
THE AMERICAN JOURNAL OF MANAGED CARE®

SUPPLEMENT

Getting to Goal: Managed Care Strategies for Children, Adolescents, and Adults With ADHD

Highlights

- Clinical Considerations for the Diagnosis and Treatment of ADHD in the Managed Care Setting
- The Role of Pharmacotherapy and Managed Care Pharmacy Interventions in the Treatment of ADHD
- ADHD in Managed Care: An Assessment of the Burden of Illness and Proposed Initiatives to Improve Outcomes
- Posttest



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Getting to Goal: Managed Care Strategies for Children, Adolescents, and Adults With ADHD

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TARGET AUDIENCE

This activity has been designed to meet the educational needs of physicians, managed care pharmacists, pharmacy directors, medical directors, quality directors, policy executives, and other key managed care administrators involved in the management of patients with attention-deficit/hyperactivity disorder (ADHD).

MEDIA

Journal supplement

EDUCATIONAL OBJECTIVES

After completing this activity, the participant should be better able to:

- Describe the overall costs associated with ADHD and related comorbidities.
- Specify the clinical and financial impact of various ADHD treatment options.
- Describe a managed care road map for improving clinical and economic outcomes for ADHD.
- Cite recommendations for health plans to assist their providers with strategies to improve HEDIS performance scores for ADHD.
- Identify a step therapy model to provide appropriate drug therapy for ADHD treatment by managed care.

STATEMENT OF NEED/PROGRAM OVERVIEW

ADHD is considered the most common neurobehavioral disorder in children, affecting an estimated 4% to 12% of school-age children. Approximately one third to one half of all pediatric mental health referrals are due to ADHD. In addition to ADHD, many children have comorbid conditions, such as anxiety disorders, conduct disorder, and learning disorders. ADHD that begins in early childhood persists into adulthood in up to two thirds of cases. According to the National Comorbidity Survey Replication (NCS-R), the estimated prevalence rate of adult ADHD in the United States is 4.4%.

Adherence is a critical aspect of care because of the chronicity of lifelong ADHD consequences from significant symptoms that continue to exhibit in adulthood. Among children with ADHD, those on medication have shown to have significantly less frequent and less costly emergency department visits. In the absence of consistent treatment, adolescents with ADHD suffer 4 times as many serious injuries and 3 times as many motor vehicle accidents versus those without ADHD or those with ADHD who are medication compliant.

The increasing incidence of ADHD is an issue for managed care organizations and their providers. Providers are already feeling stretched to deliver adequate care for neurobehavioral disorders, so there is a need to increase their comfort in prescribing medicines along with behavioral recommendations for patients with ADHD. Education is needed to learn more about the use of controlled versus noncontrolled agents. The diversion of drugs within the ADHD category remains an issue with the managed care audience; therefore, recommendations are needed that help monitor inappropriate usage.

All of the above have fostered barriers to ADHD treatment and poor adherence to treatment guidelines, including the American Academy of Child and Adolescent Psychiatry, the American Academy of Pediatrics, the National Institutes of Health, and Healthcare Effectiveness Data and Information Set (HEDIS) recommendations. By following the treatment guidelines and reducing restrictions to proper care and medications, managed care can implement an appropriate use strategy to improve outcomes for ADHD.

PHYSICIAN CONTINUING MEDICAL EDUCATION

Accreditation Statement

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Postgraduate Institute for Medicine (PIM) and Impact Education, LLC. PIM is accredited by the ACCME to provide continuing medical education for physicians.

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Getting to Goal: Managed Care Strategies for Children, Adolescents, and Adults With ADHD

This supplement to *The American Journal of Managed Care* provides information on the clinical characteristics, diagnosis, and treatment of ADHD in plan members of all ages, in addition to discussing managed care initiatives for improving therapeutic adherence and optimizing patient outcomes.

■ Participating Faculty

Julie A. Dopheide, PharmD, BCPP

Associate Professor of Clinical Pharmacy,
Psychiatry and the Behavioral Sciences
University of Southern California
Schools of Pharmacy and Medicine
Los Angeles, California

Peter S. Jensen, MD

President & CEO
The REACH Institute
REsource for Advancing Children's Health
New York, New York

Neil B. Minkoff, MD

Medical Director
Network Medical Management and Pharmacy
Harvard Pilgrim Health Care
Wellesley, Massachusetts

■ Faculty Disclosures

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Consultant:

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There are no fees for participating and receiving CME credit for this activity. During the period May 15, 2009, through November 30, 2010, participants must (1) read the learning objectives and faculty disclosures; (2) study the educational activity; (3) complete the posttest by recording the best answer to each question in the answer key on the evaluation form; (4) complete the evaluation form; and (5) mail or fax the evaluation form with answer key to Postgraduate Institute for Medicine.

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Despite typically being categorized as a childhood condition, attention-deficit/hyperactivity disorder (ADHD) affects plan members of all ages. In addition to being unrecognized and underdiagnosed in older patient demographics, ADHD features several characteristics that contribute to suboptimal outcomes and a significant burden of illness in managed care. The disorder presents differently in every age group and is frequently associated with psychiatric comorbidities, making accurate diagnosis difficult for primary care physicians who are often ill-equipped to identify and treat neurobehavioral conditions due to a lack of formal training in behavioral health. As a means of overcoming these challenges, managed care organizations have a number of potential interventions at their disposal that may be applied in the primary care, pharmacy, and healthcare administrative settings. Education serves as the foundation of these initiatives, fostering awareness of ADHD among providers and patients alike, but with different goals in mind. Proven assessment scales and evidence-based treatment algorithms can help to educate and assist providers in diagnosing and treating the condition, with which they may lack familiarity. Conversely, patient educational initiatives help improve treatment adherence by promoting realistic expectations and making patients aware of potential adverse events associated with pharmacotherapy. Further interventions, such as pharmacy database monitoring and the prescribing of extended-release formulations of stimulants, may also be employed to promote treatment adherence and alleviate concerns over drug diversion and abuse. This supplement reviews the clinical characteristics, diagnosis, and treatment of ADHD in plan members of all ages, in addition to discussing managed care initiatives for improving therapeutic adherence and optimizing patient outcomes.

Clinical Considerations for the Diagnosis and Treatment of ADHD in the Managed Care Setting

Peter S. Jensen, MD

The effective treatment of attention-deficit/hyperactivity disorder (ADHD) in the managed care setting presents a number of challenges for health plan stakeholders. Although frequently characterized as a childhood disorder, ADHD affects patients across a diverse range of ages with a myriad of different age-specific presentations. First described by Dr Heinrich Hoffman in 1845, the disorder currently known as ADHD was initially identified in children.¹ Among the primary research on the topic was a series of lectures by Sir George F. Still in 1902 describing a group of hyperactive children who would today be diagnosed as having ADHD combined type.² It was not until nearly several decades later when some of the first studies of adults with similar disorders would be published.³

Combined with the typical presentation of ADHD in children and adolescents, this extensive history of identifying ADHD as a childhood disorder has led to the underdiagnosis of adults with the condition. However, while the disorder is certainly most visible in childhood, affecting 8% to 10% of school-aged children and accounting for 30% to 50% of all childhood mental health referrals, ADHD persists into adolescence in 40% to 70% of cases, and into adulthood in 50% or more of cases.⁴⁻⁹ The prevalence of ADHD in US adults is 4.4%, which represents an estimated 8 million individuals with this underrecognized and untreated condition.^{9,10}

Beyond the varying age-specific clinical presentations of ADHD, accurate recognition and diagnosis of the disorder is further clouded by the frequent presence of psychiatric comorbidities, many of which in some cases are more prevalent than ADHD.¹⁰ Contributing to these challenges is the fact that managed care providers in the primary care setting are often ill-equipped to diagnose and identify ADHD and its many comorbid psychiatric conditions due to a lack of formalized training in behavioral health.¹¹

The burden of illness arising from the persistence of ADHD throughout all stages of life and the difficulties associated with the accurate diagnosis and treatment of the disorder are varied and significant. Challenges experienced by patients of different ages with ADHD include lower academic and occupational achievement, lower rates of high school graduation, a higher incidence of sexually transmitted diseases, a greater number of altercations with law enforcement, higher rates of alcohol and drug abuse, and an increased prevalence of anxiety and depression.¹²

Abstract

Although symptoms of attention-deficit/hyperactivity disorder (ADHD) are certainly most visible in children, the syndrome persists into adolescence in 40% to 70% of cases and into adulthood in 50% or more of cases. Accurate recognition of the disorder is clouded by the frequent presence of psychiatric comorbidities. Contributing to these challenges, managed care providers in primary care are often inexperienced in identifying and treating ADHD in adults because of a lack of formalized training. As such, special consideration must be given to each individual age group and includes identifying common clinical presentations, characterizing the disorder and its comorbidities, applying validated rating scales as screening and treatment outcome measures, and individually assessing patients' optimal response to determine the best course of therapy. Pharmacotherapy is often initiated to target ADHD symptoms with either a stimulant medication or nonstimulants. In addition, behavioral interventions are often applied to treat comorbidities and associated impairments of ADHD.

(*Am J Manag Care.* 2009;15:S129-S140)

For author information and disclosures, see end of text.

To provide adequate care for this broad spectrum of patients with ADHD and to overcome the significant burden of illness associated with the disorder, special consideration must be given to each individual age group in terms of diagnosis and treatment. This comprehensive approach includes identifying common clinical presentations, characterizing the disorder and its comorbidities, applying consensus-based diagnostic scales, and individually assessing patients for treatment with pharmacotherapy and/or psychotherapy/behavioral therapy.

The benefits of a comprehensive treatment approach go beyond merely improving the quality of care for patients with ADHD. Health economic and pharmacoeconomic analyses have demonstrated that effective management of patients with ADHD can yield cost savings for health plans and employers in terms of reduced injuries, motor vehicle accidents, incidence of substance abuse disorders, and emergency department visits.¹³⁻¹⁵ Improved management of patients with ADHD has also been shown to result in improved academic achievement by children and adolescents and higher workplace productivity by adults, demonstrating the value of effective ADHD therapy among the entire population of patients with this burdensome disorder.¹⁶

Disorder Characterization

ADHD is a disorder that is usually characterized by serious and persistent difficulties, resulting in inattentiveness or distractibility, impulsivity, and hyperactivity, typically becoming apparent and sometimes resolving in childhood, but with the potential to extend indefinitely into adult life. The potential for ADHD to span different patient age groups contributes to the complexity of diagnosing the disorder, with varying clinical presentations based on the patients' developmental stage. The lack of a simple clinical standard or test for ADHD further complicates the diagnosis of the disorder; however, the advent of the American Psychiatric Association's (APA) *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)* ADHD criteria and a number of proven, age-specific assessment scales have served to alleviate some of the challenges that managed care organizations are facing.^{9,17} The application of these assessment scales to different age groups of

patients with ADHD is subsequently reviewed in the discussion of diagnosis and assessment.

According to the *DSM-IV-TR*, ADHD is defined as being present in patients with 6 or more of the following symptoms of inattention or hyperactivity-impulsivity for at least 6 months to an extent that is disruptive and inappropriate for his or her developmental level¹⁷:

Inattention

1. Often does not pay close attention to details or makes careless mistakes in schoolwork, work, or other activities
2. Often has trouble keeping attention on tasks or play activities
3. Often does not seem to listen when spoken to directly
4. Often does not follow instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions)
5. Often has trouble organizing activities
6. Often avoids, dislikes, or does not want to perform tasks that take a lot of mental effort for a long period of time (such as schoolwork or homework)
7. Often loses items needed for tasks and activities (eg, toys, school assignments, pencils, books, or tools)
8. Is often easily distracted
9. Is often forgetful in daily activities

Hyperactivity

1. Often fidgets with hands or feet or squirms in seat
2. Often gets up from seat when remaining in seat is expected
3. Often runs about or climbs when and where it is not appropriate (adolescents or adults may feel very restless)
4. Often has trouble playing or enjoying leisure activities quietly
5. Is often "on the go" or often acts as if "driven by a motor"
6. Often talks excessively

Impulsivity

1. Often blurts out answers before questions have been finished
2. Often has trouble waiting one's turn
3. Often interrupts or intrudes on others (eg, butts into conversations or games)

In addition to meeting the symptom criteria, the *DSM-IV* criteria specify that in patients with ADHD, some of the symptoms that cause impairment were present before age 7 years, some of the impairment from the symptoms is present in 2 or more settings (eg, at school/work and at home), and there is clear evidence of significant impairment in social, school, or work functioning; the symptoms do not occur only during the course of a pervasive developmental disorder, schizophrenia, or other psychotic disorder; and the symptoms are not better accounted for by another mental disorder (eg, mood disorder, anxiety disorder, dissociative disorder, or a personality disorder).¹⁷ Recent studies of adults with ADHD are challenging the *DSM-IV* and *DSM-IV-TR*'s age-of-onset criteria, suggesting little difference in functional impairment and response to methylphenidate in adults who meet the full criteria for ADHD including onset before age 7 and those who meet all the criteria except age of onset.¹⁸ It should also be noted that many adults with and without ADHD cannot reliably identify when their symptoms first began.

According to the *DSM-IV* definition, 3 types of ADHD have been identified: (1) predominantly inattentive, (2) predominantly hyperactive-impulsive, and (3) combined. The primarily inattentive type of ADHD, in which the criteria is met for inattention but not for hyperactivity-impulsivity, is present in 20% to 30% of clinic-referred cases and the prevalence of this subtype appears to increase with age. In the primarily hyperactive-impulsive type, which has a prevalence of less than 15% of clinic-referred children and is almost nonexistent in adults, the criteria are met for hyperactivity-impulsivity but not inattention. Finally, in the most common type of ADHD in children—the combined type, present in 50% to 75% of cases—the criteria are met for both inattention and hyperactivity-impulsivity.¹⁷ This is the most studied subtype and the only one for which we have data on longitudinal course.

