



# Effective Health Care Program

## Attention Deficit Hyperactivity Disorder: Effectiveness of Treatment in At-Risk Preschoolers; Long-Term Effectiveness in All Ages; and Variability in Prevalence, Diagnosis, and Treatment

### Executive Summary

#### Background and Clinical Context

Children with attention deficit hyperactivity disorder (ADHD), a condition characterized by inattention, overactivity, and impulsivity, are most frequently identified and treated in primary school. Population studies indicate that 5 percent of children worldwide show impaired levels of attention and hyperactivity. Boys are classified with ADHD approximately twice as frequently as girls, and primary school-age children approximately twice as frequently as adolescents. ADHD symptoms exist on a continuum in the general population and are considered a “disorder” to a greater or lesser degree, depending on the source of identification (e.g., parent or teacher), extent of functional impairment, diagnostic criteria, and the threshold chosen for defining a “case.” The developmentally excessive levels of inattention, overactivity, and impulsivity characteristic of ADHD are present from an early age. However, preschoolers with early signs of ADHD may also have co-occurring oppositional noncompliant behaviors, temper tantrums, and aggression that overshadow symptoms

#### Effective Health Care Program

The Effective Health Care Program was initiated in 2005 to provide valid evidence about the comparative effectiveness of different medical interventions. The object is to help consumers, health care providers, and others in making informed choices among treatment alternatives. Through its Comparative Effectiveness Reviews, the program supports systematic appraisals of existing scientific evidence regarding treatments for high-priority health conditions. It also promotes and generates new scientific evidence by identifying gaps in existing scientific evidence and supporting new research. The program puts special emphasis on translating findings into a variety of useful formats for different stakeholders, including consumers.

The full report and this summary are available at [www.effectivehealthcare.ahrq.gov/reports/final.cfm](http://www.effectivehealthcare.ahrq.gov/reports/final.cfm).



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of inattention and overactivity and confound the diagnosis. These behaviors may be given the more general label of disruptive behavior disorder (DBD), which includes oppositional defiant disorder (ODD) and conduct disorder (CD), as well as ADHD. If not already identified at an early age, preschool youngsters with ODD frequently meet criteria for ADHD by grade school.

## History

Although the condition now classified as ADHD was first described clinically in 1902,<sup>1</sup> few widely available treatments were developed for children with difficulties with attention, hyperactivity, and impulsiveness until the 1950s, when the syndrome was identified as “minimal brain damage” or “hyperkinetic syndrome.” At about the same time, methylphenidate (MPH; brand name, Ritalin) was developed to target the condition. The use of pharmacotherapy has increased through the years, along with refinements in understanding and recognition of the condition as a disorder, as reflected by its inclusion into generally accepted classification systems, such as the Diagnostic and Statistical Manual, or DSM (included in DSM-II in 1968), and International Classification of Diseases, or ICD (included in ICD-9 in 1977). The changes in labels over time reflect the contextual understanding of the condition as one of both environmental and biological etiology—from “defects of moral control” in the Edwardian typology, through “minimal brain dysfunction” in the 1960s, to attention deficit hyperactivity disorder with identified subtypes in the 1980s and 1990s. Diagnosis of ADHD and prescriptions for its treatment have grown exponentially, particularly in North America, where the preferred DSM-IV criteria identify greater numbers of children than the ICD-10 diagnosis of “hyperkinetic disorder” used more commonly in Europe. In the 1970s, the psychostimulants were classified as controlled substances due to rising concerns about misuse and abuse, and data collection regarding their use became mandatory. During the same time period, dextroamphetamine (DEX) and MPH were evaluated as effective treatments for children with the syndrome characterized by inattention and hyperactivity.

By the end of the 1960s, approximately 150,000 to 200,000 children were treated with stimulants, which represented 0.002 percent of the U.S. child population at that time.<sup>2</sup> Comparisons over time are difficult, since issues of definitions, informants, and reporting cloud the picture; however, from 1991 to 1999, prescriptions for MPH increased from 4 million to 11 million, and prescriptions for amphetamines from 1.3 million to 6 million.<sup>3</sup> The U.S. National Survey of Child Health (NSCH) provides a 2003 estimate of 4.4 million children who were identified at some point as having ADHD, which represents 7.8 percent of that population, and 2.5 million (56 percent of those identified) were receiving medication for this condition.<sup>4</sup> Within the United States, the estimated prevalence of adult ADHD stands at 4.4 percent.<sup>5</sup> The International Narcotics Control Board, using a denominator of standardized defined daily doses (S-DDDs), reports that the medical use of MPH in the United States has increased from 7.14 S-DDDs per 1,000 inhabitants per day in 2004 to 12.03 S-DDDs per 1,000 inhabitants per day in 2008. Within the same time period, and using the same definitions, MPH consumption increased from 4.22 to 6.12 S-DDDs/day/1,000 inhabitants in Canada and from 1.38 to 3.67 S-DDDs/day/1,000 inhabitants in the United Kingdom.<sup>6</sup> Controversy continues, with ongoing concerns identified about misuse in the community, as well as a mismatch between who is identified and who is treated. The controversy around accurate diagnosis is particularly heightened with documented increases in diagnosis of younger children and associated increases in treatment with psychoactive medications.

## Social Burden

Throughout childhood and adolescence, clinically significant ADHD is often associated with concurrent oppositional and aggressive behaviors, and also anxiety, low self-esteem, and learning disabilities. Symptoms are clinically significant when they cause impaired functioning; they generally interfere with academic and behavioral functioning at school, and they may also disrupt family and peer relationships. While ADHD can begin before children enter school, it is most commonly identified and treated in primary school, around ages 7 to 9 years. Over the years, the literature examining

interventions has largely focused on the primary school–age group, with the hope that intervening at this stage will diminish the adolescent risks of dropping out of school; initiating substance use, with its associated conduct, mood, and anxiety disorders; and dangerous driving. Preschoolers treated for ADHD most often have co-occurring noncompliant behaviors, temper, and aggression that impair their relationships with family and care providers, and interfere with social and emotional development. The DSM-IV criteria include subtypes: (1) predominantly inattentive, (2) predominantly hyperactive-impulsive, and (3) combined inattentive and hyperactive. In clinical samples, preschoolers are more likely to show the hyperactive-impulsive subtype,<sup>7</sup> while primary school–age children exhibit inattentive and combined subtypes, with somewhat older children and teens showing the predominantly inattentive subtype. Overall, levels of symptoms of overactivity and impulsiveness decrease with age; however, the majority of children with ADHD continue to show impairment, especially poor attention, relative to same-age peers throughout adolescence and into adulthood. The estimate of prevalence of ADHD among adults in the United States is 5.2 percent,<sup>8</sup> while worldwide it is 2.5 percent (95% confidence interval [CI], 2.1 to 3.1).<sup>9</sup>

## Scope and Purpose of the Systematic Review

The purpose of this review is to (1) critically examine the effectiveness and adverse events of interventions in preschool children with clinically significant disruptive behavior and therefore at high risk for ADHD; (2) critically examine the comparative long-term effectiveness and adverse events of interventions for ADHD (pharmacological, psychosocial, or behavioral, and the combination of pharmacological and psychosocial or behavioral interventions); and (3) summarize what is known about patterns of identification and treatment for the condition. Factors to be examined include geography, sociodemographics, temporal aspects, and provider background. This systematic appraisal also identifies gaps in the existing literature that will inform directions for future research. The Key Questions (KQs) are as follows.

**KQ1:** Among children younger than 6 years of age with ADHD or DBD, what are the effectiveness and adverse event outcomes following treatment?

**KQ2:** Among people 6 years of age or older with ADHD, what are the effectiveness and adverse event outcomes following 12 months or more of any combination of followup or treatment, including, but not limited to, 12 months or more of continuous treatment?

**KQ3:** How do (a) underlying prevalence of ADHD and (b) rates of diagnosis (clinical identification) and treatment for ADHD vary by geography, time period, provider type, and sociodemographic characteristics?

## Pharmacological Interventions Reported in This Review

We report on the following pharmacological interventions:

### Psychostimulants

- Methylphenidate (MPH)
- Dextroamphetamine (DEX)
- Mixed amphetamine salts (MAS)

### Selective norepinephrine reuptake inhibitor

- Atomoxetine (ATX)

### Alpha-2 agonist

- Guanfacine extended release (GXR)

## Nonmedication Interventions Reported in This Review

We report on the following nonmedication interventions:

- **Parent behavior training**--Manualized programs designed to help parents manage a child's problem behavior using rewards and nonpunitive consequences
- **Psychosocial interventions**--Including any one of a number of interventions aimed to assist children and their families through psychological and social therapies (e.g., psychoeducational, parent counseling, and social-skills training)

- **Behavioral interventions**--Manualized programs designed to help adults (parents, teachers, other) using rewards and nonpunitive consequences
- **School-based interventions**--Interventions in which teachers are primary intervenors and where the intervention takes place in a classroom or school setting

## Methods

### Search Strategy

There is no limit to publication date for studies to be included for KQ1, and the databases were searched from their inception date to May 31, 2010. Studies for KQ2 were limited to publications from 1997 to 2010 inclusive because the Agency for Healthcare Research and Quality (AHRQ) has already reviewed long-term treatment of ADHD for dates before 1997.<sup>10</sup> For KQ3, publications dated back to 1980 were included.

The following databases were searched for KQ1 and KQ2: MEDLINE®, Cochrane CENTRAL, Embase, PsycInfo, and ERIC (Education Resources Information Center). For KQ3, the Cochrane Library and ERIC database were excluded from the scope of the search because prevalence data were the focus of this question. However, Medline, Embase, and PsycInfo were explored.

