

The Black Book of ADHD

David W. Goodman, MD

ABSTRACT

In 1998, the American Medical Association Scientific Counsel wrote that attention-deficit/hyperactivity disorder (ADHD) is “one of the best researched disorders in medicine”. Since then, rapidly emerging research coupled with increased interest by clinicians and the public have advanced the identification, diagnosis, and treatment of ADHD in patients of all ages. In treating patients with ADHD and their families, we hope that symptoms are reduced throughout the day leading to improved functioning, enhanced self-confidence, and better quality of life for all involved. Because of the volume of information, there is a need for clinicians to have rapid access to up to date reviews of clinically relevant information to assist in the accurate diagnosis and effective treatment of ADHD and associated psychiatric comorbidities. For the clinician, satisfaction comes from playing an instrumental role in facilitating this optimal outcome. This educational review presents information in brief text and tables for quick reference for the busy practitioner.

INTRODUCTION

“The Black Book of Attention-Deficit/Hyperactivity Disorder” is a concise presentation of rapidly accessible information important to clinicians diagnosing and treating these patients and their families. I have attempted to cull through the literature and present clinically relevant information in text and table format so that you can quickly find what you

FOCUS POINTS

- Diagnostic accuracy is increased by establishing age of onset of symptoms, chronicity of symptom course, presenting symptom threshold and impairments, and family history of attention-deficit/hyperactivity disorder while ruling out co-existing psychiatric disorders.
- Diagnostic prioritization facilitates instituting an effective treatment algorithm.
- Effective pharmacologic treatments take into consideration issues of safety, tolerability and adherence.
- Psychotherapeutic approaches are selected for the individual needs of the patient and family.

need to address the issues of the patient in front of you. I hope you find the format useful for the intended purpose and we welcome feedback for future editions.

Attention-deficit/hyperactivity disorder (ADHD) has been established as a valid psychiatric disorder in children for many years. In 1998, the American Medical Association Scientific Counsel wrote that ADHD is “one of the best researched disorders in medicine”.¹ The explosion of neuroimaging research in the past 10 years has demonstrated clear differences in the ADHD brain from dopamine receptor density in the basal ganglion² to morphologic differences in white matter,³ basal ganglion,⁴ and cerebellum⁵ to rate differences in the neurodevelopment of the frontal cortex.^{4,6} Heritability of 76% has been established with family, twin, and adoption studies.⁷ With a growing number of prospective longitudinal studies of ADHD children followed 10–20 years into adulthood,⁸ we have come to understand that up

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to 65% of these children will continue to have persistent and impairing ADHD symptoms. From these findings and epidemiologic data, the prevalence of ADHD in children is 7.8% (4.5 million)⁹ and 4.4% (9–10 million)¹¹ in adults in the United States. Of the children with ADHD, <60% have been treated in the past year while only <15% of the ADHD adults have been treated in the past year.¹⁰

The criteria for diagnosing ADHD and its subtypes are enumerated by the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision.¹¹ The original symptom criteria were field tested in children 5–17 years of age¹² and not in older patients with ADHD. Therefore, when diagnosing adults, clinicians and researchers have had to extrapolate the symptoms that appear at older ages. This clinical extrapolation has been aided by following children with ADHD into adolescence and adulthood to see which symptoms persist with impairment and which subside. With age, some patients develop compensatory skills to limit the interference they experience from their symptoms. Although impairments may not appear evident, these patients are often working harder daily to achieve what someone else achieves with little effort.

As individuals with ADHD ages, life presents ever-changing demands often requiring a greater ability to remember and organize daily tasks. Children with ADHD not diagnosed in childhood because they did not present with disruptive behavior or severe academic decline may face challenges later in life as the demands of adulthood exceed their ability to compensate. It is at this time they may present to clinicians with complaints of frustration, demoralization, anxiety, and depression. Given the high prevalence rate in children and adults relative to other psychiatric disorders, an ADHD assessment should be included in every initial mental health evaluation.

In recent years, research has focused on the concurrent psychiatric comorbidities that can complicate the diagnostic process. In children, oppositional defiant disorder and conduct disorder were commonly understood and identified. With emerging research, anxiety and mood disorders in children with ADHD have necessitated greater clinical acumen for accurate diagnoses. The same diagnostic complexities are introduced in older patients with ADHD. The onset of substance abuse, major depression, bipolar disorder, and anxiety disorders add a new dimension to developing a treatment algorithm in the presence of ADHD. Diagnostic prioritization of multiple concurrent disorders is necessary to construct a treatment algorithm. The goal is to effectively treat one disorder without worsening the other disorders. For children and adolescents, the American Academy of Child and Adolescent Psychiatry guidelines lay out a systematic approach to the treatment of ADHD and co-existing disorders. For adults, there are no such guidelines established.

Because of our understanding of ADHD as a potentially life-long disorder, the American Psychiatric Association committee working on diagnostic revisions for the forthcoming *DSM-V* will consider the research accumulating on the presentation of ADHD across the life span. This means that symptom descriptions will need to be age congruent and the threshold number of symptoms will be reconsidered. The age of onset before 7 years of age is likely to be increased because individuals with inattentive type are typically diagnosed after 7 years of age.¹³ However, remember that ADHD is a childhood disorder that may persist into adulthood so the age of onset needs to be set in childhood/early adolescence. The criteria of impairment in ≥ 2 domains is likely to remain because this is a disorder that impacts multiple domains of life. However, the degree of impairment and the domains may require greater clarification because adaptive skills, IQ, and environmental structure may alter the appearance of impairments.¹¹ The work to be done for the forthcoming *DSM-V* will greatly broaden and enhance our ability to identify ADHD accurately in all age groups.

This educational review has been divided into specific topics. “Neurobiology” reviews the epidemiology of child and adults with ADHD in the US and internationally, and a review of neuroimaging findings. “Diagnosis” presents the diagnostic criteria in the *DSM-IV-TR*; a review of extrapolated diagnostic criteria for adults; a list of ADHD rating scales for children, adolescents, and adults, and defines and reviews executive dysfunction and functional impact of ADHD. “Treatment Guidelines” reviews the current ADHD treatment guidelines for child, adolescent, and adults with ADHD established by the current meta-analyses of research findings; treatment algorithms for pure ADHD and ADHD with co-existing psychiatric comorbidities. “Treatment Options” provides a list of medications available and approved by the US Food and Drug Administration, a list of stimulant delivery vehicles, distinguishing efficacy from effectiveness of treatments, a review of complementary treatments and research findings in controlled studies, a review of current safety considerations and side effects for ADHD medications in age specific populations, and a review of psychotherapies employed.

The rapidly emerging research coupled with increased interest by clinicians and the public at large will advance the diagnosis and treatment of ADHD in patients of all ages. We hope that in treating patients with ADHD and their families symptoms are reduced throughout the day leading to improved functioning, enhanced self-confidence, and better quality of life for all involved. For you, the clinician, satisfaction comes from playing an instrumental role in facilitating this optimal outcome. I hope this article provides you with the assistance to achieve this goal.

CONCLUSION

With decades of research on childhood ADHD, the validity of the disorder is well substantiated. Although adult ADHD was presented in psychiatric literature in the mid-1970s, the emerging body of literature on ADHD across the lifespan has exploded in the last 2 decades. New technologies have allowed science to investigate genetic markers. Neuro-imaging has facilitated a better understanding of developmental, structural, molecular, and functional difference in the brains of children and adults with ADHD. Longitudinal studies have verified that 1 in 2 children with ADHD will continue to have impairing symptoms into adulthood. The negative consequences of untreated ADHD have been enumerated across the lifespan of patients with ADHD. High rates of psychiatric comorbidities add complexity to the diagnostic assessment and prioritization in order to formulate a thoughtful treatment algorithm. The psychiatric literature is extensive for clinical guidance when treating children; however there remains a paucity of adult studies that offer clinical guidance for the treatment of adults with ADHD and co-existing psychiatric disorders.

Efficacy trials for children have clearly demonstrated the benefits of medication and behavioral psychotherapies tailored to the specific symptoms and needs of the child and family. Although limited, a growing body of efficacy trials in adult ADHD over the past 20 years also demonstrates the benefit of medications and specific therapies. The specific approval of medications by the FDA in the past 7 years to treat adults with ADHD helps encourage the identification and treatment of these patients. Advances

in medication delivery systems have introduced different mechanisms in order to extend the duration of action. Safety issues have been recently highlighted by the FDA and physicians need to be knowledgeable about assessing medical risk factors in patients. With the treatment of adults versus children, physicians have new considerations in treatment like pregnancy, substance abuse, and poly-pharmaceutical treatment of concurrent medical conditions (ie, cardiovascular disease, diabetes, hypertension, pain syndromes). Patients often use complementary and alternative treatments without substantial controlled trial efficacy. The conceptual distinction between efficacy and effectiveness will become increasingly relevant as treatment comparative trials look at the economics of treatment.

Because formal training in ADHD is highly variable and virtually absent for adult ADHD, many physicians find they need to learn about this disorder in clinical practice. Summarizing this literature into clinically relevant and rapidly accessible information is critical to facilitating this educational pursuit. This article presents a portion of the tables and text from the book, in which you will find additional tables and information on rating scales, child treatment algorithms for comorbid disorders, and elaboration of Americans with Disabilities Act and Individual Education Plan criteria. This educational review presents the distillation of literature into clinical topics, and is written in table format for a fast read. The unique format of this article and its presentation of up-to-date clinically relevant information makes it a useful addition to the library of clinicians caring for ADHD patients and their families. **PP**

TABLE 1
PREVALENCE OF ADHD BY AGE^{9,10,25-33}

Child	8.7% United States ²⁵ 7.8% United States ⁹	6.7% United States ²⁶
Adolescent	16.4% China ²⁸	8.5% Finland ²⁷
Adult	4.4% United States ¹⁰ 7.3% France ²⁹ 5.2% United States ²⁹ 5.0% Netherlands ²⁹ 4.1% Belgium ²⁹ 3.1% Germany ²⁹	2.8% Italy ²⁹ 1.9% Colombia ²⁹ 1.9% Mexico ²⁹ 1.8% Lebanon ²⁹ 1.2% Spain ²⁹

Persistence of ADHD from Childhood to Adulthood

- 60% to 85% childhood into teen years³⁰⁻³²
- 46% by parent report; childhood into adulthood³³
- 49% to 54% using a developmental definition (<93rd percentile on symptoms relative to age-matched controls) of the disorder³³

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TABLE 2
FUNCTIONAL AND DEVELOPMENTAL DIFFERENCES IN ADHD BRAINS^{3,6,42,43}

<i>Neuroanatomy</i>	<i>Imaging Technique</i>	<i>Findings</i>
Differences in dopamine activity in caudate and limbic regions	PET	Reduced dopamine activity in response to MPH given intravenously
Neurodevelopmental trajectory	MRI	2-year delay in cortical thickening in medial and superior prefrontal and precentral regions
Differences in activation of neural networks for tasks	fMRI	Activation of bitemporal regions (controls activate dorsal anterior cingulate gyrus)

Although neuroimaging research has been able to show multiple differences in ADHD brains versus controls (both children and adults), these results have not yet demonstrated their utility in the clinical setting. At present, there is no support to use neuroimaging for diagnosis or treatment selection for ADHD in any age group.