The *DSM-IV-TR* defines ADHD according to the extent that the symptoms are disruptive and inappropriate for a patient's developmental level because of the different age-specific clinical presentations across patient groups.¹⁷ Generally speaking, hyperactivity and impulsivity are most obvious in childhood, and tend to decline somewhat with age. In preschool children (aged 3-5 years), ADHD is char-

acterized by a range of associated behavioral and developmental problems, such as difficulty completing developmental tasks (eg, toilet training), decreased and/or restless sleep, insatiable curiosity, family difficulties (eg, obtaining and keeping babysitters), vigorous and often destructive play, the demanding of parental attention (which is sometimes argumentative), delays in motor or language development, excessive temper tantrums (becoming more severe and frequent), and low levels of compliance (especially in boys).^{19,20} The presentation of ADHD in school-aged children (aged 6-12 years) is characterized by incomplete homework with careless errors; the blurting out of answers before questions have been completely asked (ie, disruptiveness in class); interrupting or intruding on others; an inability to stay in one's seat and acting like the "class clown"; and a perception of "immaturity" (eg, unwillingness or inability to complete chores at home).²⁰

Once a patient with ADHD has reached adolescence (aged 13-18 years), the excessive motor activity tends to decrease, and he or she may have a sense of inner restlessness rather than hyperactivity.²⁰ Schoolwork is still often disorganized in this age group, and the patient may show poor follow-through and/or fail to work independently, but now the patient may engage in "risky" behaviors, exemplified by speeding and driving mishaps. ADHD in adolescents may also be characterized by difficulty with authority figures, poor self-esteem, poor peer relationships, and anger or emotional lability.²⁰ The characteristics and presentation of ADHD in adults is similar but at a more advanced developmental level and may include vocational underachievement/failure, risk taking/fatal accidents, substance abuse disorders, antisocial personality disorder/criminal activity, unplanned pregnancy, the acquisition of sexually transmitted diseases, hopelessness, frustration, and apathy.²¹ Basically, as the disorder progresses over the course of a patient's lifetime, childhood symptoms decline while functional impairment persists or worsens into adulthood.^{17,22} For example, although more than 60% of adults (aged 18-20 years) from a cohort of 128 male patients followed over 4 years achieved full syndromic remission (<8 of 14 possible *DSM-IV-TR* symptoms), less than 30% achieved symptomatic remission (<5 *DSM-IV-TR* symptoms), and only approximately 10% achieved functional remission

(<5 DSM-IV-TR symptoms and a score >60 on the Global Assessment of Functioning Scale) (Figure 1).^{17,22}

In addition to the various presentations of ADHD across the different developmental stages of patient groups affected by the disorder, several potential psychiatric comorbidities exist with the disorder.^{10,17} These may include oppositional defiant disorder (ODD), conduct disorder, anxiety disorders (ie, generalized anxiety disorder, obsessive-compulsive disorder, and posttraumatic stress disorder), depression, bipolar disorder, tic disorders, and learning disabilities.¹⁰ In children, ODD and conduct disorder are the most common comorbid psychiatric disorders observed with ADHD in clinic samples, occurring in about 50% of cases, followed by mood, anxiety, and learning disorders, respectively (Figure 2).^{23,24} For adults, anxiety disorders are the most prevalent comorbidity, being observed in 47.1% of ADHD cases (Figure 3).¹⁰ Combined with the different presentations of ADHD in different age groups, these comorbidities can often make acknowledgment of the condition more difficult and further cloud diagnosis.

Diagnosis and Assessment

The DSM-IV-TR criteria are used to diagnose ADHD in all age groups, although some have questioned whether more specific criteria should be

developed for ADHD in adults (ie, Wender Utah Criteria).²⁵ In addition, several age-specific assessment scales, based on the DSM-IV-TR criteria, exist for diagnosing ADHD in children, adolescents, and adults (Tables 1A-C).^{4,10,26,27}

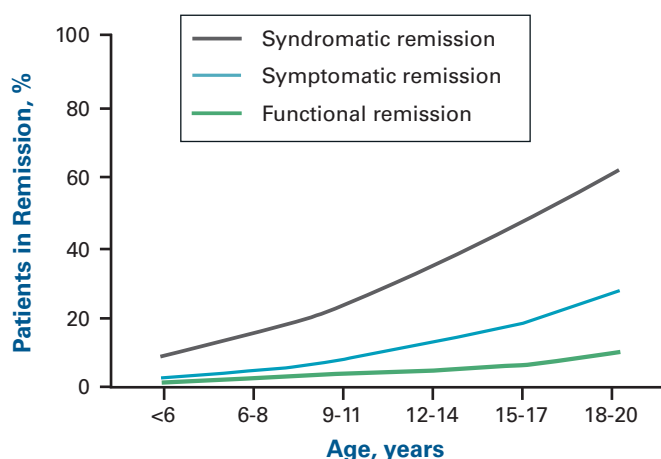
These scales are based on items that correspond to the DSM-IV symptoms. Parents and teachers typically complete these scales for children; parents, teachers, and the patients themselves being the informant for the adolescent scales; and the patients themselves being the informant in the adult scales. There is typically only modest agreement among different informants. Most scales have different norms for different age groups and for different sexes, which can help the clinician determine if a child's behavior is truly developmentally inappropriate.

In applying these assessment scales, it is important for providers in a managed care setting to consider the common comorbid conditions with ADHD discussed previously, as the presence of other disorders may impact ADHD treatment, especially when a more serious disorder is present that requires a different treatment, such as bipolar disorder or major depression. Furthermore, providers must also consider a differential diagnosis in light of normal but active behavior that seemingly overlaps somewhat with ADHD. Among the most common differential diagnoses for ADHD-like behavior are age-appropriate activities, the reaction of a child to a disorganized or chaotic environment, oppositional behavior without ADHD, other psychiatric disorders, and sleep deprivation.¹⁷

Therapeutic Considerations

Taking into account the different ages, presentations, comorbidities, and environmental factors affecting the diverse population of patients with ADHD, therapy for the disorder must be tailored to meet the needs of each individual patient. Pharmacotherapy—primarily stimulants—has long been a common treatment method for patients with ADHD and is backed by robust safety and efficacy data.²⁸ Behavioral therapy and/or psychotherapy represent other options for the treatment of ADHD, which can be performed either alone or in combination with pharmacotherapy. Either method of therapy or combination of therapies can be applied to children, adolescents, and adults.

■ **Figure 1.** Levels of Attention-Deficit/Hyperactivity Disorder Remission in Relation to Patient Age (n = 128)



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■ **Table 1A. Childhood ADHD Rating Scales**

| Rating Scale | Patient Age, years | Sex |
|--|--------------------|-------------|
| NICHQ Vanderbilt Assessment Scales—PARENT and TEACHER Information and Follow Up | 6-12 | Male/female |
| Attention Deficit Hyperactivity Disorder Rating Scale (ADHD-RS) | 5-18 | Male/female |
| CPRS-R:L ADHD Index [Conners' Parent Rating Scale (1997) Revised Version: Long Form, ADHD Index Scale] | 6-17 | Male/female |
| CTRS-R:L ADHD Index [Conners' Teacher Rating Scale (1997) Revised Version: Long Form, ADHD Index Scale] | 6-17 | Male/female |
| CPRS-R:L DSM-IV Symptoms [Conners' Parent Rating Scale (1997) Revised Version: Long Form, DSM-IV Symptoms Scale] | 6-17 | Male/female |
| CTRS-R:L DSM-IV Symptoms [Conners' Teacher Rating Scale (1997) Revised Version: Long Form, DSM-IV Symptoms Scale] | 6-17 | Male/female |
| SSQ-O-I [Barkley's School Situations Questionnaire-Original Version (1989) Number of Problems Settings Scale] | 6-11 | Female |
| SSQ-O-II [Barkley's School Situations Questionnaire-Original Version (1989) Mean Severity Scale] | 6-11 | Female |
| ADHD indicates attention-deficit/hyperactivity disorder; <i>DSM-IV</i> , <i>Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition</i> . American Academy of Pediatrics. <i>Pediatrics</i> . 2000;105(5):1158-1170. | | |

■ **Table 1B. Adolescent ADHD Rating Scales**

| Rating Scale | Symptoms Assessed | Informant |
|---|---------------------------|--------------------|
| Attention Deficit Hyperactivity Disorder Rating Scale (ADHD-RS) | ADHD | Adolescent |
| Brown Attention Deficit Disorder Scales | ADHD (attention problems) | Adolescent |
| Child Attention Profile | ADHD | Teacher |
| Conners' Parent Rating Scale (revised) | ADHD | Parent |
| <i>DSM-IV</i> Behavior Checklists | ADHD | Parent, adolescent |
| Attention Problems Scale-Teacher Report Form | ADHD | Teacher |
| Behavior Assessment System for Children (BASC) Parent Rating Scale | Psychopathology | Parent |
| Children and Adolescent Service Center (CASC) Teacher Rating Scale | Psychopathology | Teacher |
| Child Behavior Checklist | Psychopathology | Parent |
| Conners-Wells' Adolescent Self-Report Scale | Psychopathology | Adolescent |
| ADHD indicates attention-deficit/hyperactivity disorder; <i>DSM-IV</i> , <i>Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition</i> . Pliszka S, et al. <i>J Am Acad Child Adolesc Psychiatry</i> . 2007;46(7):894-921. | | |

In looking at the most common form of treatment for patients with ADHD—pharmacotherapy—a number of options exist. Specifically, stimulant medications, such as methylphenidate, dexamethylphenidate, mixed amphetamine salts, dextroamphetamine, and lisdexamfetamine, are the most common form of pharmacotherapy for the treatment of ADHD. In 2006, more than 80% of the medications prescribed to children for the

management of ADHD were stimulants, with non-stimulants such as atomoxetine being prescribed in less than 20% of cases.²⁹

Stimulant medications inhibit the reuptake of norepinephrine and dopamine; in addition, amphetamines increase catecholamine release. For this reason, stimulants are typically divided into 2 main classes: methylphenidate/dexamethylphenidate and dextroamphetamine/mixed amphetamine salts. Re-

■ **Table 1C.** Adult ADHD Rating Scales

| Rating Scale | Description |
|---|--|
| Brown Attention Deficit Disorder Scale | Rates inattention/executive dysfunction; includes items that extend beyond <i>DSM-IV</i> criteria |
| Conners' Adult ADHD Rating Scale | Large item set of developmentally relevant items; <i>DSM-IV</i> subscale maps onto diagnosis; self- and other report assessments |
| Wender-Reimherr Adult Attention Deficit Disorder Scale | Retrospective symptom scales provide age-of-onset data; not as closely tied to <i>DSM-IV</i> criteria; provides additional information on broader range of symptoms than the <i>DSM-IV</i> , in line with the Wender Utah Criteria |
| Barkley's Current Symptoms Scale | Dimensional scale using actual <i>DSM-IV</i> items but not adapted for adults; rates frequency of behaviors in past 6 months; self- and other report assessments |
| Adult Self-Report Scale V1.1 | 18-Item symptom assessment and 6-item screener; <i>DSM-IV</i> criteria made developmentally relevant for adults; rates frequency but not severity of symptoms on a 0-4 scale |
| Adult Investigator Symptom Report Scale | Interviewer-administered scale; 18 items based on <i>DSM-IV-TR</i> ADHD criteria adapted for adults; integrates age-appropriate prompts to ensure adequate probing about breadth of adult symptoms |
| ADHD indicates attention-deficit/hyperactivity disorder; <i>DSM-IV</i> , <i>Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition</i> . | |

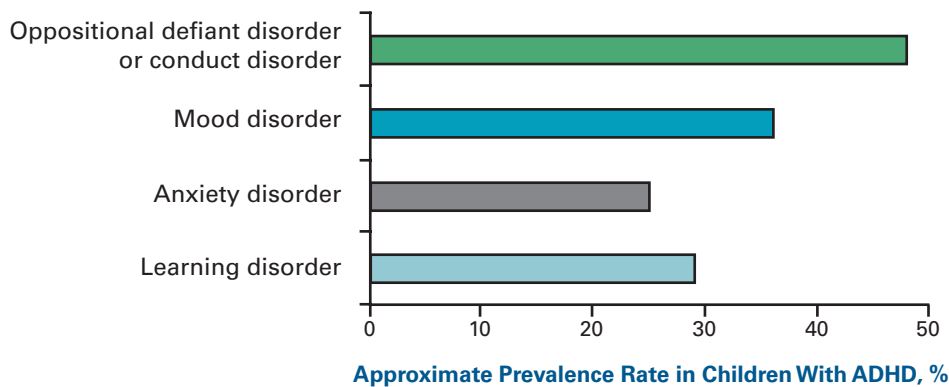
■ **Table 2.** Comparison of Stimulants for the Treatment of ADHD

| Drug | Onset, hour | Duration, hour | Dosing Range |
|---|-------------|----------------|--------------------------------|
| Methylphenidate IR | 0.5 | 2-4 | 5-20 mg 3 times daily |
| Methylphenidate SODAS | 0.5-1 | 6-8 | 10-30 mg twice daily |
| Methylphenidate OROS | 1-3 | 8-12 | 18-72 mg once daily in morning |
| Methylphenidate transdermal | 0.5-1 | 12 | 10-30 mg once daily in morning |
| Dexmethylphenidate IR | 0.5 | 4-6 | 2.5-10 mg twice daily |
| Dexmethylphenidate XR | 0.5-1 | 8-12 | 5-20 mg once daily in morning |
| Mixed amphetamine salts IR | 0.5 | 3-5 | 2.5-20 mg twice daily |
| Mixed amphetamine salts XR | 0.5-1 | 8-12 | 10-30 mg once daily in morning |
| Lisdexamfetamine | 2-4 | 12 | 10-70 mg once daily in morning |
| IR indicates immediate release; OROS, osmotic-release oral system; SODAS, spheroidal oral drug absorption system; XR, extended release. | | | |

cently, a number of extended-release formulations of existing stimulant medications have been developed to prolong the duration of action and provide more convenient once-daily dosing. These agents may offer improvements in medication adherence versus multiple-daily-dosed agents. A comparison of commercially available stimulants, including onset, duration, and dosing range, is presented in [Table 2](#).³⁰⁻³²

