosis of ADHD, collection of corroborating collateral information (e.g., childhood medical records, work evaluations, school transcripts, observer reports) is strongly recommended.[8,14] Free, research-supported observer forms include the Current Behaviour Scale – Partner Report and the retrospective Childhood Behaviour Scale – Parent Report.[14]

If a patient's evaluation findings are consistent with ADHD, the diagnosis is further classified by presentation type, disease severity, and remission status.[1] ADHD's presentation type and severity can change over time, and patients can go into remission. In the absence of a clear ADHD diagnosis, the patient may be referred to cognitive behavior therapy for distress regarding cognition or to brief psychoeducational counseling for concentration concerns.

Diagnostic Recommendations

Clarifying which symptoms are most distressing to the patient at the time of evaluation is important because there are often

TABLE 2 (continued)

DSM-5-TR ADHD Diagnostic Criteria and Classifications

Specify whether:

F90.2 Combined presentation: If both Criterion A1 (inattention) and Criterion A2 (hyperactivity-impulsivity) are met for the past 6 months.

F90.0 Predominantly inattentive presentation: If Criterion A1 (inattention) is met but Criterion A2 (hyperactivity-impulsivity) is not met for the past 6 months.

F90.1 Predominantly hyperactive/impulsive presentation: If Criterion A2 (hyperactivity-impulsivity) is met and Criterion A1 (inattention) is not met for the past 6 months.

Specify if:

In partial remission: When full criteria were previously met, fewer than the full criteria have been met for the past 6 months, and the symptoms still result in impairment in social, academic, or occupational functioning.

Specify current severity:

Mild: Few, if any, symptoms in excess of those required to make the diagnosis are present, and symptoms result in no more than minor impairments in social or occupational functioning.

Moderate: Symptoms or functional impairment between "mild" and "severe" are present.

Severe: Many symptoms in excess of those required to make the diagnosis, or several symptoms that are particularly severe, are present, or the symptoms result in marked impairment in social or occupational functioning.

ADHD = attention-deficit/hyperactivity disorder; DSM-5-TR = *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed., text revision.

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comorbid psychiatric concerns. Common psychiatric comorbidities, substantial symptom overlap with other disorders, and potential malingering complicate adult ADHD diagnosis. Diagnostic self-report tests tend to lack specificity and result in a high false-positive rate if used alone.[21-27] Given ADHD's high heritability and persistence from childhood, however, a family history of ADHD in a first-degree relative or personal history of a childhood ADHD diagnosis greatly increases the likelihood of ADHD in an adult.[2-4,9] A comprehensive combination of a clinical evaluation, screening, diagnostic testing, and collateral information is often sufficient to make an accurate diagnosis in these cases.

In patients without a first-degree relative with ADHD or personal history of a childhood ADHD diagnosis, particularly if corroborating collateral information is lacking or confounding comorbid mental illness is suspected, neuropsychological diagnostic testing should be considered. Neuropsychological testing, which is performed by or under supervision of a licensed neuropsychologist or psychologist, incorporates symptom validity testing and performance measures (e.g., working memory, sustained attention, task omissions, commission errors, reaction time, response time variability) and can assist with diagnosis when combined with self-report and collateral information.[22,28-32] The financial burden of this testing to the patient should be a consideration. Medicare/Medicaid reimbursement rates for neuropsychological testing costs are $75 to $150 per hour. The process involves hours of testing and interpretation of results, and the overall cost of evaluation can reach thousands of dollars.[33,34]

NONPHARMACOLOGIC TREATMENTS

Although pharmacologic regimens are the first-line treatment for adult ADHD, psychotherapy is an option to avoid medication. Many types of therapy can help, but symptoms often improve with cognitive behavior therapy. There is also evidence that mindfulness and cognitive remediation are effective interventions for core symptoms. There is weaker evidence for the use of group dialectical behavior therapy and hypnotherapy due to the small sample sizes, lack of suitable control conditions, and a high risk of bias.[35] In many cases, cognitive behavior therapy for ADHD in adults addresses psychoeducation and adaptive coping skills, and involves the patient's partner or family members.[36]

PHARMACOLOGIC TREATMENTS

Table 4 summarizes pharmacotherapy options for ADHD in adults.

