

# ***AHRQ Comparative Effectiveness Review Surveillance Program***

**CER # 44:** Attention Deficit Hyperactivity Disorder (ADHD): Effectiveness of Treatment in At-Risk Preschoolers; Long-term Effectiveness in All Ages; and Variability in Prevalence, Diagnosis, and Treatment

**Original release date:** October, 2011

**Surveillance Report:** July, 2012

## **Key Findings:**

- Key Question 1: Conclusion on adverse events for MPH possibly out of date due to new U.S. Food and Drug Administration (FDA) data.
- Key Question 2: Conclusion on adverse events possibly out of date due to new FDA data on AEs with Methylphenidate (MPH) and FDA, UK Medicines and Healthcare products Regulatory Agency (MHRA), and Health Canada warning re Atomoxetine (ATX) and increased blood pressure. However, two new cohort studies show medication does not increase risk of serious cardiovascular events in general population.
- Key Question 3: Conclusions regarding prevalence in adults (by sex) are probably out of date. Conclusion regarding prevalence by age probably out of date.

## **Summary Decision**

This CER's priority for updating is **Low**

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None of the investigators has any affiliations or financial involvement that conflicts with the material presented in this report.



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# **1. Introduction**

Comparative Effectiveness Review (CER) #44 was originally released in October, 2011.<sup>1</sup> Therefore, our surveillance assessment began in April, 2012. At that time, we contacted experts involved in the original CER get their opinions as to whether the conclusions had changed. We also conducted an updated electronic literature search. Every month since the CER's original release, we received many applicable warnings from the U.S. Food and Drug Administration (FDA), Health Canada, and UK Medicines and Healthcare products Regulatory Agency (MHRA) on the included medications.

## **2. Methods**

### **2.1 Literature Searches**

We conducted a limited literature search covering January 1, 2010 to June 7, 2012, using the identical search strategy used for the original report. This search included five high-profile general medical interest journals (Annals of Internal Medicine, British Medical Journal, Journal of the American Medical Association, Lancet, and the New England Journal of Medicine) and four specialty journals (Behavior Modification, Journal of Abnormal Child Psychology, Journal of Child Psychology & Psychiatry, Journal of Clinical Child & Adolescent Psychology). The specialty journals were those most highly represented among the references for the original report. This search resulted in 88 titles / abstracts to review. Appendix A includes the search strategy.

### **2.2 Study selection**

We used the same inclusion and exclusion criteria as the original CER.

### **2.3 Expert Opinion**

We shared the conclusions of the original report with eight experts in the field (including the original project leader, suggested field experts, original technical expert panel (TEP) members) for their assessment of the need to update the report and their recommendations of any relevant new studies. Six subject matter experts responded in addition to the original project leader.. Appendix C shows the questionnaire matrix that was sent to the experts.

### **2.4 Check for qualitative and quantitative signals**

The authors of the original CER conducted meta-analyses on the efficacy of parent behavioral training. There was no pooling of medication studies or adverse events; results were summarized descriptively. We looked for both quantitative and qualitative signals.

## 2.5 Compilation of Findings and Conclusions

For this assessment we constructed a summary table that includes the key questions, the original conclusions, the findings of the new literature search, the expert assessments, and any FDA reports that pertained to each key question. We categorized whether the conclusions need updating using a 4-category scheme:

- Original conclusion is still valid and this portion of the CER does not need updating
- Original conclusion is possibly out of date and this portion of the CER may need updating
- Original conclusion is probably out of date and this portion of the CER may need updating
- Original conclusion is out of date.

We used the following factors when making our assessments:

- If we found no new evidence or only confirmatory evidence and all responding experts assessed the CER conclusion as still valid, we classified the CER conclusion as still valid.
- If we found some new evidence that might change the CER conclusion, and /or a minority of responding experts assessed the CER conclusion as having new evidence that might change the conclusion, then we classified the CER conclusion as possibly out of date.
- If we found substantial new evidence that might change the CER conclusion, and/or a majority of responding experts assessed the CER conclusion as having new evidence that might change the conclusion, then we classified the CER conclusion as probably out of date.
- If we found new evidence that rendered the CER conclusion out of date or no longer applicable, we classified the CER conclusion as out of date. Recognizing that our literature searches were limited, we reserved this category only for situations where a limited search would produce prima facie evidence that a conclusion was out of date, such as the withdrawal of a drug or surgical device from the market, a black box warning from FDA, etc.

