Lifetime persistence of symptoms that began before age 7 is required for ADHD diagnosis in adults

Current PSYCHIATRY

ADHD in adults

Matching therapies with patients' needs

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Mr. Z, age 42, is referred by his primary care physician with symptoms suggesting attention-deficit/hyperactivity disorder (ADHD). Mr. Z has seen his physician sporadically for 10 years and acknowledges not following dietary and exercise advice. He has had intermittent "minor" depression, is overweight, and is a smoker with a family history of cardiovascular disease and diabetes.

A salesman, Mr. Z recently was promoted to an administrative position that substantially increased his paperwork. He is having difficulty performing his job because of longstanding forgetfulness and disorganization. He says he feels "like I'm in grade school again, lost in paperwork." He also describes a recent educational assessment for his son, age 7, who may have ADHD. Similarities between Mr. Z's and his son's early childhood academic struggles are striking.

Like Mr. Z, adults with ADHD commonly seek treatment when increasing stressors and demands overwhelm their cognitive-attentional abilities. Some may be "healthy" men and women without psychiatric histories, whose disorganization, forgetfulness, or impulsivity contributes to functional impairment, including nonadherence with medical advice. For others, such as those with known psychiatric disorders, ADHD may be a hidden comorbidity contributing to seemingly refractory depression or anxiety disorder.

Despite growing evidence related to adult ADHD, individualizing and maintaining treatment over time can be challenging for clinicians and patients. Fortunately, new tools and multiple stimulant and nonstimulant medications can help you screen for, assess, and treat adult ADHD.

continued

Adult ADHD

Table 1

Adult Self-Report Scale-v1.1 WHO 6-question screening tool for ADHD*

Check the box that best describes how you have felt and conducted yourself over the past 6 months. Please give the completed questionnaire to your healthcare professional during your next appointment to discuss the results	Never	Rarely	Some-times	Often	Very often
1. How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?					
2. How often do you have difficulty getting things in order when you have to do a task that requires organization?					
3. How often do you have problems remembering appointments or obligations?					
4. When you have a task that requires a lot of thought, how often do you avoid or delay getting started?					
5. How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?					
6. How often do you feel overly active and compelled to do things, like you were driven by a motor?					

Add the number of checkmarks that appear in the darkly shaded area. Four (4) or more checkmarks indicate that your symptoms may be consistent with adult ADHD. It may be beneficial for you to talk with your healthcare provider about an evaluation.

* Intended for use by persons age 18 and older
ADHD: attention-deficit/hyperactivity disorder; WHO: World Health Organization
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Begin assessment with orienting questions, such as 'Do you remember your first grade teacher, your school, where you lived?'

ADHD diagnosis

To diagnose ADHD in an adult patient, first establish that symptoms have existed from childhood to adulthood. One approach is to review DSM-IV-TR criteria for ADHD with your patient and ask him or her to reflect on childhood symptoms and dysfunction. Begin with orienting questions, such as "Do you remember your first grade teacher, your school, where you lived?" ADHD symptoms might have been present even if the patient maintained acceptable grades, particularly in elementary school, as dedicated parents or teachers might have contributed to early academic success.

Next, turn to diagnostic language that captures ADHD symptoms in adults. For example, the 18-item World Health Organization Adult ADHD Self-Report Scale (ASRS-v1.1) prompts individuals to self-report DSM-IV ADHD symptoms, and a 6-item subset (***Table 1***) is a highly specific screener (see ***Related Resources, page 62***). The ASRS is most reliable in adults with limited psychiatric comorbidity.[1]

Adults often describe fluctuations in symptom severity over time. Symptoms may have less impact with more physically demanding work—such as sales—and greater impact with organizationally demanding work—such as administration.

Base your summary ADHD diagnosis on DSM-IV-TR criteria, including:

- lifetime persistence of symptoms, beginning before age 7
- functional impairment in ≥2 life settings, such as work, school, or home
- lack of another medical or psychiatric condition sufficient to explain the symptoms.

