



Evidence Based Clinical Practice Guideline

Outpatient evaluation and management of Attention Deficit/Hyperactivity Disorder

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Target Population

Inclusion: Intended primarily for use in:

- Children who present with inattention, hyperactivity, impulsivity, academic underachievement, or behavior problems 5 to 18 years of age (for preschool aged children see Appendix 1)

Exclusion:

- Child with autism spectrum disorder or PDD^a
- Child with mental retardation
- Child who is better accounted for by another mental disorder (such as schizophrenia or other psychotic disorder) or a CNS^b dysfunction (such as tumor, injury, complex seizure disorder)

Target Users

Includes but is not limited to (in alphabetical order):

- Community primary care physicians and practitioners
- Patient / family
- Patient Care staff
- Psychiatrists
- Psychologists
- Residents
- Social workers
- Teachers / other school personnel

^a PDD: pervasive developmental disorder

^b CNS: central nervous system

Introduction

References in parentheses () Evidence strengths in [] (See last page for definitions)

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common chronic behavioral diagnoses encountered by primary care physicians who care for children. Nationally, ADHD is reported to affect approximately 9% of males and 3% of females in the elementary-school age population (*Cuffe 2001 [C]*, *Barbareisi 2002 [D]*, *Brown 2001 [S]*, *Wolraich 1996 [O]*). Data recently collected by the Child Policy Research Center at Cincinnati Children's Hospital Medical Center (CCHMC) identified a prevalence of physician-diagnosed ADHD ranging from 3.5 to 9.2 percent within the Greater Cincinnati region, reflecting national rates (*CPRC 2000 [O]*).

ADHD is clinically manifested in a child by symptoms of inattention, hyperactivity, and impulsivity, leading to impairment in school or social functions (daycare, camps, or other social settings). It is often brought to the attention of the primary care clinician in the setting of school difficulties, expulsion from school or daycare, or severe dysfunction in a variety of social settings.

The cost of care and the utilization of resources required to treat children with ADHD imposes a substantial burden on the healthcare system. Management of this disorder results in, on average, 6 office visits and 10 prescriptions filled per child per year, costing \$1151 per child with ADHD, compared with \$712 for the average child (*Chan 2002 [D]*). Annual costs for injury-related health services have been calculated at \$498 per child with ADHD, compared with costs of \$216 per child without ADHD (*Leibson 2001 [C]*). Additional service costs are related to the management of comorbid psychological, developmental and psychiatric problems that occur in 30-50% of ADHD patients (*Green 1999 [M]*, *Brown 2001 [S]*, *August 1996 [O]*).

Adolescents have been included in this guideline (in contrast to the AAP^c guidelines) (*AAP 2001 [S]*, *AAP 2000 [S]*) because 45%-85% of children diagnosed with ADHD in elementary school continue to manifest core symptomatology as well as social and educational dysfunction in middle and high school (*Smith 2000 [M]*, *Faraone 2002 [C]*, *Biederman 1996 [C]*, *Schaughency 1994 [C]*, *Barkley 1991 [C]*, *Mannuzza 1991 [C]*, *Robin 1999 [S]*, *Faigel 1995 [S]*). Persistence is frequently complicated by emerging comorbid psychiatric diagnoses (*Cuffe 2001 [C]*, *Mannuzza 1998 [C]*, *Barkley 1990 [C]*). See Appendix 1.

^c AAP: American Academy of Pediatrics

Children less than 5 years of age have been excluded because of 1) the difficulty with differentiating emerging and established ADHD pathology from interactional behaviors that fall within the spectrum of normal social/emotional development, (*Kadesjo 2001 [C], Byrne 2000 [C], Rappley 1999 [D], Blackman 1999 [S], Thomas 1997 [S]*) and 2) the current paucity of studies which document efficacy and safety of medications for ADHD treatment in this age group (*Handen 1999 [B], Rappley 1999 [D], Blackman 1999 [S]*). See Appendix 1.

This guideline provides evidence based recommendations for the evaluation and management of children with ADHD who are between the ages of 5-18 years. The guideline objectives are to improve diagnostic accuracy, treatment outcomes, and patient/parent satisfaction.

Etiology

The etiology of ADHD is unknown. It is believed to be the result of a complex interaction of genetic, psychosocial, environmental and biological risk factors. The single strongest identifiable risk factor is genetics, though the specifics are not well understood. Other risk factors which have been studied are: stress, such as that caused by poverty, neglect or abuse; diet; perinatal conditions; *in utero* exposure to nicotine, alcohol or cocaine; exposure to certain toxins in the environment; prematurity; and early television exposure (*Bhutta 2002 [M], Christakis 2004 [O]*). Mediators to these risk factors are access to high quality health care, supportive parenting behaviors and early diagnosis and treatment of the condition and related comorbidities.

ADHD is the expression of a deficit, both in the quantity and function, of neurotransmitters. This deficit prevents normal transmission of information in the brain, leading to behaviors which hinder attention and learning. Empirical studies of brain neurochemistry (CSF^d) have demonstrated depletion of norepinephrine and its metabolites, in the *locus coeruleus*, thus preventing arousal; and depletion of dopamine and its metabolites, in the *nucleus accumbens*, thus inhibiting ability to sustain attention and to filter distractions (*Kotimaa 2003 [C], Gottesman 2003 [S], Mercugliano 1999 [S], Miller 1998 [S], Cantwell 1996 [S]*).

^d CSF: cerebral spinal fluid

Guideline Recommendations

Assessment and Diagnosis

It is recommended that primary care clinicians initiate an evaluation for ADHD in children meeting inclusion criteria for this guideline (see Target Population) (*Wasserman 1999 [C], Sleator 1981 [C], Mulhern 1994 [D], AAP 2000 [S]*).

Overt symptoms, resulting in educational and/or social impairment, are usually brought to the attention of primary care physicians by parents and/or teachers. More subtle symptoms, such as inattention or academic underachievement, may need to be inquired about at well-child visits of school-aged children as part of routine developmental screening (*AAP 2000 [S]*). Screening may take the form of direct questioning or a pre-visit questionnaire; subjects to cover include the child's academic performance, behavior in multiple settings (home, school, social), success with making and maintaining friendships, and mood.

Note: It has been shown that "any parental concern" about inattention, impulsivity, overactivity or ADHD/ADD-by-name^e has a sensitivity of 87% and a specificity of 47% (*Mulhern 1994 [D]*).