## 2.6 Determining Priority for Updating

We used the following two criteria in making our final conclusion for this CER:

- How much of the CER is possibly, probably, or certainly out of date?
- How out of date is that portion of the CER? For example, would the potential changes to the conclusions involve refinement of original estimates or do the potential changes mean some therapies are no longer favored or may not exist? Is the portion of the CER that is probably or certainly out of date an issue of safety (a drug withdrawn from the market, a black box warning) or the availability of a new drug within class (the latter being less of a signal to update than the former)?

## **3. Results**

### **3.1 Search**

The literature search identified 88 titles. After title and abstract review, we selected 16 for full text review. The remaining 72 were rejected because they were editorials, letters, animal studies, individual case reports, or did not include topics of interest. Twenty-two additional articles were reviewed at the suggestion of the experts.

Thus, 38 articles went on to full text review. Twenty-one articles were rejected because they did not meet the original CER inclusion criteria. Many of these were short-term studies of medication efficacy in adults. Key question one of the CER included short-term studies of medication in pre-school children; however, for Key question two, (on patients over six years old), the CER included only “long-term” results at least one-year follow-up. The remaining 17 studies were abstracted into an evidence table (Appendix B).<sup>2-18</sup>

### **3.2 Expert Opinion**

We reached out to seven of the original technical expert panel members of which we received six responses.

### **3.3 Identifying qualitative and quantitative signals**

Table 1 shows the original key questions, the conclusions of the original report, the results of the literature and drug database searches, the experts’ assessments, and the recommendations of the Southern California Evidence-based Practice Center (SCEPC) regarding the need for update.

**Table 1. Summary Table**

Conclusions From CER Executive Summary	RAND Literature Search	FDA/ Health Canada/MHRA (UK)	Expert Opinion EPC Investigator, Other Experts	Conclusion from SCEPC
<b>Key Question 1: Effectiveness of interventions for ADHD and Disruptive Behavior Disorders (DBD) in children younger than 6 years of age</b>				
<p><b>Parent Behavior Training:</b> Parent behavioral interventions are an efficacious treatment option for preschoolers with DBD and show benefit for ADHD symptoms. 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.</p>	<p>New systematic review (Arkin, 2012)<sup>12</sup> supports the conclusion. Another systematic review (Furlong, 2012)<sup>13</sup> found behavioral / cognitive behavioral parenting programs effective and cost effective. Another review (Fabiano, 2009)<sup>11</sup> presented separate results for single-subject research, pre-post studies with no control group, and between-group studies. The latter meet inclusion criteria for the AHRQ CER; the pooled results support our findings.</p> <p>Two new RCTs show short term efficacy of parenting behavior training for ADHD symptoms. (Webster-Statton, 2011; Day, 2012)<sup>10 18</sup></p>	<p>NA</p>	<p>All 6 experts agreed the conclusion is still valid. Two experts suggested one study each that support the conclusion.</p>	<p>Up-to-date</p>
<p><b>Multicomponent Home and School or Daycare-Based Interventions:</b> 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 parent behavior training (PBT) sessions. Relative</p>	<p>No new studies.</p>	<p>NA</p>	<p>Three experts agreed the conclusion is still valid; the other three did not know.</p>	<p>Up-to-date</p>

