Complete Summary

GUIDELINE TITLE

Evidence based clinical practice guideline for outpatient evaluation and management of attention deficit/hyperactivity disorder.

BIBLIOGRAPHIC SOURCE(S)

Cincinnati Children's Hospital Medical Center. Evidence based clinical practice guideline for outpatient evaluation and management of attention deficit/hyperactivity disorder. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2004 Apr 30. 23 p. [145 references]

GUIDELINE STATUS

This is the current release of the guideline.

**** REGULATORY ALERT ****

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- May 2, 2007, Antidepressant drugs: Update to the existing black box warning on the prescribing information on all antidepressant medications to include warnings about the increased risks of suicidal thinking and behavior in young adults ages 18 to 24 years old during the first one to two months of treatment.
- August 21, 2006, Dexedrine (dextroamphetamine sulfate): Changes to the BOXED WARNING, WARNINGS and PRECAUTIONS sections of the prescribing information.
- September 29, 2005, Strattera (atomoxetine): Manufacturer asked to revise the prescribing information to include a boxed warning and additional warning statements that alert health care providers of an increased risk of suicidal thinking in children and adolescents.
- August 2005, Adderall: Return to Canadian market after February 2005 marketing suspension.
- October 15, 2004, Antidepressants: Public Health Advisory issued asking manufacturers of all antidepressant drugs to revise the labeling for their products to include a boxed warning and expanded warning statements that alert health care providers to an increased risk of suicidality (suicidal thinking and behavior) in children and adolescents being treated with these agents.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Attention deficit/hyperactivity disorder

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Pediatrics
Psychiatry
Psychology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Nurses
Patients
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Social Workers

GUIDELINE OBJECTIVE(S)

To improve diagnostic accuracy, treatment outcomes, and patient/parent satisfaction

TARGET POPULATION

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 in the original guideline document)

This guideline is not intended for children with:

- Autism spectrum disorder or pervasive developmental disorder
- Mental retardation
- Other mental disorders (such as schizophrenia or other psychotic disorder) or central nervous system dysfunction (such as tumor, injury, complex seizure disorder)

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. History and physical exam
2. Behavioral assessment
3. Diagnosis
4. Comorbidity assessment

Management/Treatment

1. Establishing a basis for the treatment plan
2. Discussing treatment options with family, including combined medication and behavioral therapy, medication alone, and behavior therapy alone
3. Medication treatment, stimulants being the first-line medication
4. Behavior therapy including group parent training and environmental modification at home and school in the form of daily routines
5. Treatment monitoring and follow-up including monitoring target outcomes and adverse effects
6. Consults and referrals
7. Family education

MAJOR OUTCOMES CONSIDERED

Not stated

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

To select evidence for critical appraisal by the group, the Medline, EmBase and the Cochrane databases were searched to generate an unrefined, "combined

evidence" database using a search strategy focused on answering clinical questions relevant to attention deficit/hyperactivity disorder (ADHD) and employing a combination of Boolean searching on human-indexed thesaurus terms (Medical Subject Headings [MeSH] using an OVID Medline interface) and "natural language" searching on words in the title, abstract, and indexing terms. The citations were reduced by: eliminating duplicates, review articles, non-English articles, and adult articles. The resulting abstracts were reviewed by a methodologist to eliminate low quality and irrelevant citations. During the course of the guideline development, additional clinical questions were generated and subjected to the search process.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Evidence Based Grading Scale:

A: Randomized controlled trial: large sample
B: Randomized controlled trial: small sample
C: Prospective trial or large case series
D: Retrospective analysis
E: Expert opinion or consensus
F: Basic laboratory research
S: Review article
M: Meta-analysis
Q: Decision analysis
L: Legal requirement
O: Other evidence
X: No evidence

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The recommendations contained in this document were formulated by an interdisciplinary working group, which performed systematic and critical literature reviews and examined current local clinical practices.

During formulation of these guidelines, the committee members have remained cognizant of controversies and disagreements over the management of these patients. They have tried to resolve controversial issues where possible and, when not possible, to offer optional approaches to care in the form of information that includes best supporting evidence of efficacy for alternative choices.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Cost of Care

The cost of care and the utilization of resources required to treat children with attention deficit/hyperactivity disorder (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 $1,151 per child with ADHD, compared with $712 for the average child. 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. Additional service costs are related to the management of comorbid psychological, developmental and psychiatric problems that occur in 30–50% of ADHD patients.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guidelines have been reviewed and approved by clinical experts not involved in the development process, senior management, Risk Management & Corporate Compliance, the Institutional Review Board, other appropriate hospital committees, and other individuals as appropriate to their intended purposes.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Each recommendation is followed by evidence grades (A-X) identifying the type of supporting evidence. Definitions of the evidence grades are presented at the end of the "Major Recommendations" field.