PET=positron emission tomography; MPH=methylphenidate; MRI=magnetic resonance imaging; fMRI=functional magnetic resonance imaging.

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TABLE 3
DSM-IV CRITERIA FOR ADHD¹¹

I. Either A or B

A. At least six of the following symptoms of inattention have been present for at least 6 months to an extent that is disruptive and inappropriate for developmental level:

- Often does not give close attention to details or makes careless mistakes in work or other activities
- Often has trouble keeping attention on tasks or play activities
- Often does not seem to listen when spoken to directly
- Often does not follow instructions and fails to finish duties in the workplace (not due to oppositional behavior or failure to understand instructions)
- Often has trouble organizing activities
- Often avoids, dislikes, or does not want to do things that take a lot of mental effort for a long period of time
- Often loses things needed for tasks and activities
- Is often easily distracted
- Is often forgetful in daily activities

B. At least six of the following symptoms of hyperactivity-impulsivity have been present for at least 6 months to an extent that is disruptive and inappropriate for developmental level:

Hyperactivity

- Often fidgets or squirms in seat
- Often gets up from seat when remaining in seat is expected
- Often feels very restless
- Often has trouble enjoying leisure activities quietly
- Is often “on the go” or often acts as if “driven by a motor”
- Often talks excessively

Impulsivity

- Often blurts out answers before questions have been finished
- Often has trouble waiting one’s turn
- Often interrupts or intrudes on others

II. Some symptoms that cause impairment were present before 7 years of age

III. Some impairment from the symptoms is present in two or more settings (eg, at school, work, and at home)

V. The symptoms do not happen 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

Based on these criteria, three subtypes of ADHD are identified:

- ADHD, combined type: if both criteria 1A and 1B are met for the previous 6 months
- ADHD, predominantly inattentive type: if criterion 1A is met but criterion 1B is not met for the previous 6 months
- ADHD, predominantly hyperactive-impulsive type: if criterion 1B is met but criterion 1A is not met for the previous 6 months

ADHD-residual type: diagnostic criteria achieved in childhood, however current symptoms do not reach diagnostic threshold criteria

ADHD-not otherwise specified: current symptoms reach diagnostic symptom threshold, however diagnostic threshold criteria were not reach in childhood

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TABLE 4
EXECUTIVE FUNCTION⁷⁰ AND DYSFUNCTION⁷¹

<i>Executive Functions</i>	<i>Description</i>
Set shifting	Changing activity or solution strategy (instead of doing something the same way over and over)
Planning/organizing	Managing current and future tasks
Working memory	Holding and manipulating information in one’s mind
Inhibition	Holding back from initial responses (ie, withholding judgment or doing what is expected rather than what one wants)
Initiation	Ability to get started (even on an undesirable task)
Task monitoring	Keeping track of behavior

Rates of Executive Dysfunction in Children and Adults With and Without ADHD			
	<i>ADHD+EF*</i>	<i>Non-ADHD Controls†</i>	<i>Outcomes vs. Controls</i>
Child	33%	12%	ADHD+EF: Higher risk of grade retention, LDs, lower academic achievement
Adult	31%	16%	ADHD+EF: Lower levels of education, occupation and overall SES

* Defined by 1.5 SD from mean of controls on more than two executive function measures. (Adjusted for gender, age, IQ, LD, and SES).

† Did not meet *DSM-IV* criteria for ADHD

EF=executive function; LD=learning disability; SES=social economic status; *DSM-IV*=*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*.

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TABLE 5
FUNCTIONAL IMPACTS OF ADHD

Children/Adolescents

Accidents/Injuries

- Higher risk of bicycle/pedestrian injury, head injury, multiple injuries, admissions to ICU⁷²

Educational

- Higher rates of grade retention⁸
- 8x higher risk for school expulsion or dropout⁷³
- Higher rates of associated learning disabilities⁸
- Lower rates of high school or college completion⁸⁹

Social

- Lack of friendships⁷⁴
- Less well liked by peers compared to non-ADHD peers⁷⁵
- Difficulty retaining peer status⁷⁶⁻⁷⁸

Substance/Alcohol/Tobacco

- 2x higher risk for tobacco smoking^{79,80}
- 2.5x higher risk for alcohol abuse
- 2x higher risk for substance abuse⁸⁰

Sexual Activity

- 4x more likely to have contracted an STD⁷⁸
- 10x higher risk for unplanned pregnancy⁸
- Higher risk for STDs and multiple partners⁸¹

Driving

- 2x to 6x higher rates of suspended or revoked driver's license, more traffic violations and speeding tickets, more motor vehicle accidents, and greater vehicular damage⁸²⁻⁸⁶

Medical costs

- 9 year median cost per person: \$4,306 (ADHD) versus \$1,944 (non-ADHD)⁸⁷

Adults^{82,88-91}

Education

- Less likely to finish college⁸⁹
- Lower educational attainment than patient IQ would predict⁹²

Marital/Social/Sex

- 4x higher risk to contract an STD⁸¹
- Nearly 2x higher risk of divorce/separation⁸⁹
- Less satisfied with social relationships⁸⁹
- Poorer relationship with their parents⁸⁹

Substance/Alcohol/Tobacco

- 2x to 3x higher rates of substance abuse disorder^{10,93}
- 2x to 3x higher rates of cigarette smoking⁹⁴
- Severity of ADHD symptoms associated with increased use of tobacco, marijuana, and alcohol into adulthood⁹⁵

Occupational/Workplace^{82,88-91}

- More likely to be fired from or quit a job impulsively
- Receive a lower salary⁸⁹
- Have poorer work performance scores
- More likely to have more frequent job changes over 10 years⁸⁹
- 3x more likely to be currently unemployed⁸⁹
- Lower occupational attainment than patient IQ would predict⁹²

Legal

- 2x more likely to have been arrested⁸⁹
- 3x more likely to be convicted⁹⁶
- 15x more likely to be incarcerated⁹⁶
- Greater tendency toward antisocial/criminal behavior⁸⁹

Financial

- Household income significantly lower than controls⁹⁰

Medical Costs

- Higher accident claims and significantly higher cost/accident: \$483 (ADHD) versus \$146 (controls)⁹⁷
- Family members of individuals with ADHD has 1.6 times more medical claims versus controls⁹⁸

Many of the differences are compared to age-matched controls and are statistically significant.

ICU=intensive care unit; STD=sexually transmitted disease.

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TABLE 6

ADHD AND COMORBIDITIES BY AGE GROUP

*The Preschoolers with ADHD Treatment Study (PATS)*⁹⁹
(n=302; 3–6 years of age)

ADHD alone	30.4%
ADHD plus oppositional defiant disorder	52.3%
ADHD plus communication disorder	21.9%
ADHD plus anxiety	12.3%
ADHD plus other comorbidities	4.3%

*Multi-modal Treatment Study (MTS)*¹⁰⁰
(n=579; 7–10 years of age)

ADHD alone	31%
ADHD plus oppositional defiant disorder	40%
ADHD plus anxiety disorder	34%
ADHD plus conduct disorder	14%
ADHD plus tic disorder	11%
ADHD plus mood disorder	4%

*National Comorbidity Survey Replication (NCSR)*¹⁰

(n=3,199; 18–44 years of age)

ADHD plus mood disorder (total)	38.3%
Bipolar disorder	19.4%
Major depression	18.6%
Chronic dysthymia	12.8%
ADHD plus anxiety disorder (total)	47%
Social phobia	29.3%
Posttraumatic stress disorder	11.9%
Panic disorder	8.9%
Generalized anxiety disorder	8.0%
Agoraphobia	4.0%
Obsessive-compulsive disorder	2.7%
ADHD plus substance use disorder	15.2%

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TABLE 7

CLINICAL QUESTIONS USED IN THE ASSESSMENT OF CARDIOVASCULAR RISK IN CHILDREN AND ADOLESCENTS WITH ADHD¹⁰³⁻¹⁰⁵

American Academy of Pediatrics recommendations (2008):

1. The AAP continues to recommend a careful assessment of all children, including those starting stimulants, using a targeted cardiac history and a physical examination, including a careful cardiac examination.
2. Given current evidence, the AAP encourages primary care and subspecialty physicians to continue currently recommended treatment for ADHD, including stimulant medications, without obtaining routine ECGs or routine subspecialty cardiology evaluations for most children before starting therapy with these medications.

Patient history:

1. History of fainting or dizziness (particularly with exercise)
2. Chest pain or shortness of breath with exercise
3. Unexplained, noticeable change in exercise tolerance
4. Palpitations, increased heart rate, or extra or skipped heart beats
5. History of heart murmur other than innocent or functional murmur or history of other heart problems
6. Intercurrent viral illness with chest pains or palpitations
7. Rheumatic fever
8. History of high blood pressure
9. Seizures
10. Current medications (prescribed and over the counter)
11. Health supplements (herbal, vitamins, sports drinks, etc)

Family history:

1. Sudden cardiac death or heart attack in members <35 years of age
2. Sudden or unexplained death in someone young
3. Sudden death during exercise
4. Cardiac arrhythmias
5. Hypertrophic cardiomyopathy or other cardiomyopathy, including dilated cardiomyopathy and right ventricular cardiomyopathy (right ventricular dysplasia)
6. Long-QT syndrome, short QT syndrome, or Brugada syndrome
7. Wolff-Parkinson-White syndrome or similar abnormal rhythm conditions
8. Event requiring resuscitation in young members (<35 years of age), including syncope requiring resuscitation
9. Marfan syndrome

AAP=American Academy of Pediatrics; ECGs=electrocardiograms.