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Adult ADHD

Table 2

Administering medications approved for adult ADHD

Drug	Recommended dosage*	Comments
Stimulants		
Extended-release mixed amphetamine (Adderall XR)	20 mg	Initial prescription of 10-mg XR capsules allows gradual titration
Extended-release OROS methylphenidate (Concerta)	18 to 72 mg/d	Initial prescription of 18-mg OROS MPH capsules allows gradual titration
Extended-release dexmethylphenidate (Focalin XR)	10 mg/d; maximum 20 mg/d	Dosing is one-half the typical dosing of racemic MPH
Lisdexamfetamine (Vyvanse)	30 mg/d; maximum 70 mg/d	May be adjusted weekly in 10-mg or 20-mg increments
Nonstimulant		
Atomoxetine (Strattera)	80 mg/d; maximum 100 mg/d	Initial dosage of 40 mg/d can be increased to target dosage after a minimum of 3 days; can be given as a morning dose or divided evenly between morning and evening doses

* FDA-approved dosages as listed in the package inserts of these medications
ADHD: attention-deficit/hyperactivity disorder; MPH: methylphenidate; OROS: osmotic release oral system; XR: extended-release formulation

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Clinically, some patients appear to tolerate 1 stimulant class (such as methylphenidate or amphetamine) over another

CASE CONTINUED

'All the time, every day'

Mr. Z completes the ASRS self-report symptom checklist and brings his wife to the next appointment. He rated all 6 screening symptoms and most others as occurring "often" or "very often." He describes functional impairments "essentially all the time, basically every day" at work, home, and socially. His wife confirms these symptoms and the frustrations and conflicts they have caused.

Mr. Z describes ADHD symptoms from early elementary school to college. He was held back in kindergarten for being "immature," his academic performance was inconsistent, and he "just got by…by cramming" in high school and college. His school performance pattern does not suggest a learning disability; he did not need special help in 1 subject more than others, and under pressure he could achieve average grades.

Medical review excludes explanations other than ADHD for his inattention, restlessness, and impulsivity. You conclude that Mr. Z meets criteria for ADHD, combined subtype, and discuss medication treatment.

FDA-approved medications

Medication for ADHD is appropriate only if symptoms are impairing. Five effective and generally well-tolerated medications are FDA-approved for adults with ADHD (*Table 2*):

- extended-release mixed amphetamine (Adderall XR)
- extended-release OROS methylphenidate (Concerta)
- extended-release dexmethylphenidate (Focalin XR)
- atomoxetine (Strattera)
- lisdexamfetamine (Vyvanse).

Efficacy. A meta-analysis of 29 pediatric ADHD trials across 30 years demonstrated greater effect size for stimulant class medications (immediate- and long-acting), compared with nonstimulant medications (including bupropion, atomoxetine, and modafinil).[2] This finding is consistent with the American Academy of Child and Adolescent Psychiatry's recommendation of stimulant medications as first-line agents for pediatric ADHD.[3] A similar meta-analysis

of 6 controlled studies of methylphenidate-class medications in adults found a large mean effect size (0.9), with greater effects associated with higher doses.[4]

Atomoxetine, a norepinephrine reuptake inhibitor, is the only nonstimulant medication FDA-approved for ADHD in adults. More than 6,000 children, adolescents, and adults have taken atomoxetine in clinical trials for ADHD (Lilly, prescribing information), with 4 years of open treatment data showing benefit being maintained over time.[5]

Tolerability. Although ADHD medications are generally well-tolerated by healthy adults, assess for a history of potential contraindications:

- unstable medical condition, hyperthyroidism, glaucoma
- treatment with a monoamine oxidase inhibitor or other pressor agents because of possible effects on blood pressure and heart rate
- use of cytochrome P450 2D6 inhibitors, which may increase atomoxetine steady-state plasma concentrations
- cardiovascular disease or family history of early cardiac disease (***Box 1***)[6,7]
- history of or active substance use disorder, such as alcohol dependence, cocaine or heroin abuse
- history of psychosis, bipolar disorder, or an active clinically significant psychiatric comorbidity (major depression, agitated state, suicidality).

Clinically, some patients appear to tolerate 1 class of stimulant (such as methylphenidate or amphetamine) over another. Consider switching to an alternate stimulant if your patient has bothersome side effects—mild low appetite, insomnia, tension, or jitteriness—or has received limited or partial benefit during an initial stimulant trial.