Assessment and Diagnosis

It is recommended that primary care clinicians initiate an evaluation for attention deficit/hyperactivity disorder (ADHD) in children meeting inclusion criteria for this guideline (see "Target Population" field) (Wasserman et al.,1999 [C]; Sleator & Ullmann, 1981 [C]; Mulhern, Dworkin, & Bernstein, 1994 [D]; "Clinical practice guideline: diagnosis," 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 ("Clinical practice guideline: diagnosis," 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/attention deficit disorder (ADD)-by-name has a sensitivity of 87% and a specificity of 47% (Mulhern, Dworkin, & Bernstein, 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 Diagnostic and Statistical Manual of Mental Disorders, 4th Edition *(DSM-IV)* criteria (see Appendix 2 in the original guideline document)
- 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
- 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 et al., 1999 [M]; O'Brien et al.,2003 [C]; Crystal et al., 2001 [C]; "Clinical practice guideline: diagnosis," 2000 [S]; Miller & Castellanos, 1998 [S]). See Appendix 2 in the original guideline document.

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 & Castellanos, 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, Kelly, & Walker, 1995 [C]; Elia et al., 1994 [C]; Weiss et al., 1993 [C]; Spencer et al., 1995 [D]; Tuthill, 1996 [O])
- Imaging or electroencephalogram (EEG) studies (Castellanos et al., 2002 [C]; Lyoo et al., 1996 [D]; Castellanos et al., 1996 [O]; Kuperman et al., 1996 [O]; Shaywitz et al., 1983 [O])
- Computerized performance tests (CPT)

  Note: CPT have been found to lack sufficient sensitivity and specificity to warrant their use in ADHD screening (Newcorn et al., 2001 [C]; Schatz, Ballantyne, & Trauner, 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 central nervous system (CNS) injury (Dykman & Ackerman, 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 ("Clinical practice guideline: diagnosis," 2000 [S]).

Note: Despite a report of high factual knowledge of ADHD, mothers frequently and incorrectly attribute ADHD-related behaviors to purposeful noncompliance rather than to skills deficits and cognitive limitations (Harrison & Sofronoff, 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 ("Clinical practice guideline: diagnosis," 2000 [S]).

   Note: Teachers using ADHD-specific tools are able to accurately distinguish between children with and without a diagnosis of ADHD (Green et al., 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 et al., 2003 [C], Wolraich et al., 1998 [C]). Available in the American Academy of Pediatrics/National Initiative for Children´s Health Quality (AAP/NICHQ) ADHD Practitioners´ Toolkit.
   - 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 et al., 2003 [C]; Danckaerts et al., 1999 [C]; Schaughency et al., 1994 [C]; Brown et al., 2001 [S], "Clinical practice guideline: diagnosis," 2000 [S], Local Expert Consensus [E]).

   Note: It is not recommended that global, or broad band scales (such as the Child Behavior Checklist [CBCL], Devereaux Scales of Mental Disorders [DSMD], and Conners Teacher Rating Scale [CTRS]) 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 et al., 1999 [M]; "Clinical practice guideline: diagnosis," 2000 [S]).

Diagnosis

See Table 1 in the original guideline document for definitions, in terms useful to nonclinicians, 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 et al., 1999 [C]; American Psychiatric Association [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 ("Clinical practice guideline: diagnosis," 2000 [S]). See Appendix 2 in the original guideline.
2. It is recommended that the diagnosis include the specific subtype of ADHD:
    - Predominantly hyperactive
    - Predominantly inattentive
    - Combined type

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

    Note 1: Combined type is the most common type at 65% of the total (Biederman et al., "Influence of gender," 2002 [C]; McBurnett et al., 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 et al., "Influence of gender," 2002 [C]). Relative lack of disruptive behavior in the inattentive type often results in delayed initial evaluation for ADHD in girls (Gershon, 2002 [M]; "Clinical practice guideline: diagnosis," 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 to 50% of ADHD patients (Green et al., 1999 [M]; "Clinical practice guideline: diagnosis," 2000 [S], Biederman, Newcorn, & Sprich, 1991 [S], August et al., 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 et al., 2003 [C]; Wolraich et al., 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% oppositional defiant disorder/character disorder [ODD/CD]; and 7% depression or bipolar disorder) (Doyne et al., 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 & Teicher, 1996 [C]), learning disabilities, and developmental disabilities.

Important comorbidities for which to screen, and their associated coexisting prevalence ("Clinical practice guideline: diagnosis," 2000 [S]), include:

- Oppositional defiant disorder (ODD): 35.2% (95% CI 27.2, 43.8)

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

- Conduct disorder: 25.7% (95% CI: 12.8, 41.3)
- Anxiety disorders: 25.8% (95% CI: 17.6, 35.3)
- 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 to 25% (Green et al., 1999 [M]; "Clinical practice guideline: diagnosis," 2000 [S]; Biederman, Newcorn, & Sprich, 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 et al., 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, Visser, & White, 2003 [C]). Awareness of the risk for positive family comorbidity also provides an opportunity for appropriate referral for other family members (Harrison & Sofronoff, 2002 [C]).

   Note 1: Maternal depression has been found to be associated with the presence of ADHD in children (Grupp-Phelan, Whitaker, & Naish, 2003 [C]; Lesesne, Visser, & White, 2003 [C]; Chi & Hinshaw, 2002 [C]; Cunningham & Boyle, 2002 [C], Harrison & Sofronoff, 2002 [C]; Johnston et al., 2002 [C]; McCormick, 1995 [C]; Fergusson & Lynskey, 1993 [C]; Faraone & Biederman, 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 et al., 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, Wagner, & Grumbach, 2002 [S]; "Clinical practice guideline: treatment," 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 et al., 2001 [C]; Lavigne et al., 1998 [C]; Robin, 1999 [S]).

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

B. **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 in the original guideline)
- Helping families set and monitor specific outcome goals as a part of the comprehensive treatment plan

(Jessop & Stein, 1994 [A]; Bodenheimer, Wagner, & Grumbach, 2002 [S]; "Clinical practice guideline: treatment," 2001 [S]; Perrin, 2000 [S]; Robin, 1999 [S]; Perrin, Shayne, & Bloom, 1993 [S]; Ziring et al., 1999 [X]; "General principles," 1997 [X]; AAP, "Pediatric Services," 1993 [X]; AAP, "Psychosocial Risks," 1993 [X]).

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 ("Clinical practice guideline: treatment," 2001 [S]; Swanson et al., 1999 [S]).

   Selected outcomes may include specific goals within these domains:

   - Academic
   - Behavioral/emotional
   - Social/family
   - Safety

(AAP & Nader, 1993 [S]). See Table 3 below.

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

Table 3: Selected Outcomes

Academic • 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*
Behavioral/Emotional • 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
Social/Family • 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
Safety • 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

B. **Treatment**

1. It is recommended that findings from the Multimodal Treatment Study of Children with ADHD (MTA) be used as a primary guide for making treatment decisions in children with ADHD ("NIMH Treatment Study follow-up: 24-month outcomes," 2004 [A]; "A 14-month randomized clinical trial," 1999 [A]; "NIMH Treatment Study follow-up: changes in effectiveness," 2004 [C]).

   Under the intensive intervention conditions of the MTA (see Appendix 4 in the original guideline), 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 in the original guideline document). Outcomes have been reported after 14 months of initial intervention and after 10 additional months of follow-up ("NIMH Treatment Study follow-up: 24-month outcomes," 2004 [A]; "A 14-month randomized clinical trial," 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 below.

   Table 5. Methylphenidate (MPH) mg/day at study endpoint

Treatment group	14 month	24 month
Combined	31.1 $\pm$ 11.7	30.43 $\pm$ 14.46
Med. Alone	38.1 $\pm$ 14.2	37.7 $\pm$ 17.70
P value	$\leq$ .001	.0013

   ("NIMH Treatment Study follow-up: 24-month outcomes," 2004 [A]; Vitiello et al., 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 ("NIMH Treatment Study follow-up: 24-month outcomes," 2004 [A]; "NIMH Treatment Study follow-up: changes in effectiveness," 2004 [C]).

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

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) ("NIMH Treatment Study follow-up: 24-month outcomes," 2004 [A]; "A 14-month randomized clinical trial,"1999 [A]; "NIMH Treatment Study follow-up: changes in effectiveness," 2004 [C]). Effectiveness and safety longer than 24 months has not been systematically studied (Ingram, Hechtman, & Morgenstern, 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 et al., "A randomized," 2002 [A]; Greenhill et al., 2002 [A]; Wolraich et al., 2001 [A]; Pelham et al., 2001 [B]). These longer acting dosing strategies increase the range of medication options open to families.

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 et al., 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 et al., 2001 [M]).

Note 3: Early concerns that stimulant medication may precipitate or exacerbate motor tics are unsupported by clinical trials ("Treatment of ADHD," 2002 [A]; Varley et al., 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 et al., 2001 [A]; Efron, Jarman, & Barker, 1997 [A]; Carlson & Kelly, 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 to 9.9 years of age who were treated with stimulants for ADHD, compared with an untreated group ("NIMH Treatment Study follow-up: changes in effectiveness," 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 et al., 2003 [M]; Barkley et al., 2003 [C];

Molina & Pelham, 2003 [C]; Biederman et al., 1999 [C]; "Clinical practice guideline: treatment," 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 et al., 1997 [B]; Gucuyener et al., 2003 [C]; "Clinical practice guideline: treatment," 2001 [S]).

See Table 6 in the original guideline document 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 et al., 2001 [A]; Greenhill et al., 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 ("Clinical practice guideline: treatment," 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, Short, & Manos, 2001 [C]; Greenhill et al., 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 et al., 2001 [C]; "Clinical practice guideline: treatment," 2001 [S]).

3. It is recommended that if one stimulant does not achieve desired outcomes, then another medication be considered (Faraone & Biederman, 2002 [M]; Faraone, Biederman, & Roe, 2002 [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 ("Clinical practice guideline: treatment," 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 ("Clinical practice guideline: treatment," 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, Fletcher, & Swanson, 1999 [M]; Prince et al., 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 et al., 2002 [A]; Michelson et al., 2002 [A]; Spencer et al., "Results," 2002 [A]; Michelson et al., 2001 [A]; Biederman et al., "Efficacy of atomoxetine," 2002 [B]; Spencer et al., "A double-blind comparison," 2002 [B]; Spencer et al., 2001 [C]).
- Bupropion has been shown effective in treating ADHD symptoms in one randomized controlled trial in children but has not been studied in comparison to stimulants in this population (Conners et al., 1996 [A]).
- Tricyclic antidepressants have been shown effective in treating ADHD symptoms (Jadad et al., 1999 [M]; Spencer et al., "A double-blind comparison," 2002 [B]).

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

See Table 7 in the original guideline 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 to 27 weeks duration have resulted in successful outcomes ("Clinical practice guideline: treatment," 2001 [S], Pelham & Fabiano, 2000 [S], Barkley, 1998 [S]; Pelham, Wheeler, & Chronis, 1998 [S]; Turner, Calhoun, & Adams, 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 ("NIMH Treatment Study follow-up: 24-month outcomes," 2004 [A]; "A 14-month randomized clinical trial," 1999 [A]; "Clinical practice guideline: treatment," 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) ("Clinical practice guideline: treatment," 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 ("NIMH Treatment Study follow-up: 24-month outcomes," 2004 [A]; "Diagnosis and treatment," 1998 [S]; Semansky & Koyanagi, 2003 [X]).

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 ("NIMH Treatment Study follow-up: 24-month outcomes," 2004 [A]; "A 14-month randomized clinical trial," 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 et al., 2001 [B]; Baumgaertel, 1999 [S], Chan, Rappaport, & Kemper, 2003 [O]; Bussing et al., 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. <u>Adherence to treatment plan</u>.

      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, Charach, & Schachar, 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 et al., 2002 [O]).

Note 2: Systems of care, such as flowsheets, preprinted 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 (McInerny, Meurer, & Lannon, 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) ("A 14-month randomized clinical trial," 1999 [A]; "Clinical practice guideline: treatment," 2001 [S]; Swanson et al., 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 et al., 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 ("Clinical practice guideline: treatment," 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
     - other overriding influence of a coexisting condition

   ("Clinical practice guideline: treatment," 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 Individuals with Disabilities Education Act (IDEA)])
- Education and information (CCHMC Family Resource Center, Jack H. Rubinstein Library)
- Clinical trials

See Appendix 3 in the original guideline.

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 et al., 2004 [O]).

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 in the original guideline document)

The AAP/NICHQ Toolkit provides many materials and information to assist in this education. Refer to the "Patient Resources" field for information for patients and parents.