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TABLE 8
EFFICACY VS. EFFECTIVENESS

	<i><u>Efficacy</u></i>	<i><u>Effectiveness</u></i>
Purpose	Determine treatment effect; submission to the FDA for disorder treatment indication	Care of patient and treatment of disorder/disease
Setting	Clinical trial, research center	Naturalistic, community setting
Subject Population	Recruited subjects	Referred patients
Inclusion Criteria	Specific diagnostic criteria by interview/screen	General clinical diagnostic impression for disorder/disease
Exclusion Criteria	No or limited comorbidities (medical or psychiatric)	Comorbidities included (medical or psychiatric) leading to greater clinical considerations
Study/Treatment Design	Single treatment without confounding variables	Treatment may be delivered with confounding variables (ie, other medications or concurrent disorders)
Subject Motivation	High due to study compensation and free service	Moderate because of treatment cost and perceived risk:benefit
Adverse Events	Spontaneous report by subjects; potential for underreporting	Specific side-effect questions; potential for more accurate assessment or over-reporting
Tolerance of Adverse Events	Higher due to study compensation and motivation to participate in a study	Low due to concern about side effects and medication cost
Statistic Measure	<i>P</i> value (<.05) (The event did not occur by chance)	Effect size (measures the magnitude of difference between active agent and comparator/placebo)
Compliance	High due to study compensation, free service, and participation in a study	Moderate due to medication cost and risk, expectation of benefit
Outcome	Optimized by dosing, a diagnostic specific, and motivated subject population	Possibly compromised by co-existing factors

As a clinician, it is important to understand two concepts that determine the benefits of treatments: efficacy and effectiveness. Efficacy and effectiveness are concepts to evaluate the degree of benefit a treatment offers a disorder/disease. However, the settings under which these conclusions are reached are very different. Trials for drug efficacy follow set guidelines that use recruited subjects who usually have no comorbidities so as to determine whether a treatment clearly works for a specific disorder/disease. Although efficacy is determined by this methodology, the clinicians often find that research subjects are infrequently the patients seen in clinical practice. Therefore, the outcome of the treatment in a practice setting may not be similar to the research outcome because of several confounding factors not considered during the research trial. For the clinician, understanding these differences allows for a clearer translation of clinical research findings into clinical practice. The Table enumerates the differences between efficacy and effectiveness.

FDA=Food and Drug Administration.

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TABLE 9
ADHD MEDICATION APPROVAL DATES BY THE FDA FOR ADOLESCENTS AND ADULTS¹¹⁰

<i><u>Drug</u></i>	<i><u>Active Constituent</u></i>	<i><u>FDA Approval Date</u></i>	<i><u>Drug</u></i>	<i><u>Active Constituent</u></i>	<i><u>FDA Approval Date</u></i>
ADHD medications approved by the FDA for the treatment of ADHD in adolescents			ADHD medications approved by the FDA for the treatment of ADHD in adults		
Adderall	Mixed amphetamine salts	2/13/1996	Strattera	Atomoxetine	11/26/2002
Concerta	Methylphenidate	8/1/2000	Adderall XR	Mixed amphetamine salts	8/14/2004
Methylin ER	Methylphenidate	9/5/2000	Focalin XR	Dexmethylphenidate	6/13/2005
Metadate CD	Methylphenidate	4/3/2001	Vyvanse	Lisdexamfetamine	4/24/2008
Adderall XR	Mixed amphetamine salts	11/10/2001	Concerta	Methylphenidate	6/28/2008
Focalin	Dexmethylphenidate	11/13/2001	No short-acting stimulant medication is approved by the FDA for the treatment of adults with ADHD.		
Ritalin LA	Methylphenidate	6/5/2002			
Strattera	Atomoxetine	11/26/2002			
Methylin chewable	Methylphenidate	4/15/2003			
Focalin XR	Dexmethylphenidate	5/26/2005			
Intuniv	Guanfacine hydrochloride	9/2/2009			

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TABLE 10
MEDICATIONS APPROVED BY THE FDA FOR ADHD^{34,58}

<i>Brand Name (Manufacturer)</i>	<i>Dose Form</i>	<i>Typical Starting Dose</i>	<i>FDA Max/Daily</i>	<i>Off-Label Max/Day</i>	<i>Comments</i>
<i>α2 agonist</i>					
Intuniv (Shire)	1, 2, 3, 4 mg tablets	1 mg	4 mg	Not yet known	Not a scheduled II medication. Consider in ADHD medication sensitive children, adjunct treatment, or concurrent tics; monitor for somnolence, headache, fatigue, GI upset, decreased BP, dizziness
<i>Amphetamine Preparations</i>					
<u>Short-acting</u>					
Adderall* (Shire)	5, 7.5, 10, 12.5, 15, 20, 30 mg tablets	3–5 years: 2.5 mg QD; ≥6 years: 5 mg QD-BID	40 mg	>50 kg: 60 mg	Short-acting stimulants often used as initial treatment in small children (<16 kg), but have disadvantage of BID-TID. Dosing to control symptoms throughout day. Once-daily, long-acting stimulants are now recommended as first line medication
Dexedrine* (GlaxoSmithKline)	5 mg capsules	3–5 years: 2.5 mg QD	40 mg	>50 kg: 60 mg	
DextroStat (Shire)	5, 10 mg capsules	≥6 years of age: 5 mg QD-BID	60 mg	>50 kg: 60 mg	
<u>Long-acting</u>					
Adderall XR* (Shire)	5, 10, 15, 20, 25, 30 mg capsules	≥6 years: 10 mg QD	30 mg	>50 kg: 60 mg	Longer acting stimulants offer greater convenience, confidentiality, and compliance with single daily dosing but may have greater problematic effects on daytime appetite and sleep; all three medications may be opened and sprinkled on soft foods
Dexedrine spansule (GlaxoSmithKline)	5, 10, 15 mg capsules	≥6 years: 5–10 mg QD-BID	40 mg	>50 kg: 60 mg	
Vyvanse (Shire)	20, 30, 40, 50, 60, 70 mg capsules	30 mg QD	70 mg	Not yet determined	
<i>Methylphenidate Preparations</i>					
<u>Short-acting</u>					
Focalin (Novartis)	2.5, 5, 10 mg capsules	2.5 mg BID	20 mg	50 mg	Short-acting stimulants often used as initial treatment in small children (<16 kg) but have disadvantage of BID-TID. Dosing to control symptoms throughout day. Once-daily long-acting stimulants are now recommended as first line medication
Methylin* (Mallinckrodt Pharma)	5, 10, 20 mg tablets	5 mg BID	60 mg	>50 kg: 100 mg	
Ritalin* (Novartis)	5, 10, 20 mg	5 mg BID	60 mg	>50 kg: 100 mg	
<u>Intermediate-acting</u>					
Metadate ER (UCB Pharma)	10, 20 mg capsules	10 mg QAM	60 mg	>50 kg: 100 mg	Longer acting stimulants offer greater convenience, confidentiality, and compliance with single daily dosing but may have greater problematic effects on daytime appetite and sleep
Methylin ER (Mallinckrodt Pharm)	10, 20 mg capsules	10 mg QAM	60 mg	>50 kg: 100 mg	
Ritalin SR* (Novartis)	20 mg	10 mg QAM	60 mg	>50 kg: 100 mg	
Metadate CD (UCB Pharma)	10, 20, 30, 40, 50, 60 mg	20 mg QAM	60 mg	>50 kg: 100 mg	Metadate CD and Ritalin LA caps may be opened and sprinkled on soft food
Ritalin LA (Novartis)	10, 20, 30, 40 mg	20 mg QAM	60 mg	>50 kg: 100 mg	
<u>Long-acting</u>					
Concerta (McNeil)	18, 27, 36, 54 mg capsules	18 mg QAM	72 mg	108 mg	Swallow whole with liquids; nonabsorbable tablet shell may be seen in stool.
Daytrana patch (Shire)	10, 15, 20, 30 mg patches	Begin with 10 mg patch QD, then titrate up by patch strength	30 mg	Not yet known	Recommended wear-time is 9 hours resulting in 12 duration of action. Daily placement by alternating hips. Erythematous rash may limit use
Focalin XR (Novartis)	5, 10, 15, and 20 mg capsules	5 mg QAM	30 mg	50 mg	Can be sprinkled on soft food
<i>Selective Norepinephrine Reuptake Inhibitor</i>					
Strattera (Eli Lilly)	10, 18, 25, 40, 60, 80, and 100 mg capsules	Children and adolescents <70 kg: 0.5 mg/kg/day for 4 days; then 1 mg/kg/day for 4 days; then 1.2 mg/kg/day; adult starting dose: 40 mg/day	Lesser of 1.4 mg/kg or 100 mg; adult therapeutic dose: 80–100 mg/day	Lesser of 1.8 mg/kg or 100 mg; adult trials to 120 mg	Not a schedule II medication Consider if active substance abuse or severe side effects of stimulant intolerance (mood lability, tics); give QAM or divided doses BID; do not open capsule; monitor closely for suicidal thinking and behavior, clinical worsening, or unusual changes in behavior

* Generic formulation available

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TABLE 11

MEDICATIONS USED FOR ADHD THAT ARE NOT APPROVED BY THE FDA FOR ADHD^{34,58}

<i>Generic Class/ Brand Name</i>	<i>Dose Form</i>	<i>Typical Starting Dose</i>	<i>Maximum Per Day</i>	<i>Comments (by compound)</i>
<i>Antidepressants</i>				
Bupropion Wellbutrin* (GSK, Teva)	75, 100 mg tablets	Lesser of 3 mg/kg/day or 150 mg/day	Lesser of 6 mg/kg or 300 mg, with no single dose >150 mg	Lowers seizure threshold; contraindicated if current seizure disorder. Bupropion lowers seizure threshold; the extended release preparations lower the risk; contraindicated if current seizure disorder Usually given in divided doses, BID for children, TID for adolescents, for both safety and effectiveness. In children and adolescents, the dosing is BID for all preparations In adults, bupropion is dosed BID, while SR and XL are dosed QAM to 300 mg; and split dose at 450 mg QD
Wellbutrin SR* (GSK, Allscripts)	100, 150, 200 mg tablets	150 mg	450 mg in adults	
Wellbutrin XL* (GSK, Pharma PAC)	150, 300 mg tablets	150 mg	450 mg in adults	
Imipramine Tofranil* (Mallinkrt Pharm, Sandoz)	10, 25, 50, 75 mg tablets	1 mg/kg/day	Lesser of 4 mg/kg or 200 mg	In children and adolescents, obtain baseline ECG before starting imipramine and nortriptyline
Nortriptyline Pamelor* (Sandoz, Mallinkrt Pharm); Aventyl* (Eli Lilly)	10, 25, 50, 75 mg capsules	0.5 mg/kg/day	Lesser of 2 mg/kg or 100 mg	In children and adolescents, obtain baseline ECG before starting imipramine and nortriptyline
<i>α2-Adrenergic agonists</i>				
May be used alone or as adjuvant to another medication for ADHD				
Clonidine Catapres* (Boehringer Ingelheim; Physicians TC)	0.1, 0.2, 0.3 mg tablets	<45 kg: 0.05 mg QHS; titrate in 0.05-mg increments BID, TID, QID; >45 kg: 0.1 mg QHS; titrate in 0.1- mg increments BID, TID, QID	27–40.5 kg: 0.2 mg; 40.5–45 kg: 0.3 mg; >45 kg: 0.4 mg	Effective for impulsivity and hyperactivity; tics worsening from stimulants; sleep disturbances Taper off to avoid rebound hypertension
Guanfacine Tenex* (ESP Pharma)	1, 2 mg tablets	45 kg: 0.5 mg QHS; titrate in 0.5-mg increments BID, TID, QID; > 45 kg: 1 mg QHS; titrate in 1-mg increments BID, TID, QID	27–40.5 kg: 2 mg; 40.5–45 kg: 3 mg; >45 kg: 4 mg	Effective for impulsivity and hyperactivity; tics worsening from stimulants Taper off to avoid rebound hypertension

* Generic formulation available.

