Research Prioritization Topic Brief

Topic 1: “Attention Deficit Hyperactivity Disorder (ADHD)”

Comparative effectiveness of treatment options for attention deficit hyperactivity disorder (ADHD) in children.

PCORI Scientific Program Area: Assessment of Prevention, Diagnosis and Treatment Options

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### Introduction

**Overview/definition of topic**

**DESCRIPTION OF CONDITION**
- Attention Deficit Hyperactivity Disorder (ADHD) is a neurobehavioral disorder (i.e., pertaining to a person’s neurological state by observation of his/her behavior) that begins in childhood and could affect the entire lifespan
- ADHD is a highly heritable condition\(^1\) with genetic, biologic, and developmental factors all playing a role
- There is no single diagnostic or genetic test for ADHD, therefore early diagnosis is often impossible
- Diagnosis is based on behavioral signs or symptoms

### Relevance to patient-centered outcomes

**SYMPTOMS**
- Difficulties with paying attention, controlling impulsive behaviors, and/or being overly active

**PATIENT-CENTERED OUTCOMES\(^2,3\)**
- Children with ADHD are at increased risk of:
  - Learning problems and academic underachievement
  - Difficulties relating to peers and forming friendships
  - Major injuries
  - Early sexual activity and pregnancy
  - Substance abuse and/or dependence
  - Legal difficulties
  - Occupational difficulties

### Burden on Society

**Recent prevalence in populations and subpopulations**

**PREVALENCE\(^3\)**
- One of the most common chronic health conditions affecting school-age children
  - Approximately 9.5% of children ages 4-17 (5.4 million) diagnosed as of 2007
  - Prevalence of reported cases is increasing
- Boys (13.2%) more likely to be affected than girls (5.6%)
- Highest rates of ADHD are among children covered by Medicaid and multiracial children
### Effects on patients’ quality of life, productivity, functional capacity, mortality, use of health care services

<table>
<thead>
<tr>
<th>QUALITY OF LIFE</th>
<th>When untreated, ADHD has a significant impact on quality of life, psychosocial functioning, and family life</th>
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<tbody>
<tr>
<td>PRODUCTIVITY</td>
<td>When untreated, ADHD significantly affects the productivity of both patients and their family members</td>
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<td>HEALTH CARE SERVICE UTILIZATION</td>
<td>As of 2007, 2.7 million children ages 4-17 (66.3% of those diagnosed with ADHD) were receiving drug treatment³</td>
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<td>Children with ADHD are more likely to have hospital inpatient, hospital outpatient, and emergency department admissions³</td>
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<td>Children with ADHD are more likely to have contact with a mental health professional, use prescription drugs, and have frequent health care visits³</td>
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<td>Average ADHD-related expenditures were $1,319 per patient in 2007¹⁰</td>
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### How strongly does this overall societal burden suggest that CER on alternative approaches to this problem should be given high priority?

ADHD is a common disorder affecting a large number of individuals that can have a significant impact on psychosocial, social, educational, and/or occupational functioning throughout the lifespan. While drug treatment is most often used, wider implementation of behavioral treatment with or without drug treatment may improve outcomes, reduce need for medication treatment, and reduce associated side effects.

### Options for Addressing the Issue
Based on recent systematic reviews, what is known about the relative benefits and harms of the available management options?

For children under 6 years of age at risk of developing ADHD:
- There is strong evidence for parent-administered behavior training (training parents to use effective discipline strategies such as rewards and nonpunitive consequences to manage their child’s behavior). There are four different programs of behavior training interventions for parents, with some shared common therapeutic components.\(^4\)
  - Potential harms: no evidence\(^4\)
- There is limited evidence for methylphenidate (MPH) therapy (only one good study)\(^5,6\) Preschool ADHD Treatment Study (PATS) showed MPH to be effective\(^5,6\)
  - Potential harms: Young children have more dose-related side effects and interference with growth.\(^4\) In addition, MPH is less effective in children with three or more psychological conditions in addition to ADHD.\(^4\)

For those 6 years of age and older with a diagnosis of ADHD:
- Drugs used for controlling inattention, overactivity, and impulsivity have been shown to maintain effectiveness and safety for 12 to 24 months.\(^4\)
- It is less certain whether drugs are effective and safe over the longer term.\(^4\)
- Drug treatments and interventions that combine drug and behavioral treatments are more effective than behavioral treatments alone.\(^4\) This finding is based largely on the Multimodal Treatment Study of Children with ADHD (MTA).\(^7\)
  - The MTA study also suggests that (1) children with ADHD and comorbid anxiety respond equally well to behavioral treatment and medication; (2) children with ADHD and comorbid oppositional defiant disorder (ODD) or conduct disorder (CD) require medication for benefit; and (3) behavioral treatments in addition to medication may be most important for minorities.\(^8\)
- There is insufficient evidence to comment on longer-term outcomes for ADHD symptoms following behavioral training for parents, children, or for academic interventions\(^4\)

What could new research contribute to achieving better patient-centered outcomes?