Extended-release formulations. Early adult studies demonstrated the efficacy of immediate-release stimulants, but adults with ADHD's inherent deficits in organization and memory may have higher adherence rates and greater success with once-daily, extended-release formulations.[8-11] Unless your patient wants to begin with small, short-acting dosages (5 to 10 mg) or desires to target treatment to specific times of day (such as in the morning for administrative work only), many appreciate once-daily formulations. Extended-release formulations also may be the simplest stimulants with which to begin ADHD treatment.

continued

Box 1

Managing cardiovascular risk of stimulant use in adults

Serious cardiovascular events and sudden death have occurred in adults and children treated with stimulants.[6] Agents used for attention-deficit/hyperactivity disorder (ADHD) have not been shown to cause sudden cardiac death, but the FDA requires stimulants' labeling to warn about this risk in patients with structural cardiac abnormalities. The warning advises against using stimulants in adults with cardiomyopathy, serious heart rhythm abnormalities, or coronary artery disease.

When treating adults with ADHD, look to advisories about cardiovascular monitoring in children with ADHD. Before initiating medications, do a physical exam focused on cardiovascular disease risk factors and obtain a patient and family health history of:

- fainting or dizziness
- sudden or unexplained death in someone young
- sudden cardiac death or "heart attack" in family members age <35 years.

The American Academy of Pediatrics, American Academy of Child and Adolescent Psychiatry, and American Heart Association concur that electrocardiography (ECG) is not mandatory in cardiovascular assessment and monitoring during ADHD pharmacotherapy.[7] This author (PH) refers cardiovascular questions to a primary care physician or cardiologist.

During ADHD treatment, monitor vital signs and refer patients with emergent cardiac symptoms or concerns to a cardiologist. Expect increases in blood pressure (1 to 4 mm Hg) and heart rate (2 to 6 bpm) during treatment with methylphenidate and amphetamine-class stimulants as well as with atomoxetine. Do not expect significant changes in ECG parameters (PR, QRS, and QTC intervals).

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An ECG is not considered mandatory in cardiovascular assessment and monitoring during ADHD drug therapy

Adult ADHD

Clinical Point

Extended-release formulations may be the simplest stimulants with which to begin treatment in adults with ADHD

Box 2

Strategies to cover 'wear-off' of long-acting stimulants

Combining short- and long-acting stimulants may cover hours when attention-deficit/hyperactivity (ADHD) symptoms emerge despite therapy with a long-acting agent.[12,13] Ask patients who report lack of full-day coverage if the once-daily, extended-duration formulation they are taking works well until a certain time of day. Then consider adding a similar-class immediate-release stimulant at this time to cover the later hours.

If a patient reports partial response throughout the day—such as early in treatment—begin by optimizing the long-acting agent's dosage. Keep a target daily dose in mind, based on FDA recommendations and clinical trial data. For example, an adult weighing 80 kg may respond optimally to a combination of 60 mg of a long-acting methylphenidate (MPH) in the morning, followed by 10 to 20 mg of an immediate-release MPH in mid-afternoon.

The later stimulants are taken in the day, the more likely insomnia may emerge as an adverse effect. Some patients adjust to this problem within the first weeks of treatment. If insomnia remains impairing, reduce the stimulant dose or consider switching to a shorter duration medication or to the nonstimulant atomoxetine.

Over time, patients may benefit from an immediate-release form:

- added for certain times of day—such as in late afternoon, when the morning extended-release dose has worn off (***Box 2***)[12,13]
- to use as an alternative to extended-release formulations when more or less flexibly is desired, such as on weekends.

CASE CONTINUED

Feeling 'calm, less frenetic'

During the next 6 months, you start Mr. Z on stimulant treatment at robust dosing consistent with his weight (90 kg). He complains that extended-duration methylphenidate (MPH)—titrated to 90 mg/d—doesn't last into the late afternoon, and he feels mildly tense with a low appetite. Because of an apparent partial response and relatively mild adverse effects, you discontinue MPH and try an extended-duration amphetamine, titrated to 60 mg.