In children and adolescents without a predominating psychiatric comorbidity, practice guidelines for ADHD, such as those from the American Academy of Pediatrics and the American Academy of

Child and Adolescent Psychiatry, recommend prescribing a stimulant medication first, followed by another stimulant medication trial before switching to a nonstimulant, such as atomoxetine, bupropion, or a tricyclic antidepressant.^{4,33} This general course of treatment with pharmacotherapy holds true for adults, based on years of clinical experience and sound safety and efficacy data reported with stimulant use in all 3 age groups.²⁷ Furthermore, these guidelines have been applied in the construction of published treatment algorithms, which may be used by providers to assist in making therapeutic decisions ([Figure 4](#)).^{4,33}

■ Figure 2. Common Comorbid *DSM-IV* Disorders in Children With ADHD

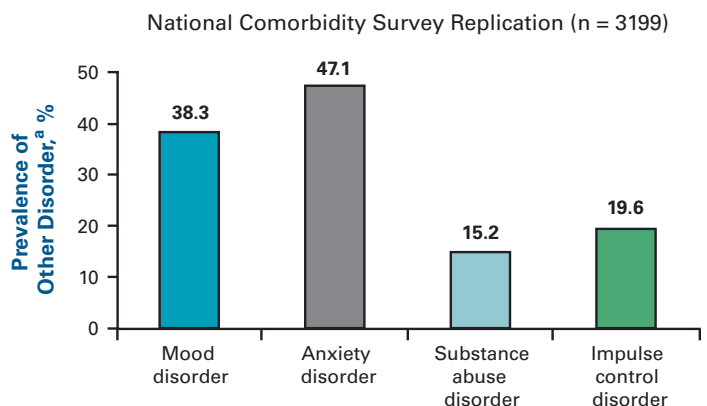
ADHD indicates attention-deficit/hyperactivity disorder; *DSM-IV*, *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*.

Sources: Pliszka SR. *J Clin Psychiatry*. 1998;59(suppl):50-58. Spencer T, et al. *Pediatric Clin North Am*. 1999;46(5):915-927.

Despite the obvious clinical benefits of stimulant medications in children, adolescents, and adults with ADHD, the relative risk of a number of adverse events associated with these agents should be considered before prescribing. Common (10%-50%) adverse effects associated with stimulant medications include decreased appetite, insomnia, headache, stomachache, and irritability.^{23,32} Not life-threatening, these adverse events are more of a nuisance, and can usually be managed by adjusting the dose or dosing schedule of the drug, switching medications, or adding medications to treat the adverse events. Uncommon (1%-10%) and rare (<1%) adverse effects associated with stimulant medication treatment for patients with ADHD include tics, dysphoria, extreme overfocus, and hallucinations.^{23,32} One serious adverse event, sudden cardiac death, has been associated with ADHD medication use in patients at risk for cardiovascular events or those with a cardiovascular defect. Among others without such risk factors, the risk has not been found to be greater than the general population of children and adolescents not receiving ADHD medication.^{34,35} The American Heart Association recommends electrocardiogram monitoring for patients receiving either stimulant or nonstimulant medications who are at risk of sudden death due to a strong family history of heart disease.³⁶

In addition to the adverse events associated with stimulants, consideration should be given to the fact that most stimulant medications prescribed for patients with ADHD are Schedule II controlled substances. The Schedule II designation indicates

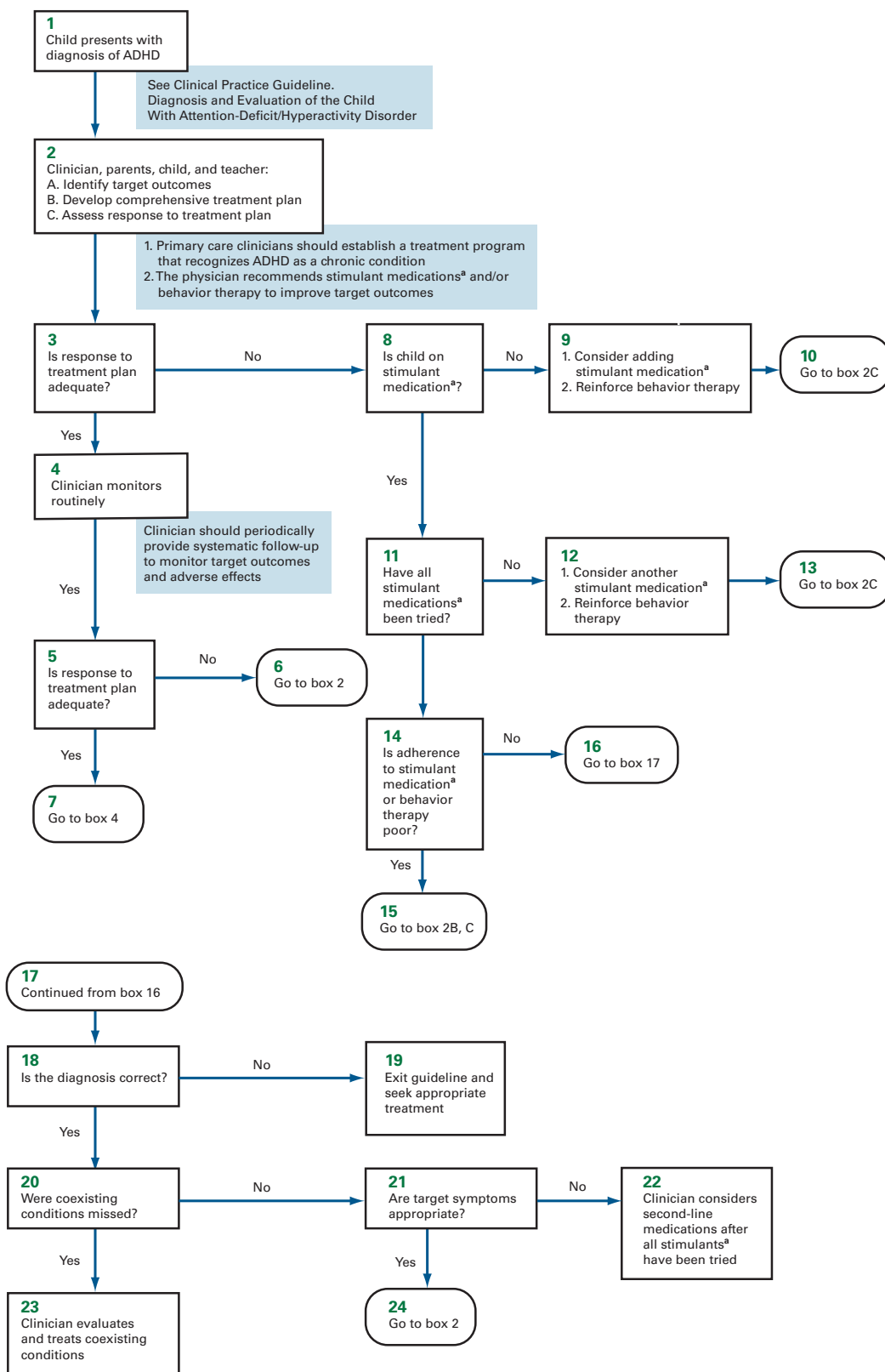
a legitimate medical use for a particular drug with a high probability of abuse. Since a diagnosis of ADHD already confers a higher risk of substance abuse, the prescribing of stimulants to adult and adolescent patients with ADHD may seem counterintuitive.³⁷⁻⁴⁰ However, many prescribing safeguards are built into the Schedule II designation, such as no refills and mandatory “hard copy” prescriptions, which reduce the likelihood of abuse. Furthermore, while some studies indicate that patients receiving treatment for ADHD demonstrate a reduced risk for substance abuse,³⁷ recent findings from the largest multicenter trial evaluating therapy for ADHD—the Multimodal Treatment

■ Figure 3. Common Comorbid *DSM-IV* Disorders in Adults With ADHD

ADHD indicates attention-deficit/hyperactivity disorder; *DSM-IV*, *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*.

^aAmong respondents with ADHD, reported comorbid disorder within the previous 12 months.

■ **Figure 4.** American Academy of Pediatrics Treatment Algorithm for School-Aged Children With ADHD



^aExcluding pemoline.

Reprinted with permission from American Academy of Pediatrics. *Pediatrics*. 2001;108(4):1035.

Study of Children with ADHD (MTA)—indicate that the actual risk for substance abuse neither increased nor decreased as a function of having been prescribed stimulants.^{41,42} Nevertheless, in patients diagnosed with ADHD who have an existing substance abuse problem, nonstimulant medications, such as atomoxetine or bupropion, should be considered.⁴⁰

Prior to initiating an ADHD medication, a number of key issues should be considered. First, a baseline assessment of ADHD symptoms and treatment targets, as well as sleeping and eating patterns should be established. Importantly, a thorough physical examination and medical history, including family history of illness, should be conducted to determine if there are any medical contraindications or concerns.^{43,44} Likewise, the baseline assessment ADHD symptoms and treatment targets should be performed in a comprehensive manner across different settings with different people (eg, home, school, day care, work) to capture the effects of therapy in the patient's real-world setting.⁴³ For children with ADHD, this assessment can be achieved by talking to parents and children while self-assessment scales are more appropriate for adolescents and adults.⁴⁵ Furthermore, careful consideration should be given to the dose and dosing schedule of the medication prescribed. Starting a patient at too low a dose and/or on a dosing schedule spaced too far apart are common reasons for medication failure, highlighting the importance of prescribing the recommended therapeutic doses of medications and employing extended-release formulations when appropriate.⁴³ Collectively, these measures can assist in choosing or switching to the optimal form of pharmacotherapy or in making the determination as to whether behavioral interventions are appropriate.⁴⁵

As mentioned previously, behavioral interventions likewise play an important role in the treatment of ADHD, both alone and in combination with pharmacotherapy. The aforementioned MTA demonstrated the role of behavioral interventions with respect to pharmacotherapy for ADHD in children.⁵ In the MTA, 579 elementary school children (aged 7-10 years) with *DSM-IV* ADHD combined type were randomized to 1 of 4 treatment groups⁵:

1. Medication alone (85% of children treated with stimulants)

2. Psychosocial/behavioral treatment alone
3. Combination of medication and psychosocial behavioral treatment
4. Routine community care

The outcome measure of interest in the trial was assessed at 14 months, and the separate and combined effects of medication and psychosocial/behavioral therapy were included in this assessment.⁵ Although medication alone was superior to behavioral intervention alone in patients with ADHD and no predominating psychological comorbidities, both interventions were equally effective in treating patients with ADHD plus anxiety or depressive disorders.⁵ Based on these findings, the researchers concluded that both courses of therapy serve separate but equally important roles in the treatment of ADHD. Pharmacotherapy effectively reduces the core symptoms of ADHD and makes it easier to implement a successful behavioral program, whereas behavioral interventions may lower the dose of medication required and target behaviors that may not be addressed as well by medication.⁵

Several different types of behavioral interventions exist for children, adolescents, and adults with ADHD. In children and sometimes adolescents, these interventions are typically directed at both the child or adolescent and the parent or primary caregiver.¹ Intensive behavioral therapy for the child or adolescent has been shown to decrease substance abuse and delinquency, lower medication dose, and reduce parental stress by changing the child or adolescent's thinking and coping habits and improving his or her organizational skills.^{46,47} Behavioral therapy may also be administered to the child or adolescent to improve his or her self-image and explore self-defeating patterns of behavior.¹ An important part of any management strategy for children or adolescents with ADHD, parent training and education is based on giving parents the tools to manage their child's behavior and encourage medication adherence.¹ These interventions have been shown to be highly effective for assisting parents in fostering regular medication habits, identifying target behaviors, providing positive reinforcement, and encouraging skill development.⁴⁶

Behavioral interventions for adults with ADHD typically consist of educational initiatives. Since

there is no caregiver (ie, no parent or guardian) in these cases, the interventions are focused directly on the patient in order to inform and assist in managing his or her ADHD. Educational interventions provide patients with information about their disorder and how to manage it most effectively, through the use of organization “props” (eg, calendars, personal digital assistants) and other organization techniques.¹ Other behavioral interventions likewise assist in organization, by creating a routine schedule for patients to keep with their therapist, and can improve patient self-image by helping them recognize that they have a disorder that must be managed effectively.¹

Conclusion

ADHD has a significant impact on patient quality of life and the managed care bottom line as well. This effect is not only realized among children, but adolescents and adults alike, where the disorder is often underrecognized and undertreated. Contributing to the burden of managing patients with ADHD is the myriad of presentations and comorbidities observed among the broad spectrum of patients with the disorder. These complexities associated with ADHD often present problems in diagnosis and treatment for managed care providers, who may already be overburdened or lack significant formalized training in behavioral health.

While pharmacotherapy, particularly with stimulants, is the most commonly employed and widely effective form of therapy for the treatment of ADHD, a comprehensive ADHD treatment plan should include behavioral and educational interventions when appropriate. However, implementation of this type of treatment plan often requires a multidisciplinary team approach of healthcare professionals, teachers, and parents to be truly effective. Beyond initiating a comprehensive treatment plan, regular feedback and monitoring is essential to maximize the effectiveness of the interventions and evaluate responses to interventions.