Study authors were contacted via email for missing outcome or design data. Reference lists of included papers were screened for possibly relevant papers that had not already been screened. Gray literature, including review data from regulatory agencies such as the Food and Drug Administration, was identified by the Center and searched manually.

Reference lists of studies determined to be eligible at full-text screening were reviewed. Any potentially relevant citations were cross-checked within our citation database, and any references not found within the database were retrieved and screened at full text.

## Criteria for Inclusion/Exclusion of Studies in the Review

### Target Population

For KQ1, the population includes children younger than 6 years of age with a diagnosis of ADHD or DBD (including ODD and CD) by DSM or ICD criteria. In addition, we included samples in which children showed clinically significant symptoms, defined by referral to treatment or high scores on screening measures.

For KQ2, the population includes people 6 years of age and older who have been diagnosed with ADHD by DSM or ICD criteria and treated for ADHD, or are a control group of people with ADHD.

For KQ3, the population includes people of any age who have been diagnosed with ADHD or treated for ADHD. Because much of the data come from cross-sectional, survey, and medical databases using drug treatments and survey symptom checklists to identify people with ADHD, a DSM or ICD diagnosis is not required for inclusion.

### Types of Comparators

We identified and included studies with comparative intervention groups. From a design hierarchy perspective, comparative group designs provide stronger evidence for efficacy and effectiveness than noncomparative designs.

The interventions (either alone or in combination) may be compared with any of the following:

- Placebo
- Same pharmacologic agent of different dose or duration
- Other pharmacologic agent
- Behavioral intervention
- Psychosocial intervention
- Academic intervention
- Any combination of pharmacologic, academic, behavioral, or psychosocial interventions

## Outcomes

No limits have been placed on the effectiveness or adverse event outcomes included in this report. Numerical or statistical results of any effectiveness or adverse event outcomes are included. Effect sizes are reported as standardized mean differences (SMDs) whereby the difference in outcome (using continuous measures) between the intervention and comparison groups is divided by the pooled standard deviation to estimate intervention effectiveness. By convention, 0.2 represents a small effect, 0.5 a moderate effect, and 0.8 a large effect.<sup>11</sup> The SMD is used as a summary statistic in meta-analysis when the studies use different instruments to measure the same outcome. The data are standardized to a uniform scale before they can be combined. The SMD expresses the size of the intervention effect in each study relative to the variability observed in that study.<sup>12</sup>

## Methodology for KQ3

For the prevalence question, we searched the literature and screened the resulting citations up to the full-text examination using systematic review methodology, with question screening and agreement by two raters who used preset inclusion/exclusion criteria for all decisions. All abstracts of the resulting reports were examined, and those that reported data directly addressing prevalence, clinical identification, and treatment of ADHD as specified in KQ3 were selected. The process of external review identified additional references, which were subsequently incorporated into the final document.

## Assessment of Methodological Quality of Individual Studies

We interpret methodological quality to include primarily elements of risk of bias (systematic error) related to the design and conduct of the study. We selected the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies<sup>13</sup> and applied it in KQ1 and KQ2. Studies were reviewed independently by two raters and, where conflicts were unresolved, by a third. No similar tool for evaluating epidemiological and health service studies was used. The process for preparing this report included peer

review by experts in the field of inquiry. For KQ3, we included additional studies recommended for inclusion by the reviewers, all of which had been identified in previous steps through the search methodology.

## Rating the Body of Evidence

We assessed the overall strength of the body of evidence using the context of the GRADE approach, modified as the Grading System as defined by AHRQ.<sup>14,15</sup> Although we included papers that were not randomized controlled trials, several factors suggested by the GRADE approach may decrease the overall strength of evidence (SOE):

- Study limitations (predominantly risk-of-bias criteria)
- Type of study design (experimental versus observational)
- Consistency of results (degree to which study results for an outcome are similar between studies, that variability is easily explained)
- Directness of the evidence (assessment of whether interventions can be linked directly to the health outcomes)
- Precision (degree of certainty surrounding an effect estimate for a specific outcome)

The ratings were arrived at through discussion among two or more of the investigators. Only papers rated as “good” were included in these analyses, since they represent the best available data at this point in time.

## Conclusions

### KQ1. Treatment of Preschoolers With Disruptive Behavior Disorders

For the management of preschoolers with disruptive behavior disorders, including children considered to be at risk for ADHD, we found evidence pertaining to two broad categories of treatment: behavioral interventions and psychostimulant medication. We pooled results for eight good-quality studies to evaluate the effect of parent behavior training (PBT) on child disruptive behavior in preschoolers (SMD = -0.68; 95% CI, 0.88 to -0.47). See Figure A. By analogy, we used the single

good-quality study of the effectiveness of methylphenidate on child behavior in preschoolers (SMD = -0.83; 95% CI, -1.21 to -0.44). Both interventions appear to be effective. The SOE for use of PBT was judged high due to number of studies and consistency of results. The SOE for methylphenidate was judged low because there is only one good-quality study.

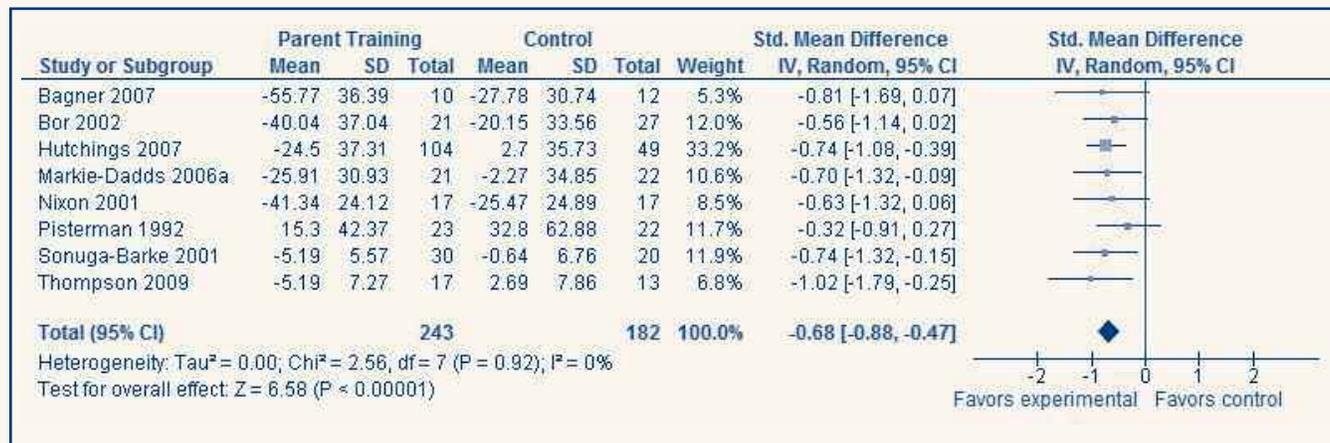
Very few randomized controlled trials (RCTs) offer information about PBT interventions designed specifically for preschoolers with ADHD. There are primarily four standardized programs of behavior training interventions for parents of preschoolers with DBD that have been developed by separate research groups in the past 25 years. While each program has its own specific features, the Triple P (Positive Parenting of Preschoolers program),<sup>16-22</sup> Incredible Years Parenting Program,<sup>23-27</sup> Parent-Child Interaction Therapy,<sup>28-35</sup> and New Forest Parenting Program<sup>36-39</sup> share common therapeutic components and are documented in manuals to ensure intervention integrity when disseminated. These programs are designed to help parents manage their child's problem behavior with more effective discipline strategies using rewards and nonpunitive consequences. An important aspect of each is to promote a positive and caring relationship between parents and their child. Primary outcomes are improved child behavior and improved parenting skills. Each program also includes educational components regarding childhood behavior problems and common developmental issues. Programs may include coaching

or consultation to support parents' efforts. The New Forest Parenting Program was specifically designed to address ADHD symptoms.

Twenty-eight RCTs show that PBT is an efficacious treatment for preschoolers with DBD; eight of these studies documented improvement specifically in ADHD symptoms. These meta-analyses confirm that long-term extension (followup) studies for the RCTs of PBT suggest that the benefits are maintained for several years. However, no long-term study (lasting 12 months or more) of PBT alone included untreated comparison groups, and attrition was high, from 24 percent at 18 months to 54 percent at 3 to 6 years, limiting interpretation of the results. A recent study examining PBT with and without school-based teacher or child interventions included a no-treatment control. This study showed maintenance of benefits of PBT at 2 years.<sup>40</sup> Studies do not comment on adverse events related to PBT.

Meta-analyses were performed to evaluate the overall strength of effect of PBT interventions on disruptive behavior, including ADHD, in preschoolers and on parent sense of competence. These meta-analyses confirmed that PBT improves parent-rated child behavior as well as parent-rated confidence in parenting skills. The SMD for PBT on child behavior was not significantly different, although slightly increased, when three studies with "fair" internal validity were included in the analysis (SMD = -0.76; 95% CI, -0.95 to -0.57).

**Figure A. Effect of PBT on preschool child behavior outcomes (eight “good” studies)**



**Note:** Includes RCTs rated as “good” quality (assumes correlation between postscore and prescore of 0.3). Means are post/pre differences; standard mean difference reflects the difference of these differences.

CI = confidence interval; df = degrees of freedom; PBT = parent behavior training; RCT = randomized controlled trial; SD = standard deviation.

**Studies:**

Bagner DM, Eyberg SM. Parent-child interaction therapy for disruptive behavior in children with mental retardation: a randomized controlled trial. *J Clin Child Adolesc Psychol* 2007;36(3):418-29. PMID:17658985.