Conclusions From CER Executive Summary	RAND Literature Search	FDA/ Health Canada/MHRA (UK)	Expert Opinion EPC Investigator, Other Experts	Conclusion from SCEPC
2 years.				
<p><b>Medication: MPH:</b> With evidence drawn primarily from the Preschool ADHD Treatment Study (PATS) study, Methylphenidate (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.</p>	No new efficacy studies.	<p><b>FDA</b> – October, 2011: Migraine and obsessive compulsive disorder add to list of possible side effects for MPH.  <b>FDA</b> –June, 2012: Serious allergic reactions, slowing of childhood growth, eyesight changes, and seizures (in patients with a history of seizures) reported.</p>	Five experts agreed the conclusion is still valid. The other expert stated that a study in process (not yet published) suggests that MPH is less efficacious and less well tolerated in preschoolers than in older children.	Possibly out-of-date regarding safety
<b>Key Question 2: Long-term (&gt;1 year) effectiveness of interventions for ADHD in people 6 years and older</b>				
<p><b>Medication Treatment: MPH, ATX (SOE low):</b> 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. Atomoxetine (ATX) is effective for ADHD symptoms and well tolerated over 12 months.</p>	Two new retrospective cohort studies by the same research group (Cooper, 2011; Habel, 2011) <sup>2,3</sup> reported on cardiovascular AEs. Among young and middle-aged adults, current or new use of ADHD medications, compared with nonuse or remote use, was not associated with an increased risk of serious cardiovascular events. Apparent protective associations likely represent healthy-user bias. In children and adolescents, use of ADHD medications was not associated with an increased risk of serious cardiovascular events	<p><b>FDA</b> – October, 2011: MPH - Migraine and obsessive compulsive disorder added to list of possible side effects.  <b>FDA</b> –June, 2012: MPH- Serious allergic reactions, slowing of childhood growth, eyesight changes, and seizures (in patients with a history of seizures) reported.  <b>FDA</b> – April, 2011: ATX - Parathesia added to list of possible side effects, along with allergic reactions such as anaphylaxis, angionuerotic edema, and urticaria.  <b>FDA</b> – April, 2011: ATX - Warning issued for severe liver injury, orthostatic hypotension, syncope.  <b>FDA</b> – October, 2011: ATX – Warning issued for increased blood pressure in patients with pheochromocytoma.  <b>UK MHRA</b> – October, 2011: ATX – Should not be used by patients with severe cardiovascular disorders, due to blood pressure increase.  <b>Health Canada</b> – October, 2011: ATX – Should not be used in patients with heart problems or where increased blood pressure or heart rate would be problematic.</p>	Five experts agreed the conclusion is still valid; the other did not know. One expert suggested two studies of lisdexamfetamine dimesylate and two studies of clonidine for ADHD.	Possibly out-of-date regarding safety
<p><b>Medication Treatment: GXR (SOE Insufficient):</b></p>	No new studies.	No new information.	Four experts agreed the conclusion is still valid.	Up-to-date

<b>Conclusions From CER Executive Summary</b>	<b>RAND Literature Search</b>	<b>FDA/ Health Canada/MHRA (UK)</b>	<b>Expert Opinion EPC Investigator, Other Experts</b>	<b>Conclusion from SCEPC</b>
<p>Only one study of guanfacine extended release (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.</p>			<p>Two disagreed with the original conclusion, in that GXR is FDA approved for augmenting MPH for ADHD and that's not discussed here.</p>	
<p><b>Combined Psychostimulant Medication and Behavioral Treatment:</b> 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.</p> <p>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.</p>	<p>No new studies on combined medication and behavioral treatment.</p>	<p><b>FDA</b> – October, 2011: Migraine and obsessive compulsive disorder add to list of possible side effects for MPH.  <b>FDA</b> –June, 2012: Serious allergic reactions, slowing of childhood growth, eyesight changes, and seizures (in patients with a history of seizures) reported.</p>	<p>All six experts agreed the conclusion is still valid. One pointed out that parent training is the primary intervention; meds are rarely sufficient for ODD treatment.</p>	<p>Up-to-date</p>
<p><b>Behavioral/Psychosocial:</b> There is insufficient</p>	<p>One new RCT (Safren, 2010)<sup>5</sup> compared cognitive behavioral treatment (CBT) to relaxation and</p>	<p>NA</p>	<p>One expert agreed the statement is still valid.</p>	<p>Up-to-date</p>