GSK=GlaxoSmithKline; SR=sustained release; XL=extended release; ECG=electrocardiogram.

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TABLE 12
STIMULANT PREPARATIONS DELIVERY SYSTEMS

<u>Preparation</u>	<u>Stimulant</u>	<u>Description</u>	<u>Duration of Action for Children</u>
Liquid	Methylphenidate (Methylin), dextroamphetamine (Liquadd)	Liquid, immediate delivery	3–4 hours
Immediate release tablet	Methylphenidate (Ritalin, Metadate, Methylin), dexamethylphenidate (Focalin), dextroamphetamine (Dexedrine), mixed amphetamine salts (Adderall)	No delivery system; immediate delivery	3–4 hours
Chewable tablet	Methylphenidate (chewable Methylin)	No delivery system; immediate delivery	3–4 hours
Slow Release Matrix	Methylphenidate SR (Ritalin SR)	Wax matrix	4–6 hours
Beaded*	Mixed-amphetamine salts XR (Adderall XR); methylphenidate (Metadate CD); dextro-amphetamine (Dexedrine spansules)	Double-beaded; immediate-release bead followed by 2nd release 4 hours later; ph-dependent polymer	Up to 12 hours
SODAS*	Dexamethylphenidate XR (Focalin XR), methylphenidate LA (Ritalin LA)	SODAS® (Spheroidal Oral Drug Absorption System); immediate release bead then 2nd release bead later	Up to 12 hours
OROS	Methylphenidate OROS (Concerta)	OROS® (Oral Release Osmotic System; osmotic push device delivers MPH with an ascending pharmacokinetic profile over 8 hours	Up to 12 hours
Patch	Methylphenidate patch (Daytrana)	DOT® (Delivery Optimized Thermodynamics) Matrix transdermal system; cutaneous gradient diffusion	Variable depending on wear time; 12 hours with 9-hour wear time
Prodrug†	Lisdexamfetamine (Vyvanse)	No delivery system; duration of action determined by enzymatic hydrolysis of lysine from dextroamphetamine	Up to 13 hours



The preparation (vehicle of delivery) determines the rate of absorption of the stimulant into the circulation and this determines the duration of action of the medication. The half-life of the compound always remains the same regardless of the vehicle of delivery as it is established once the compound is metabolized in the blood circulation. Adverse events may be related to the compound and/or the preparation. Side effect intolerance to one preparation may not predict sensitivity to another preparation of the same compound. Given the broad range of available preparations, clinicians should be able to find an appropriate choice for their patient.

* Can be sprinkled on soft food

† Can be dissolved in water; duration of action remains the same

SR=sustained release; ER=extended release; LA=long-acting.

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TABLE 13
CYP INHIBITORY EFFECTS OF ADHD MEDICATIONS¹¹³

<i>Medication</i>	<i>1A2</i>	<i>2C9</i>	<i>2C19</i>	<i>2D6</i>	<i>3A4</i>
Amphetamine	0	0	0	0	0
Methylphenidate	0	0	0	0	0
Atomoxetine	0	0	0	0*	0
Bupropion	?	?	?	+++	?
Desipramine	0	0	0	0	0

The table represents the potential for pharmacokinetic drug interactions, potential inhibitory effects of ADHD medications on the CYP enzymes and the resultant pharmacokinetic inhibition of other substrates. Because patients may be taking multiple medications, it is useful to anticipate changes in drug metabolism because this may lead to unintended side-effects. This table demonstrates that only bupropion has clinically relevant potential inhibitory effects on any medication that is metabolized by CYP 2D6. The addition of a drug metabolized by CYP 2D6 to bupropion would likely cause elevated drug blood levels that might result in unexpected side-effects. Except for bupropion, there appears to be no likely inhibitory kinetic drug interaction with ADHD medications and other drugs. This only accounts for kinetic (metabolism) interactions not pharmacodynamic interactions where two drugs interact at related receptor sites (potential of tremor with caffeine and stimulant might have an additive effect when used together).

* *in vivo*

CYP=cytochrome P450; 0=no inhibition; +++=clinically significant inhibition.

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TABLE 14
PREGNANCY AND ADHD MEDICATIONS¹¹⁴⁻¹¹⁸

Category B*

- Guanfacine extended release

Category C†

- Amphetamines, methylphenidates, atomoxetine

Breast milk and breast-feeding

- Amphetamine and methylphenidates are detectable in breast milk
- Amphetamines have been detected in infant urine
- The AAP considers amphetamines a contraindication for breastfeeding
- It is not known whether guanfacine is excreted into breast milk

* The maximum recommended human dose of 4 mg/day on a mg/m² basis resulted in no evidence of harm to the fetus. There are no adequate and well-controlled studies of guanfacine in pregnant women.

† Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

AAP=American Academy of Pediatrics.

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TABLE 15
COMPLIMENTARY AND ALTERNATIVE MEDICINE TREATMENTS FOR CHILDHOOD ADHD^{119,120}

CAM treatments are defined as any treatment other than traditional treatments with prescription medication and/or psychotherapies. Complementary treatment means that it is used in combination with traditional treatments. Alternative treatment means that it is used in lieu of traditional treatment. The use of these treatments as an alternative to traditional treatments may delay the start of effective measures. The use of CAM treatments for ADHD in children ranges from 12% to 64%.¹¹⁹⁻¹²² Interestingly, only 11% of parents revealed to the physician using CAM with their child.¹²² Many factors contribute to its continued use despite poor quality research and lack of positive findings. Both physicians and parents may delay the use of prescription medications because of a prejudice fueled by information highlighting safety considerations. When using CAM treatments, time frames and target symptoms should be established in order to judge the benefits, as with any treatment in medicine. In order to assess efficacy with high quality data, the following table only includes well designed, controlled trials or reviews of multiple studies.

<i>Agent</i>	<i>Ages (years)</i>	<i>N</i>	<i>Trial Design</i>	<i>Outcome</i>
Homeopathy ¹²³	6–12	43	Randomized, double-blind, randomized, controlled vs. placebo, 18 weeks	No significant differences on Conner's Global Index-Parent, Conner's Global Index-Teacher, Conner's Parent Rating Scale-Brief, Continuous Performance Test, and the Clinical Global Impression Scale.
Homeopathy ¹²⁵	6–16	62	Initial responders were randomized, placebo controlled, 14 weeks	Except for a very small significant improvement on CGI parent ratings in the Frei study, there was no benefit of homeopathic treatment in these trials
Homeopathy ¹²⁶	Mean age=10	43	Quasi-randomized, placebo controlled, 30 days, treatment changes at 10 day intervals	
Homeopathy ¹²⁷	7–10	20	Randomized, placebo controlled, compared with MPH, 60 days	
Homeopathy ¹²⁸	Mean age=9	43	Randomized, placebo controlled, 12 weeks	
Hypericum perforatum (St John's wort) ¹²⁴	6–17	54	Randomized, double-blind, randomized, controlled vs. placebo, 8 weeks	No significant difference on the ADHD-RS IV
Pycnogenol ¹²⁹	Children	61	Randomized, placebo controlled trial, 4 weeks	Significant findings on parent and teacher ratings
Pycnogenol ¹³⁰	Adults	24	Randomized, placebo controlled trial, MPH comparator, 3 week crossover design	No difference to placebo on all measures