After laying the foundation of a comprehensive ADHD management approach for plan members with the disorder, providers can maximize its effectiveness by using evidence-based diagnostic scales and treatment algorithms. With such proven tools

readily available, a comprehensive treatment approach for ADHD is within reach, after which improved outcomes for the diverse range of patients with ADHD will likely follow in the managed care setting.

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Address correspondence to: Peter S. Jensen, MD, President, CEO, The REACH Institute, 450 Seventh Ave, Ste 1107, New York, NY 10123. E-mail: Peter.Jensen@TheReachInstitute.org.

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The Role of Pharmacotherapy and Managed Care Pharmacy Interventions in the Treatment of ADHD

Julie A. Dopheide, PharmD, BCPP

Despite the availability of effective behavioral interventions for the treatment of attention-deficit/hyperactivity disorder (ADHD), the dominant role of pharmacotherapy as a mode of management for patients with ADHD within a managed care setting cannot be ignored. Approximately 54% of children aged 6 to 11 years who have been diagnosed with ADHD receive prescription drug therapy for their disorder.¹ Furthermore, the use of pharmacotherapy for the treatment of ADHD has increased dramatically in other childhood age groups, with the number of children younger than 9 years of age receiving drug therapy for the disorder growing nearly 75% over the past 4 years.² This rise translates into a 412% increase in healthcare spending on medications for ADHD in younger children over that same time period.² Even in adults, where ADHD is far less recognized and diagnosed, drug therapy is on the rise: the 18% increase in the number of adult patients (aged 20-64 years) using medications for the treatment of ADHD from 2003 to 2004 ranked second among all drug categories, with only the growth in rheumatologic drug users (25%) being greater.²

The widespread application and rapid growth of pharmacotherapy in the treatment of patients with ADHD is not a new phenomenon. Drug therapy—psychostimulant therapy in particular—has been employed in the treatment of patients with ADHD for decades and is supported by robust efficacy and safety data.^{3,5} Furthermore, medication management has been demonstrated to be the most cost-effective form of therapy for ADHD.³ However, although 75% to 90% of children with ADHD display reductions in ADHD symptoms with medication management,⁶ the Multimodal Treatment Study of Children with ADHD (MTA) suggests that less than half display “normalization,” depending on which type of treatment they receive; thus, 56% of children receiving high-quality medication management are “normalized,” while only 34% and 25% receiving intensive behavioral therapy and routine community care, respectively, are normalized.⁷ Psychostimulants have been demonstrated to have increased efficacy relative to nonstimulants (eg, comparator trials of atomoxetine vs stimulants) in the treatment of patients with ADHD.^{3,5} Not surprisingly, psychostimulants are typically first-line therapy for the treatment of ADHD in treatment guidelines published by a number of professional organizations, such as the American Academy of Pediatrics (AAP) and the American Academy of Child and Adoles-

Abstract

Pharmacotherapy plays a primary role in the management of attention-deficit/hyperactivity disorder (ADHD), despite the availability of effective behavioral interventions. Psychostimulants are the most commonly prescribed form of pharmacotherapy for patients with ADHD and their benefits in managed care are severalfold, leading not only to symptom resolution and improved quality of life for patients, but also reduced costs for payers and purchasers. The use of these agents requires careful consideration and management by health plan stakeholders for optimal effectiveness. Concerns regarding medication adherence, in addition to the potential for diversion and abuse of psychostimulants, highlight the importance of effective pharmacotherapy management in patients with ADHD. Initiatives promoting medication adherence, such as patient/parent education, provider follow-up, and adverse effect management, are crucial for ensuring treatment success. Once-daily, extended-release formulations of stimulants may also contribute to improving medication adherence, as may managed care pharmacy interventions such as pharmacy database monitoring.

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For author information and disclosures, see end of text.

cent Psychiatry (AACAP).^{3,8} The clinical practice guidelines published by both of these nationally recognized institutions recommend prescribing a stimulant medication first, followed by another stimulant medication if ineffective or poorly tolerated before switching to a nonstimulant, in children and adolescents with ADHD and without a predominating psychiatric comorbidity requiring a different type of treatment, such as depression or obsessive-compulsive disorder.^{3,8}

The benefits of effective pharmacotherapy for ADHD in managed care are severalfold, leading not only to symptom improvement and improved quality of life for patients and their families, but also reduced costs for payers and purchasers. For example, a meta-analysis of 62 randomized controlled trials reported that the use of psychostimulants improved teachers' and parents' ratings of disruptive behavior in students with ADHD.⁹ Furthermore, among children with ADHD, those receiving pharmacotherapy demonstrate significantly less frequent and less costly emergency department visits.¹⁰ Conversely, in the absence of consistent treatment, adolescents with ADHD suffer 4 times as many serious injuries and 3 times as many motor vehicle accidents versus those without ADHD or those with ADHD who are medication compliant.¹¹ Although somewhat controversial, several studies suggest that substance abuse disorders occur at a rate 3 to 4 times greater among patients with untreated ADHD versus those managed with psychostimulants.¹²

While offering significant benefits, pharmacotherapy for patients with ADHD still requires careful consideration and management by health plan stakeholders for optimal effectiveness. In recently published literature from the MTA study, researchers again highlighted the benefits of an individually titrated psychostimulant regimen, with the caveat that this therapy needs to be intensely managed to be effective.¹³ Echoing the sentiments of the AAP and AACAP, Swanson et al concluded that therapy should be tailored to the individual, with consideration given to each patient's clinical presentation, comorbidities, and treatment goals.¹³ Behavioral interventions should be applied in conjunction with pharmacotherapy to effectively manage psychiatric comorbidities and potentially lower the dose of medication necessary for symp-

tom resolution.¹³ In addition, initiatives promoting medication adherence, such as patient/parent education, provider follow-up, and adverse effect management, are crucial for ensuring treatment success. Once-daily, extended-release (XR) formulations of stimulants may also contribute to improving medication adherence, as can managed care pharmacy interventions such as pharmacy database monitoring.¹⁴⁻¹⁶ As the use of pharmacotherapy for the treatment of patients with ADHD continues to rise, these proactive measures can help to ensure that managed care organizations receive an adequate return on investment for their drug spending on patients with ADHD.

Overview of Pharmacotherapy in the Treatment of ADHD

The catecholamine dysfunction theory of ADHD suggests that the disorder is etiologically linked imbalanced levels of specific neurotransmitters—specifically, dopamine and norepinephrine. Dopamine is believed to play a role in the inattention and hyperactivity, and reward/motivational deficits associated with the disorder, whereas low levels of norepinephrine are believed to play a role in inattention and executive functioning. Psychostimulants prescribed for the treatment of ADHD serve to increase levels of neurotransmitters by inhibiting the reuptake of dopamine and norepinephrine in the neural synapse, as well as through inhibition of monoamine oxidase. The 2 main classes of psychostimulants available, methylphenidate and amphetamine, feature a phenethylamine pharmacophore that is common to dopamine and norepinephrine, allowing these agents to compete with the neurotransmitters for transporter receptor binding (**Figure 1**).

The first evidence of psychostimulant use in the treatment of patients with ADHD was a study published in 1937 by Charles Bradley, MD.¹⁷ Dr Bradley reported that treatment of so-called “behavior problem children” with a racemic mixture of amphetamine resulted in improved academic performance and subdued emotions without a lack of interest.¹⁷ What is now the most commonly prescribed psychostimulant for the treatment of patients with ADHD—methylphenidate—became available years later in 1955, although at the time it was not indicated for the treatment of patients

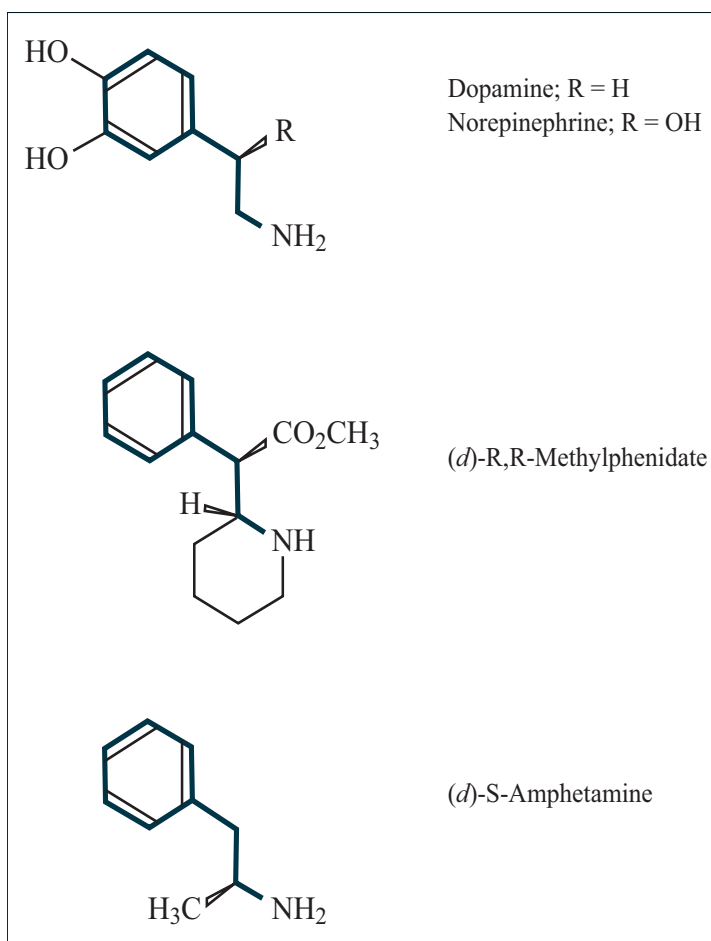
with ADHD.¹⁸ By 1957, methylphenidate was available in various forms from different manufacturers, and clinicians began prescribing the agent for the treatment of patients with ADHD, known at the time as hyperactivity of minimal brain dysfunction.¹⁸ After nearly 50 years of use of the immediate-release formulation of methylphenidate, several XR formulations of the agent were introduced in 1999, revolutionizing its ease of use and associated adherence levels.¹⁸ In recent years, immediate-release and XR formulations of other stimulants, such as dexamethylphenidate, mixed amphetamine salts, dextroamphetamine, and lisdexamfetamine, have also been approved for the treatment of patients with ADHD. The first and only nonstimulant to be approved for the treatment of ADHD, atomoxetine, was introduced in 2003; however, this agent is currently prescribed in less than 20% of patients with ADHD receiving pharmacotherapy, with psychostimulants making up the remaining majority share of prescriptions for the disorder.¹⁹

Prior to the prescribing of any of these aforementioned stimulant or nonstimulant medications for the treatment of patients with ADHD, health plan providers must accurately diagnose and adequately characterize the patient's disorder. These considerations assist in choosing the most appropriate agent and dose for each individual patient, thus optimizing therapy. A comprehensive assessment of the patient also allows the clinician to determine to what extent behavioral interventions alone or in combination with pharmacotherapy may be appropriate as part of the treatment plan.

Stimulants Versus Nonstimulants

After diagnosis and disorder characterization, providers have a wide range of pharmacotherapeutic options available for the treatment of patients with ADHD. As mentioned previously, available child and adolescent treatment guidelines recommend prescribing a psychostimulant as first-line therapy, followed by another psychostimulant if first-line therapy does not produce an adequate response.^{3,8} In the majority of patients, nonstimulants are only recommended after 2 failed stimulant trials.^{3,8} Although no formal guidelines exist for the treatment of ADHD in adults, available data demonstrating the effectiveness of psychostimulants

■ **Figure 1.** Phenethylamine Pharmacore (in Bold) Common Among the Psychostimulants Methylphenidate and Amphetamine and the Neurotransmitters Dopamine and Norepinephrine



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warrant a similar approach to pharmacotherapy in this age group.²⁰

As ADHD was originally identified and characterized in children, the majority of commercially available psychostimulants are indicated only in the treatment of ADHD in children and adolescents. The dose form, typical starting dose, and maximum dose per day of these agents are outlined in [Table 1](#).³ Note that the recently introduced intermediate- and long-acting formulations are dosed only once daily, compared with dosing 2 or 3 times a day for short-acting formulations. However, MTA researchers reported that optimal psychostimulant therapy was achieved with 3-times-daily dosing of immediate-release methylphenidate.¹³

Table 1. Characteristics of Psychostimulants Approved for the Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents³

| Generic Class/Brand Name | Dose Form | Typical Starting Dose | FDA Maximum/Day | Off-Label Maximum/Day |
|-------------------------------------|-------------------------------------|--|-----------------|-----------------------|
| Amphetamine preparations | | | | |
| Short-acting | | | | |
| Adderall ^a | 5, 7.5, 10, 12.5, 15, 20, 30 mg tab | 3-5 y: 2.5 mg qd; ≥6 y: 5 mg qd-bid | 40 mg | >50 kg: 60 mg |
| Dexedrine ^a | 5 mg cap | 3-5 y: 2.5 mg qd | | |
| DextroStat ^a | 5, 10 mg cap | ≥6 y: 5 mg qd-bid | | |
| Long-acting | | | | |
| Dexedrine spansule | 5, 10, 15 mg cap | ≥6 y: 5-10 mg qd-bid | 40 mg | >50 kg: 60 mg |
| Adderall XR | 5, 10, 15, 20, 25, 30 mg cap | ≥6 y: 10 mg qd | 30 mg | >50 kg: 60 mg |
| Lisdexamfetamine | 30, 50, 70 mg cap | 30 mg qd | 70 mg | Not yet known |
| Methylphenidate preparations | | | | |
| Short-acting | | | | |
| Focalin | 2.5, 5, 10 mg cap | 2.5 mg bid | 20 mg | 50 mg |
| Methylin ^a | 5, 10, 20 mg tab | 5 mg bid | 60 mg | >50 kg: 100 mg |
| Ritalin ^a | 5, 10, 20 mg | 5 mg bid | 60 mg | >50 kg: 100 mg |
| Intermediate-acting | | | | |
| Metadate ER | 10, 20 mg cap | 10 mg qam | 60 mg | >50 kg: 100 mg |
| Methylin ER | 10, 20 mg cap | 10 mg qam | 60 mg | >50 kg: 100 mg |
| Ritalin SR ^a | 20 mg | 10 mg qam | 60 mg | >50 kg: 100 mg |
| Metadate CD | 10, 20, 30, 40, 50, 60 mg | 20 mg qam | 60 mg | >50 kg: 100 mg |
| Ritalin LA | 10, 20, 30, 40 mg | 20 mg qam | 60 mg | >50 kg: 100 mg |
| Long-acting | | | | |
| Concerta | 18, 27, 36, 54 mg cap | 18 mg qam | 72 mg | 108 mg |
| Daytrana patch | 10, 15, 20, 30 mg patches | Begin with 10-mg patch qd, then titrate up by patch strength | 30 mg | Not yet known |
| Focalin XR | 5, 10, 15, 20 mg cap | 5 mg qam | 30 mg | 50 mg |

bid indicates twice a day; FDA, US Food and Drug Administration; qam, every morning; qd, every day; tid, 3 times a day.
^aShort-acting formulations of methylphenidate may be dosed up to 20 mg 2 or 3 times a day in adults.
Adapted from Pliszka S; AACAP Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2007;46(7):894-921.