Definitions:

Evidence Based Grading Scale:

A: Randomized controlled trial: large sample
B: Randomized controlled trial: small sample
C: Prospective trial or large case series
D: Retrospective analysis
E: Expert opinion or consensus
F: Basic laboratory research
S: Review article
M: Meta-analysis
Q: Decision analysis
L: Legal requirement
O: Other evidence
X: No evidence

CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document for outpatient evaluation and management of attention deficit/hyperactivity disorder.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence is identified and classified for each recommendation (see "Major Recommendations") using the following scheme:

Evidence Based Grading Scale:

A: Randomized controlled trial: large sample
B: Randomized controlled trial: small sample
C: Prospective trial or large case series
D: Retrospective analysis
E: Expert opinion or consensus
F: Basic laboratory research
S: Review article
M: Meta-analysis
Q: Decision analysis
L: Legal requirement
O: Other evidence
X: No evidence

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Improved diagnostic accuracy, treatment outcomes, and patient/parent satisfaction

POTENTIAL HARMS

- In children on methylphenidate (MPH), dextroamphetamine, or Adderall, side effects include trouble sleeping, poor appetite, anxiousness, stomachaches, headaches, and stimulant rebound behavior
- Mild growth suppression (0.96 cm/year; 2.0 kg/year) over two years has been documented in children ages 7 to 9.9 years of age who were treated with stimulants for attention deficit/hyperactivity disorder (ADHD), compared with an untreated group
- There is concern that desipramine may be unsafe. However, evidence is weak to support this concern for therapeutic doses. There are potentially serious adverse effects of tricyclic overdose.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

These recommendations result from review of literature and practices current at the time of their formulations. This protocol does not preclude using care modalities proven efficacious in studies published subsequent to the current revision of this document. This document is not intended to impose standards of care preventing selective variances from the guidelines to meet the specific and unique requirements of individual patients. Adherence to this pathway is voluntary. The physician in light of the individual circumstances presented by the patient must make the ultimate judgment regarding the priority of any specific procedure.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Proposed implementation strategies include:

- An attention deficit/hyperactivity disorder (ADHD) Task Force to evaluate institutional and community barriers to optimum care for children with ADHD
- Presentation at Grand Rounds
- Distributing the National Initiative for Children's Health Quality (NICHQ) Toolkit to 300 community physicians
- A series of workshops for presentation to community physicians on using the Vanderbilt form
- Required curricula added to the pediatric residency training program addressing mental health.
- An institutional process implemented to improve access for consult requests, referrals and behavior therapy
- A full-time administrator to test and implement tools and education process to improve care by community pediatricians

IMPLEMENTATION TOOLS

Clinical Algorithm
Patient Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Cincinnati Children's Hospital Medical Center. Evidence based clinical practice guideline for outpatient evaluation and management of attention deficit/hyperactivity disorder. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2004 Apr 30. 23 p. [145 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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GUIDELINE DEVELOPER(S)

Cincinnati Children's Hospital Medical Center - Hospital/Medical Center

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Cincinnati Children's Hospital Medical Center

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ADHD Team Members 2004

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The guideline was developed without external funding. All Team Members and Clinical Effectiveness support staff listed have declared whether they have any conflict of interest.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Cincinnati Children's Hospital Medical Center.

Print copies: For information regarding the full-text guideline, print copies, or evidence-based practice support services contact the Children's Hospital Medical Center Health Policy and Clinical Effectiveness Department at HPCEInfo@chmcc.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Guideline highlights. Attention deficit hyperactivity disorder. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2004 Jan.

Electronic copies: Available in Portable Document Format (PDF) from the Cincinnati Children's Hospital Medical Center.

PATIENT RESOURCES

The following are available:

- Attention deficit hyperactivity disorder (ADHD): Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2004 Jun. Electronic copies: Available from the Cincinnati Children's Hospital Medical Center Web site.
- Structuring your child´s homework. Cincinnati (OH): Cincinnati Children´s Hospital Medical Center; 2003 Dec. Electronic copies: Available from the Cincinnati Children's Hospital Medical Center Web site.
- ADHD resources. Cincinnati (OH): Cincinnati Children´s Hospital Medical Center; 2003 Dec. Electronic copies: Available from the Cincinnati Children's Hospital Medical Center Web site.

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NGC STATUS

This NGC summary was completed by ECRI on August 24, 2004. The information was verified by the guideline developer on October 12, 2004. This summary was updated by ECRI on February 11, 2005, following the release of a public health advisory from the U.S. Food and Drug Administration regarding Adderall and related products. This summary was updated by ECRI on August 15, 2005, following the U.S. Food and Drug Administration advisory on antidepressant medications. This summary was updated by ECRI on October 3, 2005, following the U.S. Food and Drug Administration advisory on Strattera (atomoxetine). This summary was updated by ECRI on August 28, 2006 following the updated U.S. Food and Drug Administration advisory on Adderall. This summary was updated by ECRI on September 7, 2006 following the updated U.S. Food and Drug Administration advisory on Dexedrine. This summary was updated by ECRI Institute on November 6, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs.

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