<b>Conclusions From CER Executive Summary</b>	<b>RAND Literature Search</b>	<b>FDA/ Health Canada/MHRA (UK)</b>	<b>Expert Opinion EPC Investigator, Other Experts</b>	<b>Conclusion from SCEPC</b>
evidence to draw conclusions on long term outcomes for persons 6 years and older with a diagnosis of ADHD.	education in adults. At 12 months, CBT group showed improved ADHD outcomes compared to relaxation and education.		One expert did not know. The others disagreed with the original statement and suggested studies.	
<b>Parent Behavior Training:</b> There is insufficient evidence to draw conclusions for persons 6 years and older with a diagnosis of ADHD.	No new studies with follow-up of at least one year.	NA	One expert agreed the conclusion is still valid. One expert did not know. The other four experts disagreed with the original statement and suggested studies.	Up-to-date
<b>Academic Interventions:</b> 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.	One new RCT (Safren, 2010) <sup>5</sup> compared cognitive behavioral treatment (CBT) to relaxation and education in adults. At 12 months, CBT group showed improved ADHD outcomes compared to relaxation and education.	NA	Four experts agreed the conclusion is still valid. One expert did not know. The other expert suggested studies.	Up-to-date
<b>Key Question 3: Underlying prevalence of ADHD, rates of diagnosis, and treatment by geography, time period, provider type, and sociodemographic characteristics</b>				
<b>Prevalence (Geography):</b> 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	One new telephone survey conducted in France (Lecendreux, 2011) <sup>15</sup> found prevalence was 4.7% for boys and 2.2% in girls (age 6 to 12 years). In contrast, survey of a national representative population of Germans (de Zwann, 2012) <sup>16</sup> found 4.8% of female and 4.6% of male adults reported having ADHD.	NA	Five experts agreed the conclusion is still valid. One expert did not know.	Up-to-date

Conclusions From CER Executive Summary	RAND Literature Search	FDA/ Health Canada/MHRA (UK)	Expert Opinion EPC Investigator, Other Experts	Conclusion from SCEPC
<p><b>Prevalence (Time period):</b> 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.</p>	<p>No new studies reporting longitudinal prevalence data.</p>	<p>NA</p>	<p>Four experts agreed the conclusion is still valid. One expert did not know. One expert did not answer.</p>	<p>Up-to-date</p>
<p><b>Prevalence socioeconomic status (SES) (SES):</b> 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>	<p>According to recent U.S. data (CDC, 2010)<sup>7</sup> rate of ADHD in children living at or below poverty level is 11.6%, compared to 8.6% in families with income more than 200% of poverty level.</p>	<p>NA</p>	<p>Four experts agree the conclusion is still valid. Two experts did not know.</p>	<p>Up-to-date</p>
<p><b>Prevalence (Sex):</b> Most studies illustrate a sex difference in the prevalence of ADHD (males &gt; females).</p>	<p>New studies of children<sup>7,9,15</sup> reported significantly higher prevalence in boys, while the one new study of adults<sup>16</sup> did not find any association between ADHD and sex.</p>	<p>NA</p>	<p>Five experts agreed the conclusion is still valid. The other expert mentioned that the gender ratio is 1 to 1 in adults.</p>	<p>Conclusion probably out-of-date regarding adults</p>
<p><b>Prevalence (Age):</b> The age group ≈5-10 years appears to experience the highest prevalence. ADHD research detailing prevalence in adults is lacking</p>	<p>According to recent U.S. data (CDC, 2010)<sup>7</sup> rate of ADHD is 13.6% in ages 15 to 17 and 6.6% in ages 4 to 10.</p>	<p>NA</p>	<p>All six experts disagreed with the statement that research on ADHD prevalence in adults is lacking. They suggested many studies. In fact, the</p>	<p>Conclusion probably out-of-date</p>