Of these psychostimulants, only mixed amphetamine salts, XR; dexamethylphenidate XR; lisdexamfetamine; and osmotic release oral system (OROS) methylphenidate have received approval from the US Food and Drug Administration (FDA) for use in adults.²¹ Beyond their effect on symptoms of ADHD in children, adolescents, and adults, psychostimulants have also demonstrated clinical worth in a variety of related neurobehavioral domains, such as oppositional and aggressive behaviors, academic achievements, and social skills.²²

The most common adverse events associated with psychostimulants include insomnia, nervousness, irritability, anxiety, jitteriness, headache, stomachache, and decreased appetite.²⁰ Although stimulants can increase pulse and blood pressure modestly, this is rarely a clinical problem, and recent data indicate that the risk for sudden cardiac death in patients receiving stimulant pharmacotherapy does not exceed the base rate in the general population.²³ Furthermore, this sudden cardiac death incidence is often associated with preexisting

structural cardiac defects, other complicating circumstances, or a positive family history.²³ There has also been some concern regarding the worsening of tic disorders in association with psychostimulant therapy.²⁴ However, standard doses of stimulants do not exacerbate or precipitate tic disorders in most patients, and apparent medication-induced exacerbations may decline spontaneously even without discontinuation of therapy.²⁴ Likewise, the chronic use of psychostimulants appears to acutely decrease growth rates in children, although the effects of these agents on weight and height have generally been considered to be of minimal clinical significance.²⁵ Despite the fact that growth appears to stabilize over time in group studies, it remains important to consider and closely monitor individuals being treated.²⁶

The abuse potential of psychostimulants has led to the classification of most of these commercially available agents as Schedule II controlled substances. In a Web survey of students from a Midwestern public school district in grades 6 through 11, illicit use of psychostimulants was reported by 4.5% of respondents.²⁷ Another online survey demonstrated that the incidence of stimulant misuse and abuse appears to increase significantly among college students, where 16% reported abusing or misusing a prescribed stimulant.²⁸ Drug diversion—another managed care concern associated with psychostimulants—was even more apparent than misuse among the aforementioned middle and high school survey respondents, with 23.3% reporting having been approached to sell, give, or trade their prescription drugs.²⁷ While misuse is a definite issue, a number of safeguards are built into the Schedule II designation that are designed to prevent these instances of abuse and diversion, such as mandatory hard-copy prescriptions, no refills on prescriptions, and 30-day limits on drug supplies. Furthermore, concern over stimulant abuse has decreased as newer XR formulations have been introduced to the market. For example, OROS methylphenidate demonstrated no detection or likeability in subjects tested every hour for 10 hours after ingestion in one study.²⁹ Although some reports have suggested that treatment for patients with ADHD is associated with a significantly reduced risk of substance abuse, recent findings from the National Institute of Mental Health's MTA have not uncovered any systematic

relationship.^{30,31} Still, nonstimulant pharmacotherapy is usually preferred in patients with a history of substance abuse.

Atomoxetine, a selective norepinephrine reuptake inhibitor and the only nonstimulant approved by the FDA for the treatment of ADHD, is indicated for use in children, adolescents, and adults. Dosing for this agent follows a weight-based schedule because plasma levels vary considerably as a function of body weight, with a recommended target dose of 1.2 mg/kg.³² A longer period than that of psychostimulants is often required before the full effects of atomoxetine are observed.³³ The therapeutic benefits of atomoxetine often persist into the evening or even the following morning when the agent is dosed during the day; however, patients typically need 2 to 4 weeks of regular dosing with the agent to realize therapeutic benefits, compared with 1 to 2 hours with psychostimulants.³³ The most common adverse events associated with atomoxetine therapy include dry mouth, insomnia, decreased appetite, nausea and vomiting, sexual difficulties, dizziness, and increased blood pressure and heart rate.³² Irritability and increased aggression have also been observed, particularly in individuals with comorbid mood or behavioral syndromes, and hepatotoxicity has been reported in rare instances.³² The potential advantages of atomoxetine over psychostimulants with regard to adverse events are decreased insomnia and growth-related effects. There is also less potential for abuse than for stimulants, and this agent appears not to be well suited for those who display tics, which are exacerbated by stimulants.

Managed Care Pharmacy Interventions

Prescribing and use of the aforementioned stimulant and nonstimulant pharmacotherapy for patients with ADHD can have a significant financial impact on managed care. In fact, estimates of the annual cost for treating children with ADHD range from \$2 billion to \$11 billion, with pharmacotherapy making up a significant portion of those expenditures.³⁴ Among adults, one analysis demonstrated total medical and drug costs for patients treated with pharmacotherapy as ranging from \$2000 to \$4000 during a 6-month period.³⁵ Furthermore, this spending on agents for the treatment of patients with ADHD shows no signs of slowing down anytime in the near future. Despite making up only 1.8% of

plan cost, pharmacotherapy for ADHD increased 5.6% in utilization in 2007, with a 6.8% increase in unit cost also contributing to increased spending.²

When considering these rising costs associated with pharmacotherapy for patients with ADHD in managed care, it is obvious that plans have invested a significant amount of resources toward treating the disorder. To ensure a sound return on this investment, stakeholders must implement pharmacy interventions to manage the use of pharmacotherapy and promote improved outcomes. This process begins by addressing a key component of treatment for patients with ADHD: medication adherence.

Adherence is a critical aspect of care due to the chronicity of lifelong ADHD and the consequences resulting from significant symptoms that continue to exhibit into adulthood. Without consistent, adequate treatment, these symptoms remain minimally managed and can impact patient quality of life, as well as lead to increased costs for payers and purchasers. Similar to interventions promoting medication adherence for other conditions, patient/parent education serves as the foundation for addressing adherence in patients with ADHD.

An important part of any management strategy for children, adolescents, or adults with ADHD, patient/parent education is designed to counsel patients and/or parents on the benefits and adverse events associated with all psychopharmacologic treatments. By helping a patient and/or parent understand why a medication is being prescribed and what potential positive and negative effects to expect, managed care organizations can foster realistic expectations regarding treatment and minimize anxiety should adverse events occur.

In children and adolescents with the disorder, managed care stakeholders may be best served by focusing such educational interventions on parents or guardians, since they are better suited to understand the implications of treatment adherence and can have a profound impact on the behavior of the patient. Parent training and education are based on the premise of giving parents the tools to manage their child's behavior and encourage medication adherence.³⁶ These interventions have been shown to be highly effective for assisting parents in fostering regular medication habits, identifying target

behaviors, providing positive reinforcement, and encouraging skill development.³⁷

When addressing adolescent or adult patients with ADHD, who are capable of fully understanding the implications of treatment adherence, educational efforts should be targeted directly at the patients themselves. It is important to discuss the standard messages regarding target outcomes and potential drug adverse events. In particular, because a noticeable proportion of high school and college students receiving prescription drugs for the treatment of ADHD are likely to be approached regarding their medication, it is useful to discuss this potential problem.

As a means of improving the effectiveness of educational efforts for promoting medication adherence in the treatment of patients with ADHD, plans may also implement adherence monitoring measures to track adherence and target nonadherent patients for intervention. These pharmacy monitoring interventions may be as simple as basic pharmacy database monitoring or more involved and sophisticated, as in the case of the Stimulant Adherence Measure described by Charach et al.¹⁴ The Stimulant Adherence Measure is a semistructured telephone interview designed to elicit a detailed description of medication use from parents and children that takes 5 to 15 minutes to complete.¹⁴ In the study, the researchers compared use of the Stimulant Adherence Measure to use of the Medication Event Monitoring System (MEMS®)—a device that records the date and time the pill container was opened using an electronic computer chip in the cap—for monitoring adherence to pharmacotherapy for ADHD. Charach et al reported that the telephone interview method employed in the Stimulant Adherence Measure demonstrated good to excellent agreement with the proven yet costly MEMS.¹⁴

The effective management of adverse events associated with drug therapy is another means of improving adherence among patients with ADHD. Management begins with a comprehensive physical examination prior to the initiation of therapy as well as initiating therapy at a low dose and sequentially titrating upward to minimize adverse events. Furthermore, in many cases, lowering the medication dose is the first step to minimizing or even completely resolving the occurrence of adverse events (**Table 2**). It should be noted, how-

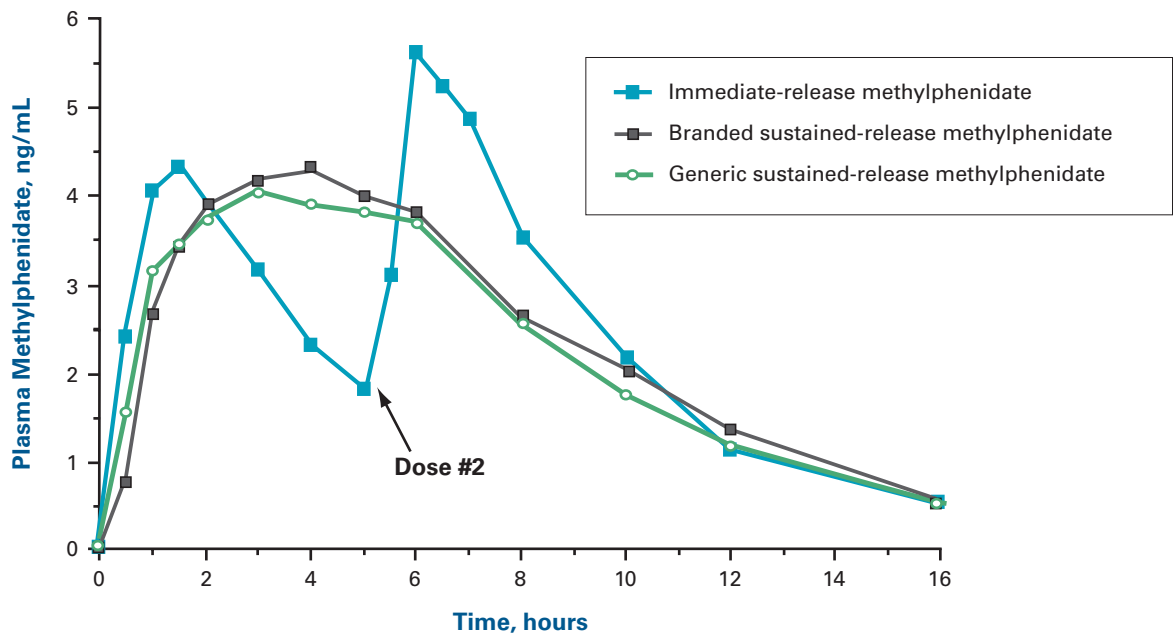
■ **Table 2.** Strategies for the Management of Various Safety Considerations and Potential Adverse Events Associated With Pharmacotherapy for Attention-Deficit/Hyperactivity Disorder

| Pharmacologic Treatment | Safety Considerations/ Potential Adverse Events | Management Strategies |
|--|---|---|
| Methylphenidate | | |
| Immediate release (short-acting; ie, dextro, levo-MPH, d-MPH) | Risk for tachycardia, arrhythmia, sudden death Risk for growth suppression Risk for tics Potential for abuse and diversion Risk for hallucinations Risk for GI adverse events (abdominal pain, vomiting, decreased appetite) | Heart rate/BP monitoring, ECG and/or echocardiogram in high-risk cases; baseline ECG not recommended Baseline height/weight with periodic monitoring; dietary consultation and/or nutritional supplementation Decrease anxiety; monitor for appearance/exacerbation of tics; adjust dose; change medication Counsel; nonstimulants; extended-release formulations of stimulants Inquire about vision symptoms; discontinue use if hallucinations occur Inquire about GI symptoms; decrease dose if these occur |
| Extended release (intermediate- and long-acting; ie, MPH-LA, MPH-CD, OROS MPH, d-MPH XR) | Presumed same risk for cardiovascular adverse events as IR, but not studied Risk for growth suppression and tics similar to or lower than IR formulations Possible lower potential for abuse and diversion, but not well studied | See recommendations for IR formulations |
| Transdermal system | Risk for skin erythema, rash Risk for other side effects similar to oral MPH Possible lower potential for abuse and diversion, but no data currently | Observation; topical creams; rotation of administration site |
| Amphetamine | | |
| Immediate release (d-AMP, MAS) | Overall risks are similar to MPH, with some individual variations | See recommendations of MPH |
| Extended release (d-AMP, spansule, MAS-XR, lisdexamfetamine) | Presumed risks similar to IR formulation Possible lower potential for abuse and diversion | See recommendations of MPH |
| Atomoxetine | | |
| | Risk for hepatotoxicity Possibility of suicidal thinking Risk for sedation Risk of tachycardia, arrhythmia, sudden death No abuse potential | Baseline history; follow clinically for abdominal pain/jaundice Weekly monitoring for suicidal ideation/behavior when beginning treatment or changing dose Dose twice a day, or bedtime dosing Heart rate/BP monitoring; ECG and/or echocardiogram in high-risk cases; baseline ECG not recommended |
| AMP indicates amphetamine; BP, blood pressure; d, dextro; ECG, electrocardiogram; GI, gastrointestinal; IR, immediate release; LA, long acting; MAS, mixed amphetamine salts; MPH, methylphenidate; OROS, osmotic release oral system; XR, extended release. | | |

ever, that some adverse events are idiosyncratic and cannot be managed successfully by dose reduction. In these cases, intolerability should be managed by switching to a different agent or by administering supportive care when appropriate.