General

Comprehensive assessment of patients for ADHD involves six components:

- screening for the specific symptoms of ADHD by both parents/caregivers **and** teachers/school personnel
- determining whether symptoms are causing educational, social and/or behavioral impairment at home and in school or other social settings
- meeting other *DSM-IV*^f criteria (Appendix 2)
- screening for comorbidities
- comprehensive review of patient's medical history
- comprehensive physical exam.

History

It is recommended that evidence obtained includes information, delineated in the *DSM-IV*, regarding:

- core symptoms of ADHD (inattention, hyperactivity and impulsivity) in more than one setting
- age of onset
- duration of symptoms

^e ADD: Attention Deficit Disorder

^f *DSM-IV*: Diagnostic and Statistical Manual of Mental Disorders, 4th Edition.

- degree of functional impairment in more than one setting, including:
 - academic performance
 - family relationships and friendships
 - independence in activities of daily living
 - self-esteem
 - disruptional and unsafe behaviors
- comorbid psychiatric conditions
- medical/social conditions that produce ADHD-like symptoms (e.g. conditions producing chronic sleep deprivation; obstructive sleep apnea; neurobehavioral side effects of medications taken for other chronic conditions; physical, sexual, and emotional abuse)
- past medical history (looking for previously diagnosed conditions that are associated with a risk of developing ADHD, e.g. meningitis, lead toxicity, fetal cocaine and alcohol exposure)

(Green 1999 [M], O'Brien 2003 [C], Crystal 2001 [C], AAP 2000 [S], Miller 1998 [S]). See Appendix 2.

Physical Examination

It is recommended that a comprehensive physical examination be performed to exclude physical conditions whose symptoms mimic those of ADHD. Examples include hypothyroidism, anemia, visual and auditory impairment, and chronic adenoidal/tonsillar hypertrophy (Miller 1998 [S]).

Laboratory Studies

It is recommended that other diagnostic tests **not** be routinely conducted in an evaluation for ADHD. This includes:

- lead or thyroid testing (Kahn 1995 [C], Elia 1994 [C], Weiss 1993 [C], Spencer 1995 [D], Tuthill 1996 [O])
- imaging or EEG studies (Castellanos 2002 [C], Lyoo 1996 [D], Castellanos 1996 [O], Kuperman 1996 [O], Shaywitz 1983 [O])
- CPT (computerized performance tests)
 - Note:** CPT have been found to lack sufficient sensitivity and specificity to warrant their use in ADHD screening (Newcorn 2001 [C], Schatz 2001 [C]).
- complete psychological testing or neuropsychology testing
 - Note:** This would be useful for children with a positive screen for comorbid learning disability, borderline low IQ or subclinical CNS injury (Dykman 1991 [C]).
- chromosome or genetic testing.

Behavioral Assessment

1. It is recommended that diagnostic information be obtained directly from parents/caregivers in the form of questionnaires and an interview that is structured to elicit information about family structure and dynamics, parenting styles and expectations, and

pertinent family educational and psychiatric history (AAP 2000 [S]).

Note : Despite a report of high factual knowledge of ADHD, mothers frequently and incorrectly attribute ADHD-related behaviors to purposeful non-compliance rather than to skills deficits and cognitive limitations (Harrison 2002 [C]).

2. It is recommended that diagnostic information be obtained directly from the classroom teacher(s) and other school professional(s) in the form of questionnaires, report cards, and written comments about classroom performance (AAP 2000 [S]).
 - Note:** Teachers using ADHD-specific tools are able to accurately distinguish between children with and without a diagnosis of ADHD (Green 1999 [M]).
3. It is recommended that narrow band scales be used in conjunction with questionnaires that assess social and educational impairment and screen for the presence/absence of comorbid psychiatric conditions. Tools that have been developed for efficient use by primary care clinicians in children and adolescents include:
 - Vanderbilt form: comprehensive form that screens for symptoms, impairment and comorbidity (Wolraich 2003 [C], Wolraich 1998 [C]). Available in the [AAP/NICHQ^g ADHD Practitioners' Toolkit^h](#).
 - combination of the Conners Scales + DSM-IV checklist + comorbidity screening.
 - for adolescents: add Conners'-Wells' Adolescent Self-Report Scale to one of the above options. (Steinhausen 2003 [C], Danckaerts 1999 [C], Schaughency 1994 [C], Brown 2001 [S], AAP 2000 [S], Local Expert Consensus [E]).

Note: It is not recommended that global, or broad band scales (such as the CBCLⁱ, DSMD^j and CTRS^k) be used in making the diagnosis of ADHD. These tools assess overall functioning and symptoms for other psychiatric disorders, require more time to administer and interpret, have to be purchased from their copyright holders, and do not specifically focus on the ADHD diagnosis (Green 1999 [M], AAP 2000 [S]).

^g NICHQ: National Initiative for Children's Health Quality

^h Toolkit website: <http://www.nichq.org/resources/toolkit/>

ⁱ CBCL: Child Behavior Checklist

^j DSMD: Devereaux Scales of Mental Disorders

^k CTRS: Conners Teacher Rating Scale

Table 1: Definitions*

Term	Definition
ADHD Subtype: <ul style="list-style-type: none"> • predominantly hyperactive-impulsive • predominantly inattentive • combined type 	Detailed symptoms for each subtype are listed in Appendix 2. Children show both hyperactive and impulsive behavior, but can pay attention. Children have several symptoms of inattention; children are not overly active. Children show all three symptoms: inattention, impulsivity and hyperactivity.
Comorbidity: <ul style="list-style-type: none"> • oppositional defiant disorder (ODD) • conduct disorder (CD) • anxiety disorders • mood disorders/depression • learning disabilities (LD) 	Children tend to lose their temper easily and annoy others, are defiant and hostile. Children tend to break rules, destroy property and violate the rights of others. Children have extreme feelings of fear, worry or panic which may produce physical symptoms. Children are depressed, or have bipolar disorder, mania or other mood conditions. Children have conditions making it difficult to master specific skills such as reading or math.

*Understanding ADHD, parent brochure in the [AAP/NICHQ Toolkit](#)

Diagnosis

See Table 1 for definitions, in terms useful to non-clinicians, of ADHD subtypes and comorbidities discussed in this guideline.