For children under 6 years of age:
- There is a need for studies that compare drug treatments to behavioral treatments or combined drug and behavioral treatment as in the MTA study (which looked at intensive medication management alone, intensive behavioral treatment alone, and a combination of both) in older children. For the youngest children, it would be beneficial to assess which strategies have the best patient-centered outcomes
- Since most studies have used different behavioral strategies it would also be beneficial to assess the relative efficacy of key components of behavioral treatment programs in an effort to see what strategies are most practical

For those over 6 years of age:
- There is a need for more information on the long-term outcomes of behavioral and pharmacologic therapies
- The optimal follow-up and monitoring schedule for patients with ADHD is not known.\(^9\)
<table>
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<th>Question</th>
<th>Response</th>
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| Have recent innovations made research on this topic especially compelling? | • Existing studies of drug treatments tested older, short-acting stimulant medications, such as methylphenidate and amphetamine.  
• Studies of newer, long-acting medications (e.g., extended release methylphenidate, extended release dextroamphetamine, extended release amphetamine, dextroamphetamine mixed salts, amphetamine, dextroamphetamine mixed salts atomoxetine, and lisdexamfetamine dimesylate) are needed. Such studies should ideally compare these medications to short-acting stimulant medications as well as behavioral therapies. |
| How widely does care now vary?                                         | • Rates of diagnosis vary considerably in relation to access to local health care services and availability of medical providers.  
• Rates of drug usage vary by age and sex; children age 11-17 years are more likely than those age 4-10 to take medication; boys are 2.8 times more likely than girls to take medication.  
• Children of relatively low socioeconomic status are more likely to have ADHD and less likely to receive treatment than children of relatively high socioeconomic status  
• Low socioeconomic and minority status are both associated with shorter duration of drug use, thus reducing treatment efficacy. |
| What is the pace of other research on this topic (as indicated by recent publications and ongoing trials)? | ClinicalTrials.gov:  
• Ongoing trials: 215  
• Completed trials: 394  
NIH reporter:  
544 projects/307 publications |
| How likely is it that new CER on this topic would provide better information to guide clinical decision making? | For children under 6 years of age, new CER could provide better data on:  
• The comparative effectiveness of behavioral strategies versus drug versus a combination of the two  
• The comparative effectiveness of newer ADHD medications, which are approved for children over 6 years of age but are being prescribed off-label to children younger than 6, although they have not been studied in this population  
• Which components of behavioral treatment programs are most practical  
For people over 6 years of age, new CER could provide better data on:  
• Long-term outcomes of behavioral versus drug therapies  
• Differences in outcomes based on age, sex, race, ethnicity, socioeconomic status, or other comorbid conditions |
| Potential for New Information to Improve Care and Patient-Centered Outcomes |
| What are the facilitators and barriers that would affect the implementation of new findings in practice? | FACILITATORS:  
• Large numbers of children and adults with ADHD  
• Significant impact on psychosocial function  
• Desire for alternatives to drug treatments because of concerns about side effects  
BARRIERS:  
• Lack of time for medical providers to adequately assess patients  
• Lack of training for medical providers in diagnosis and treatment of ADHD  
• Lack of availability of behavioral treatment programs in certain locations  
• Reimbursement for treatment  
• Cost and practicality of conducting long-term follow-up studies |
How likely is it that the results of new research on this topic would be implemented in practice right away?

- It is likely that new data suggesting superiority of particular medications over others could be implemented quickly in people over the age of 6, as these medications are already approved for this age group.
- It is likely that new data on the effectiveness of different drug treatments would not be implemented quickly in children under the age of 6, as these medications would need FDA approval in this age group and there is likely to be considerable concern regarding side effects. However, since many of these agents are already being used off-label in this age group, it may be possible to expedite this process.
- It is likely that new data on the effectiveness of different behavioral programs or their component parts could be implemented quickly if these programs are already available.
- It is unlikely that new data on the effectiveness of different behavioral programs or their component parts could be implemented quickly if these programs are not already available as there would be delay while these programs are created.

Would new information from CER on this topic remain current for several years, or would it be rendered obsolete quickly by subsequent studies?

- There are a large number of completed and ongoing studies in this topic area; however, many studies are small in size.
- Both the larger PATS and MTA studies have remained current for many years. It is likely that new information with more current therapies (medication and psychosocial) would remain relevant for many years.

REFERENCES:


APPENDIX: TOPIC QUESTIONS

Nominated by Agency for Healthcare Research and Quality (AHRQ):

1) For children less than 6 years of age with disruptive behavior disorder or ADHD, what is the comparative efficacy and effectiveness of specific psychosocial treatments alone compared with pharmacological treatments alone or in combination with psychosocial treatments for patient outcomes?

2) For people ages 6 years or older with ADHD, what are the comparative long-term outcomes for the available psychosocial and pharmacological treatments?

3) Among children less than 6 years of age with disruptive behavior disorder or ADHD, what is the relative/comparative efficacy of key components of psychosocial treatment programs? These might include the relative efficacy of specific parent training compared with treatment components targeting the child, or the efficacy of variants in psychosocial treatment service delivery that allow flexibility for parental preferences compared with those that do not.

4) For people ages 6 years or older with ADHD, which specific sociodemographic, baseline clinical characteristics, and neurobiological features predict a positive treatment response with respect to patient outcomes?