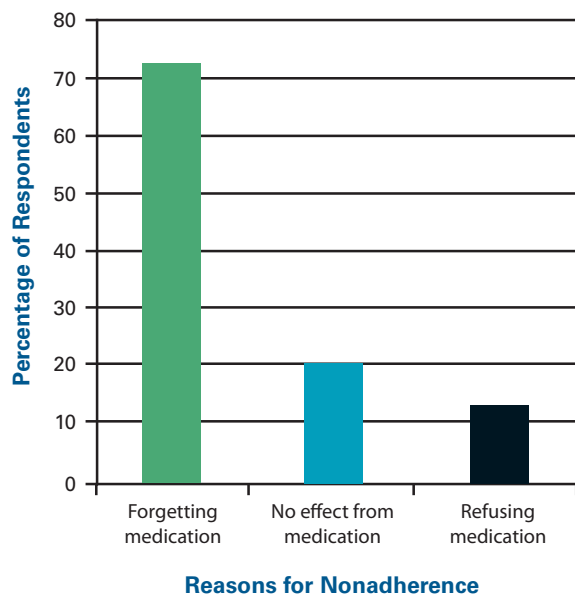
Beyond the implications of patient education and management of adverse events, the actual choice of agent can have a profound effect on medication adherence.¹⁶ As mentioned previously, over the past decade, several XR formulations of psycho-

■ Figure 2. Pharmacokinetic Profile of Immediate-Release Methylphenidate (twice/day) Compared With That of the Branded and Generic Sustained-Release Products



Source: Patrick KS, et al. *Biopharm Drug Dispos.* 1989;10:165-171.

■ Figure 3. Reasons for Poor Adherence to Medications for the Treatment of Attention-Deficit/Hyperactivity Disorder¹⁶



stimulants have been introduced that require only once-daily dosing, as opposed to immediate-release formulations that must be dosed 2 to 3 times a day. These XR formulations maintain effective plasma concentrations of the active agent over 8 to 12

hours, whereas immediate-release formulations must be dosed again after approximately 4 hours (Figure 2).³⁸

When considering that forgetting medication is among the most common reasons for nonadherence, these XR formulations that allow for minimal dosing are likely to cause the patient to experience higher adherence rates (Figure 3).¹⁶ Another common reason for nonadherence (at least among children), refusing medication, may also be alleviated by newer formulations that increase ease of administration, such as the methylphenidate patch or granulated formulations that can be sprinkled on or in food or drink.

Conclusion

Pharmacotherapy has demonstrated significant benefits in improving outcomes in many patients with ADHD, which can in turn reduce direct and indirect costs for payers and purchasers. Specifically, treatment with psychostimulants has demonstrated robust effects on ADHD symptoms. However, these agents come at a cost that has been increasing on a yearly basis, in conjunction with their utilization. It is obvious that management is necessary on the part of managed care organizations to maximize the return on their investment.

A number of pharmacy-led interventions may prove beneficial to managed care stakeholders for improving outcomes and maximizing the effectiveness of prescription drug therapies. These interventions are founded on the principle of promoting medication adherence, which is crucial in the treatment of patients with ADHD when considering the chronicity of the disorder. Patient/parent education efforts, adherence monitoring, management of adverse events, and the use of XR formulations are among some of the most effective means of achieving higher rates of medication adherence in the treatment of patients with ADHD. These interventions, which can be either partially or exclusively implemented and managed by managed care pharmacy, allow for optimal use of pharmacotherapy for the treatment of patients with ADHD, benefiting patients, purchasers, and payers alike.

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Address correspondence to: Julie A. Dopheide, PharmD, BCPP, Associate Professor of Clinical Pharmacy, Psychiatry and the Behavioral Sciences, University of Southern California, Schools of Pharmacy and Medicine, 1985 Zonal Ave, Los Angeles, CA 90089. E-mail: dopheide@pharmacy.usc.edu.

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ADHD in Managed Care: An Assessment of the Burden of Illness and Proposed Initiatives to Improve Outcomes

Neil B. Minkoff, MD

Attention-deficit/hyperactivity disorder (ADHD) has a profound impact on managed care due to its broad-reaching effects on every age group of patients. Although traditionally recognized as a childhood disorder, longitudinal and cross-sectional studies indicate that ADHD persists into adolescence and adulthood in the majority of cases and is estimated to affect nearly 8 million adults.¹⁻⁵ Unfortunately, adult ADHD is often unrecognized by managed care stakeholders and the general public, leading to late or missed opportunities to effectively treat this disorder in adults. In fact, while approximately half of patients with ADHD are diagnosed before age 13, more than one third (35%) are not diagnosed until after age 18.¹

The characteristics of ADHD, which can vary significantly among patients and patient age groups, result in chronic problems with attention and impulse control; this, in turn, contributes to difficulties with productive functioning in academic, social, and workplace settings.⁶ The implications of these difficulties are often overwhelming and outline the significant burden of illness associated with ADHD, which is realized in diminished quality of life for patients and their families as well as increased costs or loss of revenue for payers and employers. Whether this burden is embodied by poor academic performance among children, dangerous and abusive behavior among adolescents, or decreased earning potential among adults, it is worthy of significant consideration from managed care stakeholders.⁶

On the clinical side, evidence-based care has already contributed to successful efforts by healthcare providers to alleviate a portion of the burden of illness associated with ADHD. However, considering the chronicity and persistence of the disorder and associated impairments, further intervention may be necessary on the part of managed care organizations (MCOs) to foster sound clinical practices and optimal care. The diverse and complex clinical presentations of patients with ADHD, coupled with the prevalent occurrence of psychiatric comorbidities, make the disorder difficult to recognize and diagnose for already overburdened providers in the primary care setting, who may be lacking formalized training in behavioral health.⁷ Educational initiatives and evidence-based screening tools, such as behavior rating scales and treatment algorithms, play a role in

Abstract

Attention-deficit/hyperactivity disorder (ADHD) often results in persistent problems with attention and impulsivity; these problems, in turn, contribute to impairments in a wide range of functions that affect academic, social, and workplace performance. The chronic and cumulative effects of these difficulties can be overwhelming and outline the significant burden of illness associated with ADHD, which is realized in diminished quality of life for patients and their families and increasing costs or loss of revenue for payers and employers. This burden warrants significant consideration and action from managed care stakeholders to foster sound clinical practice and optimal care. For example, educational interventions and evidence-based tools can be implemented to assist providers with accurate diagnosis and more effective treatment. Furthermore, extensive data documenting the benefits of pharmacotherapy and provider follow-up have demonstrated that initiatives designed to encourage treatment adherence may be the best investment for managed care plans seeking to improve outcomes in patients with ADHD.

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For author information and disclosures, see end of text.

assisting providers with diagnosis and treatment.^{5,8,9} Furthermore, data documenting the safety and efficacy of pharmacotherapy and provider follow-up have demonstrated that initiatives designed to encourage treatment adherence—such as medication tracking and the National Committee for Quality Assurance’s (NCQA) Healthcare Effectiveness Data and Information Set (HEDIS) measures—may be the best investment for plans seeking to improve outcomes in patients with ADHD.¹⁰ The foundation of such programs should again be centered on education, but also directed at patients and parents of patients who should be made aware of the benefits and potential adverse effects of treatment.¹¹ Comprehensive efforts such as these may prove imperative for improving patient outcomes in the treatment of ADHD when considering the complexity and significant burden of illness associated with the disorder.

Burden of Illness

When characterizing the burden of illness associated with ADHD, perhaps the most evident component is the economic impact of the disorder. ADHD contributes to rising costs for payers, employers, and patients, realized not only in the direct medical costs associated with the disorder, but also the indirect costs of reduced productivity, lost earning potential, and other socioeconomic factors. Breaking down the direct medical costs of ADHD further, studies have documented increasing costs immediately related to treating the disorder itself, as well as costs associated with treating comorbidities and other medical needs resulting from the effects of the disorder.

In terms of direct expenditures, estimates of the annual costs of treating children with ADHD range from \$2 billion to \$11 billion, with pharmacotherapy contributing significantly to these expenditures.¹² The scenario is similar among adults, where 6-month estimates of the total medical and drug costs for ADHD range from \$2000 to \$4000.¹³ Psychiatric comorbidities associated with the disorder may have an even more profound impact on payer bottom lines, with yearly estimates totaling \$58.3 billion for drug abuse, \$85.8 billion for alcohol abuse, and \$43.7 billion for depression.^{14,15} These costs become noteworthy when considering the increased incidence of substance abuse among

individuals with ADHD and an increased likelihood of other unhealthy habits potentially leading to further medical costs, such as smoking and illicit sexual behavior.^{16,17} Children with the disorder are more likely to smoke and to start smoking at a younger age than those without ADHD.¹⁶ Individuals with ADHD also have an onset of sexual intercourse at an earlier age, more sexual partners, more early pregnancies, and more sexually transmitted diseases than individuals without the disorder.¹⁷ In addition, compared with controls, patients with ADHD have higher incidences of antisocial personality disorder, major depressive disorder, and anxiety disorder.¹⁸ An increased incidence of accidents and emergency department visits among individuals with ADHD also contributes to the medical costs resulting from the effects of the disorder. Adolescents with untreated ADHD have 4 times as many serious injuries and 3 times as many motor vehicle accidents than those without ADHD or those taking medication for ADHD.¹⁹

The indirect costs associated with ADHD, while less evident than direct costs, may bear even greater weight in contributing to the disorder’s overall burden of illness, particularly for patients and employers. Patients with ADHD experience distraction and inattention that can potentially lead to decreased academic and workplace performance and, ultimately, lost income and revenue.⁶ Studies have shown that, compared with individuals without ADHD, those with ADHD had lower educational achievement. Furthermore, patients with ADHD with a high school degree earn significantly less than their counterparts without ADHD.⁶ In fact, on average, those individuals with ADHD have household incomes that are more than \$10,000 lower for high school graduates and \$4334 lower for college graduates, compared with those without ADHD.⁶ Furthermore, approximately 50% of individuals with ADHD indicated that they have lost or changed jobs due to their disorder, and many individuals with the disorder are often considered last for promotions or raises.⁶

Less obvious but no less significant than the economic burden of ADHD is the quality-of-life and behavioral dysfunctional impact of the disorder. ADHD is a highly disabling disorder with a significant effect on a broad range of areas of functioning, including education, employment,

and interpersonal relationships. This reduced functioning has resulted in individuals with the disorder reporting lower self-image or optimistic point of view and lower levels of satisfaction with all aspects of life.¹⁸ In turn, the general pessimism resulting from chronic academic, social, and occupational dysfunction has been documented to lead to negative outcomes on a personal level for individuals with ADHD, such as a higher prevalence of marital problems and increased criminal behavior.^{4,20} In fact, studies have shown that individuals with ADHD, compared with those without ADHD, are more likely to be divorced and/or arrested.²⁰ These varied and significant components of the burden of illness associated with ADHD, in addition to the complex nature of the presentations and comorbidities of the psychiatric disorder itself, validate the need for intervention beyond that applied to other disorders and conditions on the part of managed care stakeholders.

Improving Outcomes in ADHD: A Road Map for MCOs

As a means of improving patient outcomes in ADHD, MCOs should seek to optimize care in every phase of the treatment continuum—from diagnosis to follow-up. However, before a patient can even be diagnosed with the disorder, an ongoing relationship must exist between the provider and the patient that fosters trust and a cooperative approach to care where the patient takes an active role in ensuring treatment success. The patient-centered medical home (PCMH) is such a model for care where each patient has an ongoing relationship with a personal physician who leads a team that takes collective responsibility for patient care, including arranging for appropriate care with other qualified physicians and specialists.²¹ Serving as a “command center” from which care is planned and directed, the PCMH provides an ideal setting for applying the first steps in adequate care—diagnosis and treatment selection—and culminating in the implementation of interventions to promote adherence to the therapy selected.