1. It is recommended that a child meet *DSM-IV* criteria as the requirement for the diagnosis of ADHD (McBurnett 1999 [C], APA 2000 [X], AAP 1996 [X]). The criteria require that symptoms alone are not sufficient for diagnosis, but that functional impairment in combination with symptoms be present in 2 or more settings (AAP 2000 [S]). See Appendix 2.
2. It is recommended that the diagnosis include the specific subtype of ADHD:
 - predominantly hyperactive,
 - predominantly inattentive, or
 - combined type.

Knowing the subtype of ADHD may help to predict degree and type of functional impairment (McBurnett 1999 [C]).

Note 1: Combined type is the most common type at 65% of the total (Biederman 2002 [C], McBurnett 1999 [C]).

Note 2: Girls are 2.2 times (95%CI: 1.2, 4.0) more likely than boys to have the inattentive type than boys (Biederman 2002 [C]). Relative lack of disruptive behavior in the inattentive type often results in delayed initial evaluation for ADHD in girls (Gershon 2002 [M], AAP 2000 [S]).

Comorbidity

1. It is recommended that the practitioner screen for potential comorbidities in addition to assessing for ADHD specific symptoms, since comorbid psychological, developmental and psychiatric problems occur in 30-50% of ADHD patients (Green 1999 [M], AAP 2000 [S], Biederman 1991 [S], August 1996 [O]). The presence of comorbid conditions will influence treatment plans; see Management section.

Note 1: The Vanderbilt form is a comprehensive form that screens for comorbidity as well as for core symptoms and impairment (Wolraich 2003 [C], Wolraich 1998 [C]).

Note 2: Locally, data collected from pediatricians in the Cincinnati area and analyzed by the Cincinnati Pediatric Research Group (CPRG) show that 47% of ADHD patients also have a comorbid condition (21.7% learning disabled; 13.5% ODD/CD; and 7% depression or bipolar disorder) (Doyme 2004 [O]).

Comorbid and primary psychiatric disorders often masquerade as ADHD, confounding the diagnostic process. Conditions requiring consideration that may present with many of the core symptoms of ADHD include childhood bipolar disorder, mood disorders, anxiety disorders, early thought disorders, conduct disorder, childhood abuse and neglect (Glod 1996 [C]), learning disabilities and developmental disabilities.

Important comorbidities for which to screen, and their associated coexisting prevalence (AAP 2000 [S]), include:

- oppositional defiant disorder (ODD): 35.2% (95%CI¹ 27.2, 43.8)

Note: Higher scores on hyperactivity/impulsivity predict higher scores on ODD over a 2-year period (Burns 2002 [C]).

- conduct disorder: 25.7% (95%CI: 12.8, 41.3)
- anxiety disorders: 25.8% (95%CI: 17.6, 35.3)

¹ 95%CI: 95% Confidence Interval expresses the uncertainty (precision) of a measured value; it is the range of values within which we can be 95% sure that the true value lies. A study with a larger sample size will generate more precise measurements, resulting in a narrower confidence interval.

- mood disorders/depression:
18.2% (95%CI: 11.1, 26.6)
- learning disabilities (LD)
Note: Due to differences in diagnostic criteria and definition of LD, variability in reported comorbidity varies widely, but is most likely to be in the range of 12% -25% (Green 1999 [M], AAP 2000 [S], Biederman 1991 [S]).

2. It is recommended that information regarding family histories of ADHD and psychiatric disorders be elicited as part of the intake history. Family histories positive for these conditions are frequently present in patients who are being evaluated for ADHD (Faraone 1996 [C], McCormick 1995 [C]). The existence of these conditions in parents and/or siblings, either as established or potential diagnoses, has important implications in terms of constructing successful treatment plans for children with ADHD (Lesesne 2003 [C]). Awareness of the risk for positive family comorbidity also provides an opportunity for appropriate referral for other family members (Harrison 2002 [C]).

Note 1: Maternal depression has been found to be associated with the presence of ADHD in children (Grupp-Phelan 2003 [C], Lesesne 2003 [C], Chi 2002 [C], Cunningham 2002 [C], Harrison 2002 [C], Johnston 2002 [C], McCormick 1995 [C], Fergusson 1993 [C], Faraone 1997 [S]).

Note 2: A large longitudinal study of siblings of children with ADHD found a 26% prevalence of ADHD and significantly increased rates of 10 other disorders commonly associated with ADHD, compared to significantly increased rates of only 3 disorders in siblings of control subjects (Faraone 1996 [C]).

Management

A. Establishing a basis for the treatment plan

1. It is recommended that **primary care** clinicians establish a treatment plan that is based on the concept of ADHD as a chronic condition (Bodenheimer 2002 [S], AAP 2001 [S]). Young children who meet criteria for the diagnosis and respond to treatment for ADHD are likely to have a relapsing and remitting course into the teenage and young adult years (Cuffe 2001 [C], Lavigne 1998 [C], Robin 1999 [S]).

Note: Care for children with ADHD over time includes consideration of principles for comprehensive chronic care (Jessop 1994 [A]). See Table 2.

Table 2 Principles of Comprehensive Chronic Care

- Ensuring accessibility to and continuity of primary healthcare
- Overseeing care coordination, including support for comorbid conditions and non-healthcare services for patients and families
- Providing developmentally appropriate information about ADHD as the child matures and as new evidence becomes available
- Providing ADHD-specific anticipatory guidance for each appropriate stage of childhood or episode of family transition
- Maintaining watchful awareness for and providing appropriate discussion of stress and psychosocial risks for the family unit or individual family members
- Ensuring that families' concerns about raising a child with ADHD are being heard and understood
- Ensuring that families are aware of support and information resources for families of ADHD children (see Appendix 3)
- Helping families set and monitor specific outcome goals as a part of the comprehensive treatment plan

(Jessop 1994 [A], Bodenheimer 2002 [S], AAP 2001 [S], Perrin 2000 [S], Robin 1999 [S], Perrin 1993 [S], AAP 1999 [X], AAP 1997 [X], AAP 1993b [X], AAP 1993a [X])

