Comparative Effectiveness Review
Number 44

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.

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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,[1] 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.[2] 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.[3] 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.[4] Within the United States, the estimated prevalence of adult ADHD stands at 4.4 percent.[5] 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.[6] 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,[7] 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,[8] while worldwide it is 2.5 percent (95% confidence interval [CI], 2.1 to 3.1).[9]

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.[10] 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.[11] 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.[12]

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[13] 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.[14,15] 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),[16-22] Incredible Years Parenting Program,[23-27] Parent-Child Interaction Therapy,[28-35] and New Forest Parenting Program[36-39] 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.[40] 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).

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

Intervention	Level of Evidence	Conclusion
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

Intervention	Level of Evidence	Conclusion
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	Context and cultural overlay influence how ADHD is understood from country to country, and thus how it is treated. Underlying prevalence does not appear to vary much between nations and regions, once differences in methodologies for ascertainment are taken into account
	Time period	Since identified as a clinical entity in 1902 in the context of mandatory education, prevalence of cases identified has increased. 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.
	SES	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.
	Sex	Most studies illustrate a sex difference in the prevalence of ADHD (males > females).
	Age	The age group ≈5-10 years appears to experience the highest prevalence. ADHD research detailing prevalence in adults is lacking
Clinical Identification	Service provider	Appreciation of the combined neurodevelopmental and environmental etiologies and magnitude of impairment due to the condition has increased over the past 4 decades. Providers vary in level of expertise in diagnosis of ADHD, as well as in familiarity with screening instruments and classification systems
	Location	Rates of diagnosis vary considerably due to cultural context, access to health care services, and provider type. Significant regional variations are noted within the United States. Prevalence is reported to average 7.8%, with variability from 5.0% in Colorado to 11.1% in Alabama. In special populations, such as the incarcerated, rates as high as 25.5% have been noted.[107]
	Informant	Parent and teacher observations have been accepted by some researchers in population studies in lieu of clinician diagnosis. The NSCH[4] 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. Rates of diagnosis vary considerably due to cultural context. Some ethnicities are more likely to seek help or accept the diagnosis than others.
	Sex	Boys are identified as having ADHD more frequently than girls.
	Age	Primary school–age children are identified as having ADHD more frequently than older children. Formerly thought to disappear in adulthood, it is now recognized that ADHD may persist throughout the lifespan.

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	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. 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.
	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.[6]
	SES	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. Lower SES and minority ethnicity are associated with shorter duration of medication use. Insurance status may influence access to specialist providers in the United States.
	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.

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