Diagnosis and Treatment Selection

Accurate diagnosis and appropriate treatment are hallmarks of interventions for improving outcomes in any disease or condition; however, certain

inherent characteristics of psychiatric conditions such as ADHD require special consideration in managed care in light of their divergence from often more common, nonbehavioral illnesses. Psychiatric disorders provide a particular challenge in that many providers in the primary care setting lack the formalized training necessary to optimally diagnose and treat patients with these conditions; this is a unique challenge in the behavioral health specialty, where primary care physicians (PCPs) are often called on to act as specialists as opposed to referring patients to an actual specialist, which is typically the case for conditions specific to other specialties, such as oncology or neurology.⁷ Furthermore, the standard organization and routing of care to specialty providers within conventional MCOs offers little assistance in alleviating this apparent disconnect. In fact, diverting patients with psychiatric conditions to more appropriately trained professionals within managed behavioral health often results in the fragmentation of care due to the most commonly employed systems of resource allocation and benefit design in the current managed care landscape. Fortunately, a number of options exist for stakeholders seeking to overcome the barriers to optimal care for patients with psychiatric conditions, such as proven assessment scales, which aid PCPs in diagnosis, and treatment algorithms and guidelines, which aid in guiding appropriate treatment.^{5,8,9}

With no clear-cut biological diagnostic markers, patients with ADHD and other psychiatric disorders are more difficult to diagnose than their nonpsychiatric counterparts. Whereas the presence and severity of nonbehavioral conditions, such as diabetes and cardiovascular disease, may be established by assessing levels of hemoglobin A1C and low-density lipoprotein cholesterol, respectively, or other similarly well-defined markers, the diagnosis of ADHD is more subjective and less absolute. Still, the symptoms of ADHD are well characterized, particularly in children, and easy to elicit from parents and teachers. The diagnostic process is more complicated for adults, especially when parents or previous school or medical records are unavailable.

As a means of simplifying the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)* criteria and creating a much-needed, more user-friendly interface for the

diagnosis of ADHD in patients in the primary care setting, several rating scales have been developed by various organizations and academic institutions that quantify the symptoms of ADHD in an easy-to-use, question-and-answer format.²² Three different sets of these rating scales exist—1 for each of the 3 different subsets of patients with ADHD: children, adolescents, and adults.^{5,8,9} Although each of these sets of rating scales is based on the universal *DSM-IV-TR* criteria for ADHD, each is also tailored toward the unique presentation of ADHD symptoms in their respective age group.

The sets of rating scales for children and adolescents typically include questions regarding the patient's functioning in the academic setting, since this is where the symptoms of ADHD are most burdensome and evident in school-aged patients.^{8,9} Furthermore, the childhood and adolescent scales typically focus on parents and/or teachers as the primary respondent, since these parties are best equipped to provide an objective opinion on behavior and academic functioning in younger patients who may not fully understand the line of questioning or appreciate the importance of candid and honest answers.^{8,9} Some adolescent scales, however, query the patient directly, because adolescents are more advanced from a maturity and developmental standpoint. The childhood and adolescent scales currently in common practice for the diagnosis of ADHD include the following^{8,9}:

Childhood Rating Scales

- National Initiative for Children's Healthcare Quality (NICHQ) Vanderbilt Assessment Scales—PARENT and TEACHER Information and Follow Up
- Attention Deficit Hyperactivity Disorder Rating Scale (ADHD-RS)
- Conners' Parent Rating Scale (1997) Revised Version: Long Form, ADHD Index Scale (CPRS-R:L ADHD Index)
- Conners' Teacher Rating Scale (1997) Revised Version: Long Form, ADHD Index Scale (CTRS-R:L ADHD Index)
- Conners' Parent Rating Scale (1997) Revised Version: Long Form, *DSM-IV* Symptoms Scale (CPRS-R:L *DSM-IV* Symptoms)
- Conners' Teacher Rating Scale (1997) Revised Version: Long Form, *DSM-IV* Symptom Scale (CTRS-R:L *DSM-IV* Symptoms)

- Barkley's School Situations Questionnaire-Original Version (1989) Number of Problems Settings Scale (SSQ-O-I)
- Barkley's School Situations Questionnaire-Original Version (1989) Mean Severity Scale (SSQ-O-II)
- Swanson, Nolan, and Pelham Rating Scale (1992): Version 5 (SNAP-IV)

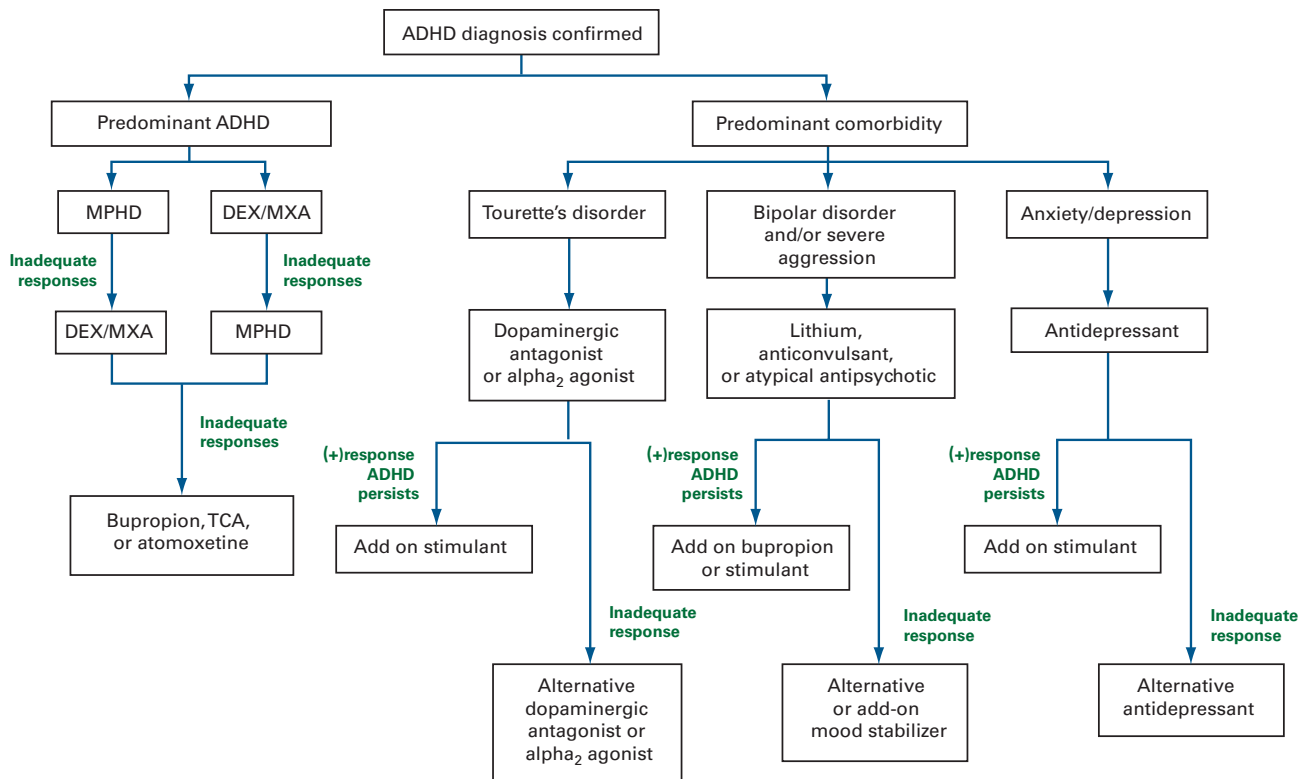
Adolescent Rating Scales

- Attention Deficit Hyperactivity Disorder Rating Scale (ADHD-RS)
- Brown Attention Deficit Disorder Scales
- Child Attention Profile
- Conners' Parent Rating Scale (revised)
- *DSM-IV* Behavior Checklists
- Attention Problems Scale-Teacher Report Form
- Behavior Assessment System for Children (BASC) Parent Rating Scale
- Child and Adolescent Service Center (CASC) Teacher Rating Scale
- Child Behavior Checklist
- Conners-Wells' Adolescent Self-Report Scale

Differing from the sets of childhood and adolescent rating scales, the set of ADHD rating scales for adults focuses on the patients themselves as the primary respondents.⁵ These scales feature a similar question-and-answer format, with responses being quantified to a corresponding score to determine a diagnosis of ADHD; however, as patients in this age group have typically advanced beyond the traditional academic setting, the questions are directed toward assessing symptoms in a workplace setting or in other adult-specific scenarios.⁵ The adult scales currently in common practice for the diagnosis of ADHD include the following⁵:

Adult Rating Scales

- Brown Attention Deficit Disorder (ADD) Scale
- Conners' Adult ADHD Rating Scale (CAARS)
- Wender-Reimherr Adult Attention Deficit Disorder Scale
- Barkley's Current Symptoms Scale
- Adult Self-Report Scale V1.1
- Adult Investigator Symptom Report Scale (AISRS)

■ **Figure.** ADHD Treatment Algorithm Accounting for Predominant Disorder or Comorbidities

ADHD indicates attention-deficit/hyperactivity disorder; DEX, dextroamphetamine; MPHD, methylphenidate; MXA, mixed-salts amphetamine; TCA, tricyclic antidepressant.

Reprinted with permission from Dopheide JA, Theesen KA, Malkin M. Psychiatric disorders of childhood treatments. DiPiro JT, et al, eds. *Pharmacotherapy: A Pathophysiological Approach*. 6th ed. New York, NY: McGraw-Hill; 2005:1145-1154.

Once the diagnosis of ADHD is made, PCPs may still require guidance in choosing appropriate targets for therapy, which take each individual's symptoms, level and duration of impairment, and comorbidity into account. Rationally derived treatment algorithms have been developed by the American Academy of Pediatrics (AAP) and the American Academy of Child and Adolescent Psychiatry (AACAP) that provide systematic and stepwise treatment recommendations.^{8,9} These valuable tools can assist the prescriber who has had little formal training in diagnosis and treatment of ADHD.²³ Similarly, treatment guidelines serve the same role as treatment algorithms in guiding the evidence-based and appropriate treatment of a disease or condition. However, whereas treatment algorithms typically provide this information in a simplified graphic format, treatment guidelines are often presented in the form of a full-text document. The 2 most prominent guidelines for the treatment

of ADHD in children and adolescents were published by the AAP and AACAP, respectively.^{8,9} At present, no nationally recognized treatment guidelines exist for the treatment of ADHD in adults. It is important to note that both treatment algorithms and treatment guidelines may be adopted from an outside source such as a professional organization or generated within a health plan for distribution to the provider network. In either case, these evidence-based considerations should serve as the foundation for a step-therapy model that can be promoted by plans and serve as a general guideline to providers for making decisions on the most extensively documented clinically and cost-effective form of treatment: pharmacotherapy.

Dictated by existing algorithms and treatment guidelines, the general approach for a step-therapy model in patients with ADHD should be based on the selection of a primary psychostimulant, followed by another psychostimulant trial in the event

of an inadequate response (Figure).²³ If a second psychostimulant provides an inadequate response or poor tolerability after trials of wide dosing ranges, nonstimulant pharmacotherapy should be selected. In patients with psychiatric comorbidities, or in patients in whom there are substance abuse concerns, alternative courses of therapy may be considered, such as nonstimulant pharmacotherapy or behavioral interventions as first-line treatment (Figure).²³ Combining pharmacotherapy with medication is often helpful when there is significant comorbidity and a wide range of symptoms and impairments that extend beyond ADHD.²⁴

Promoting Treatment Adherence

Given the high prevalence of ADHD among children and adolescents and the potential for the disorder to persist into adulthood, managed care stakeholders need to develop a strategy for the effective long-term management of this chronic condition. Once an accurate diagnosis of ADHD has been made and an appropriate treatment has been selected, this effective long-term management should be based on initiatives to monitor and promote treatment adherence. This management includes not only adherence to prescribed pharmacotherapy, but also adherence to behavioral interventions and provider follow-up. Without appropriate adherence to therapy, treatment cannot be optimized and little to no improvement in outcomes will be realized.

Education forms the foundation on which treatment adherence is based: If a patient does not fully realize and understand the proven benefits and potential adverse effects associated with a particular treatment, he or she may be more likely to discontinue therapy or adhere to therapy in an inconsistent manner.¹¹ The physician's office is the most ideal setting in which to deliver this crucial information, since PCPs often have the trust and undivided attention of a patient during these visits. Office visits are also crucial for assessing treatment success and adherence and managing potential adverse events associated with therapy. The office setting is also an area that has demonstrated significant need for improvement in the treatment of ADHD. Researchers in one study reported that only 25% of patients have a follow-up visit with their PCP in the 30 days following their first prescription for the

treatment of ADHD, and this number is only 4% higher in psychiatric settings.²⁵ Furthermore, only 53% of physicians surveyed reported routine follow-up visits for children diagnosed with ADHD.²⁶

The NCQA's HEDIS measure for Follow-Up Care for Children Prescribed ADHD Medication is one example of a quality initiative currently in use for improving medication and follow-up adherence.¹⁰ The measure is defined in 2 parts¹⁰:

- Percentage of children aged 6 to 12 years with a prescription for ADHD medication who had 1 follow-up visit with a practitioner during the 30-day initiation phase
- Percentage of children aged 6 to 12 years with a prescription for ADHD medication who remained on the medication for at least 210 days and had at least 2 additional follow-up visits with a practitioner within 9 months after the end of the initiation phase

While current performance for both components of the measure remains modest, with 33.7% and 38.7% of participating commercial plans achieving compliance for the initiation and continuation/maintenance phases, respectively, it remains a valuable tool for assessing the quality of care for patients with ADHD in terms of follow-up and medication adherence (Table).¹⁰ Before the introduction of the measure, no nationally accepted standard existed for plans to determine their performance in these 2 components of care for patients with ADHD.

Considering the value of the NCQA HEDIS measures for the treatment of ADHD as a means of monitoring and improving follow-up adherence, plans should seek interventions to improve provider adherence to these 2 components of care. Rewarding provider performance in the measures serves as an ideal starting point, by encouraging PCPs to apply the measures through an incentive-based program. Incentives may be either financial, such as bonuses or adjusted fee schedules, or nonfinancial, such as public performance reporting and honor rolls. Regardless of their nature, these incentives must be adequate enough to make physicians take notice and adjust their behavior and clinical practices accordingly.