Stimulant Medications

Stimulants are a first-line therapy for adult ADHD given the robust data supporting their effectiveness. Stimulants include permutations of amphetamine and methylphenidate. Although there are multiple formulations, a systematic review concluded

TABLE 3

Diagnostic Tools for Adult ADHD

Diagnostic tool	Description	Availability
ADHD Lifespan Functioning Interview	18-item questionnaire Asks about family, social, school, occupational, antisocial behavior/legal, and substance use history	Free at https://www.psychology-services.uk.com/adhd.htm
Adult ADHD Investigator Symptom Rating Scale	18-item questionnaire based on DSM-IV criteria	Free by emailing adultADHD@med.nyu.edu
Adult ADHD Rating Scale IV with Adult Prompts	18-item questionnaire based on DSM-IV criteria	Free by emailing adultadhd2@nyulangone.org
Adult ADHD Self-Report Scale (v1.1) Symptom Checklist	18-item questionnaire Official instrument of the World Health Organization	Free at https://add.org/adhd-questionnaire
Barkley Adult ADHD Rating Scale-IV	27 items for current ADHD symptoms 18 items for childhood ADHD symptoms Based on DSM-IV	Purchase at https://www.russellbarkley.org/
Brown Executive Function/Attention Scales for Adults	Structured interview up to 90 minutes Asks about clinical history, early schooling, family history, physical health, substance use, and sleep habits	Purchase at https://www.pearsonassessments.com
Conners 4th Edition	Highest specificity with embedded validity indicators Short and long structured interview versions Long version can take up to 90 minutes Asks about childhood and adult histories	Purchase at https://www.pearsonassessments.com
Diagnostic Interview for ADHD in Adults-5	Structured interview up to 90 minutes Asks about childhood and adult histories	Purchase at www.divacenter.eu
Structured Clinical Interview for DSM-5	Structured interview guide for making any major DSM-5 diagnosis Includes an adult ADHD module	Purchase at https://www.appi.org/Products/Interviewing/Structured-Clinical-Interview-for-DSM-5-Disorders and https://www.appi.org/Products/Interviewing/Quick-Structured-Clinical-Interview-for-DSM-5-Diso
Weiss Symptom Record II and Functional Impairment Rating Scale – Self	18 items for ADHD 69 items for function across 7 domains Based on DSM-IV Also includes items for developmental/learning delays, mood/behavior/personality disorders, motor disorders, psychosis, suicide, stress, sleep/eating habits, substance use, and addiction	Free at https://mhscales.com/wfirs and https://mhscales.com/wsr
Wender-Reimherr Adult Attention-Deficit Disorder Scale	Measures the severity of symptoms in adults with ADHD using the Utah criteria Useful to assess mood lability symptoms	Purchase at https://www.aacp.com/article/buy_now/?id=69

ADHD = attention-deficit/hyperactivity disorder; DSM-IV = *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed.