Bor W, Sanders MR, Markie-Dadds C. The effects of the Triple P-Positive Parenting Program on preschool children with co-occurring disruptive behavior and attentional/hyperactive difficulties. *J Abnorm Child Psychol* 2002;30(6):571-87. PMID:12481972.

Hutchings J, Gardner F, Bywater T, et al. Parenting intervention in Sure Start services for children at risk of developing conduct disorder: pragmatic randomised controlled trial. *BMJ* 2007;334(7595):678. PMID:17350966.

Markie-Dadds C, Sanders MR. Self-directed Triple P (Positive Parenting Program) for mothers with children at-risk of developing conduct problems. *Behav Cogn Psychother* 2006;34(3):259-75. PMID:2006330159.

Nixon RDV. Changes in hyperactivity and temperament in behaviourally disturbed preschoolers after parent-child interaction therapy (PCIT). *Behav Change* 2001;18(3):168-76.

Pisterman S, Firestone P, McGrath P, et al. The effects of parent training on parenting stress and sense of competence. *Can J Behav Sci* 1992;24(1):41-58.

Sonuga-Barke EJ, Daley D, Thompson M, et al. Parent-based therapies for preschool attention-deficit/hyperactivity disorder: a randomized, controlled trial with a community sample. *J Am Acad Child Adolesc Psychiatry* 2001;40(4):402-8. PMID:11314565.

Thompson MJJ, Laver-Bradbury C, Ayres M, et al. A small-scale randomized controlled trial of the revised new forest parenting programme for preschoolers with attention deficit hyperactivity disorder. *Eur Child Adolesc Psychiatry* 2009;18(10):605-16. PMID:2009502208.

Five studies examining combinations of PBT and school or daycare interventions for preschool children at risk for DBD and/or ADHD suggest that adding classroom teacher consultation may be important for children in low socioeconomic status (SES) communities, but not for families with educated parents who live in communities with resources. Three of these five studies followed children for 12 months, while the other two assessed children following completion of the initial kindergarten year and at a 2-year followup. Without reinforcement, benefits of the kindergarten treatment classroom disappeared at 2 years. Direct comparisons of identical interventions offered to families of different SES have not yet been performed.

An additional two studies<sup>41,42</sup> examined PBT with specific teacher behavior training and child training as combination interventions, with children in a no-treatment condition for 8 months (on a wait list) used as the comparison condition. All behavioral interventions showed benefits relative to no-treatment controls. A dose response to the number of PBT sessions attended by parents was also identified.<sup>41</sup> These two additional pieces of evidence (that benefits of PBT compared to no treatment are maintained for 8 months or more and that the effect on child behavior improvement is greater when the parent attends more PBT sessions) both enhance the overall SOE for effectiveness of PBT.

Fifteen reports representing 11 investigations of psychostimulant medication use in preschoolers, primarily immediate release MPH, suggest that it is efficacious and safe; however, the evidence comes primarily from short-term trials lasting days to weeks with small samples.<sup>7,43-56</sup> The Preschool ADHD Treatment Study (PATS)<sup>7,51-54</sup> addresses a number of important methodological limitations and clinical concerns, examining the potential additional benefit of optimized dose of immediate release MPH for 4 weeks following a series of 10 PBT sessions. As above, the PATS study suggests that MPH is effective for improving parent-rated child behavior in preschoolers. The SMD for pharmacological intervention was essentially the same when two RCTs<sup>47,48</sup> evaluating MPH that were judged to be of “fair” quality were included with the PATS study in a meta-analysis.

In the intervention studies for preschoolers, adverse events were documented for medication interventions,

as described above, but not for PBT or school-based interventions. Careful attention to details regarding adverse events and their impact on medication adherence offers clear information about long-term (up to 10 months) effectiveness and safety in this age group. Parent- and teacher-reported ADHD symptoms improved concurrently with parents’ noting increased mood problems.<sup>7</sup> The PATS study offers information about both the potential benefits and limitations of stimulant medication use in very young children. Limitations include the following: preschool children experience more dose-related adverse events than older children, stimulants interfere with rates of growth,<sup>53</sup> and the presence of three or more comorbid conditions and psychosocial adversity are associated with lessened effectiveness of psychostimulant medication following PBT.<sup>52</sup> Only 60 percent of those enrolled in the study entered the open-label medication titration component following PBT. Following medication titration and the RCT phase, approximately 46 percent continued in the 10-month open-label extension phase, suggesting that even under ideal clinical monitoring conditions, concerns about tolerability and parent preferences play an important role in providing optimum care for young children with ADHD. Long-term extension studies following children after PBT are few; however, RCTs comparing PBT, teacher training, child training, and combinations of the above demonstrate that benefits following PBT, and combined parent and teacher training, are present at 1 year postintervention.<sup>41,42</sup> Some, but not all, studies show maintenance of benefits at 2 years; greater improvement and maintenance of improvement is more likely when parents participate in a greater number of PBT sessions. In the studies lasting up to 2 years, some children received nonprotocol co-interventions of medication. To date, no studies have examined the benefits of combining PBT and psychostimulant medication.

Our results using the GRADE approach to assign SOE are summarized in Table A. The SMD for behavior improvement is -0.68 (95% CI, -0.88 to -0.47). The SMD for behavior improvement following MPH intervention in the PATS study is of similar size but greater variability, -0.83 (95% CI, -1.21 to -0.44). There are important differences in the goals of the interventions, as PBT most often targets a range of disruptive behavior whereas the PATS study targeted

ADHD behaviors. Both interventions are effective, with no adverse events reported for PBT, while there are adverse effects with MPH. This favors the use of PBT for preschoolers at risk for ADHD due to disruptive behavior. A direct comparison has not yet been done.

## **KQ2. Long-Term Effectiveness and Safety of Interventions in People Age 6 and Older**

### **Pharmacologic Agents**

The body of literature examining long-term effectiveness and safety is most robust among samples of children ages 6–12 years at recruitment, mostly boys with ADHD, combined subtype (ADHD-C), and for studies examining pharmacotherapeutic interventions for the core symptoms of ADHD. Studies evaluating long-term outcomes in children younger than 6 years of age were discussed in the results for KQ1 of this review. This section summarizes details from studies of pharmacologic agents.

The long-term effectiveness and safety of several psychostimulants (e.g., MPH immediate release amphetamine [MPH-IR], OROS MPH [Osmotic-controlled Release Oral delivery System methylphenidate], DEX, MAS, and sequential combinations of psychostimulants), the norepinephrine reuptake inhibitor ATX, and the noradrenergic agonists clonidine and GXR have been examined prospectively in children and adolescents age 6 and over. One cohort describes psychostimulants without distinguishing between MPH and DEX agents,<sup>57,58</sup> while other reports describe amphetamine, MPH-IR, DEX, MAS, and OROS MPH.<sup>58-65</sup> Four reports describe cohorts of participants in trials of the norepinephrine reuptake inhibitor ATX;<sup>66-69</sup> one of these is an extension of clinical trials in adults. Two reports focus on the safety and continued efficacy of the noradrenergic agonist GXR.<sup>70,71</sup> Three additional RCTs compare MPH with the combination of MPH and psychosocial and/or behavioral interventions lasting 14 months to 2 years.<sup>72-77</sup> One of these, the Multimodal Treatment of ADHD Study (the MTA Study), also compared medication management of MPH to psychosocial and behavioral intervention alone and to a community control group. Twelve of 21

clinical trials or extension studies reviewed were funded wholly or in part by industry. The agents examined were all shown to be efficacious for control of inattention, overactivity, and impulsiveness for at least 12 months and up to 3 years, and few serious adverse events were noted, although GXR appears to be less well tolerated than other agents examined. Global ratings of impairment also indicate continued benefit throughout the extension studies for patients still receiving medications. Placebo-controlled discontinuation trials, where patients receiving treatment are allocated to continue or to stop treatment, are few; one trial discontinued treatment with amphetamine after 15 months, another discontinued MPH following 12 months and compared these participants with those in an ongoing psychosocial intervention,<sup>75</sup> and another examined relapse in children receiving ATX for 12 months. Attrition from the trials occurs for a variety of reasons, including adverse events and ineffectiveness. Retention of participants on active treatment at 12 months varies across studies and agents, from a high of 98 percent for MPH-IR to 75 percent for amphetamine, 63 percent for OROS MPH, 58 percent for MAS XR (extended release), 56 percent for ATX, and 43 percent for GXR. In general, those who remain on medication show continued benefit, and few adverse events are reported for them. With a majority of the studies funded by industry, there may be enhanced representations of effectiveness and safety.

Psychostimulants continue to provide control of ADHD symptoms and are well tolerated for months to years at a time. The MTA study clearly demonstrates that MPH improved ADHD symptoms and overall functioning alone or in combination with psychosocial/behavioral interventions for 14 months<sup>74</sup> and up to 24 months.<sup>73,76</sup> In the MTA study, the SMD for improved symptoms following 14 months of medication management is -0.54 (95% CI, -0.79 to -0.29) and is -0.70 (95% CI, -0.95 to -0.46) for 14 months of combined medication and psychosocial/behavioral interventions. Overall, few available studies make direct comparisons of long-term outcomes of psychostimulants. Barbaresi et al.<sup>59</sup> compare MPH and DEX use in a population-based retrospective cohort of boys and girls followed from birth to late adolescence. The mean duration of treatment for any single agent was 3.5 years ± 3.1

years. The youngest and oldest children in the study showed less benefit and more adverse effects. More boys than girls showed a positive response to DEX. Fewer children experienced adverse events with MPH than with DEX. Concerns about adverse events led to discontinuation of medications for 15 to 20 percent of children age 6 and over using MAS XR.<sup>63,65</sup> Concerns about exacerbation of tics with stimulants appear to be unfounded, although the sample size remains small and may result in type II error.<sup>58,62</sup> Use of psychostimulants slows the rate of growth, and increases blood pressure and heart rate to a small degree.<sup>53,57,62,64,65,78</sup> At a group level, the mean changes are clinically insignificant, although on rare occasions individuals discontinue an agent because of changes in vital signs.<sup>65</sup>

Overall, the benefits and safety of MPH for symptom control and general functioning are clearly documented, primarily for boys ages 7-9 years at initiation with ADHD-C. There are many similarities between MPH immediate release and other preparations of psychostimulants, both in terms of efficacy and in the side effect profile. Therefore, many researchers and clinicians assume all psychostimulants are effective and safe for extended periods of time. The documentation for this assertion is not yet robust.