Table 3 Selected Outcomes

<p>Academic</p> <ul style="list-style-type: none"> • Improved grades; improved academic productivity* • Improved attention to details* • Fewer careless mistakes* • Improvement in following directions, fewer reminders necessary* • Improved organization: brings supplies to class, remembers to bring in homework*
<p>Behavioral / Emotional</p> <ul style="list-style-type: none"> • Decreased school or bus detentions, school suspensions, daily report cards or other behavioral markers* • Improved success with star charts or reward schedules / systems • Improved self esteem • Improved behavior in public places • Improved compliance with classroom or home rules
<p>Social / Family</p> <ul style="list-style-type: none"> • Improved family relationships* • Improved compliance with parental requests* • Improved sibling interactions* • Increased independence in specified activities of daily living • Improved peer relations* • Demonstrates good sportsmanship, waits turn
<p>Safety</p> <ul style="list-style-type: none"> • Home: less climbing or running in inappropriate situations • Bicycle: helmet wearing, riding safety • Car: seatbelt wearing, driving safety • Decrease in number of injuries

*May be measured by Vanderbilt Rating Scale

2. It is recommended that 3 to 6 desired outcomes be selected by the family to guide management, the goal of which is to maximize function. Therefore, it is suggested that the selected outcomes be related to

the specific impairments attributable to the ADHD core symptoms exhibited by the child. When identifying target outcomes, it is important to include input from the family, child, teacher and others, as appropriate, who provide supervisory care for the child (AAP 2001 [S], Swanson 1999 [S]).

Selected outcomes may include specific goals within these domains:

- academic
- behavioral / emotional
- social / family
- safety

(Nader 1993 [S]). See Table 3.

Note: Children and adolescents with ADHD are at elevated risk for a wide variety of injury outcomes compared to those without behavior disorders (Brehaut 2003 [C], Hoare 2003 [C], Barkley 2002 [C], Schwebel 2002 [C]).

B. Treatment

1. It is recommended that findings from the MTA (Multimodal Treatment Study of Children with ADHD) be used as a primary guide for making treatment decisions in children with ADHD (MTA Cooperative Group 2004 [A], MTA Cooperative Group 1999 [A], MTA Cooperative Group 2004 [C]).

Under the intensive intervention conditions of the MTA (see Appendix 4), a treatment strategy employing a **combination of medication and behavior therapy** has been shown to be more effective than medication therapy alone, behavior therapy alone or usual community care (see Table 4). Outcomes have been reported after 14 months of initial intervention and after 10 additional months of follow-up (MTA Cooperative Group 2004 [A], MTA Cooperative Group 1999 [A]).

Note 1: With combined therapy, final adjusted daily doses of stimulants used were lower, compared with the medication-only arm of the study. See Table 5.

Table 5 MPH mg/day at study endpoint

Treatment group	14 month	24 month
Combined	31.1 ± 11.7	30.43 ± 14.46
Med. Alone	38.1 ± 14.2	37.7 ± 17.70
p value	≤ .001	.0013

(MTA Cooperative Group 2004 [A], Vitiello 2001 [A])

Note 2: Treatment effect was shown to be reduced by 50% in the 10 month follow-up phase, though 24-month outcomes continued to favor combination and medication therapy groups over the behavior therapy and usual community care groups. Further analysis revealed that symptom reemergence was

partially explained by discontinuation of medication during the follow-up phase (MTA Cooperative Group 2004 [A], MTA Cooperative Group 2004 [C]).

2. It is recommended that treatment options and their relative effects be discussed with the family.

Table 4 Percentage of Patients with Normalized*Behavior, by Therapy Type

Treatment group	14 month		24 month	
Classmates without ADHD	88%			
Combined Therapy (Comb)	68%	Comb+Med vs. Beh+CC p<.001	48%	Comb+Med vs. Beh+CC p=.0003
Medication Alone (Med)	56%	Comb vs. Med p<.04	37%	Comb vs. Med p=.86
Behavioral Alone (Beh)	34%	Beh vs. CC p<0.1	32%	Beh vs. CC p=0.16
Usual Community Care (CC)	25%		28%	

Legend: Comb+Med is both the combined therapy and the medication-alone groups. Beh+CC is both the behavior-alone and the usual community care groups.

*“Normalized” defined as a score ≥ 1.0 cutoff value using the SNAP-IV^m scale, a measure of ADHD symptomatology and outcomes. (MTA Cooperative Group 2004 [A], Swanson 2001 [A])

Medications

1. It is recommended, for a treatment plan that includes medication, that stimulants be the first line medication for the treatment of ADHD in children without complex comorbidity. This is based on data suggesting a very high efficacy and overall safety profile for periods as long as 24 months with short-acting stimulants (MPH) (MTA Cooperative Group 2004 [A], MTA Cooperative Group 1999 [A], MTA Cooperative Group 2004 [C]). Effectiveness and safety longer than 24 months has not been systematically studied (Ingram 1999 [S]).

The relatively recent development of long-acting/slow release technology permits once-a-day dosing formulations. These medications demonstrate safety and efficacy profiles similar to traditional short-acting stimulants (Biederman 2002 [A], Greenhill 2002 [A], Wolraich 2001 [A], Pelham 2001 [B]). These longer acting dosing strategies increase the range of medication options open to families.

^m SNAP-IV Rating Scale: Swanson, Nolan, and Pelham Questionnaire. <http://www.ADHD.net>

Note 1: Benefits of longer-acting medications may include elimination of the burden of medication administration by school personnel or other supervisory care providers, decreased stigma associated with medication administration away from home which may be experienced by the child, improved compliance, and decreased opportunity for abuse of the medication (*Pelham 2001 [B]*).

Note 2: Effectiveness of MPH in improving the hyperactivity index is more pronounced on teacher rating scales than on parent rating scales at 14 months (*Schachter 2001 [M]*).

Note 3: Early concerns that stimulant medication may precipitate or exacerbate motor tics is unsupported by clinical trials (*Tourette's Syndrome Study Group 2002 [A]*, *Varley 2001 [D]*).

Note 4: In children on MPH, dextroamphetamine or Adderall®, side effects include trouble sleeping, poor appetite, anxiousness, stomachaches, headaches and stimulant rebound behavior (*Ahmann 2001 [A]*, *Efron 1997 [A]*, *Carlson 2003 [C]*).

Note 5: Mild growth suppression (0.96 cm/year; 2.0 kg/year) over two years has been documented in children ages 7-9.9 years of age who were treated with stimulants for ADHD, compared with an untreated group (*MTA Cooperative Group 2004 [C]*). The effect on ultimate adult height and weight has not been studied.