TABLE 4

Pharmacotherapy Options for the Treatment of ADHD in Adults

Medication*	Dosage†	Adverse effects	Cost‡
Stimulants			
Dextroamphetamine/amphetamine (Adderall)	IR: 5 mg once or twice daily (maximum: 40 mg per day) ER: 10 to 20 mg once daily in the morning (maximum: 60 mg per day)	Loss of appetite, insomnia, tachycardia, headache, weight loss, dry mouth	IR: $20 ($340) for 10 mg ER: $30 ($225) for 10 mg
Dextroamphetamine (Zenzedi, Xelstrym)	IR/ER: 5 mg once or twice daily (maximum: 60 mg per day) Patch: 9-mg patch worn for 9 hours, off for 15 hours (maximum: 18 mg worn for 9 hours)	Nausea, anorexia, insomnia, abdominal discomfort, fever, nervousness	IR: $30 ($40) for 10 mg ER: $30 ($730) for 10 mg Patch: — ($500)
Methylphenidate	IR: 5 mg once daily (maximum: 60 mg per day divided into 2 or 3 doses) SR: 20 mg daily in the morning (maximum: 60 mg per day) ER (12 hour): 10 mg twice daily (maximum 60 mg per day) ER (24 hour): 10 mg daily in the morning (maximum: 60 mg per day) Concerta: 18 mg daily (maximum: 72 mg per day)	Decreased appetite, headache, dry mouth, insomnia, abdominal discomfort, nausea, anorexia	Varies
Dexmethylphenidate (Focalin)	IR: 2.5 mg twice daily (maximum: 20 mg per day) ER: 10 mg once daily (maximum: 40 mg per day)	Anorexia, nausea, abdominal discomfort, dry mouth, anxiety, insomnia	IR: $20 ($55) for 10 mg ER: $50 ($170) for 10 mg
Lisdexamfetamine (Vyvanse)	30 mg once daily (maximum: 70 mg per day)	Decreased appetite, insomnia, abdominal discomfort, nausea, anorexia	$75 ($400) for 30 mg
Nonstimulants (selective norepinephrine reuptake inhibitors)			
Atomoxetine (Strattera)	40 mg once daily for at least 3 days (maximum: 100 mg per day divided into 1 or 2 doses; may titrate to maximum in 2 to 4 weeks)	Nausea, vomiting, abdominal discomfort, fatigue, insomnia, erectile dysfunction, somnolence, dry mouth	$30 ($450) for 40 mg
Viloxazine (Qelbree)	200 mg once daily (maximum: 600 mg per day	Increased diastolic blood pressure, tachycardia, nausea, headache, abdominal discomfort	— ($350) for 200 mg

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ADHD = attention-deficit/hyperactivity disorder; ER = extended release; IR = immediate release; SR = sustained release.

*—All brand-name pharmacotherapies were reviewed on https://www.accessdata.fda.gov.

†—Starting dosages appear first with increases and maximums noted where appropriate. Dosage may vary based on kidney disfunction, age > 65 years, and other comorbidities.

‡— Estimated lowest GoodRx price for one month's treatment. Actual cost will vary with insurance and by region. Generic price listed first; brand name price in parentheses. Information obtained at https://www.goodrx.com (accessed July 1, 2024; zip code: 66211).

TABLE 4 (continued)

Pharmacotherapy Options for the Treatment of ADHD in Adults

Medication*	Dosage†	Adverse effects	Cost‡
Antidepressant (off-label use)			
Bupropion (Wellbutrin)	IR: 100 mg twice daily for 3 days, then 100 mg three times daily (maximum: 450 mg per day) SR: 150 mg once daily for 3 days, then 150 mg twice daily (maximum: 400 mg per day divided into 2 doses) ER: 150 mg once daily for 4 days, then may increase to 300 mg daily (maximum: 450 mg per day)	Seizures, glaucoma, mania, insomnia, agitation, suicidal ideation, hallucination, anxiety, tachycardia, weight loss, headache	IR: $10 (—) for 100 mg SR: $25 ($500) for 150 mg ER: $25 ($2,000) for 150 mg

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*—All brand-name pharmacotherapies were reviewed on https://www.accessdata.fda.gov.

†—Starting dosages appear first with increases and maximums noted where appropriate. Dosage may vary based on kidney disfunction, age > 65 years, and other comorbidities.

‡— Estimated lowest GoodRx price for one month's treatment. Actual cost will vary with insurance and by region. Generic price listed first; brand name price in parentheses. Information obtained at https://www.goodrx.com (accessed July 1, 2024; zip code: 66211).

that most adults with ADHD have a favorable response to stimulants, with some studies indicating a preference for amphetamines over methylphenidate.[37] Approximately 70% of adults with ADHD have immediate improvement in attentiveness and reduced distractibility, with moderate to large effect sizes. Effects are seen within 1 hour of administrating immediate-release or controlled-release formulations. Controlled-release formulations, which remain effective for 6 to 10 hours, may improve compliance because they require only once-daily dosing.[38]

Potential adverse effects of stimulants include insomnia, headaches, elevated blood pressure, elevated heart rate, decreased appetite, weight loss, dry mouth, anxiety, and depression. Because of their potential to persistently increase blood pressure or heart rate, stimulants are contraindicated in those with uncontrolled hypertension, angina, a history of myocardial infarction, arrhythmias, significant heart valve disease, or cardiomyopathy. Before initiating stimulant therapy, electrocardiography may be recommended for some patients, based on their symptoms, conditions, and personal or family cardiovascular history. Stimulants are also contraindicated in those who are pregnant or have a history of tics, drug addiction, alcohol misuse, severe anorexia, or psychosis.[8,14,39]