Atomoxetine is both safe and effective for ADHD symptoms over 12 to 18 months among children and for up to 3 years in adults. Unlike studies of other agents, two studies offer direct comparison with placebo for examination of relapse prevention, offering clear evidence of effectiveness in children and teens.<sup>66,67</sup> Buitelaar et al.<sup>67</sup> demonstrated improved symptoms following 12 months of ATX, with SMD of -0.40 (95% CI, -0.61 to -0.18). However, teacher-reported outcomes do not document a statistically significant superiority of ATX over placebo after 1 year of treatment, as children randomized to placebo also maintained benefits to some degree following the clinical trial. The study set a high threshold for relapse (i.e., a return to 90% of baseline symptom score), and in this context, the vast majority of those on ATX (97.5 percent) as well as those on placebo (88 percent) did not relapse.<sup>67</sup> Discontinuation in children and teens appears to be higher (26 percent) due to ineffectiveness and lower (3 percent) due to adverse events than with other agents, although these are not direct comparisons.<sup>67</sup> These findings are consistent with those from an RCT lasting

less than 12 months showing that ATX is less effective than OROS MPH for ADHD symptoms.<sup>79</sup> As with psychostimulants, the group means for blood pressure and heart rate show small but clinically insignificant increases.<sup>68,69</sup> Adler et al. offer the only study of a pharmacologic intervention over an extended time period (3 years) in adults with ADHD.<sup>68</sup> Symptom improvement was maintained for those on ATX, and discontinuation due to adverse events was somewhat higher for adults (11 percent) than for children (3 percent).

An extension study of guanfacine suggests that this agent is also effective in controlling ADHD symptoms for up to 2 years; however, high rates (40 to 60 percent) of somnolence, headache, and fatigue occur when it is used as a monotherapy, especially in the initial 6 to 8 months of treatment.<sup>70</sup> A second study examined concurrent use of psychostimulants and noted improved tolerance to these adverse effects.<sup>71</sup> Changes in vital signs occur, but no clear group trends are noted. Individuals may develop clinically significant hypotension and bradycardia.<sup>70,71</sup> Serious adverse events noted include syncope, and 1 percent of participants developed clinically significant changes on electrocardiogram (ECG), such as asymptomatic bradycardia. As GXR has not been available as long as ATX, conclusions as to its general usefulness are premature. The clinically significant ECG changes noted in 1 percent of children may warrant increased cardiac monitoring for this agent.

Overall, pharmacologic agents used for controlling the symptoms of inattention, overactivity, and impulsivity of ADHD show maintenance of effectiveness and safety for 12 to 24 months. Following that, attrition from use interferes with the ability to draw conclusions. Along with decreased symptoms, overall functioning is improved, although studies do not control for adjunctive nonpharmacological interventions. A byproduct of the placebo-controlled relapse prevention studies has been the opportunity to collect long-term comparison data suggesting that some children show maintenance of gains on placebo, which may indicate that maturation may also be contributing to benefits seen when young people remain on medications for several years. The majority of children who participate in the trials of newer agents are school-aged boys with ADHD-C and few comorbid conditions.

## **Psychosocial and Behavioral Interventions, Alone and in Combination With Medication**

Investigations comparing psychosocial/behavioral interventions, alone and in combination with psychostimulant medication management, showed that both medication and combined medication/behavioral treatment are more effective in treating ADHD and ODD symptoms than psychosocial or behavioral interventions alone.<sup>72-76</sup> These results apply to children, primarily boys ages 7–9 years of normal intelligence with ADHD-C, especially during the first 2 years of treatment. The combination of psychosocial and behavioral treatment with medication may have a slight advantage during the first 14 months (SMD = -0.70; 95% CI, -0.95 to -0.46), especially for children with multiple comorbidities.<sup>80</sup> However, combined treatment is equivalent to medication alone in controlling ADHD and ODD symptoms for up to 2 years if the child shows an early favorable response to medication.<sup>76</sup>

### **Longer Term Outcomes**

Evaluation of long-term outcomes following interventions for ADHD is complex due to multiple patterns of services used and very few studies available, with only two RCTs of well-characterized clinical samples, both of boys ages 7–9 years with DSM-IV ADHD-C. The best quality data come from the MTA study, with publications about outcomes at 14 months (the length of the initial RCT), 24 months, and 3 years, and a publication regarding 6- and 8-year followup data.<sup>73,74,81,82</sup> The initial RCT compared 14 months of management with MPH-IR to three other interventions: psychosocial and behavioral treatment; the combination of medication management and psychosocial and behavioral treatment; and standard community care. Three years after initiation, the four intervention groups showed comparable outcomes. The majority of ADHD children who received interventions were maintaining improved functioning, although they did not match the functional levels of the non-ADHD comparison group. A small proportion returned to previous levels of poor functioning over time.<sup>83</sup>

In the MTA trial, no clear relationship was identified between duration of medication use and psychiatric or overall functional outcomes at 3 years or beyond.<sup>82,84</sup> In

contrast, a few long-term cohort studies lasting 5 years or more suggest that increased duration of medication was associated with improved grade retention and academic achievement, and may also lessen onset of substance use disorders as well as ODD, conduct, anxiety, and depressive disorders.<sup>85-88</sup> These cohort studies provide longer duration of followup into late adolescence and adulthood, but most rely on participant recall to provide information regarding medication use, except for one that used linked administrative, clinical, and educational data to examine a birth cohort.<sup>87</sup> No prospective studies have been designed to investigate the question of long-term functional outcomes directly.

Very few studies describe long-term outcomes of treatments for ADHD on academic or school-based outcomes. There appear to be long-term academic benefits with medication interventions in some domains (e.g., improved absenteeism and grade retention).<sup>85,86</sup> Combining psychosocial/behavioral and academic skills interventions with medication offers no additional gains over medication alone, at least for children with ADHD without comorbid learning disabilities.<sup>89</sup> The psychosocial/behavioral intervention in the MTA study included a home and school focus on homework that successfully improved homework completion for up to 2 years.<sup>90</sup> Interventions directed at academic skills in classroom-based programs result in academic enhancement in a range of areas, but sustained intervention is required to provide continued academic growth over time.<sup>91,92</sup>

The types of interventions and domains of academic functioning and school outcomes under investigation vary widely across studies, making it difficult to compare results. In addition, few of the studies controlled for child characteristics such as learning disabilities and overall intellectual abilities. Additional aspects to consider are the challenges inherent in examining the multiple co-interventions offered in home, school, and clinic settings over extended lengths of time.

Our results using the GRADE approach to assign SOE are summarized in Table B. The evidence for long-term effectiveness of pharmacologic agents for improving ADHD symptoms is based on a single good study for methylphenidate with SMD = -0.54 (95% CI, -0.79 to

-0.29) and a single good study for atomoxetine with SMD = -0.40 (95% CI, -0.61 to -0.18). These studies followed the children for 12 or 14 months and showed benefit with few adverse effects, thereby resulting in low strength of evidence for longer term effectiveness for each of these agents. Similarly, there is a single good study showing benefits for the combination of methylphenidate and psychosocial interventions, with SMD = -0.70 (95% CI, -0.95 to -0.46). Overall there is insufficient information to comment on longer term outcomes for ADHD symptoms following behavior training for children, or for parents, or for academic interventions.

### **KQ3. Variability in Prevalence, Diagnosis, and Treatment**

One worldwide pooled prevalence estimate of ADHD among those 18 years of age or younger is 5.29 percent (95% CI, 5.01 to 5.56), although the percentage use of stimulants in the United States in selected subsets (e.g., Medicaid recipients) exceeds this rate.<sup>93</sup> More boys than girls have ADHD, and children in the age group 5–10 years show the highest prevalence. In addition, some studies suggest children from lower SES demonstrate higher levels of symptoms. Research detailing prevalence in other age groups worldwide is generally lacking, with few studies examining prevalence among preschoolers, adolescents, or adults. Primary sources of variability among studies were diagnostic criteria and informant. Table C summarizes information regarding the underlying prevalence of ADHD, rates of diagnosis, and treatment by geography, time period, provider type, and sociodemographic characteristics.