Conclusions From CER Executive Summary	RAND Literature Search	FDA/ Health Canada/MHRA (UK)	Expert Opinion EPC Investigator, Other Experts	Conclusion from SCEPC
			original CER contains several studies on prevalence in adults.	
<p><b>Treatment (Location):</b> 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.</p>	No new studies.	NA	Five experts agreed the conclusion is still valid. One expert did not know.	Up-to-date
<p><b>Treatment (Provider):</b> Family practitioners in many jurisdictions, particularly those with limited access to specialists, report significant pressure from parents and teachers to prescribe stimulant medications.</p>	A new review of medical records (Faraone, 2004) <sup>17</sup> of adults with ADHD showed primary care providers (PCPs) were the least aggressive in diagnosing ADHD in adults. Psychiatrists were significantly more likely to use pharmacotherapy.	NA	Two experts agreed this conclusion is still valid. One expert feels the conclusion is “probably” valid. Two experts do not know. One expert asked for where this info came from. (We will send references.)	Up-to-date
<p><b>Treatment (Informant):</b> 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</p>	No new studies.	NA	Two experts agreed this conclusion is still valid. One expert feels the conclusion is “probably” valid. Three experts do not know.	Up-to-date

Conclusions From CER Executive Summary	RAND Literature Search	FDA/ Health Canada/MHRA (UK)	Expert Opinion EPC Investigator, Other Experts	Conclusion from SCEPC
over time than repeated community surveys do.				
<b>Treatment (Time):</b> 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 (S-DDD), 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>1</sup>	A new review of medical records (Faraone, 2004) <sup>17</sup> of adults with ADHD showed that only 25% had been diagnosed in childhood or adolescence.	NA	All six experts agree this conclusion is still valid.	Up-to-date
<b>Treatment (SES):</b> 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.	No new studies.	NA	Five experts agreed the conclusion is still valid. One did not know.	Up-to-date.
<b>Treatment (Sex):</b> Only sparse comparative data are available examining rates of treatment by sex once ADHD is diagnosed.	A new retrospective analysis of national prescription databases in Nordic countries (Zoega, 2011) <sup>14</sup> reported men were 2 times more likely than women to have used ADHD drugs. Among children, boys were over 4 times as likely as girls.	NA		Up-to-date

<sup>1</sup> 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).

<b>Conclusions From CER Executive Summary</b>	<b>RAND Literature Search</b>	<b>FDA/ Health Canada/MHRA (UK)</b>	<b>Expert Opinion EPC Investigator, Other Experts</b>	<b>Conclusion from SCEPC</b>
<b>Treatment (Age):</b> Medication treatment prevalence is higher for primary school-age children than for adolescents or adults.	A new retrospective analysis of national prescription databases in Nordic countries (Zoega, 2011) <sup>14</sup> reported usage was highest for ages 11-15 in males for Iceland, Norway, and Sweden, but ages 7-10 in Finland. For females, use was highest for ages 11-15 in Iceland and Sweden, 7-10 in Finland, and 16-20 in Norway.	NA	All six experts agreed the conclusion is still valid.	Up-to-date for U.S.

Legend: ATX= Atomoxetine; MDD=Major Depressive Disorder; MPH=Methylphenidate; MRI=Magnetic Resonance Imaging; NSSRI=selective serotonin reuptake inhibitor; PTSD=Post-Traumatic Stress Disorder; SCEPC=Southern California Evidence-based Practice Center; SNPs=Small Nuclear Polymorphisms; TBI=Traumatic Brain Injury; TCA=tricyclic antidepressant

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# **Appendices**

**Appendix A: Search Strategy**

**Appendix B: Evidence Table**

**Appendix C: Questionnaire Matrix**

## Appendix A. Search Methodology

### DATABASES SEARCHED & TIME PERIOD COVERED:

Medline on OVID – 2010-06/07/12

Embase, PsycINFO, Cochrane – 2010-06/07/2012

### LANGUAGE:

English

### SEARCH STRATEGIES:

#### Medline:

exp "Attention Deficit and Disruptive Behavior Disorders"/ OR exp Attention Deficit Disorder with Hyperactivity/ OR ("attention deficit" OR adhd).mp. OR Hyperkinesis/ OR child behavior disorders/ OR impulse control disorders/ OR inattent\*.mp. OR (disrupt\* adj4 disorder?).tw.

OR Conduct Disorder/ or "attention deficit and Disruptive Behavior Disorders".mp. or attention deficit disorder with hyperactivity.mp. or Conduct Disorder\*.mp.