Note 6: A meta-analysis of 6 studies, including a 13-year prospective study, showed use of stimulants in childhood is associated with a decrease in the risk for subsequent substance abuse, contrary to popular belief. The weight of observational studies to date in children and adolescents with ADHD shows that those who are untreated with stimulant medications are at greater risk for future substance abuse (*Wilens 2003 [M]*, *Barkley 2003 [C]*, *Molina 2003 [C]*, *Biederman 1999 [C]*, *AAP 2001 [S]*, *Local Expert Consensus [E]*).

Note 7: Though the Physician's Desk Reference (PDR) warns that MPH may lower the convulsive threshold, a controlled study shows that in patients with epilepsy and ADHD, seizure activity does not increase when MPH is added to antiepileptic drug treatment (*Gross-Tsur 1997 [B]*, *Gucuyener 2003 [C]*, *AAP 2001 [S]*).

See Table 6 for dose and pharmacodynamics information for commonly used stimulant medications.

2. It is recommended that careful and systematic dosing titration be performed to determine the optimal dosing for a given child (*Vitiello 2001 [A]*, *Greenhill 2001 [C]*).

Begin titration with a low dose and increase dosage, as frequently as **weekly**, until there is an adequate response on the selected outcomes or until unacceptable side effects are observed. During titration, use follow-up parent and teacher rating scales to measure symptoms and side effects (*AAP 2001 [S]*). It may be preferable to start a child on a short-acting formulation to determine the optimal dosing before titrating a long-acting formulation.

Note 1: Pharmacokinetic data indicates that optimal stimulant dosing varies widely among patients of similar weight and is dependent more on differences in individual patient metabolism (*Findling 2001 [C]*, *Greenhill 2001 [C]*).

Note 2: Drug holidays and/or medication scheduling may be tailored to the preferences and needs of the family as necessary to achieve selected outcomes (*Greenhill 2001 [C]*, *AAP 2001 [S]*).

3. It is recommended that if one stimulant does not achieve desired outcomes, then another medication be considered (*Faraone 2002a [M]*, *Faraone 2002b [M]*).

Note: An undesired idiosyncratic response to one stimulant does not predict failure with another stimulant. 80% of children with ADHD will eventually respond to one of the stimulants if medication response is monitored systematically (*AAP 2001 [S]*).
4. It is recommended, when 2 or more stimulants have been tried without success, that 2nd tier medications be considered by clinicians if they are familiar with their use (*AAP 2001 [S]*).
 - Clonidine or guanfacine may be effective adjuncts to stimulant treatment for children with ADHD, as they improve symptoms and counteract insomnia and appetite suppressant side effects common to stimulant use (*Connor 1999 [M]*, *Prince 1996 [D]*).
 - Atomoxetine is not as well studied as the stimulant medications, but in clinical trials has shown comparable efficacy and profile of side effects (*Kratochvil 2002 [A]*, *Michelson 2002 [A]*, *Spencer 2002 [A]*, *Michelson 2001 [A]*, *Biederman 2002 [B]*, *Spencer 2002 [B]*, *Spencer 2001 [C]*).
 - Bupropion has been shown effective in treating ADHD symptoms in one randomized controlled trial in children but has not been studied in

Table 6 Stimulant Medications

Stimulant medication	Minimum starting dose	Maximum daily dose*	Time to maximum effect	Duration of action	Mechanism of action
Short-Acting					
methylphenidate (MPH) <ul style="list-style-type: none"> • generic <ul style="list-style-type: none"> ○ Methylin™ ○ Metadate® • Ritalin® 	5 mg bid	60 mg	2 hr	3-5 hr	Selective inhibition of the pre-synaptic <u>dopamine</u> transporter
d-methylphenidate <ul style="list-style-type: none"> • Focalin™ 	2.5 mg bid	20 mg	1-2 hr	2-5 hr	
dextroamphetamine <ul style="list-style-type: none"> • generic • Dexedrine® • Adderall® (3:1 ratio of d:l isomers) 	5 mg bid	40 mg	3 hr	4-6 hr	Selective inhibition of the pre-synaptic <u>norepinephrine</u> and <u>dopamine</u> transporter
Intermediate- and Long-Acting					
methylphenidate (MPH) <ul style="list-style-type: none"> • generic-SR <ul style="list-style-type: none"> ○ Methylin™ ER ○ Metadate® ER • Ritalin-SR® • Concerta® • Metadate® CD • Ritalin LA® 	** 10 mg/day 20 mg/day 18 mg/day 10 mg/day 20 mg/day	60 mg 60 mg 54 mg 60 mg 60 mg	5 hr 5 hr 6-8 hr 5 hr 5 hr	8 hr 8 hr 12 hr 8-12 hr 8-12 hr	Selective inhibition of the pre-synaptic <u>dopamine</u> transporter
dextroamphetamine <ul style="list-style-type: none"> • Dexedrine® Spansule® • Adderall XR® (3:1 ratio of d:l isomers) 	** 5 mg/day 10 mg/day	40 mg 30 mg	1-4 hr 7 hr	9 hr 12 hr	

CCHMC Formulary, manufacturers' prescribing information and Biederman, 2002 [A].

*This column is the manufacturer's recommended maximum dose, not evidence-based. A safe and effective dose without side effects may be higher than this for an individual patient, as determined through careful and systematic dosing titration.

**Extended release tablets may be used in place of the immediate release tablets when the equivalent dosage:duration ratio is met.