TABLE 15

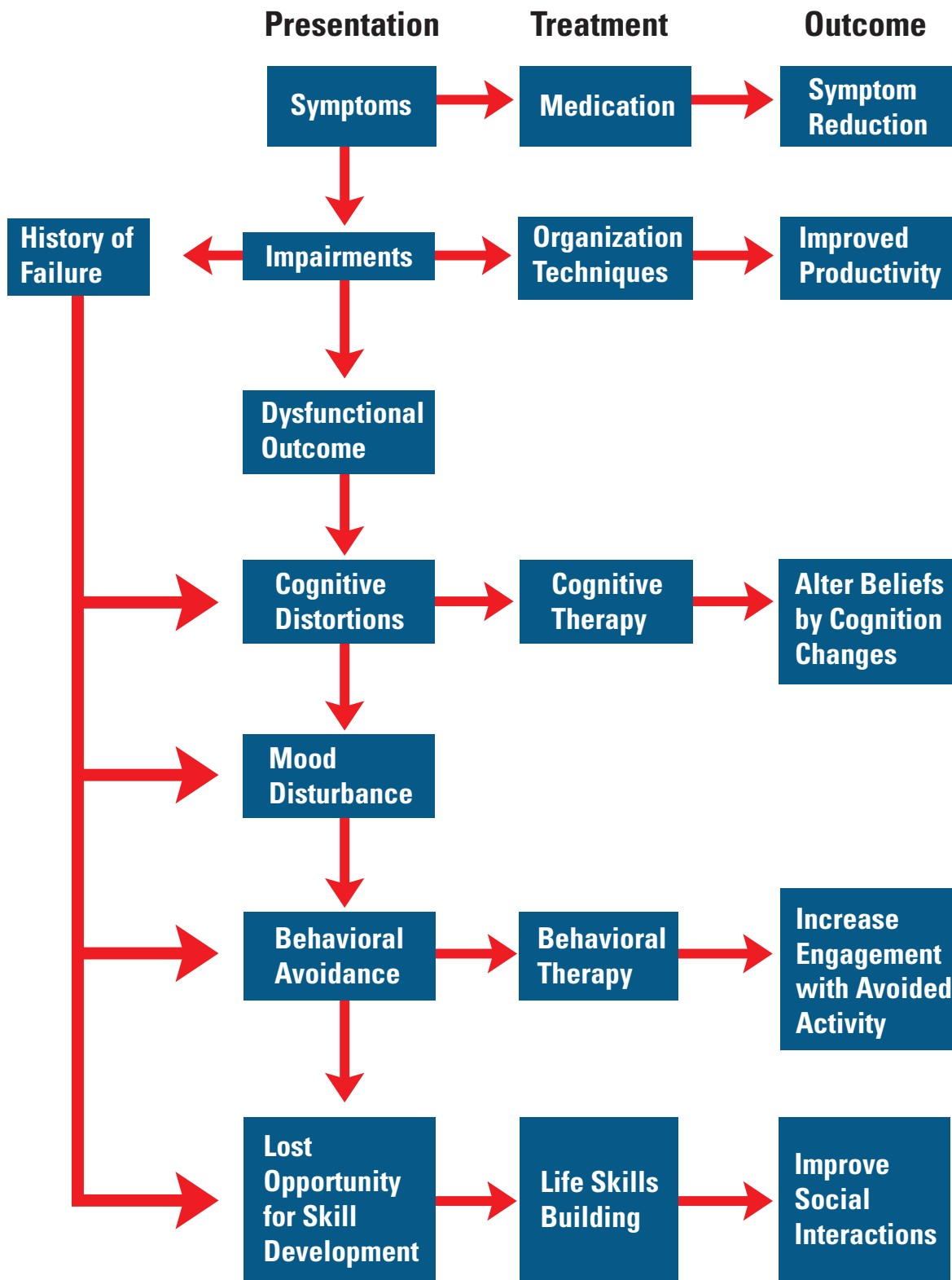
COMPLIMENTARY AND ALTERNATIVE MEDICINE TREATMENTS FOR CHILDHOOD ADHD (CONT.)^{119,120}

<i>Agent</i>	<i>Ages (years)</i>	<i>N</i>	<i>Trial Design</i>	<i>Outcome</i>
Feingold Diet ^{131,132}	Children	Largest trial N=40	Review of studies	Replication studies found no benefit
Sugar elimination ¹³³	Children		Review of studies	No association found
Megavitamins ¹³⁴	Children	41	Randomized, controlled, crossover trial, 24 weeks	No differences; elevated liver enzymes, significantly more disruptive classroom behavior with megavitamins; elevated liver enzymes
Omega fatty acids ¹³⁵	6–12	54	Randomized, placebo-controlled, augmentation study to stimulant treated subjects	No differences to placebo
Omega fatty acids ¹³⁶	6–13	50	Randomized, placebo-controlled trial; 16 weeks: some subjects medicated	No differences to placebo
Omega fatty acids ¹³⁷	6–12	40	Randomized, placebo-controlled trial; 8 weeks; 15% subjects medicated	No differences to placebo
Omega fatty acids ¹³⁸	8–12	29	Randomized, placebo-controlled trial, 12 weeks; ADHD with LDs	Significant differences on 7 of 14 scales used
Omega fatty acids ¹³⁹	7–12	132	Randomized, placebo-controlled trial, 12 weeks; crossover extension, 12 weeks	Significant differences on parent ratings, not teacher ratings, replicated in the crossover arm
Zinc ¹⁴⁰	Mean age=9.4	400	Randomized, placebo-controlled trial, 12 weeks	Significant differences to placebo
Zinc ¹⁴¹	Mean age=7.9	44	Randomized, placebo-controlled trial; subjects medicated	Significant differences to placebo
Iron ¹⁴²	5–8	23	Randomized, placebo-controlled trial, 12 weeks	Significant difference on investigator-rated ADHD scale and on teacher not parent ratings
EEG biofeedback ¹⁴³	Children and adolescents		Review of studies	No randomized, placebo controlled trials
Acupuncture			Review of publications on PubMed (accessed February 2009)	No randomized, placebo controlled trials
Chiropractic treatments			Review of publications on PubMed (accessed February 2009)	No randomized, placebo controlled trials

CAM=complimentary and alternative medicines; MPH=methylphenidate; EEG=electroencephalogram.

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FIGURE 2
PSYCHOTHERAPIES FOR ADOLESCENTS AND ADULTS¹¹³



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TABLE 27
ADVERSE EVENTS WITH ADHD MEDICATIONS

<i>Side Effect</i>	<i>Treatment: Child</i>	<i>Treatment: Adult</i>	<i>Side Effect</i>	<i>Treatment: Child</i>	<i>Treatment: Adult</i>
Agitation	Reduce total daily dose Switch to long-acting agent Consider underlying mood disorder	Reduce total daily dose Switch to long-acting agent Consider underlying mood disorder	Headaches	Treat with OTC agents May reduce total daily dose until acclimates May change preparation of agent	Treat with OTC agents May reduce total daily dose until acclimates May change preparation of agent
Anxiety	Distinguish worry/fear from jitteriness/nervousness (below) Reduce total daily dose Switch to long-acting agent Consider underlying anxiety disorder	Distinguish worry/fear from jitteriness/nervousness (below) Reduce total daily dose Switch to long-acting agent Consider underlying anxiety disorder	Initial insomnia	Be sure this was not pre-existing to medication Move timing or eliminate afternoon dose If residual ADHD symptoms present, may use clonidine HS for sedation May use melatonin 90 minutes before bedtime	Be sure this was not pre-existing to medication Move timing or eliminate afternoon dose If residual ADHD symptoms present, may use clonidine HS for sedation May use trazadone HS May use melatonin 90 minutes before bedtime
Bruxism	Decrease total daily dose May use alpha agent May need to change compound*	Decrease total daily dose May need to change compound* May use alpha agonist Dental night guard to reduce grinding and morning headache	Irritability	Occurs shortly after dose or as a rebound experience If occurs 1–2 hours after dosing of short-acting agent, may change to long-acting agent If occurs when medication wears off, may change to long-acting agent Long-acting agents have different wear off rates, so an alternative long-acting agent may be preferable Co-existing mood disorder needs to be treated	Occurs shortly after dose or as a rebound experience If occurs 1–2 hours after dosing of short-acting agent, may change to long-acting agent If occurs when medication wears off, may change to long-acting agent Long-acting agents have different wear off rates, so an alternative long-acting agent may be preferable Co-existing mood disorder needs to be treated
Constipation	Dietary fiber, mild laxative, stool softener	Dietary fiber, mild laxative, stool softener	Jitteriness/nervousness	Reduce total daily dose If occurs 1–2 hours after dosing of short-acting agent, may change to long-acting agent. Reduce/eliminate daily caffeine intake Distinguish jitteriness/quivering from anxiety/worry	Reduce total daily dose If occurs 1–2 hours after dosing of short-acting agent, may change to long-acting agent. Reduce/eliminate daily caffeine intake Distinguish jitteriness/quivering from anxiety/worry
Decrease appetite	May or may not be desired based on child's BMI Take morning medication after meal Reduce total daily dose Change to long-acting agent	Usually welcomed to help weight loss Problematic if associated with significant weight and low BMI Reduce total daily dose Change to long-acting agent	Sweating	Check vital signs	May try hydrin or clonidine
Decrease libido	Not applicable	Dose and compound related Reduce total daily dose or change compound	Tics	Reduce dose Treat tics with guanfacine or clonidine Consider atomoxetine	Reduce dose Treat tics with guanfacine or clonidine Consider atomoxetine
Dizziness	If postural, recommend slower movement from lying to standing If related to vital sign changes, reduce total daily dose or change preparation or compound	If postural, recommend slower movement from lying to standing If related to vital sign changes, reduce total daily dose or change preparation* or compound Treat elevations in pulse and/or blood pressure	Weight loss	Take medication after morning meal Reduce total daily dose Change to long-acting agent or non-stimulant Add high caloric snacks daily	Take medication after morning meal Reduce total daily dose Change to long-acting agent or non-stimulant Add high caloric snacks daily
Dry mouth	Sugarless candy/gum Mouthwash that promotes salivation necessary for dental/gingival protection	Sugarless candy/gum Mouthwash that promotes salivation necessary for dental/gingival protection May use oral pilocarpine	Erectile Dysfunction	Not applicable	May use PDE5 agents PRN
GI upset/nausea/stomachache	Treat with OTC agents Usually subsides Try MPH patch Take with food	Treat with OTC agents Usually subsides Try MPH patch Take with food			

* "Change compound" means changing medication compound, not just the preparation of the same compound; † "Change preparation" means the compound remains the same
BMI=body mass index; PDE5=phosphodiesterase 5 inhibitors; GI=gastrointestinal; OTC=over-the-counter; MPH=methylphenidate.

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AUTHOR'S NOTE

The following references are the complete list from “The Black Book of ADHD—1st Edition” and the original numbering from that clinical handbook has been kept for this Educational Review. Although not every reference was used in this article, the inclusion of the entire reference list reflects the breath and depth of the clinical handbook’s content for readers who consider adding it to their library.