Stimulant Misuse and Diversion

Stimulant medications are classified as Schedule II substances by the U.S. Drug Enforcement Administration due to the high potential for abuse. They increase levels of dopamine in the brain, which has rewarding effects.[40] In 2021, more than 3.4 million people 18 years and older in the United States misused prescription stimulants, most commonly amphetamines.[41] An estimated 66% of people who misuse prescription stimulants get the medications from family or friends with prescriptions, and 20% obtain prescriptions themselves by presenting to clinicians with exaggerated or fabricated symptoms.[42] In adolescents and college students, nonmedical stimulant use may be as prevalent as medical use.[43]

The risk of abuse is increased among persons with a history of substance use disorder.[40] Controlled-release formulations are harder to inject or snort than immediate-release formulations and thus are less likely to be abused. Prescription stimulants are most often abused to achieve intoxication, lose weight, self-treat mental illness, or improve cognition and productivity.[41,43] About 5% of people without ADHD who use stimulants for nonmedical purposes will increase their use, leading to substance use disorder and dependence.[44] Rates of overdose deaths from noncocaine stimulants have been exponentially increasing in the United States since 2012, with more than 32,500 deaths in 2021.[45] To prevent misuse of prescribed stimulants, controlled substance agreements and monitoring methods such as random urine drug screening, patient reevaluation at least every 3 months, and local prescription drug monitoring programs may be used.[46]

Nonstimulant Medications

For those who do not respond to stimulants, have major adverse effects with stimulant use, or have a contraindication to stimulant use, nonstimulant medications approved by the U.S. Food and Drug Administration (FDA) for adult ADHD are atomoxetine and viloxazine (Qelbree), which are selective norepinephrine reuptake inhibitors.[37] One of the benefits of using

nonstimulant medications for ADHD treatment in adults is a lower risk of abuse compared with stimulants.[47] They may also be beneficial for patients with concomitant anxiety. Although nonstimulants generally take longer than stimulants to reach full effect (about 4 weeks), some patients see improvement in ADHD symptoms in as early as one week.[48]

For those who do not respond to stimulant treatment or FDA-approved nonstimulant options, off-label medications may be considered. Bupropion can be used for those with comorbid conditions such as depression, anxiety, and smoking. Clonidine and guanfacine (Intuniv), alpha-2 and alpha-2a adrenergic receptor agonists, respectively, are approved only for use in children and adolescents, but they have been used in adults despite limited evidence.[37,49] Similarly, the evidence is limited for tricyclic antidepressants, and they are not approved for ADHD at any age.[38]

MONITORING PHARMACOTHERAPY

In adults with a new ADHD diagnosis, at least monthly follow-up is appropriate until the patient has adequate functional improvement.[19] During these visits, it is important to address treatment expectations, medication adverse effects, vital signs (particularly blood pressure and heart rate in patients taking stimulants), medication effectiveness, and the need for dosing adjustments. Drug holidays during weekends and vacations are sometimes recommended, but the evidence is lacking.[14] Many of the diagnostic tools in Table 3 can also be used to reassess patients for condition improvement while they are undergoing treatment optimization.[8,14,19,20,50] If an individual becomes dependent on stimulants, rapid cessation may lead to withdrawal symptoms, including fatigue, uncontrolled body movements, irritability, and confused thoughts, which may take weeks to resolve. To reduce this risk, a taper is recommended to wean patients off high doses of stimulants.[51]

This article updates previous articles on this topic by Post and Kurlansik,[50] and Searight, et al.[52]

Data Sources: Essential Evidence Plus, PubMed, MEDLINE, Cochrane database, American Academy of Family Physicians, UpToDate, and Centers for Disease Control and Prevention were searched using an extensive list of synonyms for ADHD treatment, diagnosis, and testing. Search dates: May 2023 to January 2024, and July 2024.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Air Force, the U.S. Department of Defense, or the U.S. government.

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