Table 7 Second-Tier Medications (in alphabetical order)

Medication	Minimum starting dose	Maximum daily dose*	Mechanism of action	Comments
alpha ₂ -adrenoreceptor antagonists <ul style="list-style-type: none"> • clonidine (Catapres®) • guanfacine (Tenex®) 	off label for ADHD and for children 0.05 mg/day 1 mg/day	off label for ADHD and for children 0.4 mg 3 mg	Central alpha ₂ -adrenoreceptor antagonist	If discontinued: gradual withdrawal over 4-5 days, to prevent hypertension.
atomoxetine (Strattera™)	10 mg/day (0.5 mg/kg)	1.4 mg/kg, not to exceed 100 mg	Selective inhibition of the pre-synaptic <u>norepinephrine</u> transporter	May take up to 2 weeks for maximum effect. Caution in patients taking other drugs which increase heart rate or blood pressure.
bupropion <ul style="list-style-type: none"> • Wellbutrin® • Wellbutrin SR®** • Wellbutrin XL™** 	off label for ADHD and for children 0.5 mg/kg tid 0.7 mg/kg bid 1.4 mg/kg/day	off label for ADHD and for children 6 mg/kg, not to exceed 400 mg	Selective inhibition of the pre-synaptic <u>dopamine</u> transporter	Caution for immediate release formulation in patients with a history of seizures; this risk is decreased with use of extended release products.
tricyclic antidepressants <ul style="list-style-type: none"> • imipramine <ul style="list-style-type: none"> ○ Tofranil® ○ Tofranil-PM® • desipramine <ul style="list-style-type: none"> ○ Norpramin® 	off label for ADHD and for children age 6-12: 2 mg/kg bid adolescents: 25-50 mg/day	off label for ADHD and for children 5 mg/kg, not to exceed 150 mg	Selective inhibition of the pre-synaptic <u>norepinephrine</u> and <u>serotonin</u> transporter	Caution in patients with a family history of sudden death. Monitor blood pressure with initial treatment.

CCHMC Formulary and manufacturers' prescribing information

*This column is manufacturer's recommended maximum dose, not evidence-based. A safe and effective dose without side effects may be higher than this for an individual patient, as determined through careful and systematic dosing titration.

**Extended release tablets may be used in place of the immediate release tablets when the equivalent dosage:duration ratio is met

comparison to stimulants in this population (Conners 1996 [A]).

- Tricyclic antidepressants have been shown effective in treating ADHD symptoms (Jadad 1999 [M], Spencer 2002 [B]).

Note: There is concern that desipramine may be unsafe. However, evidence is weak to support this concern for therapeutic doses (Biederman 1995 [D]). There are potentially serious adverse effects of tricyclic overdose; review of medication safety in the home is prudent.

See Table 7 for dose and pharmacodynamics information for second-tier medications.

Behavior Therapy

Based on the nature of coexisting conditions, specific target outcomes, and family circumstances, stimulants may not be appropriate.

1. It is recommended, for a treatment plan that includes behavior therapy, that a group treatment setting be utilized. Well studied interventions of 6-27 weeks duration have resulted in successful outcomes (AAP 2001 [S], Pelham 2000 [S], Barkley 1998 [S], Pelham 1998 [S], Turner 1992 [S]).

Note 1: Improvement in symptoms and function is documented to occur with behavior therapy alone and in combination with medication; however, as with medication therapy, behavior therapy will not bring outcomes into the normal range in all cases (MTA Cooperative Group 2004 [A], MTA Cooperative Group 1999 [A], AAP 2001 [S]).

Note 2: Behavior therapy for the treatment of ADHD is defined as working with parents to assist them in structuring an environment in which the child will have clear, firm, consistent and predictable limits, rules, and consequences.

Note 3: Behavior therapy does **not** include play therapy, cognitive therapy, or cognitive-behavior therapy, all of which have been proven not to be effective for treating the core symptoms of ADHD (Barkley 1998 [S]).

Note 4: Environmental modifications are not well studied, but are usually included in behavior therapy plans for home and school in the form of daily routines (e.g. a consistent bedtime, scheduled meal times and a structured quiet time for homework) (AAP 2001 [S]).

Note 5: Practitioners can help families identify and discuss potential barriers to optimal behavior therapy such as availability of appointments, scheduling around work and school, appropriate time commitment, cost,

insurance coverage, and other system barriers (MTA Cooperative Group 2004 [A], NIH 1998 [S], Semansky 2003 [X]).

2. It is recommended that families who refuse either medication or behavior therapy be informed that, for most children, stimulants in combination with behavior therapy have been shown to be most effective and that medication therapy is more effective than behavior therapy alone (MTA Cooperative Group 2004 [A], MTA Cooperative Group 1999 [A]).

Note: Although stimulants alone have been shown to benefit a higher proportion of patients with ADHD than behavior therapy alone, behavior therapy alone is more effective than no treatment for families who refuse medication therapy.

Other Interventions

Occupational therapy, interactive metronome training, biofeedback, herbs, vitamins, elimination diets, vision therapy and food supplements have little or no quality evidence to support their effectiveness for the treatment of ADHD (Shaffer 2001 [B], Baumgaertel 1999 [S], Chan 2003 [O], Bussing 2002 [O], Local Expert Consensus [E]).

C. Treatment Monitoring and Follow-up

1. It is recommended that the clinician provide periodic follow-up for the child diagnosed with ADHD. This would include monitoring target outcomes and adverse effects by collecting relevant information from parents, teachers and the child.

Issues to be considered:

- a) Adherence to treatment plan.

Note: In a study of 71 children on stimulants, 52% adhered to medication treatment for the entire 3-year study period. Of the remaining children, who had discontinued at least once during the study period, 40% were back on stimulants at the end of the 3 years (Thiruchelvam 2001 [B]).

- b) Use of tools.

Note 1: Time and reimbursement issues were identified, by Cincinnati area community pediatricians, as barriers to optimum management of ADHD (Davis 2002 [O]).

Note 2: Systems of care, such as flowsheets, pre-printed letters or written plans which can be modified with patient-specific information have been shown to improve efficiency and quality of care. The [AAP/NICHQ Toolkit](#) contains many such tools (McInerney 2003 [X]).

- c) Dynamic nature of plan.
Developmental changes, educational expectations by grade, and other changes in the home or school environment require that the need for a change in management be evaluated.

- d) Frequency of follow-up.
Follow-up visits during the months following diagnosis allows further exploration of issues identified in the initial assessment as well as education about ADHD and living with a chronic disease. Other parameters contributing to an agreement with the family on the frequency of follow-up visits include the degree of dysfunction, complications, and adherence.

Criteria to consider when increasing the interval between visits may include:

- symptom free
- meeting desired outcome measures
- no unacceptable side effects
- no serious academic difficulties
- other family needs

2. It is recommended that the clinician have active and direct communication with schools (teachers, school counselors, school psychologists, school administrators, family outreach workers, school nurses) (*MTA Cooperative Group 1999 [A], AAP 2001 [S], Swanson 1999 [S], Local Expert Consensus [E]*).

Note 1: A standard request form, which the parent signs to authorize telephone or e-mail exchange of information, initiates the communication between physician and teacher, which is critical during assessment and titration, but continues to be crucial for monitoring treatment success.