REFERENCES

- Baughman FA Jr. Treatment of attention-deficit/hyperactivity disorder. *JAMA*. 1999; 281:1490-1491.
- Volkow ND, Wang GJ, Newcorn J, et al. Depressed dopamine activity in caudate and preliminary evidence of limbic involvement in adults with attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry*. 2007;64:932-940.
- Castellanos FX, Lee PP, Sharp W, et al. Developmental trajectories of brain volume abnormalities in children and adolescents with attention-deficit/hyperactivity disorder. *JAMA*. 2002;288:1740-1748.
- Shaw P, Lerch J, Greenstein D, et al. Longitudinal mapping of cortical thickness and clinical outcome in children and adolescents with attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry*. 2006;63:540-549.
- Castellanos FX, Giedd JN, Berquin PC, et al. Quantitative brain magnetic resonance imaging in girls with attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry*. 2001;58:289-295.
- Shaw P, Eckstrand K, Sharp W, et al. Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation. *Proc Natl Acad Sci U S A*. 2007;104:19649-19654.
- Faraone SV, Perlis RH, Doyle AE, et al. Molecular genetics of attention-deficit/hyperactivity disorder. *Biol Psychiatry*. 2005;57:1313-1323.
- Barkley RA, Murphy K, Fischman M. *ADHD in Adults: What the Science Says*. New York, NY: Guilford Press; 2008.
- Mental health in the United States: Prevalence of diagnosis and medication treatment for attention-deficit/hyperactivity disorder—United States, 2003. Available at: www.cdc.gov/mmwr/preview/mmwrhtml/mm5434a2.htm. Accessed December 16, 2008.
- Kessler RC, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. *Am J Psychiatry*. 2006;163:716-723.
- Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: American Psychiatric Association; 1994.
- Lahey BB, Applegate B, Meburne HK, et al. DSM-IV field trials for attention deficit hyperactivity disorder in children and adolescents. *Am J Psychiatry*. 1994;151:1673-1685.
- Faraone SV, Biederman J, Spencer T, et al. Diagnosing adult attention deficit hyperactivity disorder: are late onset and subthreshold diagnoses valid? *Am J Psychiatry*. 2006;163:1720-1729.
- Still GF. Some abnormal psychical conditions in children. Lecture I. *Lancet*. 1902;1:1008-1012.
- Rasmussen N. Making the first anti-depressant: amphetamine in American medicine, 1929-1950. *J Hist Med Allied Sci*. 2006;61(3):288-323.
- Bradley C. The behavior of children receiving Benzadrine. *Am J Psychiatry*. 1937;94:577-585.
- Diagnostic and Statistical Manual of Mental Disorders*. 2nd ed. Washington, DC: American Psychiatric Association; 1968.
- Conners CK. A teacher rating scale for the use of drug studies with children. *Am J Psychiatry*. 1969;126(6):884-888.
- Lauer MW, Benhoff D, Solomons G. Hyperkinetic impulse disorder in children's behavior problems. *Psychosom Med*. 1957;19(1):38-49.
- Wood DR, Reimherr FW, Wender PH, Johnson GE. Diagnosis and treatment of minimal brain dysfunction in adults: a preliminary report. *Arch Gen Psychiatry*. 1976;33(12):1453-1460.
- Mann HB, Greenspan SL. The identification and treatment of adult brain dysfunction. *Am J Psychiatry*. 1976;133(9):1013-1017.
- Diagnostic and Statistical Manual of Mental Disorders*. 3rd ed. Washington, DC: American Psychiatric Association; 1980.
- Spitzer FL, Davies M, Barkley RA. The DSM-III-R field trial of disruptive behavior disorders. *J Am Acad Child Adolesc Psychiatry*. 1990;29(5):690-697.
- Diagnostic and Statistical Manual of Mental Disorders*. 3rd ed. rev. Washington, DC: American Psychiatric Association; 1987.
- Froehlich TE, Lamphear BP, Epstein JM, et al. Prevalence, recognition, and treatment of attention deficit/hyperactivity disorder in a national sample of US children. *Arch Pediatr Adolesc Med*. 2007;161:857-864.
- Woodruff TJ, Axelrad DA, Kyle AD, Nweke O, Miller GG, Hurlay BJ. Trends in environmentally related childhood illnesses. *Pediatrics*. 2004;113:1133-1140.
- Nyman ES, Ogdie MN, Loukola A, et al. ADHD Candidate Gene Study in a Population-Based Birth Cohort: Association with DBH and DRD2. *J Am Acad Child Adolesc Psychiatry*. 2007;46(12):1614-1621.
- Leung PW, Hung SF, Ho TP, et al. Prevalence of DSM-IV disorders in Chinese adolescents and the effects of an impairment criterion: A pilot community study in Hong Kong. *Eur Child Adolesc Psychiatry*. 2008;17(7):452-461.
- Fayyad J, De Graaf R, Kessler R, et al. Cross-national prevalence and correlates of adult attention-deficit/hyperactivity disorder. *Br J Psychiatry*. 2007;190:402-409.
- Barkley RA. *Attention Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment*. New York, NY: Guilford Press; 1990.
- Beiderman J, Faraone S, Milberger S, et al. A prospective 4-year follow-up study of attention-deficit hyperactivity and related disorders. *Arch Gen Psychiatry*. 1996;53:437-446.
- Claude D, Firestone P. The development of ADHD boys: a 12 year follow up. *Can J Behav Sci*. 1995;27:226-249.
- Barkley RA ADHD-longterm course, adult outcome, and comorbid disorders. *Attention Deficit Hyperactivity Disorder: State of the Science, Best Practices*. In: Jensen PS, Cooper JY eds. Kingston, NH: Civic Research Institute; 2002;4-1-4-12.
- 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;46:894-921.
- Faraone SV, Khan SA. Candidate gene studies of attention-deficit/hyperactivity disorder. *J Clin Psychiatry*. 2006;67:13-20.
- Thapar A, Langley K, Owen MJ, O'Donovan MC. Advances in genetic findings on attention deficit hyperactivity disorder. *Psychol Med*. 2007;37:1681-1692.
- Li D, Sham PC, Owen MJ, He L. Meta-analysis shows significant association between dopamine system genes and attention deficit hyperactivity disorder (ADHD). *Hum Mol Genet*. 2006;15:2276-2284.
- Maher BS, Marazita ML, Ferrell RE, Vanyukov MM. Dopamine system genes and attention deficit hyperactivity disorder: a meta-analysis. *Psychiatr Genet*. 2002;12:207-215.
- Brookes KJ, Mill J, Guindalini C, et al. A common haplotype of the dopamine transporter gene associated with attention-deficit/hyperactivity disorder and interacting with maternal use of alcohol during pregnancy. *Arch Gen Psychiatry*. 2006;63:74-81.
- Purper-Ouakil D, Wohl M, Mouren MC, et al. Meta-analysis of family-based association studies between the dopamine transporter gene and attention deficit hyperactivity disorder. *Psychiatr Genet*. 2005;15:53-59.
- Squassina A, Lanktree M, et al. Investigation of the dopamine D5 receptor gene (DRD5) in adult attention deficit hyperactivity disorder. *Neurosci Lett*. 2008;432(1):50-53.
- Bush G, Spencer TJ, Holmes J, et al. Functional magnetic resonance imaging of methylphenidate and placebo in attention-deficit/hyperactivity disorder during the multi-source interference task. *Arch Gen Psychiatry*. 2008;65:102-114.
- Banerjee TD, Middleton F, Faraone SV. Environmental risk factors for attention-deficit hyperactivity disorder. *Acta Paediatr*. 2007;96(9):1269-1274.
- Braun JM, Kahn RS, Froehlich T, Auinger P, Lanphear BP. Exposures to environmental toxicants and attention deficit hyperactivity disorder in U.S. children. *Environ Health Perspect*. 2006;114(12):1904-1909.
- Knopik VS, Heath AC, Jacob T, et al. Maternal alcohol use disorder and offspring ADHD: disentangling genetic and environmental effects using a children-of-twins design. *Psychol Med*. 2006;36(10):1461-1471.
- Langley K, Rice F, van den Bree MB, Thapar A. Maternal smoking during pregnancy as an environmental risk factor for attention deficit hyperactivity disorder behaviour. A review. *Minerva Pediatr*. 2005;57(6):359-371.
- Thapar A, Fowler T, Rice F, et al. Maternal smoking during pregnancy and attention deficit hyperactivity disorder symptoms in offspring. *Am J Psychiatry*. 2003;160(11):1985-1989.
- Linnet KM, Dalsgaard S, Obel C, et al. Maternal lifestyle factors in pregnancy risk of attention deficit hyperactivity disorder and associated behaviors: review of the current evidence. *Am J Psychiatry*. 2003;160(6):1028-1040.
- Kotimaa AJ, Moilanen I, Taanila A, et al. Maternal smoking and hyperactivity in 8-year-old children. *J Am Acad Child Adolesc Psychiatry*. 2003;42(7):826-833.
- Milberger S, Biederman J, Faraone SV, Chen L, Jones J. Is maternal smoking during pregnancy a risk factor for attention deficit hyperactivity disorder in children? *Am J Psychiatry*. 1996;153(9):1138-1142.
- Langley K, Holmans PA, van den Bree MB, Thapar A. Effects of low birth weight, maternal smoking in pregnancy and social class on the phenotypic manifestation of Attention Deficit Hyperactivity Disorder and associated antisocial behaviour: investigation in a clinical sample. *BMC Psychiatry*. 2007;20:7:26.
- Knopik VS, Sparrow EP, Madden PA, et al. Contributions of parental alcoholism, prenatal substance exposure, and genetic transmission to child ADHD risk: a female twin study. *Psychol Med*. 2005;35(5):625-635.
- Sasaluxnanon C, Kaewpornsawan T. Risk factor of birth weight below 2,500 grams and attention deficit hyperactivity disorder in Thai children. *J Med Assoc Thai*. 2005;88(11):1514-1518.
- Mick E, Biederman J, Prince J, Fischer MJ, Faraone SV. Impact of low birth weight on attention-deficit hyperactivity disorder. *J Dev Behav Pediatr*. 2002;23(1):16-22.
- Nigg JT, Knottnerus GM, Martel MM, et al. Low blood lead levels associated with clinically diagnosed attention-deficit/hyperactivity disorder and mediated by weak cognitive control. *Biol Psychiatry*. 2008;63:325-331.
- Linnet KM, Wisborg K, Secher NJ, et al. Coffee consumption during pregnancy and the risk of hyperkinetic disorder and ADHD: a prospective cohort study. *Acta Paediatr*. 2009;98:173-179.
- Pliszka SR, Crismon ML, Hughes CW, et al. The Texas Children's Medication Algorithm Project: Revision of the algorithm or pharmacotherapy of attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2006;45:642-657.
- Chrisman A. Pediatric ADHD: Guidelines for Initiating and Monitoring Treatment. Available at: www.medscape.com/viewprogram/7656. Accessed October 29, 2008.
- DuPaul GJ, Power TJ, Anastopoulos AD, Reid R. *ADHD Rating Scales-IV: Checklists, Norms and Clinical Interpretation*. New York, NY: Guilford Press; 1998.
- Conners CK. Conners' Rating Scales-Revised. Available at: www.pearsonassessments.com/tests/crs-r.htm. Accessed October 29, 2008.
- Brown TE. Brown ADD Rating Scales for Children, Adolescents, and Adults. Available at: www.drthomasebrown.com/assess_tools/index.html. Accessed October 29, 2008.
- Wolraich ML, Lambert W, Doffing MA, et al. Psychometric properties of the Vanderbilt ADHD Diagnostic Parent Rating Scale in a referred population. *J Pediatr Psychol*. 2003;28:559-568.
- Conners CK, Erhardt D, Sparrow E. Conners' Adult ADHD Rating Scales. www.pearsonassessments.com/tests/caars.htm. Accessed October 29, 2008.
- Achenbach TM, Edelbrock C. *The Child Behavior Checklist*. Burlington, VT: University Associates in Psychiatry; 1983.
- Murphy KR, Adler LA. Assessing attention-deficit/hyperactivity disorder in adults: focus on rating scales. *J Clin Psychiatry*. 2004;65(suppl 3):12-17.
- Kessler RC, Adler LA, Gruber MJ, et al. Validity of the World Health Organization Adult ADHD Self-Report Scale (ASRS) Screener in a representative sample of health plan members. *Int J Methods Psychiatr Res*. 2007;16(2):53-65.