Clinical identification of ADHD and treatment with psychostimulants increased throughout the early 1960s to mid-1990s in North America, and use of ADHD medications of various types has continued to grow.<sup>94-96</sup> Changing patterns of ADHD medication use suggest increases among girls and adolescents. While at much lower rates, medication use (frequently off label) has also increased among preschoolers.<sup>97</sup> Agents prescribed have changed from short-acting preparations of stimulants to long-acting formulations.<sup>98</sup> Disparities occur among those who are identified and receive medication. Studies in the United States document that

more boys than girls, more whites than Hispanics or African Americans, more children living in prosperous than less affluent communities, and more children living in urban than rural centers are dispensed medication.<sup>99-102</sup> Regional variations occur both within and outside the United States. More children in the Midwest and South receive diagnoses and ADHD medications relative to the western United States. More people in the United States receive medications than in Europe and the rest of the world.<sup>98,103</sup> Not surprisingly, the source of data influences these findings. Epidemiological surveys with parents suggest a smaller increase in medication use than is indicated by insurance claims and Medicaid data sources. In addition, Medicaid data sources document that only about half those identified receive medication treatment.<sup>104</sup> Prescription data show that many who fill an initial prescription do not continue using medication for long periods of time, especially among low-income and ethnic minority youths.<sup>105,106</sup> Clinical identification by nonphysicians and nonmedication interventions for ADHD were not captured in the sources of data used. Assessing possible interactions among various factors that appear to affect patterns of diagnosis and treatment (e.g., region by time period by provider type) would be informative but is beyond the scope of this review.

Concerns regarding inaccurate identification of children and youths with ADHD in the community appear to be justified. However, the current review should be seen as preliminary, as the data to answer service use questions are incomplete and primarily reflect services available through the health sector. Some of the increased identification and treatment likely reflect acknowledgment of the disorder in children and youths who were previously undiagnosed and untreated. On the other hand, prescriptions, as captured in databases collected for insurance claims, may reflect physicians' responding to concerns raised by parents and teachers. When lack of clinical certainty exists and the intervention is relatively quick and safe, a doctor may easily respond to a request for help on an individual level with "try this and see if it helps." Studies based on epidemiological surveys rather than health insurance claims suggest a more gradual rise in identification and prescription treatment. Since children and youths with ADHD also can receive interventions at school and

through mental health centers, the patterns observed may reflect reliance on physician services by those who lack access to other alternatives. The differential changes over time in ADHD diagnoses and prescription

treatments among regions of the United States, or between the United States and Europe, also reflect cultural differences in beliefs and attitudes about the disorder and how it should be treated.

**Table A. KQ1: Effectiveness of interventions for ADHD and DBD in children younger than 6 years of age**

<b>Intervention</b>	<b>Level of Evidence</b>	<b>Conclusion</b>
Parent Behavior Training	SOE: High  SMD: -0.68 (95% CI, -0.88 to -0.47)	Parent behavioral interventions are an efficacious treatment option for preschoolers with DBD and show benefit for ADHD symptoms.  These studies support the long-term effectiveness of parent interventions for preschoolers with DBD, including ADHD symptoms, with evidence that benefits are maintained for up to 2 years. There also appears to be a dose-response effect.
Multicomponent Home and School or Daycare-Based Interventions	SOE: Insufficient	Evidence is drawn from few reports.  Where there is no socioeconomic burden, multicomponent interventions work as well as a structured parent education program in several domains.  Where there is socioeconomic burden, the treatment classroom appears to be the primary beneficial intervention, and this appears to be related to lack of parent engagement and attendance at PBT sessions. Relative benefits of the school-based intervention diminished over 2 years.
Medication (MPH Only)	SOE: Low  SMD: -0.83 (95% CI, -1.21 to -0.44)	With evidence drawn primarily from the PATS study, MPH (e.g., short-acting, immediate-release MPH) is both efficacious and generally safe for treatment of ADHD symptoms, but there has been no long-term followup in preschoolers.

**Note:** ADHD = attention deficit hyperactivity disorder; CI = confidence interval; DBD = disruptive behavior disorder; KQ = Key Question; MPH = methylphenidate; PATS = Preschool ADHD Treatment Study; PBT = parent behavior training; SMD = standardized mean difference; SOE = strength of evidence.

**Table B. KQ2: Long-term (>1 year) effectiveness of interventions for ADHD in people 6 years and older**

<b>Intervention</b>	<b>Level of Evidence</b>	<b>Conclusion</b>
Medication Treatment	SOE: Low  MPH: SMD: -0.54 (95% CI, -0.79 to -0.29)  ATX: SMD: -0.40 (95% CI, -0.61 to -0.18)	Very few studies include untreated controls.  Studies were largely funded by industry.  Psychostimulants continue to provide control of ADHD symptoms and are generally well tolerated for months to years at a time. The evidence for MPH use in the context of careful medication monitoring shows good evidence for benefits for symptoms for 14 months.  ATX is effective for ADHD symptoms and well tolerated over 12 months.
	SOE: Insufficient	Only one study of GXR monotherapy is available. It reports reduced ADHD symptoms and global improvement, although less than a fifth of participants completed 12 months.  Monitoring of cardiac status may be indicated since approximately 1% of participants showed ECG changes judged clinically significant.
Combined Psychostimulant Medication and Behavioral Treatment	SOE: Low  SMD: -0.70 (95% CI, -0.95 to -0.46)	The results from 2 cohorts indicate both medication (MPH) and combined medication and behavioral treatment are effective in treating ADHD plus ODD symptoms in children, primarily boys ages 7-9 years of normal intelligence with combined type of ADHD, especially during the first 2 years of treatment.  Several reports from one high-quality study suggest that combined medication and behavioral treatment improves outcomes more than medication alone for some subgroups of children with ADHD combined type and for some outcomes.
Behavioral/Psychosocial	SOE: Insufficient	There is not enough evidence to draw conclusions for persons 6 years and older with a diagnosis of ADHD.
Parent Behavior Training	SOE: Insufficient	There is not enough evidence to draw conclusions for persons 6 years and older with a diagnosis of ADHD.
Academic Interventions	SOE: Insufficient	One good-quality study and its extension showed that classroom-based programs to enhance academic skills are effective in improving achievement scores in multiple domains, but following discontinuation, the benefits for sustained growth in academic skills are limited to the domain of reading fluency. All other domains show skill maintenance but not continued growth.

**Note:** ADHD = attention deficit hyperactivity disorder; ATX = atomoxetine; ECG = electrocardiogram; GXR = guanfacine extended release; KQ = Key Question; MPH = methylphenidate; ODD = oppositional defiant disorder; SMD = standardized mean difference; SOE = strength of evidence.

**Table C. KQ3: Underlying prevalence of ADHD, rates of diagnosis, and treatment by geography, time period, provider type, and sociodemographic characteristics**

Issue	Factor	Conclusion
Prevalence	Geography	<p>Context and cultural overlay influence how ADHD is understood from country to country, and thus how it is treated.</p> <p>Underlying prevalence does not appear to vary much between nations and regions, once differences in methodologies for ascertainment are taken into account</p>
	Time period	<p>Since identified as a clinical entity in 1902 in the context of mandatory education, prevalence of cases identified has increased.</p> <p>Some proportion of this secular trend is due to refinement of the state of knowledge, as well as changes in definition of acceptable informant, uses of screening tests, and changes in classification systems and diagnostic categories over time. In addition, patterns of access and location of service have been used to document prevalence.</p>
	SES	<p>Some studies suggest that those of lower SES have a higher prevalence of ADHD, although those of higher SES are more likely to be treated.</p>
	Sex	<p>Most studies illustrate a sex difference in the prevalence of ADHD (males &gt; females).</p>
	Age	<p>The age group ≈5-10 years appears to experience the highest prevalence.</p> <p>ADHD research detailing prevalence in adults is lacking</p>
Clinical Identification	Service provider	<p>Appreciation of the combined neurodevelopmental and environmental etiologies and magnitude of impairment due to the condition has increased over the past 4 decades.</p> <p>Providers vary in level of expertise in diagnosis of ADHD, as well as in familiarity with screening instruments and classification systems</p>
	Location	<p>Rates of diagnosis vary considerably due to cultural context, access to health care services, and provider type.</p> <p>Significant regional variations are noted within the United States.</p> <p>Prevalence is reported to average 7.8%, with variability from 5.0% in Colorado to 11.1% in Alabama.</p> <p>In special populations, such as the incarcerated, rates as high as 25.5% have been noted.<sup>107</sup></p>
	Informant	<p>Parent and teacher observations have been accepted by some researchers in population studies in lieu of clinician diagnosis.</p> <p>The NSCH<sup>4</sup> accepted a positive response from the primary caretaker to the question, “Has a doctor or health professional ever told you that [child name] has ... ADD or ADHD?” to estimate ADHD prevalence in 2003.</p> <p>Rates of diagnosis vary considerably due to cultural context. Some ethnicities are more likely to seek help or accept the diagnosis than others.</p>
	Sex	<p>Boys are identified as having ADHD more frequently than girls.</p>
	Age	<p>Primary school–age children are identified as having ADHD more frequently than older children.</p> <p>Formerly thought to disappear in adulthood, it is now recognized that ADHD may persist throughout the lifespan.</p>

**Table C. KQ3: Underlying prevalence of ADHD, rates of diagnosis, and treatment by geography, time period, provider type, and sociodemographic characteristics (cont'd)**

Issue	Factor	Conclusion
Treatment	Location	Rates of treatment vary considerably due to location and access to providers of health care services, internationally as well as regionally or even within the same community, dependent on provider type and availability, provider remuneration, and insurance status of patient.
	Provider	Family practitioners in many jurisdictions, particularly those with limited access to specialists, report significant pressure from parents and teachers to prescribe stimulant medications.
	Informant	<p>The sociocultural experience of the parent or teacher informant may influence interpretation and reporting of behaviors, willingness and persistence in seeking professional help, and/or the acceptance of treatment.</p> <p>Accuracy and completeness of data influence prevalence estimates, as health insurance and prescription administrative databases suggest greater increase in treatment with medications over time than repeated community surveys do.</p>
	Time	The rate of psychostimulant medication has increased over the past 3 decades. More recent statistics from the International Narcotics Control Board, using a denominator of standardized defined daily doses, reports that medical use of MPH (i.e., Ritalin) in the United States has increased from 7.14 S-DDDs per 1,000 inhabitants per day in 2004 to 12.03 S-DDDs per 1,000 inhabitants per day in 2008. <sup>6</sup>
	SES	<p>Children of lower SES are identified as having ADHD more often than children of higher SES; however, the latter are more likely to receive stimulant medications.</p> <p>Lower SES and minority ethnicity are associated with shorter duration of medication use.</p> <p>Insurance status may influence access to specialist providers in the United States.</p>
	Sex	Only sparse comparative data are available examining rates of treatment by sex once ADHD is diagnosed.
	Age	Medication treatment prevalence is higher for primary school-age children than for adolescents or adults.