Alternatively, the physician may have the parent deliver the forms to the teacher, giving implied consent for information sharing.

Note 2: Teacher reports are more effective than parent reports for documenting efficacy of stimulant medication, but not as reliable as parents for reporting side effects (*Swanson 1999 [S]*).

3. It is recommended that the clinician reevaluate the child with ADHD when the treatment and management plan have not met desired outcomes (*AAP 2001 [S]*).

Unsuccessful treatment response may be due to:

- lack of adherence to the treatment regimen
- unrealistic target outcomes
- incomplete information about the child's behavior
- an incorrect diagnosis

- treatment failure, as defined by:
 - ADHD symptoms present after trials of 2 or 3 stimulant medications at maximum dose without side effects or at any dose with unacceptable side effects,
 - lack of response to behavior therapy or combination therapy in controlling the child's behaviors, or
 - the overriding influence of a coexisting condition

(*AAP 2001 [S]*).

Consults and Referrals

Primary care pediatricians may appropriately diagnose and manage most cases of ADHD, even if comorbid conditions are managed by a specialist.

Consider a consult with or referral to professionals who have expertise in child/adolescent psychology, child/adolescent psychiatry or developmental pediatrics when:

- behavior therapy is ordered
- case is complicated by comorbidity
- case is not responding to treatment
- physician is uncomfortable with any stage of the case management.

Consider referring the family to other community support resources for:

- behavior therapy
 - school psychologist
 - community psychologist
- help with 504/IEP process
 - Child Advocacy Center (Parent Training and Information Center funded by IDEAⁿ)
- education and information
 - CCHMC Family Resource Center
 - Jack H. Rubinstein Library
- clinical trials

See Appendix 3.

Note: Locally, data collected from pediatricians in the Cincinnati area and analyzed by the Cincinnati Pediatric Research Group (CPRG) show that 69% of patients with ADHD were referred for additional evaluation or assistance with management. The most common referrals were to school or community psychologists (41.2%), developmental pediatricians (16%) and psychiatrists (7.75%) (*Doyne 2004 [O]*).

ⁿ IDEA: Individuals with Disabilities Education Act (the nation's special education law)

Education

It is recommended that the family be given general education about ADHD as well as specific information appropriate to the child's developmental stage, specific deficits and selected outcomes. This education may begin as soon as the diagnosis is confirmed and be supplemented at each follow-up visit as appropriate to the needs of the family. Suggested topics include:

- ADHD as a chronic condition
- description of the disorder:
 - mechanism of action (executive functioning affected, externalizing disorder)
 - deficits (inability to organize, listen, pay attention, think clearly)
 - consequences (inability to learn, including inability to learn coping strategies)
- treatment options
- environmental modifications
- prognosis
- resources for information and support
(see Appendix 3)

The [AAP/NICHQ Toolkit](#)^o provides many materials and information to assist in this education.

Health Topics on CCHMC's website^p:

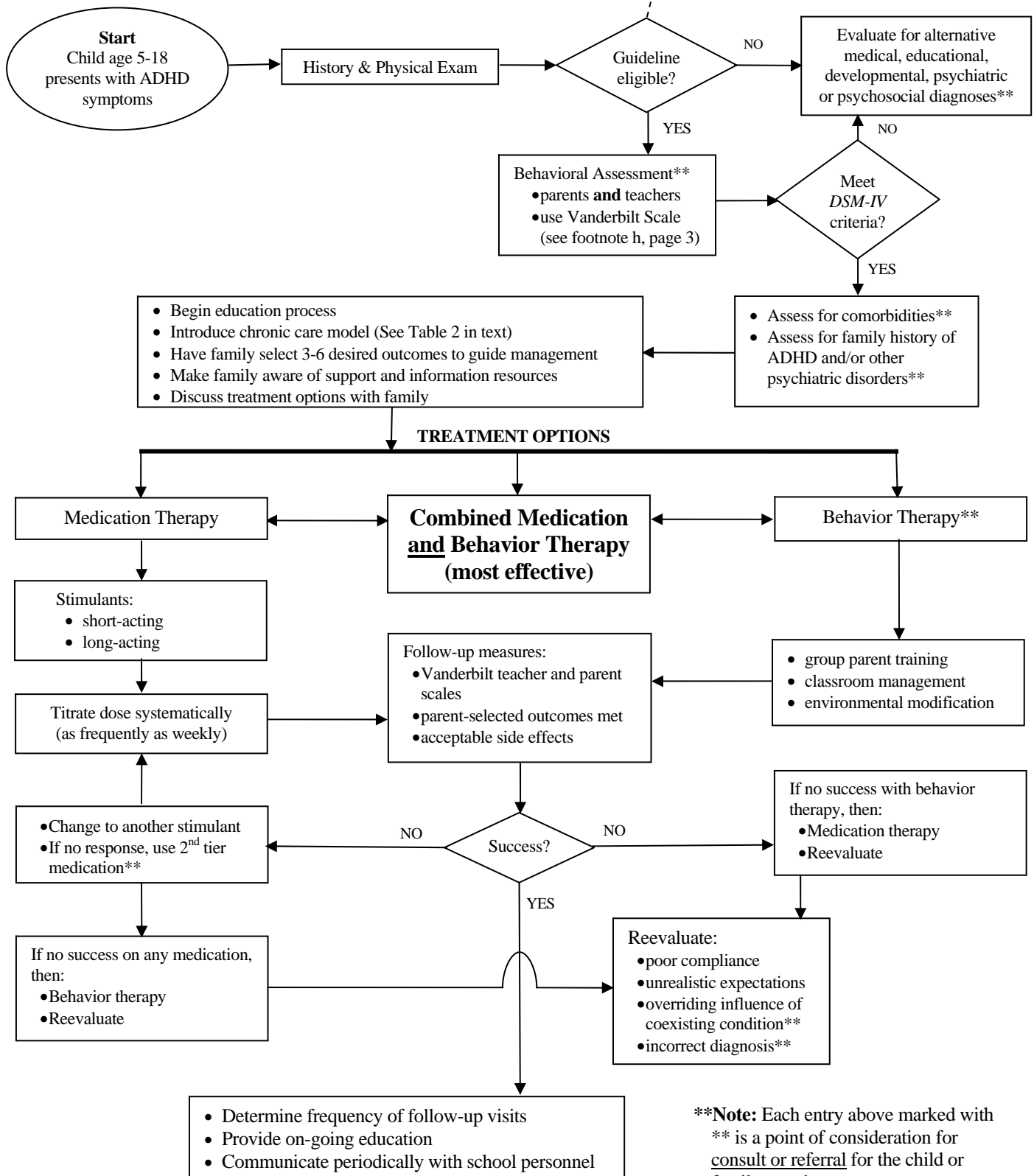
- [Attention Deficit Hyperactivity Disorder \(ADHD\)](#)
- [Structuring Your Child's Homework](#)
- [ADHD Resources for Families in Greater Cincinnati](#)