67. Brown TE. *Brown Attention-Deficit Disorder Scales*. San Antonio, TX: The Psychological Corporation; 1996.
68. Ward MF, Wener PH, Reimherr FW. The Wender Utah Rating Scale: an aid in the retrospective diagnosis of childhood attention deficit hyperactivity disorder. *Am J Psychiatry*. 1993;150(8):1285-1290.
69. Barkley RA, Murphy KR. *Attention-Deficit Hyperactivity Disorder: A Clinical Workbook*. 2nd ed. New York, NY: Guilford Press; 1998.
70. Biederman J, Monuteaux MC, Doyle AE, et al. Impact of executive function deficits and attention-deficit/hyperactivity disorder (ADHD) on academic outcomes in children. *J Consult Clin Psychol*. 2004;72:757-766.
71. Biederman J, Faraone SV, Fried R, Valera EM. *Adult ADHD: A Neurobiological Disorder with Lifetime Impact*. CME Monograph from the Adult Academic Council. January 2007. Haymarket Medical.
72. DiScala C, Lescohier I, Barthel M, Li G. Injuries to children with attention deficit hyperactivity disorder. *Pediatrics*. 1998;102(6):1415-1421.
73. Barkley RA, Fischer M, Edelbrock CS, Smallish L. The adolescent outcome of hyperactive children diagnosed by research criteria: I. An 8-year prospective follow-up study. *J Am Acad Child Adolesc Psychiatry*. 1990;29:546-557.
74. Mrug S, Hoza B, Gerdes AC, et al. Discrimination between children with ADHD and classmates using peer variables. *J Atten Disord*. 2008;(epub ahead of print).
75. Hoza B, Mrug S, Gerdes AC, et al. What aspects of peer relationships are impaired in children with attention-deficit/hyperactivity disorder? *J Consult Clin Psychol*. 2005;73(3):411-423.
76. Hoza B. Peer functioning in children with ADHD. *J Pediatr Psychol*. 2007;32(6):655-663.
77. Hoza B, Gerdes AC, Mrug S, et al. Peer-assessed outcomes in the multimodal treatment study of children with attention deficit hyperactivity disorder. *J Clin Child Adolesc Psychol*. 2005;34(1):74-86.
78. Hoza B, Mrug S, Pelham VE Jr, et al. A friendship intervention for children with Attention Deficit/Hyperactivity Disorder: preliminary findings. *J Atten Disord*. 2003;6(3):387-398.
79. Lambert NM, Hartsough CS. Prospective study of tobacco smoking and substance dependencies among samples of ADHD and non-ADHD participants. *J Learn Disabil*. 1998;31(6):533-544.
80. Elkins IJ, McGue M, Iacono WG. Prospective effects of attention-deficit/hyperactivity disorder, conduct disorder, and sex on adolescent substance use and abuse. *Arch Gen Psychiatry*. 2007;64(10):1145-1152.
81. Barkley RA, Fischer M, Smallish L, Fletcher K. Young adult outcome of hyperactive children: adaptive functioning in major life activities. *J Am Acad Child Adolesc Psychiatry*. 2006;45:192-202.
82. Murphy K, Barkley RA. Attention deficit hyperactivity disorder adults: comorbidities and adaptive impairments. *Compr Psychiatry*. 1996;37(6):393-401.
83. Barkley RA, Guevremont DC, Anastopoulos AD, DuPaul GJ, Shelton TL. Driving-related risks and outcomes of attention deficit hyperactivity disorder in adolescents and young adults: a 3- to 5-year follow-up survey. *Pediatrics*. 1993;92(2):212-218.
84. Barkley RA, Murphy KR, DuPaul GI, Bush T. Driving in young adults with attention deficit hyperactivity disorder: knowledge, performance, adverse outcomes and the role of executive functioning. *J Int Neuropsychol Soc*. 2002;8(5):655-672.
85. Fried R, Petty C, Surman C, et al. Characterizing impaired driving in adults with attention-deficit/hyperactivity disorder: A controlled study. *J Clin Psychiatry*. 2006;67:567-574.
86. Barkley R. Driving impairments in teens and adults with attention-deficit/hyperactivity disorder. *Psychiatr Clin North Am*. 2004;27:233-260.
87. Leibson CL, Katusic SK, Barbaresi WJ, Ransom J, O'Brien PC. Use and costs of medical care for children and adolescents with and without attention-deficit/hyperactivity disorder. *JAMA*. 2001;285(1):60-66.
88. Murphy KR, Barkley RA. Occupational functioning in adults with ADHD. *ADHD Report*. 2007;15(1):6-10.
89. Biederman J, Faraone SV, Spencer TJ, et al. Functional impairment in adults with self-reports of diagnosed ADHD: a controlled study of 1001 adults in the community. *J Clin Psychiatry*. 2006;67(4):524-540.
90. Biederman J, Faraone SV. The effects of attention-deficit/hyperactivity disorder on employment and household income. *MedGenMed*. 2006;8(3):12.
91. Goodman D. The consequences of attention deficit hyperactivity disorder. *J Psychiatr Prac*. 2007;13(5):318-327.
92. Biederman J, Petty CR, Fried R, et al. Educational and occupational underattainment in adults with attention-deficit/hyperactivity disorder: a controlled study. *J Clin Psychiatry*. 2008;69(8):1217-1222.
93. Biederman J, Wilens TE, Mick E, et al. Psychoactive substance use disorders in adults with attention deficit hyperactivity disorder (ADHD): effects of ADHD and psychiatric comorbidity. *Am J Psychiatry*. 1995;152:1642-1658.
94. Kollins SH, McClernon FJ, Fuemmeler BF. Association between smoking and attention-deficit/hyperactivity disorder symptoms in a population-based sample of young adults. *Arch Gen Psychiatry*. 2005;62:1142-1147.
95. Upadhyaya HP, Carpenter MJ. Is attention deficit hyperactivity disorder (ADHD) symptom severity associated with tobacco use? *Am J Addict*. 2008;17(3):295-298.
96. Mannuzza S, Klein RG, Moulton JL 3rd. Lifetime criminality among boys with attention deficit hyperactivity disorder: a prospective follow-up study into adulthood using official arrest records. *Psychiatry Res*. 2008;160(3):237-246.
97. Swensen A, Birnbaum H, Hamadi R, et al. Incidence and costs of accidents among attention-deficit/hyperactivity disorder patients. *J Adolesc Health*. 2004;35:346.e1-e9.
98. Matza LS, Paramore C, Prasad M. A review of the economic burden of ADHD. *Cost Eff Resour Alloc*. 2005;3:5.
99. Posner K, Melvin GA, Murray DW, et al. Clinical presentation of attention-deficit/hyperactivity disorder in preschool children: the Preschoolers with Attention-Deficit/Hyperactivity Disorder Treatment Study (PATS). *J Child Adolesc Psychopharmacol*. 2007;17(5):547-562.
100. Jensen PS, Hinshaw SP, Kraemer HC, et al. ADHD comorbidity findings from the MTA study: comparing comorbid subgroups. *J Am Acad Child Adolesc Psychiatry*. 2001;40(2):147-158.
101. Searight HR, Burke JM, Rottnek F. Adult ADHD: evaluation and treatment in family medicine. *Am Fam Physician*. 2000;62:2077-2086.
102. Brown TE, McMullen WJ. Attention deficit disorders and sleep/arousal disturbance. *Ann N Y Acad Sci*. 2001;931:271-286.
103. Vetter VL, Elya J, Erickson C, et al. Cardiovascular monitoring of children and adolescents with heart disease receiving stimulant drugs. A scientific statement from the American Heart Association Council on Cardiovascular Disease in the Young Congenital Cardiac Defects Committee and the Council on Cardiovascular Nursing. *Circulation*. 2008;117(18):2407-2423.
104. MedLearning Inc (Medical Education Resources, Inc 2008).
105. Perrin JM, Friedman RA, Knilans TK; Black Box Working Group; Section on Cardiology and Cardiac Surgery. Cardiovascular monitoring and stimulant drugs for attention-deficit/hyperactivity disorder. *Pediatrics*. 2008;122(2):451-453.
106. Janicak PG, Davis JM, Preskorn SH, Ayd FJ. *Principles and Practice of Psychopharmacotherapy*. 2nd ed. New York, NY: Lippincott Williams and Wilkins; 1997.
107. Cohen J. *Statistical Power Analysis of Treatment Response in a Patient*. Mahwah, NJ: Lawrence Erlbaum Associates, Inc.; 1998.
108. Faraone S. Comparing the efficacy of medications for ADHD using meta-analysis. Abstract presented at: The 159th Annual Meeting of the American Psychiatric Association; May 2006; Toronto, Canada.
109. Faraone SV. *Medscape Psychiatry and Mental Health*. 2003;8(2).
110. Haxell P. Pharmacological management of attention-deficit hyperactivity disorder in adolescents. *CNS Drugs*. 2007;21(1):37-46.
111. IDEA Parent Guide, National Center for Learning Disabilities, April 2006. Available at: www.nclld.org/images/stories/downloads/parent_center/idea2004parentguide.pdf. Accessed October 17, 2008.
112. Wilens TE, Spencer T. *Handbook of Substance Abuse: Neurobehavioral Pharmacology*. New York, NY: Plenum Press; 1998.
113. Goodman D. Treatment and assessment of adults with ADHD. In: Biederman J, ed. *ADHD Across the Life Span: From Research to Clinical Practice—An Evidence-Based Understanding*. Hasbrouck Heights, NJ: Veritas Institute for Medical Education, Inc.; 2006.
114. American Academy of Pediatrics Committee on Drugs. *Pediatrics*. 2001;108:776-789.
115. Ilett KF, Hackett LP, Kristensen JH, Kohan R. Transfer of dexamphetamine into breast milk during treatment for attention deficit hyperactivity disorder. *Br J Clin Pharmacol*. 2007;63(3):371-375.
116. Steiner E, Villen T, Hallberg M, Rane A. Amphetamine secretion in breast milk. *Eur J Clin Pharmacol*. 1984;27:123-124.
117. Spigset O, Brede WR, Zhalsen K. Excretion of methylphenidate in breast milk. *Am J Psychiatry*. 2007;164(2):348.
118. Hackett LP, Kristensen JH, Hale TW, Paterson R, Ilett KF. Methylphenidate and breast-feeding. *Ann Pharmacother*. 2006;40(10):1890-1891.
119. Stubberfield T, Parry T. Utilization of alternative therapies in attention-deficit hyperactivity disorder. *J Paediatr Child Health*. 1999;35(5):450-453.
120. Bussing R, Zima BT, Gary FA, et al. Use of complementary and alternative medicine for symptoms of attention-deficit hyperactivity disorder. *Psychiatr Serv*. 2002;53(9):1096-1102.
121. Chan E. The role of complementary and alternative medicine in attention-deficit hyperactivity disorder. *J Dev Behav Pediatr*. 2002;23(1 Suppl):S37-S45.
122. Chan E, Rappaport LA, Kemper KJ. Complementary and alternative therapies in childhood attention and hyperactivity problems. *J Dev Behav Pediatr*. 2003;24(1):4-8.
123. Jacobs J, Williams AL, Girard C, Nijke VY, Katz D. Homeopathy for attention-deficit/hyperactivity disorder: a pilot randomized-controlled trial. *J Altern Complement Med*. 2005;11(5):799-806.
124. Weber W, Vander Stoep A, McCarty RL, et al. Hypericum perforatum (St John's wort) for attention-deficit/hyperactivity disorder in children and adolescents: a randomized controlled trial. *JAMA*. 2008;299(22):2633-2641.
125. Frei H, Everts R, von Ammon K, et al. Homeopathic treatment of children with attention deficit hyperactivity disorder: a randomised, double blind, placebo controlled crossover trial. *Eur J Pediatr*. 2005;164(12):758-767.
126. Lamont J. Homeopathic treatment of attention deficit hyperactivity disorder: a controlled trial. *British Homeopathic Journal*. 1997;86:196-200.
127. Strauss L. The efficacy of a homeopathic preparation in the management of attention deficit hyperactivity disorder. *Journal of Biomedical Therapy*. 2000;18(2):197-201.
128. Jacobs J, Williams AL, Girard C, et al. Homeopathy for attention-deficit/hyperactivity disorder: a pilot randomized-controlled trial. *J Altern Complement Med*. 2005;11(5):799-806.
129. Trebaticka J, Kopasova S, Hradecna Z, et al. Treatment of ADHD with French maritime pine bark extract, Pycnogenol. *Eur Child Adolesc Psychiatry*. 2006;15(6):329-335.
130. Tenenbaum S, Paull JC, Sparrow EP, Dodd DK, Green L. An experimental comparison of Pycnogenol and methylphenidate in adults with attention-deficit/hyperactivity disorder (ADHD). *J Atten Disord*. 2002;6:49-60.
131. Feingold B. *Why Your Child is Hyperactive*. New York, NY: Random House; 1975.
132. Wender EH. The food additive-free diet in the treatment of behavior disorders: a review. *J Dev Behav Pediatr*. 1986;7(1):35-42.
133. Schnoll R, Burshteyn D, Cea-Aravena J. Nutrition in the treatment of attention deficit hyperactivity disorder: a neglected but important aspect. *Appl Psychophysiol Biofeedback*. 2003;28(1):63-75.
134. Haslam RH, Dalby JT, Rademaker AW. Effects of megavitamin therapy on children with attention deficit disorders. *Pediatrics*. 1984;74(1):103-111.
135. Voigt RG, Llorente AM, Jensen CL, et al. A randomised, double-blind, placebo-controlled trial of docosahexaenoic acid supplementation in children with attention-deficit/hyperactivity disorder. *J Pediatr*. 2001;139:189-196.
136. Stevens LJ, Zhang W, Peck L, et al. EPA supplementation in children with inattention, hyperactivity, and other disruptive behaviors. *Lipids*. 2003;38:1007-1021.
137. Hirayama S, Hamazaki T, Terasawa K. Effect of docosahexaenoic acid-containing food administration on symptoms of attention-deficit/hyperactivity disorder—a placebo controlled double-blind study. *Eur J Clin Nutr*. 2004;58:467-473.
138. Richardson AJ, Puri BK. A randomised double-blind, placebo-controlled study of the effects of supplementation with highly unsaturated fatty acids on ADHD-related symptoms in children with specific learning difficulties. *Prog Neuropsychopharmacol Biol Psychiatry*. 2002;26:233-239.
139. Sinn N, Bryan J. Effect of supplementation with polyunsaturated fatty acids and micronutrients on ADHD-related problems with attention and behavior. *J Dev Behav Pediatr*. 2007;28:82-91.
140. Blicic M, Yildirim F, Kandil S, et al. Double-blind, placebo-controlled study of zinc sulfate in the treatment of attention deficit hyperactivity disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2004;28:181-190.
141. Akhondzadeh S, Mohammadi M-R, Khademi M. Zinc sulfate as an adjunct to methylphenidate for the treatment of attention deficit hyperactivity disorder in children: a double blind and randomized trial. *BMC Psychiatry*. 2004;4:9.