**Note:** ADD = attention deficit disorder; ADHD = attention deficit hyperactivity disorder; KQ = Key Question; MPH = methylphenidate; NSCH = National Survey of Children’s Health; S-DDD = standardized defined daily dose; SES = socioeconomic status.

## Remaining Issues

Since the AHRQ review of long-term intervention studies for ADHD, published in 1997, researchers have sought opportunities to discover what has happened to the participants in earlier studies and have begun to tackle the challenges of prospective cohort studies. The primary weaknesses reflected in the literature relate to these challenges. Overall, data were difficult to compare due to lack of clarity with regard to uniformity of assessment and reporting, as well as inconsistencies in study design and the development of objective outcomes. For interventions for preschoolers with DBD, a primary challenge is distinguishing the overlying effect of normal maturation from the clinical condition; few extended studies encompass untreated comparison groups and these studies are of more complex combinations of parent, teacher, and child behavior training interventions. Only recently have investigations of PBT included direct measures of ADHD symptoms and associated functional impairments. Researchers also should describe what, if any, unintended negative consequences occur when families are offered PBT for their preschooler. For example, some parents may respond better to individual rather than group PBT sessions, and some children with comorbid developmental disorders may not respond to standard behavioral interventions. Documenting what works best for whom is an important next step in describing the overall effectiveness of the intervention.

A second important finding follows the suggestive outcome that parents from different SES groups appear to benefit from different approaches. An important subtext is the question of how approaches to PBT could be refined to be acceptable to lower SES families, as well as examining the mix of parent, teacher, and child approaches both at home and at school. Further studies examining a range of child functional outcomes are important as well. Remaining untapped as a source of information is the likelihood that “care as usual” varies in different communities, leading to diverse outcomes in comparison groups.

The lack of research in adolescents and adults with ADHD presents a major gap in the literature. Also, few study participants are girls or come from diverse racial or ethnic groups. Studies have not included subgroup analyses for those with ADHD inattentive subtype,

comorbid anxiety, or learning disorders. No clinical studies have been designed to follow children through adolescence and into adulthood, tracking the mix of interventions obtained by participants and their functional outcomes. It will be particularly challenging to coordinate observations regarding academic interventions and outcomes. No prospective studies examining nonmedication interventions have enrolled adolescents or adults identified with ADHD to investigate whether interventions at later stages of development are effective for improving function.

An important strength of research in the past decade is evidence for effective and safe medications for children, youths, and adults with ADHD. There are several documented pharmacological agents that control symptoms for 1 to 2 years. The choices help to optimize effectiveness and tolerability over this time period. Beyond 2 years, benefit appears to be highly variable. Evidence now suggests that some children experience mild decrements in their growth rate while on psychostimulants. While these are considered of little clinical significance, it is not clear if these changes may also represent potential nutritional or developmental concerns that are not yet recognized.

An opportunity and a challenge for this review was integrating information from clinical trials research with the broad picture provided by newly emerging research using a variety of large-scale databases reflecting community access to health services and use of pharmacological agents. Some of the administrative data sources were useful to explore rare but potentially serious adverse events following use of ADHD medications. On this topic, health administrative data suggest that neither cardiac events among those aged 20 years and younger nor cerebrovascular accidents in adults are more frequent among those using medications for ADHD than for persons in the general population. However, further examination using appropriate data sources (e.g., case control studies) is warranted, as adult users of psychostimulants or ATX may be at increased risk of transient ischemic attacks.

Our final question focused on the match between community prevalence of ADHD and rates of identification and treatment of the disorder. The complex issues of mental health service delivery are superimposed on the underlying sociocultural mix of

beliefs about ADHD as a health disorder and attitudes toward use of medication. While recognized as the standard for effectiveness research, clinical trials are nonetheless limited to relying on volunteer participants who are then carefully selected as pure examples of a condition and provided with a carefully controlled intervention. Epidemiological survey methods offer information on risk and protective factors in large populations but still rely on volunteers to provide information, and in that way underrepresent marginalized or transient segments of the population. The way diagnoses and interventions are actually used in day-to-day clinical practice in the community is rarely so precise or carefully controlled.

In the past two decades, increased technological advances have allowed research using existing administrative data to represent clinical practice. Insurance claims and prescription databases have become important complementary sources of health services information to investigate questions about ADHD identification and treatment in actual practice. The key limitations in this body of literature are the use of data collected for the purpose of justifying health services, the lack of quality control regarding reliability and validity of measures, and the selective nature of clinical services captured, almost exclusively pharmacological interventions. On the other hand, the size and representativeness of the sample populations offer compensatory advantages and strongly suggest that many children and youths are diagnosed who then receive suboptimal care. There appears to be little research documenting nonpharmacological interventions or educational services use for those with ADHD, which reflects a lack of infrastructure for linkage among data sources across health, education, and specialty care systems. Better synchronization of information across these complementary domains would promote population-based research and improved services delivery for ADHD.

## References

1. Still GF. Some abnormal psychological conditions in children: the Goulstonian lectures. *Lancet*. 1902;1:1008-12.
2. Mayes R, Rafalovich A. Suffer the restless children: the evolution of ADHD and paediatric stimulant use, 1900-80. *Hist Psychiatry*. 2007;18(72:Pt 4):435-57.
3. Eisenberg L. Commentary with a historical perspective by a child psychiatrist: when "ADHD" was the "brain-damaged child." *J Child Adolesc Psychopharmacol*. 2007;17(3):279-83.
4. Centers for Disease Control and Prevention. Mental health in the United States. Prevalence of diagnosis and medication treatment for attention-deficit/hyperactivity disorder--United States, 2003. *MMWR Morb Mortal Wkly Rep*. 2005;54(34):842-7.
5. Kessler RC, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. *Am J Psychiatry*. 2006;163(4):716-23.
6. Report of the International Narcotics Control Board for 2009. Comments on the Reported Statistics on Psychotropic Substances. 35-59. 2010. [www.incb.org/pdf/technical-reports/psychotropics/2009/Publication\\_Parts\\_09\\_english/Part\\_Two\\_Tables\\_EFS\\_2009.pdf](http://www.incb.org/pdf/technical-reports/psychotropics/2009/Publication_Parts_09_english/Part_Two_Tables_EFS_2009.pdf).
7. Greenhill L, Kollins S, Abikoff H, et al. Efficacy and safety of immediate-release methylphenidate treatment for preschoolers with ADHD. *J Am Acad Child Adolesc Psychiatry*. 2006;45(11):1284-93.
8. Fayyad J, de Graaf R, Kessler R, et al. Cross-national prevalence and correlates of adult attention-deficit hyperactivity disorder. *Br J Psychiatry*. 2007;190:402-9.
9. Simon V, Czobor P, Balint S, et al. Prevalence and correlates of adult attention-deficit hyperactivity disorder: meta-analysis. *Br J Psychiatry*. 2009;194(3):204-11.
10. Jadad AR, Boyle M, Cunningham C, et al. Treatment of Attention-Deficit/Hyperactivity Disorder. Evidence Report/Technology Assessment No. 11. AHRQ Publication No. 00-E005. Rockville, MD: Agency for Healthcare Research and Quality; Nov. 1999. PM:10790990.
11. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.
12. Higgins J, Green S. *Cochrane Handbook for Systematic Reviews of Interventions*, version 5.1.0; Mar. 2011.
13. Armstrong R, Waters E, Doyle J. Chapter 21, Reviews in health promotion and public health. In: *Cochrane Handbook for Systematic Reviews of Interventions*. The Cochrane Collaboration; 2008.
14. Grade Working Group. *Grading the Quality of Evidence and the Strength of Recommendations*. [www.gradeworkinggroup.org](http://www.gradeworkinggroup.org).