AND

interven\*.mp. or drug therapy/ or atomoxetine.mp. or guanfacine.mp. or lisdexamfetamine.mp. or vyvanse.mp. or ritalin.mp. or therap\*.mp. or treatment\*.mp.

NOT

(case reports or comment or congresses or consensus development conference or consensus development conference, nih or editorial or letter or meta analysis).mp.

NUMBER OF RESULTS: 2734

#### Embase:

'attention deficit disorder with hyperactivity'/exp OR 'attention deficit disorder with hyperactivity' OR 'attention deficit disorder'/exp OR 'attention deficit disorder' OR 'hyperkinesis'/exp OR 'hyperkinesis' OR 'adhd' OR 'minimal brain dysfunction'/exp OR 'minimal brain dysfunction' OR 'impulsive behavior'/exp OR 'impulsive behavior' OR inattent\* OR 'impulse control' OR hyperactiv\* OR 'impulsiveness'/exp OR 'impulsiveness' OR 'disruptive behavior'/exp OR 'disruptive behavior' OR 'attention deficit'/exp OR 'attention deficit' OR 'adhd'/exp OR adhd

AND

interven\* OR 'drug'/exp AND 'therapy'/exp OR 'drug therapy'/exp OR 'atomoxetine'/exp OR 'guanfacine'/exp OR 'lisdexamfetamine'/exp OR 'vyvanse'/exp OR 'ritalin'/exp OR therap\* OR treatment\*

AND

('clinical article'/de OR 'clinical trial'/de OR 'cohort analysis'/de OR 'comparative study'/de OR 'control group'/de OR 'controlled clinical trial'/de OR 'controlled study'/de OR 'cross-sectional study'/de OR 'double blind procedure'/de OR 'longitudinal study'/de OR 'major clinical study'/de OR 'methodology'/de OR 'prospective study'/de OR 'randomized controlled trial'/de)

AND

[humans]/lim

AND

'article'/it OR 'article in press'/it OR 'book'/it

NUMBER OF TOTAL RESULTS: 3833

PsycINFO:

"Attention Deficit Disorder with Hyperactivity" OR "Attention Deficit Disorder" OR "Hyperkinesia" OR  
adhd OR "minimal brain dysfunction" OR "impulsive behavior" OR child behavior disorder\* OR  
inattent\* OR "impulse control" OR disruptive disorder\* OR hyperactiv\*

AND

interven\* OR drug therapy OR atomoxetine OR guanfacine OR lisdexamfetamine OR vyvanse OR ritalin  
OR therap\* OR treatment\*

AND

Human

NOT

letter OR editorial OR "case report" OR "case reports" OR "case series" OR dissertation\* OR conference  
OR symposi\*

Search modes - Phrase Searching (Boolean)

NUMBER OF TOTAL RESULTS: 1562

Cochrane:

"Attention Deficit Disorder with Hyperactivity" OR "Attention Deficit Disorder" OR "Hyperkinesia" OR  
adhd OR "minimal brain dysfunction" OR "impulsive behavior" OR child behavior disorder\* OR  
inattent\* OR "impulse control" OR disruptive disorder\* OR hyperactiv\* in Title, Abstract or Keywords  
and interven\* OR drug therapy OR atomoxetine OR guanfacine OR lisdexamfetamine OR vyvanse OR  
ritalin OR therap\* OR treatment\* in Title, Abstract or Keywords, from 2010 to 2012 in Cochrane Central  
Register of Controlled Trials"

NUMBER OF RESULTS BY DATABASE: Trials [380] Methods Studies [1] Technology Assessments  
[10] Economic Evaluations [2]

LIMIT TO THE FOLLOWING JOURNALS:

JAMA, New England Journal Of Medicine, BMJ, Annals Of Internal Medicine, Lancet,  
Behavior Modification, Journal Of Abnormal Child Psychology, Journal Of Child Psychology &  
Psychiatry, Journal Of Clinical Child & Adolescent Psychology

## Appendix B. Evidence Tables

Evidence Table Key Question 1. Among children younger than 6 years of age with ADHD or DBD, what are the effectiveness and adverse event outcomes following treatment?

### Parent Training

Study	N Mean Age % