

PCC

V I S U A L S

PRIMARY CARE COMPANION TO THE
JOURNAL OF CLINICAL PSYCHIATRY

**THIS ISSUE OF PCC VISUALS
DISCUSSES THE DIAGNOSIS AND
MANAGEMENT OF ATTENTION-DEFICIT/
HYPERACTIVITY DISORDER (ADHD) IN
ADULTS IN THE PRIMARY CARE SETTING.**

To obtain credit, read the material
and complete the CME Posttest
and Registration Form.

CME OBJECTIVES

After completing this educational activity,
participants should be able to:

- Discuss the phenomenology of ADHD in adults
- Describe the process for assessing ADHD in adults
- Choose a strategy for managing an adult with ADHD
- Review the literature on the relationship of substance abuse and ADHD in adults
- Discuss the role of the primary care physician in diagnosing and managing ADHD in adults

FACULTY

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Diagnosing and Treating Attention-Deficit/Hyperactivity Disorder in Adults

JOSEPH BIEDERMAN, M.D.

With a prevalence of 4.5%,¹ attention-deficit/hyperactivity disorder (ADHD) affects so many adults that primary care physicians will encounter adult patients who have ADHD but have never been diagnosed with and/or treated for this disorder. Adults with ADHD can be identified by certain impairments that have decreased their quality of daily life since childhood. Physicians and adults with ADHD, in collaboration with other professionals or support groups if needed, should design treatment plans individualized for patients' comorbid psychiatric and medical conditions and the areas of their lives they would most like to improve. Although the long-term effects of medications for ADHD are still being evaluated, these treatments should be safe for most patients if they are prescribed and taken correctly.

Phenomenology of ADHD

JOSEPH BIEDERMAN, M.D.

In childhood, the ratio of ADHD in males and females ranges from 4:1 to 9:1, but by adulthood, the ratio is about 3:2. This difference might be caused by referral bias. Children are likely to be referred for treatment if they are disruptive, and disruptive behaviors are reported in more than twice as many boys as girls. However, adults often seek treatment on their own because of problems functioning at work and home that are caused by ADHD and comorbid conditions, not because of conduct problems. Regardless of age or gender, individuals with ADHD face impairment in all aspects of their lives that is costly to them and to society, especially if left untreated.

Prevalence of Lifetime Psychiatric Conditions in Pediatric and Adult Populations With ADHD and Controls by Gender

Several psychiatric conditions are significantly more common in individuals with ADHD than in control subjects. Similar lifetime rates of these disorders in children and adults with ADHD indicate that many of these conditions begin

in early childhood. Also, the current prevalence of comorbid conditions is in general substantially lower than the lifetime prevalence. Therefore, much of the impairment in adults with ADHD is likely caused by the disorder itself.

Condition	Pediatric (%)				Adult (%)			
	Female		Male		Female		Male	
	Control (N = 122)	ADHD (N = 140)	Control (N = 140)	ADHD (N = 120)	Control (N = 110)	ADHD (N = 50)	Control (N = 97)	ADHD (N = 78)
At least 2 anxiety disorders	5	33	4	28	15	52 ^a	10	45 ^a
Oppositional defiant disorder	4	35 ^b	11	66 ^b	2	30 ^a	3	33 ^a
Enuresis	6	25	14	32	3	26 ^a	14	27
Major depression (severe)	1	15 ^c	2	29 ^c	6	36 ^a	4	31 ^a
Conduct disorder	0	8 ^d	3	21 ^d	2	8	6	31 ^{ab}
Bipolar disorder	0	11	0	11	3	10	4	12

Data from Biederman et al.^{2,3}

^a*p* < .001 for difference between subjects with ADHD and controls of the same gender.

^b*p* < .001 for difference between females and males with ADHD.

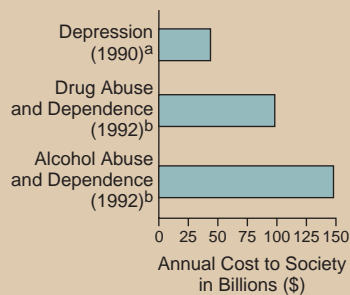
^c*p* = .002 for difference between females and males with ADHD.

^d*p* = .001 for difference between females and males with ADHD.

■ The Cost of ADHD and Comorbid Disorders

The academic toll of ADHD, including the need for special classes, extra help, and repeating a grade, is well known. However, ADHD is associated with many more costs to the patient and society. Although the economic cost of ADHD itself is unknown, the societal and medical expenses associated with some symptoms and comorbid conditions, especially when left untreated, are extensive.^{4,5} The results of untreated antisocial behaviors such as theft and vandalism can be seen in prison, where the prevalence of ADHD in adults might be 25%,⁶ which is more

Annual Costs of Conditions Commonly Comorbid With ADHD in the United States

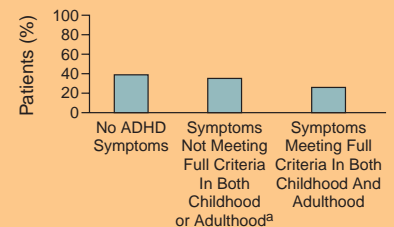


^aData from Greenberg et al.⁴

^bData from Harwood et al.⁵

than five times the estimated prevalence in the general population. ADHD must

Prevalence of ADHD in 102 Male Inmates Between 16 and 64 Years in a Utah Prison



Data from Eyestone and Howell.⁶

^aSome individuals had mild or significant symptoms in childhood alone, adulthood alone, or both or had mild symptoms at one stage and significant symptoms at another stage.

be managed to reduce the cost to patients and society. ■

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Statement of Need and Purpose

A substantial number of children who have attention-deficit/hyperactivity disorder (ADHD) continue to have symptoms well into adulthood. In adults, ADHD is often associated with substance abuse as well as co-occurring anxiety, mood, and disruptive disorders. Physicians sometimes fail to consider, detect, or treat adults for ADHD, due to a lack of information on the diagnosis and treatment of ADHD. This educational activity was designed to meet the needs of participants in the CME activities of Physicians Postgraduate Press, Inc. who have requested information on the diagnosis and management of ADHD in adults. There are no prerequisites for participating in this activity.

Accreditation Statement

Physicians Postgraduate Press, Inc. is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

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Physicians Postgraduate Press, Inc. designates this educational activity for up to 1 Category 1 credit toward the AMA Physician's Recognition Award. Each participant should claim only those credits that he/she actually spent in the educational activity.

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Faculty Disclosure

In the spirit of full disclosure and in compliance with all ACCME Essential Areas and Policies, the faculty for this CME activity were asked to complete a full disclosure statement. The information received is as follows: **Dr. Biederman** has received research support from Shire Richwood, Eli Lilly, Wyeth, Pfizer, Cephalon, Novartis, Janssen, Noven Pharmaceutical, Stanley Foundation, the National Institute of Mental Health (NIMH), the National Institute of Child Health & Human Development, and the National Institute on Drug Abuse (NIDA) and is a member of the speakers bureaus/advisory boards of GlaxoSmithKline, Eli Lilly, Pfizer, Novartis, Wyeth, Shire Richwood, Alza, Cephalon, Celltech, Noven Pharmaceutical, and McNeil; **Dr. Adler** is a consultant for, has received grant/research support and honoraria from, and is a member of the speakers/advisory boards of Novartis, Abbott, Eli Lilly, Pfizer, Merck, McNeil, and Johnson & Johnson; **Dr. Culpepper** is a consultant for Forest, Cephalon, Janssen, Eli Lilly, Pfizer, and Wyeth; **Dr. Mason** is a consultant for and a member of the speakers/advisory board of Eli Lilly; **Dr. Montano** is a consultant for Eli Lilly, GlaxoSmithKline, Organon, Forest, Roche, and Wyeth; has received grant/research support from Bristol-Myers Squibb, Eli Lilly, and GlaxoSmithKline; has received honoraria from Eli Lilly, GlaxoSmithKline, Forest, Organon, and Wyeth; and is a member of the speakers/advisory boards of Eli Lilly, GlaxoSmithKline, Forest, Organon, and Wyeth; **Dr. Roth** is a consultant for Eli Lilly; **Dr. Spencer** has received research support from Abbott, Bristol-Myers Squibb, Cephalon, Eli Lilly, GlaxoSmithKline, Janssen, McNeil, Celltech, Novartis, Pfizer, Shire Richwood, and Wyeth; is a member of the

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Disclosure of Off-Label Usage

The chair has determined that, to the best of his knowledge, bupropion and desipramine are not approved by the U.S. Food and Drug Administration for the treatment of attention-deficit/hyperactivity disorder and topiramate is not approved for the treatment of bipolar disorder. If you have questions, contact the medical affairs department of the manufacturer for the most recent prescribing information.

Acknowledgment

This PCC Visuals was derived from the symposium "Diagnosing and Treating Attention-Deficit/Hyperactivity Disorder in Adults," which was held January 17, 2003, in Boston, Mass., and the teleconference "Diagnosing and Treating Attention-Deficit/Hyperactivity Disorder in Adults in Primary Care," which was held May 13, 2003. This newsletter was independently developed by the Physicians Postgraduate Press, Inc. Office of Continuing Medical Education pursuant to an unrestricted educational grant from Eli Lilly and Company. The opinions expressed herein are those of the authors and do not necessarily reflect the views of the CME provider and publisher or the commercial supporter.

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■ Need for Primary Care Physicians to Diagnose and Treat Adults With ADHD

LARRY CULPEPPER, M.D.; OREN MASON, M.D.; C. BRENDAN MONTANO, M.D.; AND MARY ELIZABETH ROTH, M.D.

About 4.5% of adults have ADHD, which has persisted in about 70% of the 6.5% of children with the disorder.¹ Compared with the prevalence of medical conditions such as epilepsy⁷ and stroke,⁸ the prevalence of ADHD is higher in adults. Therefore, primary care physicians should expect to encounter patients who have the disorder but have never been diagnosed or treated.

Unfortunately, some primary care physicians are reluctant to diagnose and treat the disorder in adults. More education about the condition, improved treatments, and unique advantages for primary care physicians will help them to confidently diagnose and treat ADHD. ■

■ Reasons Why Primary Care Physicians Might Not Recognize or Treat ADHD

- Lack education about and understanding of ADHD
- Have few validated screening tools that they or patients can easily and quickly administer
- Have little time to spend with each patient
- Have a bias against the use of psychostimulant medications, which until recently have been the only approved medication treatment for ADHD

■ Advantages for Primary Care Physicians in Diagnosing and Treating ADHD in Adults

- May know the history of the patient and his or her family, including whether any family member has ADHD
- Can observe the patient when he or she comes to the office for a family member's visit
- Can easily keep track of the patient's accidents and illnesses and their frequency
- Can assess the patient's ADHD when the patient comes in for other treatment

■ The 3 Populations of Adults With ADHD in Primary Care

LARRY CULPEPPER, M.D.; OREN MASON, M.D.; AND MARY ELIZABETH ROTH, M.D.

Primary care physicians are likely to see 3 populations of adults with ADHD: those adults who have received continual treatment since being diagnosed in childhood, those who were diagnosed and treated in childhood but stopped care as adults, and those who have never been diagnosed or treated for ADHD. Unfortunately, the patients who are easiest to care for—those who have received continual therapy—are the least common.

Physicians must be prepared to identify and treat the other two, more common populations. Adults who have impairments such as problems with time or money management, relationships, and focusing and frequent accidents or injuries should be screened for ADHD. Regardless of whether ADHD is diagnosed in childhood or adulthood, physicians must stress that patients are unlikely to outgrow the disorder and should continue therapy to maintain a good quality of life. ■

■ Common Characteristics of the 3 Populations of Adults With ADHD

Adults who were diagnosed in childhood and have received continual care

- Know how they respond to treatment
- Saw improvement in functioning when treatment began
- Occasionally tried discontinuing therapy and experienced a worsening of symptoms
- Realize that they can overcome the dysfunction associated with ADHD

Adults who were diagnosed in childhood but stopped treatment

- Thought that they outgrew ADHD
- Experienced problems at work or in college after they stopped treatment
- Did not recognize the impact of treatment on their functioning
- Are resistant to taking medication, especially controlled substances, for the rest of their lives

Adults who have never been diagnosed or treated

- Have had poor organization, a short attention span, and difficulty focusing since childhood
- Have had to work harder than others to achieve similar goals
- Were diagnosed with another disorder such as depression but did not fully respond to treatment
- Have a family member with ADHD
- Want a better quality of life

Case Reports of Adults With ADHD

LENARD A. ADLER, M.D.

The following case reports describe symptoms and impairments commonly seen in adults with ADHD. The treatments prescribed for these patients are some of the effective options for adults with the disorder. As these reports show, gathering

a careful clinical history and listening to patients' concerns helps the clinician diagnose ADHD. Also, developing an individualized treatment plan for each adult is key to reducing the symptoms and related impairments of the disorder.

■ Patient 1: 54-Year-Old Man With Undiagnosed ADHD and Comorbid Bipolar Disorder

Patient 1 is a married Latino full-time skilled laborer. His experience shows that ADHD can be diagnosed even when a patient is hospitalized for a comorbid psychiatric disorder. Also, treatment of comorbid conditions might take precedence over treatment of ADHD.

- Reason for seeking treatment: manic episode
- Comorbid psychiatric conditions: bipolar disorder with no prior manic episodes and untreated depressive episodes; substance abuse; conduct disorder in childhood
- No known family history of ADHD
- Symptom history
 - ✓ Past: poor academic performance, talking out of turn in class, poor listening skills, fighting
 - ✓ Current: poor listening skills, feeling of restlessness, poor planning skills, irritability, euphoria, compulsive spending, inability to sleep, and refusal to follow rules, which led to discharge from the hospital
- Treatment
 - ✓ 150 mg topiramate po hs, 15 mg olanzapine hs, 1 mg clonazepam po bid for mood symptoms in hospital
 - ✓ Treatment of mood symptoms to continue during outpatient follow-up; treatment for ADHD to begin once mood symptoms are controlled

■ Patient 3: 42-Year-Old Man With Undiagnosed ADHD and No Comorbid Disorders

Patient 3 is a married Caucasian attorney. His experiences demonstrate that even highly successful individuals can have ADHD. They might function well in one domain because of coping strategies but perform poorly in others. This case also emphasizes the importance of screening adults with a family history of the disorder and listening to patients' concerns before prescribing treatment. ■

- Reasons for seeking treatment: difficulty completing work, rarely at home and distracted when there, need to write things down to remember them
- No comorbid psychiatric conditions
- Family history
 - ✓ 2 children with ADHD who are treated with stimulants
 - ✓ Father with bipolar disorder
- Symptom history
 - ✓ Past: difficulty paying attention, disorganization, climbing on furniture, interrupting others
 - ✓ Current: constant need to be busy, distractibility, interrupting others, difficulty completing tasks
- Treatment
 - ✓ Wanted a noncontrolled substance that would be effective all day without multiple doses
 - ✓ Successfully treated with 60 mg atomoxetine in the morning

■ Patient 2: 29-Year-Old Woman With ADHD Not Treated Since Childhood and Comorbid Dysthymia

Patient 2 is an unmarried African-American actress and student. Her case points out the need for thorough clinical evaluation. Symptoms of her adulthood ADHD were overlooked when the diagnosis of dysthymia was made, despite her childhood diagnosis and family history of ADHD. Concerning treatment, her medication compliance improved when she had to take only 2 instead of 3 doses per day.

- Reason for seeking treatment: underperformance at school and work that led to depression
- Comorbid psychiatric conditions: current dysthymia and conduct disorder symptoms in childhood
- Family history: sister and nephew with ADHD treated successfully with the combination of amphetamine and dextroamphetamine
- Symptom history
 - ✓ Past: fidgetiness, climbing on furniture, losing things, poor listening skills, impulsivity
 - ✓ Current: distractibility, forgetfulness, lateness, restlessness, impatience, poor organization, interrupting others
- Treatment
 - ✓ Ineffective prior treatment: the selective serotonin reuptake inhibitors fluoxetine and sertraline
 - ✓ Successful current treatment: the combination of amphetamine and dextroamphetamine: 40 mg extended-release formulation in the morning and 20 mg immediate-release formulation in the afternoon

■ Assessing Adult ADHD in Primary Care

LARRY CULPEPPER, M.D.; OREN MASON, M.D.; C. BRENDAN MONTANO, M.D.; AND MARY ELIZABETH ROTH, M.D.

The most important step in diagnosing ADHD is to take a thorough history by asking patients, and a family member if possible, questions about patients' past and current behavior. Because ADHD begins in childhood, patients will have experienced a continuum of impairment at school and work and in relationships throughout their lives.

Many adults with ADHD might not complain of obvious signs of the disorder such as failing in school or being unable to sit still. Symptoms of ADHD may change over time. For example, hyperactive behavior in childhood might evolve into having 2 or 3 active jobs in adulthood. There-

fore, primary care physicians must learn to consider the diagnosis of ADHD when patients have certain characteristics or crises that might not immediately seem tied to the disorder, as physicians would consider the diagnosis of asthma for a patient with a chronic cough. For example, patients with ADHD often come in for more frequent office visits than other patients because of mood-related symptoms or accidents. Physicians should rule out medical conditions such as vision and hearing problems and other psychiatric conditions such as bipolar disorder as the cause of patients' symptoms before making the diagnosis of ADHD.

■ Questions to Ask Adult Patients in Primary Care

Many adults with ADHD might have difficulty answering general questions like "What were you like when you were 6 or 7 years old?" or finding documentation such as report cards for their behavior in childhood. Also, physicians might not have the time or expertise to administer rating scales. Therefore, primary care physicians should ask patients focused questions that might reveal certain characteristics that indicate the presence of ADHD throughout the patients' lives.

- Do you have any family members with ADHD?
- When you were in school, how comfortable were you in the classroom setting, and were any comments made about your behavior?
- Have you always had to work harder than your peers at school and work?
- Do you procrastinate?
- Do you have problems staying organized or feel your life is chaotic?
- Do you have any problems maintaining relationships?
- How frequently have you switched jobs?
- Do you frequently have accidents or injuries?
- Do you rely on substances such as alcohol, illicit drugs, or caffeine to function?
- Have you been diagnosed with another psychiatric disorder, and has that condition been unresponsive to treatment?

■ Crises That Bring Adults With ADHD Into the Primary Care Physician's Office

When adults have a long-term pattern of crises that could be related to ADHD, physicians must consider the diagnosis of ADHD regardless of how plausible patients' explanations for their problems are.

- Substance abuse
- Injuries from motor vehicle accidents, being clumsy, or doing impulsive things such as diving into shallow water
- Crisis pregnancy
- Sexually transmitted diseases
- Emotional lability
- Depression or anxiety disorder

■ Differential Diagnosis of ADHD

Although many primary care physicians may not consider including ADHD as a differential diagnosis, the disorder shares symptoms with some common medical conditions including endocrine disorders and vision or hearing problems. With training, physicians can distinguish ADHD from other psychiatric conditions—such as adjustment, anxiety, developmental, psychotic, and substance use disorders and learning disabilities as well as mood disorders, for which ADHD is commonly misdiagnosed. Sometimes simply asking patients whether they have experienced the symptoms of a disorder will make the diagnosis clear. For example, patients with bipolar disorder might identify with having pressured thoughts, flight of ideas, and highly productive periods when they need little sleep. Those with only ADHD might not understand the symptoms being described.

Many patients with ADHD also meet criteria for comorbid disorders. For example, about 10% to 20% of patients with

Unlike ADHD, bipolar disorder is associated with

- Substantial episodic dysphoria or euphoria
- Psychotic symptoms such as delusions
- Decreased need for sleep

Unlike ADHD, major depressive disorder is associated with

- Substantial episodic dysphoria and loss of interest in activities lasting at least 2 weeks
- Appetite disturbances
- Easy fatigue and loss of energy
- Onset usually in adolescence or adulthood

ADHD have bipolar disorder, and vice versa. However, other disorders must be ruled out as the cause of symptoms of inattention, hyperactivity, and impulsivity before ADHD can be diagnosed. The illness that causes the most discomfort in the patient's life should be treated first. Periodically, the patient's condition should be reassessed and the treatment plan for each disorder modified if needed. ■

■ Assessing ADHD in Adults With an Emphasis on Using Rating Scales

KEVIN R. MURPHY, PH.D., AND LENARD A. ADLER, M.D.

Assessing whether an adult has ADHD can be difficult. Most symptoms of ADHD such as disorganization, restlessness, and distractibility are normal human characteristics that are also symptoms of many conditions commonly comorbid with ADHD. Clinical judgment must be used to decide the cause of the symptoms and to what degree the patient must be impaired to meet the clinically significant impairment criteria for diagnosis. Although there is no litmus test for ADHD, there are some essential require-

ments for making the diagnosis. Physicians should take a history of current and childhood behavior and ask questions that assess the onset, cause, and impact of symptoms. Optimally, a rating scale should also be administered to obtain information from multiple sources (e.g., patient, parent, and spouse, if possible) and to provide a standard for evaluating the number of symptoms endorsed and the severity of impairment in major life activities caused by the patient's symptoms.

■ Key Questions in Adult Assessment of ADHD

Clinicians must remember that the diagnosis of ADHD is not simply a matter of symptom endorsement or the identification of personality traits such as being energetic. At a minimum, making the diagnosis requires determining the onset, chronicity, and pervasiveness of symptoms and the resulting degree of impairment as well as ruling out alternative explanations for symptoms. Optimally, a rating scale based on criteria in the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV)⁹ should also be used.

- Are symptoms of inattention, hyperactivity, and impulsivity clearly present?
- Does objective evidence show that symptoms cause significant impairment in school, work, and social domains and in daily adaptive functioning?
- Have symptoms been observed as part of the person's behavior across situations since childhood? If not, is there a plausible reason (such as extraordinary parental support, tutors, special schools, or personal coping strategies) why symptoms were not noticed until later?
- What evidence is there that symptoms are not due to lack of effort, poor vocational match, or transient situational or environmental circumstances?
- Are symptoms better explained by another psychiatric or medical diagnosis?
- Might other psychiatric diagnoses coexist with ADHD symptoms?

■ Available Rating Scales

Rating scales help determine the presence of ADHD symptoms, evaluate treatment response, and quantify impairment. They can be a cost-effective way to quickly gather data from multiple informants such as the patient, parent, significant other, and even work supervisor. However, data might be unreliable if the informant is not familiar with the patient's behavior or if the patient's memory or psychopathology distorts his or her self-perception. Also, the presence of symptoms detected on rating scales must be supported by significant real-world functional impairment for a diagnosis of ADHD to be made.

- ADHD Rating Scale-IV (ADHD RS-IV)
- Barkley and Murphy's Current Symptom Scale
- Barkley Side Effects Rating Scale
- Behavior Assessment System for Children
- Brown Attention-Deficit Disorder Scales
- Child Behavior Checklist
- Childhood Symptom Scale
- Conners' Adult ADHD Rating Scales
- Physician's Checklist for Parents
- Swanson, Nolan, and Pelham Rating Scale
- Wender Utah Rating Scale

■ Preview of the Pilot Adult ADHD Self-Report Scale (ASRS)

Most rating scales for ADHD, such as the ADHD RS-IV, were designed and are standardized for clinician administration to children. A study is currently being conducted in adult ADHD populations to compare the validity of a pilot version of a self-administered adult ADHD symptom rating scale, the Pilot ASRS, versus the clinician-administered ADHD RS-IV.¹⁰ The Pilot ASRS is a frequency-based scale that matches the 18 items in the DSM-IV criteria,⁹ has adult-specific language, and provides a context basis for symptoms. ■

Benefits of the Pilot ASRS

- Language
 - ✓ Provides situational context for some symptoms
 - ✓ Removes 2-part questions; eg, "failure to pay close attention to details and making careless mistakes" became "making careless mistakes"
 - ✓ Uses clear, adult-specific language; eg, "losing things necessary for tasks or activities" became "misplacing or trouble finding things"
- Scoring
 - ✓ Measures only frequency of symptoms to avoid confusing patients with questions of severity
 - ✓ Includes rarely as an option: 0 = never, 1 = rarely, 2 = sometimes, 3 = often, 4 = very often

The Use of ADHD Treatments for Children and Adults

THOMAS J. SPENCER, M.D.

Because the disorder develops in childhood, most medication trials in ADHD have been conducted in children. Despite a lack of extensive testing in adults, medications found effective in children are often prescribed for adults with ADHD. A few controlled trials have found the stimulants and atomoxetine to be the safest and most

efficacious medication options for adults with the disorder. The dopaminergic and noradrenergic effects of these medications are believed to help individuals focus on stimuli, analyze data, and prepare responses.

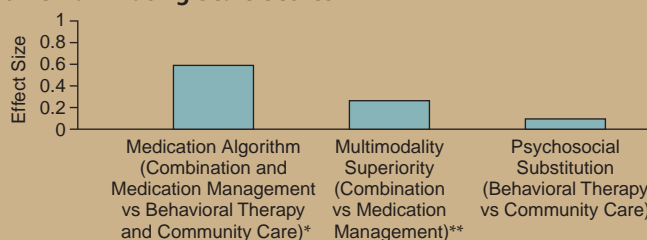
Two differences in treating children and adults are that adults generally need symptom relief later into the day and

higher doses of medication to attain substantial improvement. Fortunately, a single dose of a long-acting stimulant might provide symptom relief up to 12 hours, and the effects of atomoxetine might last longer. Further research will provide guidelines for the appropriate doses of these medications when used in adults with ADHD.

Treatment Studies in Children

The Multimodal Treatment Study in Children With ADHD (MTA) was designed to test the effectiveness of 4 treatment options: the combination of medication management and behavioral therapy, medication management alone, behavioral therapy alone, and treatment usually received in the community. Instead of relying solely on clinical judgment, the medication management groups followed an algorithm that began with 3 doses of methylphenidate per day and then tailored the medication and dose until response was established.

Effect Size of MTA Treatment Comparisons on Swanson, Nolan, and Pelham Rating Scale Scores

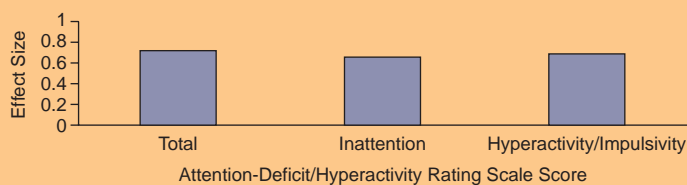


Data from Swanson et al.¹¹

* $p < .001$.

** $p < .05$.

Effect Size of Atomoxetine Versus Placebo on Attention-Deficit/Hyperactivity Rating Scale Scores



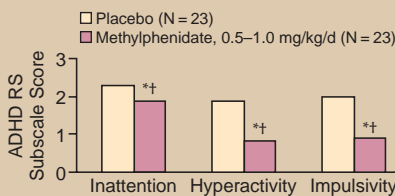
Data from Spencer et al.¹²

The effect size was greater with carefully planned medication treatment than with placebo, behavioral therapy, or less structured medication treatment. Since the MTA, the nonstimulant atomoxetine has been approved for use in children with ADHD. Although not directly compared in an adequately powered study, atomoxetine and stimulants appear to have comparable efficacy in reducing symptoms of ADHD in children.

Stimulant Studies in Adults With ADHD

Two of the most commonly used stimulants for ADHD, mixed amphetamine salts and methylphenidate, have been found efficacious in clinical trials of adults, using the ADHD Rating Scale and the ADHD RS-IV. Clinical practice and trials have also helped establish appropriate doses of immediate-release and long-acting formulations of stimulants in the absence of FDA approval and dosing guidelines in adults with ADHD.

Endpoint ADHD RS Scores in a 7-Week Crossover Trial of Placebo and Methylphenidate^a



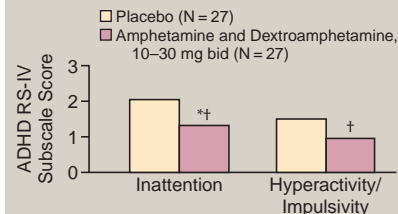
Data from Spencer et al.¹³

^aSymptoms were rated as follows: 0 = none, 1 = mild, 2 = moderate, 3 = severe.

* $p < .0001$ vs. baseline.

† $p < .001$ vs. placebo at endpoint.

Endpoint ADHD RS-IV Scores in a 7-Week Crossover Trial of Placebo and Amphetamine and Dextroamphetamine^a



Data from Spencer et al.¹⁴

^aSymptoms were rated as follows: 0 = none, 1 = mild, 2 = moderate, 3 = severe.

* $p = .001$ vs. baseline.

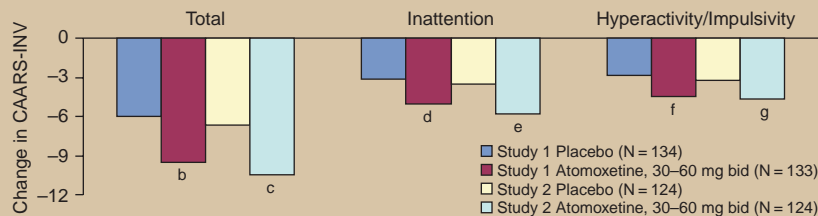
† $p < .01$ vs. placebo at endpoint.

Atomoxetine Studies in Adults With ADHD

In two large controlled trials in adults, atomoxetine was significantly more effective than placebo in reducing both inattention and hyperactivity/impulsivity scores on the atten-

tion subscale of the Conners' Adult ADHD Rating Scales. Atomoxetine is approved by the FDA for use in adults. Also, improvement might last into the evening with atomoxetine. ■

Mean Change From Baseline to Endpoint Scores on the Investigator-Rated Attention Subscale of the Conners' Adult ADHD Rating Scales (CAARS-INV) in Two 10-Week Placebo-Controlled Trials of Atomoxetine in Adults^a



Data from Michelson et al.¹⁵

^aMean baseline total scores were 33 to 35 of a possible 72, inattention scores were 18 to 20 of a possible 36, and hyperactivity/impulsivity scores were 14 to 16 of a possible 36.

^b $p = .005$, ^c $p = .002$, ^d $p = .010$, ^e $p = .001$, ^f $p = .017$, ^g $p = .013$ for the difference between atomoxetine and placebo in the individual study.

Intervention Strategies for Adults With ADHD

MARGARET D. WEISS, M.D.

Many adult psychiatrists and primary care physicians have not been trained to treat ADHD. Because adult patients with this disorder are often highly motivated and have good insight into their illness, managing ADHD is not as difficult as many clinicians believe. The growing body of research can also help clinicians recognize symptoms, set and measure goals for therapy, and determine optimal treatment(s).

Steps in Diagnosing and Treating ADHD

- Feedback session: assess symptoms, comorbid conditions, and functioning
- Psychoeducation: explain how symptoms and functioning are related
- Identification of treatment targets: establish desired improvements, outcome measures, and a time frame for achieving response
- Medication trial: select the optimal medication for the patient and alter the medication and dose as necessary
- Psychological treatment of residual impairment: help the patient find ways of modifying environments to reduce impairment; use simple, focused therapies; and suggest support groups or group therapy

Medication Treatment

Medication is a first-line treatment that is effective for many adults with ADHD. Before prescribing medication, physicians should inform patients of possible improvements as well as side effects. Medication should be chosen on the basis of its duration of action and potential for abuse and the patient's comorbid conditions, target symptoms,

preference, and family history. Doses should be titrated for each patient such that the individual obtains optimal improvement in symptoms and functioning with minimal side effects. Medication response can be measured by physicians with rating scales, and most patients can learn to observe and report changes in target symptoms.

Methodologically Sound Medication Trials in Adults With ADHD

Study	Drug	Total N	Duration, wk	Dose
Spencer et al, 1998 ¹⁶	Atomoxetine	21	7	40–80 mg/d
Spencer et al, 2001 ¹⁷	Dextroamphetamine and amphetamine	27	7	10–30 mg bid
Spencer et al, 1995 ¹⁸	Methylphenidate	23	7	0.5–1.0 mg/kg/d
Wilens et al, 1999 ¹⁹	ABT-418	32	7	37.5–75 mg/d
Wilens et al, 2001 ²⁰	Bupropion SR	38	6	100–400 mg/d
Wilens et al, 1996 ²¹	Desipramine	41	6	100–200 mg/d

Psychosocial Treatment

Although few controlled trials have been conducted on psychosocial treatment in ADHD, such therapy might help patients cope with impairments such as disorganization, forgetfulness, time mismanagement, and low self-esteem. Psychosocial treatments appropriate for adults with ADHD may need to be developed because these patients have unique attributes that might limit the effectiveness of current therapies. Behavior therapy that relies on the patient for self-monitoring might not work for impulsive patients. Cognitive strategies that require cortical function might not be effective for inattentive, impulsive, and disinhibited behaviors, which are linked to dysfunctions in the frontal areas of the cerebral cortex. ■

Proposed Psychosocial Interventions

- Psychoeducation: explain how symptoms are responsible for impairments
- Environmental restructuring: examine the benefits of using electronic devices and other people for organization and time management, identify the best time and environment for performing tasks, and eliminate coping strategies that do not work
- Family intervention: help family members understand and compensate for the patient's impairment
- Group therapy and self-help groups: provide social contacts and ongoing support through developmental transitions

Proposed Therapeutic Accommodations

- Use simple, structured, action-based, problem-solving therapies
- Allow defiant patients control and choice
- Avoid nagging
- Redirect dependency
- Follow short-term interventions with arrangements for follow-up in the community and booster sessions, if needed

■ Treating Adult ADHD in Primary Care

LARRY CULPEPPER, M.D.; OREN MASON, M.D.; AND MARY ELIZABETH ROTH, M.D.

Physicians should educate each patient about the impairment caused by ADHD and how treatment can help improve functioning. Then a stimulant or atomoxetine should be prescribed as the first-line treatment for ADHD in adults. Some patients will respond best to a particular stimulant, some to another stimulant, and some to atomoxetine. Therefore, more than one medication, with dosage titrated to the highest toler-

able and effective level, may need to be tried to build the optimal treatment plan for the patient. To evaluate which treatment is most effective, physicians should set therapeutic targets important to the individual patient and monitor them with the patient at every visit. When selecting treatment and assessing response, physicians should consider the special demands in the patient's home, occupational, and social lives.

■ Setting and Monitoring Targets for ADHD Treatment in Adults

The easiest way for primary care physicians to assess improvement in an adult with ADHD is to set and monitor 3 or 4 therapeutic targets. These targets should be objective measures that clearly show decline or improvement because some patients with ADHD are defensive about their behavior or have poor insight into their illness. The patient and physician should work together to decide which areas of functioning are most important for that individual, and the physician can write these targets on the patient's chart.

Patients who want to focus on job performance might report how often they get negative feedback, such as a warning or bad review, and positive feedback, such as an award, raise, or promotion. Some goals at home might be to pay bills on time and to complete marital counseling. Not being late or missing appointments or days of work or school are goals that could cover several areas of life.

A partner for the patient's care, such as a spouse or parent, can help the patient keep track of improvement in the thera-

Example of a Table for Monitoring Therapeutic Targets

Date of Visit	Treatment	Treatment Compliance	Progress in Therapeutic Targets		
			Being on Time to Work	Attending Marital Counseling	Paying Bills on Time
Jan 18, 2003	Methylphenidate, 30 mg extended-release in am and 10 mg immediate-release in pm	Missed about 10 pills in last mo	About 45 min late 6 d, 30 min late 3 d, and 15 min late 8 d	Went to 2 of 4 scheduled sessions	2 in on time, 1 less than 2 wk late, and 2 about 1 mo late
Feb 24, 2003	Methylphenidate, 40 mg extended-release in am and 15 mg immediate-release in pm	Missed about 8 pills in last mo	About 45 min late 1 d, 20 min late 8 d, and 10 min late 3 d	Went to 2 of 4 scheduled sessions	2 in on time, 2 about 5 d late, and 1 about 3 wk late
April 3, 2003	Dextroamphetamine and amphetamine, 30 mg extended-release in am and 15 mg immediate-extended in pm	Missed about 5 pills in last mo	About 30 min late 2 d, 15 min late 6 d, and 5 min late 1 d	Went to 3 of 4 scheduled sessions	2 in on time and 3 less than 2 wk late

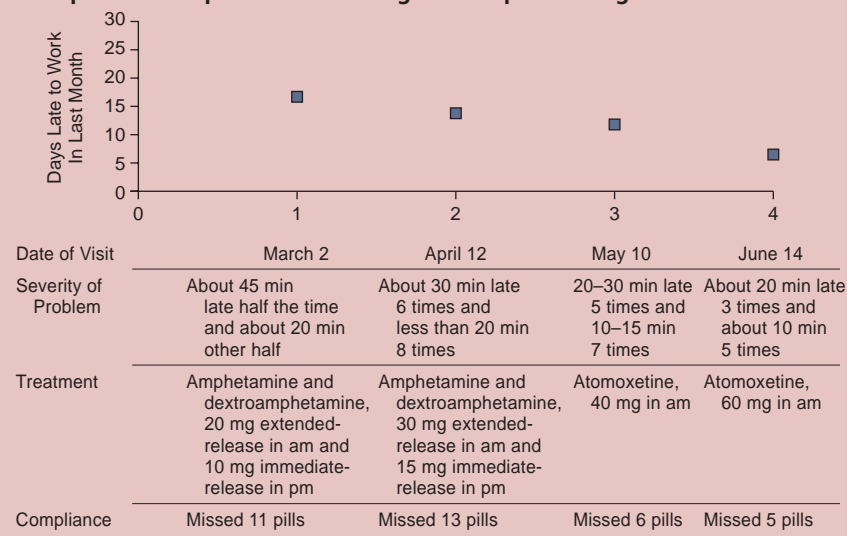
peutic targets. Every time the patient comes in, the physician can ask and record (in a table, graph, or notes) how often a problem such as lateness occurred and how severe it was.

Progress and decline in achieving established treatment goals should be monitored for a few months, at a minimum. Asking the patient how he or she is doing at the beginning of every visit can also provide valuable subjective responses from the patient and his or her partner in care. This individualized subjective and objective assessment will provide patients a unique measure of how each medication, dosage, and their level of treatment compliance affect their quality of life.

■ Special Considerations for Treating Adults With ADHD

Because symptoms evolve and responsibilities increase as individuals with ADHD age, patients' treatment plans might need to be modified to provide coverage 24 hours per day. ■

Example of a Graph for Monitoring a Therapeutic Target



- Many adults must be able to function well at all times because of children, elderly parents, spouses, and/or coworkers who rely on them
- Careless behavior such as drinking heavily, using substances, driving recklessly, and having unprotected sexual intercourse often occurs at night when a morning or afternoon dose of medication is no longer effective
- A medication might not be allowed for certain professions, eg, airline pilot
- A medication might aggravate axis III, or medical, conditions

■ Substance Use Disorders and ADHD

TIMOTHY E. WILENS, M.D.

About 50% of untreated adults with ADHD, versus about 25% of adults without ADHD, will have a substance use disorder (either substance abuse or dependence) at some point in their lives.²² Younger adults, i.e., those between the ages of 18 and 30 years, are more likely than older adults to have a current substance use disorder. The presence of other psychiatric conditions also predicts a greater risk for substance abuse. Pharmacotherapy of

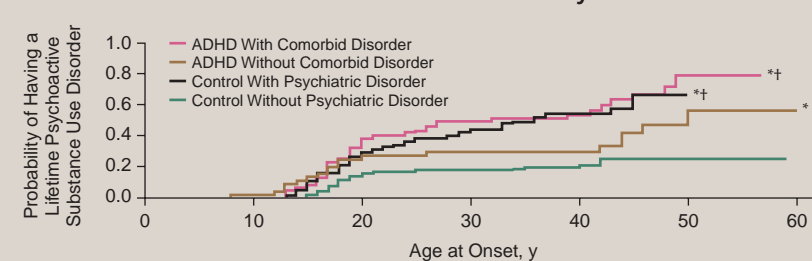
ADHD in children and adolescents may reduce the ultimate risk for substance use disorder.²³

Compared with adults without ADHD, untreated adults with ADHD begin using substances at an earlier age and will take longer to achieve remission of substance use disorders. For most patients, substance use problems should be addressed before ADHD treatment is begun. However, treating ADHD symptoms might also assist with substance use treatment.