15. Owens DK, Lohr KN, Atkins D, et al. AHRQ Series Paper 5: Grading the strength of a body of evidence when comparing medical interventions - Agency for Healthcare Research and Quality and the Effective Health-care Program. *J Clin Epidemiol.* 2010;63:513-23.
16. Markie-Dadds C, Sanders MR. A controlled evaluation of an enhanced self-directed behavioural family intervention for parents of children with conduct problems in rural and remote areas. *Behav Change.* 2006;23(1):55-72.
17. Connell S, Sanders MR, Markie-Dadds C. Self-directed behavioral family intervention for parents of oppositional children in rural and remote areas. *Behav Modif.* 1997;21(4):379-408.
18. Markie-Dadds C, Sanders MR. Self-directed Triple P (Positive Parenting Program) for mothers with children at-risk of developing conduct problems. *Behav Cogn Psychother.* 2006;34(3):259-75.
19. Bor W, Sanders MR, Markie-Dadds C. The effects of the Triple P-Positive Parenting Program on preschool children with co-occurring disruptive behavior and attentional/hyperactive difficulties. *J Abnorm Child Psychol.* 2002;30(6):571-87.
20. Sanders MR, Christensen AP. A comparison of the effects of child management and planned activities training in five parenting environments. *J Abnorm Child Psychol.* 1985;13(1):101-17.
21. Sanders MR, Bor W, Morawska A. Maintenance of treatment gains: a comparison of enhanced, standard, and self-directed Triple P-Positive Parenting Program. *J Abnorm Child Psychol.* 2007;35(6):983-98.
22. Dadds MR, McHugh TA. Social support and treatment outcome in behavioral family therapy for child conduct problems. *J Consult Clin Psychol.* 1992;60(2):252-9.
23. Lavigne JV, Lebailly SA, Gouze KR, et al. Treating oppositional defiant disorder in primary care: a comparison of three models. *J Pediatr Psychol.* 2008;33(5):449-61.
24. Jones K, Daley D, Hutchings J, et al. Efficacy of the Incredible Years Basic Parent Training Programme as an early intervention for children with conduct problems and ADHD. *Child Care Health Dev.* 2007;33(6):749-56.
25. Hutchings J, Gardner F, Bywater T, et al. Parenting intervention in Sure Start services for children at risk of developing conduct disorder: pragmatic randomised controlled trial. *BMJ.* 2007;334(7595):678.
26. Bywater T, Hutchings J, Daley D, et al. Long-term effectiveness of a parenting intervention for children at risk of developing conduct disorder. *Br J Psychiatry.* 2009;195(4):318-24.
27. Williford AP, Shelton TL. Using mental health consultation to decrease disruptive behaviors in preschoolers: adapting an empirically-supported intervention. *J Child Psychol Psychiatry.* 2008;49(2):191-200.
28. Bagner DM, Eyberg SM. Parent-child interaction therapy for disruptive behavior in children with mental retardation: a randomized controlled trial. *J Clin Child Adolesc Psychol.* 2007;36(3):418-29.
29. Hood KK, Eyberg SM. Outcomes of parent-child interaction therapy: mothers' reports of maintenance three to six years after treatment. *J Clin Child Adolesc Psychol.* 2003;32(3):419-29.
30. Matos M, Bauermeister JJ, Bernal G. Parent-child interaction therapy for Puerto Rican preschool children with ADHD and behavior problems: a pilot efficacy study. *Fam Process.* 2009;48(2):232-52.
31. Nixon RDV. Changes in hyperactivity and temperament in behaviourally disturbed preschoolers after parent-child interaction therapy (PCIT). *Behav Change.* 2001;18(3):168-76.
32. Nixon RD, Sweeney L, Erickson DB, et al. Parent-child interaction therapy: a comparison of standard and abbreviated treatments for oppositional defiant preschoolers. *J Consult Clin Psychol.* 2003;71(2):251-60.
33. Funderburk BW, Eyberg SM, Newcomb K, et al. Parent-child interaction therapy with behavior problem children: maintenance of treatment effects in the school setting. *Child Fam Behav Ther.* 1998;20(2):17-38.
34. Eyberg SM, Boggs SR, Algina J. Parent-child interaction therapy: a psychosocial model for the treatment of young children with conduct problem behavior and their families. *Psychopharmacol Bull.* 1995;31(1):83-91.
35. Schuhmann EM, Foote RC, Eyberg SM, et al. Efficacy of parent-child interaction therapy: interim report of a randomized trial with short-term maintenance. *J Clin Child Psychol.* 1998;27(1):34-45.
36. Sonuga-Barke EJ, Daley D, Thompson M, et al. Parent-based therapies for preschool attention-deficit/hyperactivity disorder: a randomized, controlled trial with a community sample. *J Am Acad Child Adolesc Psychiatry.* 2001;40(4):402-8.
37. Sonuga-Barke EJ, Thompson M, Daley D, et al. Parent training for Attention Deficit/Hyperactivity Disorder: is it as effective when delivered as routine rather than as specialist care? *Br J Clin Psychol.* 2004;43(Pt 4):4-57.
38. Sonuga-Barke EJ, Daley D, Thompson M. Does maternal ADHD reduce the effectiveness of parent training for preschool children's ADHD? *J Am Acad Child Adolesc Psychiatry.* 2002;41(6):696-702.

39. Thompson MJJ, Laver-Bradbury C, Ayres M, et al. A small-scale randomized controlled trial of the revised New Forest Parenting Programme for preschoolers with attention deficit hyperactivity disorder. *Eur Child Adolesc Psychiatry*. 2009;18(10):605-16.
40. Hanisch C, Freund-Braier I, Hautmann C, et al. Detecting effects of the indicated prevention Programme for Externalizing Problem behaviour (PEP) on child symptoms, parenting, and parental quality of life in a randomized controlled trial. *Behav Cogn Psychother*. 2010;38(1):95-112.
41. Feusner JD, Moody T, Hembacher E, et al. Abnormalities of visual processing and frontostriatal systems in body dysmorphic disorder. *Arch Gen Psychiatry*. 2010;67(2):197-205.
42. Reid MJ, Webster-Stratton C, Hammond M. Follow-up of children who received the Incredible Years intervention for oppositional-defiant disorder: maintenance and prediction of 2-year outcome. *Behav Ther*. 2003;4(4):471-91.
43. Heriot SA, Evans IM, Foster TM. Critical influences affecting response to various treatments in young children with ADHD: a case series. *Child Care Health Dev*. 2008;34(1):121-33.
44. Barkley RA. The effects of methylphenidate on the interactions of preschool ADHD children with their mothers. *J Am Acad Child Adolesc Psychiatry*. 1988;27(3):336-41.
45. Barkley RA, Karlsson J, Pollard S, et al. Developmental changes in the mother-child interactions of hyperactive boys: effects of two dose levels of Ritalin. *J Child Psychol Psychiatry*. 1985;26(5):705-15.
46. Handen BL, Feldman HM, Lurier A, et al. Efficacy of methylphenidate among preschool children with developmental disabilities and ADHD. *J Am Acad Child Adolesc Psychiatry*. 1999;38(7):805-12.
47. Musten LM, Firestone P, Pisterman S, et al. Effects of methylphenidate on preschool children with ADHD: cognitive and behavioral functions. *J Am Acad Child Adolesc Psychiatry*. 1997;36(10):1407-15.
48. Ghuman JK, Aman MG, Lecavalier L, et al. Randomized, placebo-controlled, crossover study of methylphenidate for attention-deficit/hyperactivity disorder symptoms in preschoolers with developmental disorders. *J Child Adolesc Psychopharmacol*. 2009;19(4):329-39.
49. Short EJ, Manos MJ, Findling RL, et al. A prospective study of stimulant response in preschool children: insights from ROC analyses. *J Am Acad Child Adolesc Psychiatry*. 2004;43(3):251-9.
50. Schleifer M, Weiss G, Cohen N, et al. Hyperactivity in preschoolers and the effect of methylphenidate. *Am J Orthopsychiatry*. 1975;45(1):38-50.
51. Abikoff HB, Vitiello B, Riddle MA, et al. Methylphenidate effects on functional outcomes in the Preschoolers with Attention-Deficit/Hyperactivity Disorder Treatment Study (PATS). *J Child Adolesc Psychopharmacol*. 2007;17(5):581-92.
52. Ghuman JK, Riddle MA, Vitiello B, et al. Comorbidity moderates response to methylphenidate in the Preschoolers with Attention-Deficit/Hyperactivity Disorder Treatment Study (PATS). *J Child Adolesc Psychopharmacol*. 2007;17(5):563-80.
53. Swanson J, Greenhill L, Wigal T, et al. Stimulant-related reductions of growth rates in the PATS. *J Am Acad Child Adolesc Psychiatry*. 2006;45(11):1304-13.
54. Wigal T, Greenhill L, Chuang S, et al. Safety and tolerability of methylphenidate in preschool children with ADHD. *J Am Acad Child Adolesc Psychiatry*. 2006;45(11):1294-303.
55. Firestone P, Musten LM, Pisterman S, et al. Short-term side effects of stimulant medication are increased in preschool children with attention-deficit/hyperactivity disorder: a double-blind placebo-controlled study. *J Child Adolesc Psychopharmacol*. 1998;8(1):13-25.
56. Cohen NJ. Evaluation of the relative effectiveness of methylphenidate and cognitive behavior modification in the treatment of kindergarten-aged hyperactive children. *J Abnorm Child Psychol*. 1981;9(1):43-54.
57. Charach A, Ickowicz A, Schachar R. Stimulant treatment over five years: adherence, effectiveness, and adverse effects. *J Am Acad Child Adolesc Psychiatry*. 2004;43(5):559-67.
58. Law SF, Schachar RJ. Do typical clinical doses of methylphenidate cause tics in children treated for attention-deficit hyperactivity disorder? *J Am Acad Child Adolesc Psychiatry*. 1999;38(8):944-51.
59. Barbaresi WJ, Katusic SK, Colligan RC, et al. Long-term stimulant medication treatment of attention-deficit/hyperactivity disorder: results from a population-based study. *J Dev Behav Pediatr*. 2006;27(1):1-10.
60. Hoare P, Remschmidt H, Medori R, et al. 12-month efficacy and safety of OROS MPH in children and adolescents with attention-deficit/hyperactivity disorder switched from MPH. *Eur Child Adolesc Psychiatry*. 2005;14(6):305-9.
61. Gillberg C, Melander H, von Knorring AL, et al. Long-term stimulant treatment of children with attention-deficit hyperactivity disorder symptoms. A randomized, double-blind, placebo-controlled trial. *Arch Gen Psychiatry*. 1997;54(9):857-64.