Mr. Z's blood pressure and heart rate remain stable. He begins to exercise regularly and reduce his use of tobacco and caffeine drinks, as you recommend. He says he feels "calm, less frenetic." He reports no tension on this medication and only mild reduced appetite. With a plan to continue taking the stimulant medication with regular monitoring, he then disappears from treatment.

Promoting adherence

Treatment nonadherence is an issue throughout medicine, and individuals with disorganization, forgetfulness, and impulsivity may be at higher-than-usual risk of not following through on medication regimens.

In addition, restrictions on stimulant-class medications do not permit multiple-month prescribing (refills), as is allowed with nonscheduled medications such as atomoxetine. Discuss with patients how they will obtain stimulant medications on a regular, monthly or bimonthly basis. In our experience, the practical challenges of remaining in treatment at times may limit patients' adherence to ADHD medications more than a lack of response or tolerability concerns.

Explain to patients early in treatment that they might need to try several different medications before settling on 1 that is optimally tolerated and efficacious. Because stimulants are generally quite effective for ADHD symptoms, set your goal to identify adverse effects and aim for a patient response of "this works well, and I don't feel any different on it."

CASE CONTINUED

Ready to try again

Three years later, Mr. Z returns and reports gradually discontinuing the stimulant because he "wanted to go it on my own." He functioned relatively well at first, but errors and conflicts at his job led to his dismissal.

Since then, he has been unemployed. He is increasingly depressed and reports drinking and smoking "more heavily than in college." He asks about resuming ADHD treatment.

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Mr. Z does not meet DSM-IV-TR criteria for major depressive disorder or alcohol abuse/dependence. His depressed mood appears to be linked to his marked ADHD symptoms. Mr. Z agrees to a new treatment plan that includes starting atomoxetine at 25 mg to allow for flexible titration and psychotherapy to monitor his mood and achieve sobriety.

ADHD and substance abuse

Clinical judgment determines whether an adult with ADHD and a history of substance use disorders may safely benefit from treatment with a stimulant. The relationship between ADHD and substance use disorders is of clinical concern, but ADHD medications have not been shown to increase risk for later substance use disorders in children.[14] Conversely, effective ADHD treatment appears to reduce later cigarette and substance use.[15]

Consider using a nonstimulant-class medication in adults with ADHD and active substance use disorders. In a 12-week, double-blind, controlled trial, atomoxetine improved ADHD symptoms significantly more than placebo in adults meeting DSM-IV-TR criteria for comorbid alcohol use disorders. After 4 to 30 days of alcohol abstinence, 72 patients were randomly assigned to atomoxetine, 25 to 100 mg/d (mean final dose 90 mg/d), and 75 patients to placebo. Although estimated times to initial relapse to heavy drinking did not differ:

- atomoxetine-treated subjects had 26% fewer cumulative heavy drinking days than placebo-treated subjects (P = 0.023)
- the difference in cumulative heavy drinking days between the atomoxetine and placebo groups became statistically significant after 55 days of treatment.[16]

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continued

Adult ADHD

Clinical Point

Explain to patients that they may need to try several different medications to find 1 that is optimally tolerated and efficacious

Related Resources

- World Health Organization Adult Self-Report Scale (ASRS) 18-item instrument and 6-item screener. www.med.nyu.edu/psych/psychiatrist/adhd.html.
- Volkow ND, Swanson JM. Does childhood treatment of ADHD with stimulant medication affect substance abuse in adulthood? *Am J Psychiatry* 2008;165:553-5.
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Drug Brand Names

Atomoxetine • Strattera
Bupropion • Wellbutrin
Extended-release mixed amphetamine • Adderall XR
Extended duration OROS methylphenidate • Concerta
Extended-release dexmethylphenidate • Focalin XR
Lisdexamfetamine • Vyvanse
Modafinil • Provigil

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Bottom Line

To gauge the lifetime persistence of attention-deficit/hyperactivity disorder (ADHD) in adults, begin by reviewing childhood symptoms. Then ask questions using adult-friendly language to investigate the impact of ADHD symptoms at work and at home. Medication for ADHD is appropriate only if symptoms are impairing. Consider risks vs benefits of pharmacotherapy, balancing medical or psychiatric comorbidities against the functional impairments of ADHD in adulthood.