■ Risk for and Impairment Associated With Substance Use Disorders

Problems with substance use generally develop at a younger age for subjects with ADHD than for controls. The risk for substance use disorders and the age at onset are influenced by several factors. Also, adults with ADHD who have a substance use disorder have greater impairment than do patients with only ADHD.

Age at Onset of Psychoactive Substance Use Disorder for Patients With ADHD and Controls With or Without Comorbid Psychiatric Conditions



Data from Wilens et al.²²

* $p \leq .05$ vs. control subjects without a comorbid psychiatric disorder.
† $p \leq .05$ vs. ADHD subjects without a comorbid psychiatric disorder.

Risk Factors for Substance Use in Adults With ADHD

- The presence of another psychiatric condition increases the risk for substance use disorder and predicts an earlier age at onset^a
- Conduct disorder, bipolar disorder, and major depression are associated with the earliest age at onset of substance use disorders^a
- The risk for alcohol use disorders is greater for those with drug use disorders, and vice versa^b
- The risk for substance abuse is greater for those with substance dependence, and vice versa^b

Impairment Associated With ADHD and Substance Use

- The risk for having a comorbid psychiatric condition is greater than with ADHD alone^c
- Functioning is worse than with ADHD alone^c

^aData from Wilens et al.²²

^bData from Biederman et al.²⁴

^cData from T. E. W.; A. Kwon, M.S.; J. Biederman, M.D.; et al., manuscript submitted, 2003

Treatment of ADHD and Substance Use Disorders

The strategy for treating adults with ADHD and a substance use disorder is to first address the substance use. Then ADHD and other psychiatric disorders should be treated, in the order of greatest to least impairing. Both psychotherapy and pharmacotherapy should be implemented.

The first-line medication options for adults with ADHD and a substance use disorder are bupropion or a tricyclic antidepressant, but other treatments such as atomoxetine and stimulants might also be effective. Medication that might have negative interactions with abused substances or that could be diverted should be avoided. When treating patients with ADHD and a substance use disorder, physicians must remember that some patients might have little desire to stop using substances, misuse their medication, or have difficulty complying with treatment. Therefore, management should include frequent follow-up and contingency plans for relapse or continued substance use. ■

Possible Medication Options for ADHD and Substance Use

Medication	Evidence
Bupropion	Open trials involving about 50 subjects; associated with a modest reduction in substance abuse when ADHD improved, and vice versa
Atomoxetine	Not tested in trials; believed promising because it lacks abuse liability and its specific norepinephrine action is not associated with substance abuse pathophysiology
Methylphenidate	Open and controlled trials involving about 70 subjects; ADHD symptoms significantly improved regardless of substance use; mixed results for substance use and cravings

Resources for Patients With ADHD and Physicians

LARRY CULPEPPER, M.D.; OREN MASON, M.D.;
AND MARY ELIZABETH ROTH, M.D.

ADHD in adults can generally be treated by primary care physicians, and education and collaboration with other professionals and peers can better improve the patient's quality of life. Consulting a psychiatrist might be useful if a patient does not have a clear diagnosis, does not respond well to medication, or has substantial psychiatric comorbidity. Regardless of their degree of medication response, some patients might want support from peer groups or counselors. For individualized help with organization and strategies for dealing with ADHD, patients can hire coaches, although this growing field is still unregulated. Information on diagnosing and treating ADHD is available nationwide, often in English and Spanish, through government and nonprofit organizations. Physicians should encourage their patients to share with them and other patients any local resources they find.

■ Government organizations

- ✓ National Institute for Mental Health:
<http://www.nimh.nih.gov/publicat/adhdmnu.cfm>
- ✓ Centers for Disease Control and Prevention (CDC):
<http://www.cdc.gov/ncbddd/adhd/default.htm>

■ Nonprofit organizations

- ✓ Children and Adults With Attention-Deficit/Hyperactivity Disorder (CHADD), which has chapters across the United States to provide information and support to patients and others affected by ADHD: <http://www.chadd.org>
- ✓ National Resource Center on AD/HD, which is a clearinghouse for information on ADHD that is a program of CHADD funded by the CDC: <http://www.help4adhd.org> or 800-233-4050
- ✓ Attention Deficit Disorder Association, which provides information on resources like coaching and books for young adults and adults affected by ADHD: <http://www.add.org> or 847-432-ADDA

Controversies in ADHD in Adults

LARRY CULPEPPER, M.D.; OREN MASON, M.D.; AND MARY ELIZABETH ROTH, M.D.

Although the idea that ADHD often persists into adulthood is becoming more widely accepted, controversies still surround its treatment. For example, medications such as those used to treat ADHD must be used for years to treat the disorder before their long-term benefits and adverse effects can be established. How best to treat ADHD, especially in light of its high comorbidity with other psychiatric and medical conditions, has also yet to be definitively determined.

- Should ADHD be treated for patients' entire lives?
- How will stimulants and atomoxetine alter patients' neuro pathways over the long term?
- How will stimulants and atomoxetine affect other psychiatric and medical conditions?
- These patients often have high levels of chronic stress, which could increase their risk for cardiovascular disease; should precautions such as stress testing and institution of a sympatholytic drug be taken when adults with ADHD begin stimulant treatment as a result?
- What kind of physical effects will result from drug interactions between stimulants or atomoxetine and medications for other psychiatric and medical conditions?

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Drug Names: amphetamine and dextroamphetamine (Adderall and others), atomoxetine (Strattera), bupropion (Wellbutrin and others), clonazepam (Klonopin and others), desipramine (Norpramin and others), fluoxetine (Prozac and others), methylphenidate (Concerta, Ritalin, and others), olanzapine (Zyprexa), sertraline (Zoloft), topiramate (Topamax).