62. Gadow KD, Sverd J, Sprafkin J, et al. Long-term methylphenidate therapy in children with comorbid attention-deficit hyperactivity disorder and chronic multiple tic disorder. *Arch Gen Psychiatry*. 1999;56(4):330-6.
63. McGough JJ, Biederman J, Wigal SB, et al. Long-term tolerability and effectiveness of once-daily mixed amphetamine salts (Adderall XR) in children with ADHD. *J Am Acad Child Adolesc Psychiatry*. 2005;44(6):530-8.
64. Findling RL, Biederman J, Wilens TE, et al. Short- and long-term cardiovascular effects of mixed amphetamine salts extended release in children. *J Pediatr*. 2005;147(3):348-54.
65. Weisler RH, Biederman J, Spencer TJ, et al. Long-term cardiovascular effects of mixed amphetamine salts extended release in adults with ADHD. *CNS Spectrums*. 2005;10(12 Suppl 20):35-43.
66. Michelson D, Buitelaar JK, Danckaerts M, et al. Relapse prevention in pediatric patients with ADHD treated with atomoxetine: a randomized, double-blind, placebo-controlled study. *J Am Acad Child Adolesc Psychiatry*. 2004;43(7):896-904.
67. Buitelaar JK, Michelson D, Danckaerts M, et al. A randomized, double-blind study of continuation treatment for attention-deficit/hyperactivity disorder after 1 year. *Biol Psychiatry*. 2007;61(5):694-9.
68. Adler LA, Spencer TJ, Milton DR, et al. Long-term, open-label study of the safety and efficacy of atomoxetine in adults with attention-deficit/hyperactivity disorder: an interim analysis. *J Clin Psychiatry*. 2005;66(3):294-9.
69. Wernicke JF, Faries D, Girod D, et al. Cardiovascular effects of atomoxetine in children, adolescents, and adults. *Drug Safety*. 2003;26(10):729-40.
70. Biederman J, Melmed RD, Patel A, et al. Long-term, open-label extension study of guanfacine extended release in children and adolescents with ADHD. *CNS Spectrums*. 2008;13(12):1047-55.
71. Sallee FR, Lyne A, Wigal T, et al. Long-term safety and efficacy of guanfacine extended release in children and adolescents with attention-deficit/hyperactivity disorder. *J Child Adolesc Psychopharmacol*. 2009;19(3):215-26.
72. Conners CK, Epstein JN, March JS, et al. Multimodal treatment of ADHD in the MTA: an alternative outcome analysis. *J Am Acad Child Adolesc Psychiatry*. 2001;40(2):159-67.
73. MTA Cooperative Group. National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: 24-month outcomes of treatment strategies for attention-deficit/hyperactivity disorder. *Pediatrics*. 2004;113(4):754-61.
74. MTA Cooperative Group. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. The MTA Cooperative Group. Multimodal Treatment Study of Children with ADHD. *Arch Gen Psychiatry*. 1999;56(12):1073-86.
75. Abikoff H, Hechtman L, Klein RG, et al. Symptomatic improvement in children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. *J Am Acad Child Adolesc Psychiatry*. 2004;43(7):802-11.
76. Abikoff H, Hechtman L, Klein RG, et al. Social functioning in children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. *J Am Acad Child Adolesc Psychiatry*. 2004;43(7):820-9.
77. So CY, Leung PW, Hung SF. Treatment effectiveness of combined medication/behavioural treatment with Chinese ADHD children in routine practice. *Behav Res Ther*. 2008;46(9):983-92.
78. Swanson JM, Elliott GR, Greenhill LL, et al. Effects of stimulant medication on growth rates across 3 years in the MTA follow-up. *J Am Acad Child Adolesc Psychiatry*. 2007;46(8):1015-27.
79. Newcorn JH, Kratochvil CJ, Allen AJ, et al. Atomoxetine and osmotically released methylphenidate for the treatment of attention deficit hyperactivity disorder: acute comparison and differential response. *Am J Psychiatry*. 2008;165(6):721-30.
80. Jensen PS, Hinshaw SP, Kraemer HC, et al. ADHD comorbidity findings from the MTA study: comparing comorbid subgroups. *J Am Acad Child Adolesc Psychiatry*. 2001;40(2):147-58.
81. Jensen PS, Arnold LE, Swanson JM, et al. 3-year follow-up of the NIMH MTA study. *J Am Acad Child Adolesc Psychiatry*. 2007;46(8):989-1002.
82. Molina BS, Hinshaw SP, Swanson JM, et al. The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. *J Am Acad Child Adolesc Psychiatry*. 2009;48(5):484-500.
83. Molina BS, Flory K, Hinshaw SP, et al. Delinquent behavior and emerging substance use in the MTA at 36 months: prevalence, course, and treatment effects. *J Am Acad Child Adolesc Psychiatry*. 2007;46(8):1028-40.

84. Swanson JM, Hinshaw SP, Arnold LE, et al. Secondary evaluations of MTA 36-month outcomes: propensity score and growth mixture model analyses. *J Am Acad Child Adolesc Psychiatry.* 2007;46(8):1003-14.
85. Barbaresi WJ, Katusic SK, Colligan RC, et al. Modifiers of long-term school outcomes for children with attention-deficit/hyperactivity disorder: does treatment with stimulant medication make a difference? Results from a population-based study. *J Dev Behav Pediatr.* 2007;28(4):274-87.
86. Biederman J, Monuteaux MC, Spencer T, et al. Do stimulants protect against psychiatric disorders in youth with ADHD? A 10-year follow-up study. *Pediatrics.* 2009;124(1):71-8.
87. Katusic SK, Barbaresi WJ, Colligan RC, et al. Psychostimulant treatment and risk for substance abuse among young adults with a history of attention-deficit/hyperactivity disorder: a population-based, birth cohort study. *J Child Adolesc Psychopharmacol.* 2005;15(5):764-76.
88. Mannuzza S, Klein RG, Truong NL, et al. Age of methylphenidate treatment initiation in children with ADHD and later substance abuse: prospective follow-up into adulthood. *Am J Psychiatry.* 2008;165(5):604-9.
89. Hechtman L, Abikoff H, Klein RG, et al. Academic achievement and emotional status of children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. *J Am Acad Child Adolesc Psychiatry.* 2004;43(7):812-9.
90. Langberg JM, Arnold LE, Flowers AM, et al. Parent-reported homework problems in the MTA study: evidence for sustained improvement with behavioral treatment. *J Clin Child Adolesc Psychol.* 2010;39(2):220-33.
91. Jitendra AK, DuPaul GJ, Volpe RJ, et al. Consultation-based academic intervention for children with attention deficit hyperactivity disorder: school functioning outcomes. *School Psych Rev.* 2007;36(2):217-36.
92. Volpe RJ, DuPaul GJ, Jitendra AK, et al. Consultation-based academic interventions for children with attention deficit hyperactivity disorder: effects on reading and mathematics outcomes at 1-year follow-up. *School Psych Rev.* 2009;38(1):5-13.
93. Polanczyk G, de Lima MS, Horta BL, et al. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. *Am J Psychiatry.* 2007;164(6):942-8.
94. Safer DJ, Zito JM, Fine EM. Increased methylphenidate usage for attention deficit disorder in the 1990s. *Pediatrics.* 1996;98(6):1084-8.
95. Robison LM, Sclar DA, Skaer TL, et al. National trends in the prevalence of attention-deficit/hyperactivity disorder and the prescribing of methylphenidate among school-age children: 1990-1995. *Clin Pediatr (Phila).* 1999;38(4):209-17.
96. Zuvekas SH, Vitiello B, Norquist GS. Recent trends in stimulant medication use among U.S. children. *Am J Psychiatry.* 2006;163(4):579-85.
97. Zito JM, Safer DJ, Valluri S, et al. Psychotherapeutic medication prevalence in Medicaid-insured preschoolers. *J Child Adolesc Psychopharmacol.* 2007;17(2):195-203.
98. Scheffler RM, Hinshaw SP, Modrek S, et al. The global market for ADHD medications. *Health Aff (Millwood).* 2007;26(2):450-7.
99. Bokhari F, Mayes R, Scheffler RM. An analysis of the significant variation in psychostimulant use across the U.S. *Pharmacoepidemiol Drug Saf.* 2005;14(4):267-75.
100. Bloom B, Cohen RA, Freeman G. Summary health statistics for U.S. children: National Health Interview Survey, 2007. *Vital Health Stat* 2009;(239):1-80.
101. Miller TW, Nigg JT, Miller RL. Attention deficit hyperactivity disorder in African American children: what can be concluded from the past ten years? *Clin Psychol Rev.* 2009;29(1):77-86.
102. Leslie LK, Wolraich ML. ADHD service use patterns in youth. *J Pediatr Psychol.* 2007;32(6):695-710.
103. Zito JM, Safer DJ, de Jong-van den Berg L, et al. A three-country comparison of psychotropic medication prevalence in youth. *Child Adolesc Psychiatry Ment Health.* 2008;2(1):26.
104. Froehlich TE, Lanphear BP, Epstein JN, et al. Prevalence, recognition, and treatment of attention-deficit/hyperactivity disorder in a national sample of US children. *Arch Pediatr Adolesc Med.* 2007;161(9):857-64.
105. Perwien A, Hall J, Swensen A, et al. Stimulant treatment patterns and compliance in children and adults with newly treated attention-deficit/hyperactivity disorder. *J Manag Care Pharm.* 2004;10(2):122-9.
106. Marcus SC, Wan GJ, Kemner JE, et al. Continuity of methylphenidate treatment for attention-deficit/hyperactivity disorder. *Arch Pediatr Adolesc Med.* 2005;159(6):572-8.
107. Eyestone LL, Howell RJ. An epidemiological study of attention-deficit hyperactivity disorder and major depression in a male prison population. *J Am Acad Psychiatry Law.* 1994;22(2):181-93.

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