^o Toolkit website: <http://www.nichq.org/resources/toolkit/>

^p CCHMC Health Topic website:
www.cincinnatichildrens.org/health/info

Algorithm for Outpatient Evaluation and Management of Attention Deficit/Hyperactivity Disorder

Exclude: Child with autism spectrum disorder or PDD; Child with mental retardation; Child who is better accounted for by another mental disorder or a CNS dysfunction.



****Note:** Each entry above marked with ** is a point of consideration for consult or referral for the child or family member. (See text, pg 10, for specific Consults and Referrals information.)

Appendix 1: Rationale for age inclusion/exclusion criteria

Adolescents (12-18 years of age) [included in target population]

1. There is continuing educational and social dysfunction in this group.
 - a. Significant morbidity persists in late adolescents/adults; includes family dysfunction issues (*Cuffe 2001 [C]*).
 - b. Without effective treatment of this age group the risk persists for trauma, family dysfunction, divorce and incarceration; proper treatment allows them to succeed as well as their peers (*Faigel 1995 [S]*).
 - c. 78% of children with ADHD persist into adolescence (*Robin 1999 [S]*).
2. Safety and practicality of treatment is a concern.
 - a. There is no evidence that psychostimulants are any less effective (*Klorman 1990 [B]*) and any less accepted in this age group despite some concerns about non-compliance (*Smith 2000 [M]*, *Greenhill 2002 [S]*).
 - b. Newer sustained release products are more easily controlled by the caregiver, as dosing during school hours is not required. Furthermore, newer stimulant preparations, and specifically Concerta[®], are not formulated and packaged in preparations that can be easily abused (*Greenhill 2002 [S]*).
 - c. There appears to be very little correlation between untreated controls and treated adolescents as regards the risk of substance abuse with the exception of the Conduct Disorder comorbidity (*Barkley 2003 [C]*). In fact, adolescents with ADHD who go untreated are at significant risk of future substance use disorders (SUD) (*Molina 2003 [C]*).
 - d. Many different issues present themselves in the adolescent age group including self-diagnosis, self-management and titration. In addition there is a crucial need for counseling in view of the severity of co-morbidities and the complexity of school (secondary and college) and social issues (*Robin 1999 [S]*).

Preschool Children (less than 5 years of age) [excluded from target population]

1. **Evaluation** is difficult and often not valid.
 - a. “There are clear dangers to early labeling...” “...as many as 50% of the symptoms may be transient and actually age appropriate (high activity level; impulsivity; short attention span)...” (*Blackman 1999 [S]*).
 - b. 50% of children in this age group have diagnoses (psychiatric) that persist, but 50% do “...grow out of it...” (*Lavigne 1998 [C]*).
 - c. The *American Academy of Child and Adolescent Psychiatry Practice Parameter for the Psychiatric Assessment of Infants and Toddlers* states “...behavioral problems in this age group may be related to temperament, parental expectations, constitutional factors or abuse...” (*Thomas 1997 [S]*).
2. **Treatment** response is variable and unpredictable with a greater incidence of adverse reactions.
 - a. “The results of studies (of methylphenidate) on both efficacy and side effects in preschool-aged children are mixed and inconsistent...”; “...the dilemma of safety and appropriateness...” (*Blackman 1999 [S]*).
 - b. Children (ages 4-6) are “...especially susceptible to adverse drug side effects...” (*Handen 1999 [B]*).
 - c. Treatment response is variable but early recognition might reduce risk factors (*Wilens 2002 [C]*).

Appendix 2: DSM-IV Criteria for Diagnosis of ADHD

A. Either 1 or 2

- 1) Six (or more) of the following symptoms of **inattention** have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:

Inattention

- a) often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities
- b) often has difficulty sustaining attention in tasks or play activities
- c) often does not seem to listen when spoken to directly
- d) often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions)
- e) often has difficulty organizing tasks and activities
- f) often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework)
- g) often loses things necessary for tasks or activities (e.g., toys, school assignments, pencils, books, or tools)
- h) is often easily distracted by extraneous stimuli
- i) is often forgetful in daily activities

- 2) Six (or more) of the following symptoms of **hyperactivity-impulsivity** have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:

Hyperactivity

- a) often fidgets with hands or feet or squirms in seat
- b) often leaves seat in classroom or in other situations in which remaining seated is expected
- c) often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)
- d) often has difficulty playing or engaging in leisure activities quietly
- e) is often "on the go" or often acts as if "driven by a motor"
- f) often talks excessively

Impulsivity

- g) often blurts out answers before questions have been completed
- h) often has difficulty awaiting turn
- i) often interrupts or intrudes on others (e.g. butts into conversations or games)

- B. Some hyperactive-impulsive or inattentive symptoms that caused impairment were present before 7 years of age.
- C. Some impairment from the symptoms is present in 2 or more settings (e.g., at school [or work] or at home).
- D. There must be clear evidence of clinically significant impairment in social, academic, or occupational functioning.
- E. The symptoms do not occur exclusively during the course of a pervasive developmental disorder, schizophrenia, or other psychotic disorder and are not better accounted for by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, or personality disorder).

Code based on type:

- 314.01 Attention-Deficit/Hyperactivity Disorder, **Combined Type**: if both criteria A1 and A2 are met for the past 6 months
- 314.00 Attention-Deficit/Hyperactivity Disorder, **Predominantly Inattentive Type**: if criterion A1 is met but criterion A2 is not met for the past 6 months
- 314.01 Attention-Deficit/Hyperactivity Disorder, **Predominantly Hyperactive-Impulsive Type**: if criterion A2 is met but criterion A1 is not met for the past 6 months
- 314.9 Attention-Deficit/Hyperactivity Disorder **Not otherwise specified**

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