In addition to follow-up adherence, medication adherence remains a primary concern in the treatment of patients with ADHD, as evidenced by its inclusion in the NCQA's HEDIS measure.¹⁰

However, while medication adherence is a critical component of optimal care, according to one survey, only 36% of adults with ADHD reported taking a prescription medication for the disorder.⁶ Still, a number of interventions are available for managed care stakeholders as a means of resolving this issue of poor adherence to ADHD pharmacotherapy, such as patient education, extended-release formulations of medications, and adherence monitoring.^{11,27}

As mentioned previously, patient education serves as the foundation of any initiative to improve medication adherence.¹¹ By providing patients with the necessary information regarding the benefits and potential adverse effects of their prescribed therapy, MCOs can target the single most influential party in determining medication adherence: the patients themselves.¹¹ While these educational interventions can be targeted directly at adult patients when treating that particular age group, parents or guardians are likely better suited for understanding and applying education provided in the treatment of children or adolescents with ADHD. Furthermore, parents or guardians typically have a significant influence over the behavior of child or adolescent patients, making them ideal for educational initiatives promoting treatment adherence in these younger age groups.²⁸ This approach has yielded promising results, particularly in one study where parents who were more knowledgeable about ADHD were more likely to enroll their children in both pharmacologic and nonpharmacologic treatments.²⁸ Other studies have likewise concluded that education can encourage active participation in treatment, enhance adherence to treatment regimens, and provide patients and families with important coping skills.²⁹

Although effective in promoting medication adherence, patient/parent education alone is not sufficient to address the adherence challenges associated with the treatment of ADHD. Helping patients and their families feel comfortable disclosing their concerns and/or issues associated with taking ADHD medication as prescribed remains a significant challenge that can best be addressed through the building of patient–physician trust.³⁰ Even under the ideal clinical trial conditions of the Multimodal Treatment Study of Children with ADHD, nearly 50% of parents on one or more

■ **Table.** Performance in NCQA's HEDIS Measure for Follow-Up Care of Children Prescribed ADHD Medication¹⁰

| Initiation Phase: Trends, 2005-2007 | | |
|---|------------|----------|
| Year | Commercial | Medicaid |
| 2007 | 33.7 | 33.5 |
| 2006 | 33.0 | 31.8 |
| 2005 | 32.0 | 31.4 |
| Continuation and Maintenance Phase: Trends, 2005-2007 | | |
| Year | Commercial | Medicaid |
| 2007 | 38.7 | 38.9 |
| 2006 ^a | N/A | N/A |
| 2005 | N/A | N/A |
| ADHD indicates attention-deficit/hyperactivity disorder; HEDIS, Healthcare Effectiveness Data and Information Set; NCQA, National Committee for Quality Assurance. ^a The 2006 and 2005 specifications for the commercial and Medicaid phase of the ADHD measure misstated the denominator and will not be publicly reported. Source: National Committee for Quality Assurance. 2008. | | |

instances stated that their child was taking his or her ADHD medication as prescribed, while saliva assays indicated that their child had actually not taken the medication that day.³⁰ Regardless of the cause of patient nonadherence or the reason behind parents providing inaccurate information about their children's adherence, trust in the physician, as well as the physician's ability to set patients and parents at ease to talk about these issues, is paramount.

In addition to educating patients and developing strong patient–physician relationships, the prescribing of recently introduced extended-release formulations of stimulants for the treatment of ADHD has proven effective in improving medication adherence. In fact, the simplified dosing realized through the once-daily administration of these agents has demonstrated an advantage over stimulants dosed multiple times daily in several different measures of adherence. In a retrospective analysis, treatment with extended-release methylphenidate for patients with ADHD was associated with longer treatment periods, fewer switches in therapy, increased patient adherence, and a lower usage rate of emergency department services compared with initial treatment with the conventional immediate-release formulation of the drug.²⁷

Obviously, the aforementioned interventions for improving medication adherence are wasted on

patients who are already compliant with therapy, necessitating a means of distinguishing adherent patients from nonadherent patients. Furthermore, by determining which patients to target with initiatives promoting medication adherence, managed care stakeholders can optimize their investment in such interventions. Adherence monitoring methods such as pharmacy database monitoring is one such means of identifying nonadherent patients that is based on an information technology–driven review of pharmacy claims data to determine which patients fail to fill their prescriptions in the allotted time period. One shortcoming of this method, however, is that it is based on the assumption that patients who regularly refill their medications are actually taking the drug, as opposed to throwing it away, saving it, or giving or selling it to someone else. In the treatment of patients with ADHD, where drug diversion of prescribed therapies is a real concern, the possibility that patients may be throwing, saving, or giving or selling their medication may be the case among many patients who appear to be adherent to therapy. The Schedule II distinction assigned to most of the stimulants prescribed for the treatment of ADHD features a number of safeguards against this diversion and other forms of abuse—such as mandatory hard-copy prescriptions, a no-refill mandate, and drug supplies limited to 30 days—but caution should still be exercised.

Conclusion

Patients with ADHD present a significant cost burden in managed care and on the economy in general, through reduced workplace productivity, an increased incidence of accidents, and increased criminal activity among individuals with ADHD; beyond these economic concerns, the disorder results in substantially reduced quality of life for many patients. Although once considered a childhood disorder, available data have demonstrated the chronicity of the condition across several different age strata, highlighting a significant need for quality-enhancing initiatives in managed care. Further validating the need for quality improvement is the unique and complex nature of ADHD as a psychiatric condition and one that many providers are poorly equipped to diagnose and treat in the primary care setting.

A number of potential interventions are available to managed care stakeholders for addressing the aforementioned concerns associated with the disorder. Proven rating scales and evidence-based treatment algorithms and guidelines serve to simplify the diagnosis and treatment of patients with ADHD by PCPs, thereby assisting them in making accurate determinations and sound clinical decisions. Treatment (ie, medication and follow-up) adherence, a component of care that has been demonstrated as being paramount to improved patient outcomes, likewise plays a role in the quality of care for patients with ADHD and should be fostered by means such as patient education, the NCQA HEDIS measures, the prescribing of extended-release formulations of stimulants, and pharmacy database monitoring. While such interventions will likely come at a significant cost for MCOs, the cost of inadequate or suboptimal care may prove to be even greater.

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Address correspondence to: Neil B. Minkoff, MD, Medical Director, Network Medical Management and Pharmacy, Harvard Pilgrim Health Care, 93 Worcester St, Wellesley, MA 02481. E-mail: neil_minkoff@harvard.pilgrim.org.

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Getting to Goal: Managed Care Strategies for Children, Adolescents, and Adults With ADHD

Instructions

There are no fees for participating in and receiving CME credit for this activity. During the period May 15, 2009, through November 30, 2010, participants must (1) read the learning objectives and faculty disclosures; (2) study the educational activity; (3) complete the posttest by recording the best answer to each question in the answer key on the evaluation form; (4) complete the evaluation form; and (5) mail or fax the evaluation form with answer key to:

Postgraduate Institute for Medicine
367 Inverness Parkway
Suite 215
Englewood, CO 80112
Fax: 303-790-4876

A statement of credit will be issued only upon receipt of a completed activity evaluation form and a completed posttest with a score of 70% or better. Your statement of credit will be mailed to you within 3 weeks.

Release date: **May 15, 2009**

Expiration date: **November 30, 2010**

PHYSICIAN CONTINUING MEDICAL EDUCATION

Accreditation Statement

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Postgraduate Institute for Medicine (PIM) and Impact Education, LLC. PIM is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation

Postgraduate Institute for Medicine designates this educational activity for a maximum of 1.5 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

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Accreditation Statement



Postgraduate Institute for Medicine is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

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Postgraduate Institute for Medicine designates this continuing education activity for 1.5 contact hours (0.15 CEUs) of the Accreditation Council for Pharmacy Education. (Universal Activity Number-809-999-08-254-H01-P)

Estimated time to complete activity: 1.5 hours.

After reading "Getting to Goal: Managed Care Strategies for Children, Adolescents, and Adults With ADHD" complete the program evaluation and select the 1 best answer to each of the following questions.

1. Childhood ADHD persists into adulthood in _____ of individuals.

- a. ~10%
- b. ~25%
- c. ≥50%
- d. ≥75%

2. Which type of ADHD constitutes less than 15% of all cases and predominates in childhood?

- a. Hyperactive-impulsive
- b. Hyperactive
- c. Impulsive
- d. Inattentive

3. Vocational or academic underachievement/failure, “risky” behavior, substance abuse disorders, and criminal activity are examples of the presentation of ADHD in:
- Adolescents
 - Adolescents and adults
 - Children
 - Children and adolescents
4. Which of the following serve as the informants in most childhood ADHD rating scales?
- Patients
 - Parents
 - Teachers
 - Both b and c
5. As high as 90% of children respond to which type of pharmacotherapy with minimal side effects?
- Stimulants
 - Nonstimulants
 - Antidepressants
 - Antipsychotics
6. Which of the following is a safeguard built into the Schedule II designation assigned to most stimulant medications prescribed for ADHD?
- 30-day supply limit
 - No refills
 - Hard-copy prescriptions
 - All of the above
7. The behavioral interventions employed in the treatment of adult ADHD typically centered on a(n) _____ component.
- Educational
 - Chemical
 - Creative
 - Pragmatic
8. According to the National Committee for Quality Assurance’s (NCQA) Healthcare Effectiveness Data and Information Set (HEDIS) measure for Follow-Up Care for Children Prescribed ADHD Medications, what is the goal for follow-up visits during the 9-month continuation and maintenance phase?
- ≥ 1
 - ≥ 2
 - ≥ 3
 - ≥ 4
9. Approximately what percentage of individuals with ADHD indicated that they have lost or changed jobs due to their disorder?
- 30
 - 40
 - 50
 - 60
10. Compared to treatment with immediate-release methylphenidate, which of the following agents was associated with longer treatment periods, fewer switches in therapy, increased patient adherence, and a lower usage rate of emergency department services in a retrospective analysis?
- Atomoxetine
 - Dextroamphetamine
 - Bupropion
 - Extended-release methylphenidate

OUTCOMES SURVEY

To what extent do you agree with the following statements?

(Please circle the appropriate number on the scale.)

1. When prescribing ADHD medications, current ADHD treatment guidelines recommend extended-release formulations of stimulants over immediate-release preparations.

Strongly disagree

1

2

3

4

5

6

Strongly agree
2. There are validated assessment tools to aid in the diagnosis of ADHD for adults presenting with symptoms in accordance with *DSM-IV* criteria.

Strongly disagree

1

2

3

4

5

6

Strongly agree
3. For patients with ADHD and no predominant psychiatric comorbidities, stimulant pharmacotherapy is the most clinically desirable and cost-effective approach to care.

Strongly disagree

1

2

3

4

5

6

Strongly agree
4. Appropriate pharmacotherapy in children with ADHD is associated with reduced emergency department use and medical costs.

Strongly disagree

1

2

3

4

5

6

Strongly agree
5. During the titration phase of medication initiation in children and adolescents with ADHD, observations of the patient’s behavior should be sought from multiple sources in evaluating the effect of the medication.

Strongly disagree

1

2

3

4

5

6

Strongly agree
6. The use of pharmacy database monitoring assists in improving patient outcomes by tracking medication adherence in adult ADHD patients.

Strongly disagree

1

2

3

4

5

6

Strongly agree

EVALUATION FORM

Getting to Goal: Managed Care Strategies for Children, Adolescents, and Adults With ADHD
Project ID: 6066-ES-37

To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please take a few minutes to complete this evaluation form. **You must complete this evaluation form to receive acknowledgment for completing this activity.**

Please answer the following questions by circling the appropriate rating:

1 = Strongly Disagree 2 = Disagree 3 = Neutral 4 = Agree 5 = Strongly Agree

Extent to Which Program Activities Met the Identified Objectives

After completing this activity, I am now better able to:

- Describe the overall costs associated with ADHD and related comorbidities. 1 2 3 4 5
- Specify the clinical and financial impact of various ADHD treatment options. 1 2 3 4 5
- Describe a managed care road map for improving clinical and economic outcomes for ADHD. 1 2 3 4 5
- Cite recommendations for health plans to assist their providers with strategies to improve HEDIS performance scores for ADHD. 1 2 3 4 5
- Identify a step therapy model to provide appropriate drug therapy for ADHD treatment by managed care. 1 2 3 4 5

Overall Effectiveness of the Activity

The content presented:

- Was timely and will influence how I practice 1 2 3 4 5
- Enhanced my current knowledge base 1 2 3 4 5
- Addressed my most pressing questions 1 2 3 4 5
- Provided new ideas or information I expect to use 1 2 3 4 5
- Addressed competencies identified by my specialty 1 2 3 4 5
- Avoided commercial bias or influence 1 2 3 4 5

Impact of the Activity

Name 1 thing you intend to change in your practice as a result of completing this activity:

Posttest

Please list any topics you would like to see addressed in future educational activities:

Additional comments about this activity:

Follow-up

As part of our continuous quality improvement effort, we conduct postactivity follow-up surveys to assess the impact of our educational interventions on professional practice. Please indicate if you would be willing to participate in such a survey:

- ☐ Yes, I would be interested in participating in a follow-up survey.
- ☐ No, I'm not interested in participating in a follow-up survey.

If you wish to receive acknowledgment for completing this activity, please complete the posttest by selecting the best answer to each question, complete the evaluation for verification of participation, and fax to 303-790-4876.

Posttest Answer Key

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|----|
| | | | | | | | | | |

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For Physicians Only

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