142. Konofal E, Lecendreux M, Deron J, et al. Effects of iron supplementation on attention deficit hyperactivity disorder in children. *Pediatr Neurol*. 2008;38:20-26.
143. Monastra VJ, Lynn S, Linden M, et al. Electroencephalographic biofeedback in the treatment of attention-deficit/hyperactivity disorder. *Appl Psychophysiol Biofeedback*. 2005;30(2):95-114.
144. Lerner M, Wigal T. Effects of Long-term Stimulants Therapy on Safety Outcomes in Children with ADHD. *Psychiatric Annals*. 2008;38(1):43-51.
145. Pliszka SR, Matthews RL, Braslow KJ, Watson MA. Comparative effects of methylphenidate and mixed salts amphetamine on height and weight in children with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2006;45(5):520-526.
146. Charach A, Figueroa M, Chen S, Ickowicz A, Schochar R. Stimulant treatment over 5 years effects on growth. *J Am Acad Child Adolesc Psychiatry*. 2006;45(4):415-421.
147. Zachor DA, Roberts AW, Hadgens JB, Isaacs JS, Merrick J. Effects of long-term psychostimulant medication on growth of children with ADHD. *Res Dev Disabil*. 2006;27(2):162-174.
148. Faraone SV, Biederman J, Monuteaux M, Spencer T. Long-term effects of extended release mixed amphetamine salts treatment of attention-deficit/hyperactivity disorder. *J Child Adolesc Psychopharmacol*. 2005;15(2):191-202.
149. Spencer TJ, Faraone SV, Biederman J, et al: Concerta Study Group. Does prolonged therapy with a long-acting stimulant suppress growth in children with ADHD? *J Am Acad Child Adolesc Psychiatry*. 2006;45(5):527-537.
150. Swanson JM, Elliott GR, Greenhill LL, et al. Effects of stimulant medication on growth rates across 3 Years in the MTA follow-up. *J Am Acad Child Adolesc Psychiatry*. 2007;46(8):1015.
151. Wilens TE, Biederman J, Lerner M. Concerta Study Group. Effects of once-daily osmotic release methylphenidate on blood pressure and heart rate in children with attention-deficit/hyperactivity disorder: results from a one year follow-up study. *J Clin Psychopharmacol*. 2004;24(1):36-41.
152. Wilens TE, McBurneet K, Stein M, et al. ADHD treatment with once-daily OROS methylphenidate: final results from a long-term open-label study. *J Am Acad Child Adolesc Psychiatry*. 2005;44(10):1015-1023.
153. Donner RM, Michaels MA, Ambrosini PH. Cardiovascular effects of mixed amphetamine salts extended release in the treatment of school-aged children with attention-deficit/hyperactivity disorder. *Biol Psychiatry*. 2007;61(5):706-712.
154. Findling RL, Biederman J, Wilens TE, et al, and the SLI381.301 and .302 Study Groups. Short- and long-term cardiovascular effects of mixed amphetamine salts extended release in children. *J Pediatr*. 2005;147(3):348-354.
155. Varley CK, Vincent J, Varley P, Calferon R. Emergence of tics in children with attention deficit hyperactivity disorder treated with stimulant medications. *Compr Psychiatry*. 2001;42(3):228-233.
156. Roessner V, Robatzek M, Knapp G, Banaschewski T, Tothenberger A. first-onset tics in patients with attention-deficit-hyperactivity disorder: impact of stimulants. *Dev Med Child Neurol*. 2006;48(7):616-621.
157. Palumbo D, Spencer T, Lynch J, Co-Chien H, Faraone SB. Emergence of tics in children with ADHD: impact of once-daily OROS methylphenidate therapy. *J Child Adolesc Psychopharmacol*. 2004;14(2):185-194.
158. Gadow KD, Sverd J, Sprafkin J, Nolan EE, Grossman S. Long-term methylphenidate therapy in children with comorbid attention-deficit hyperactivity disorder. *Arch Gen Psychiatry*. 1999;56(4):330-336.
159. Title 34—Education—Definition of individualized education program. Available at: http://edocket.access.gpo.gov/cfr_2007/julqtr/34cfr300.320.htm. Accessed October 17, 2008.
160. Title 34—Education—IEP Team. Available at: http://edocket.access.gpo.gov/cfr_2007/julqtr/34cfr300.321.htm. Accessed October 17, 2008.
161. Individualized Education Program. Available at: http://en.wikipedia.org/wiki/Individualized_Education_Program. Accessed October 17, 2008.
162. Kamens MW. Learning to write IEPs: a personalized, reflective approach for preservice teachers. *Intervention in School and Clinic*. 2004;40(2):76-80.
163. Katsiyannis A, Maag JW. Educational methodologies: Legal and practical considerations. *Preventing School Failure*. 2001;46(1):31-36.
164. Lewis AC. The old, new IDEA. *The Education Digest*. 2005;70(5):68-70.
165. ADA Home page. www.ada.gov. Accessed October 17, 2008.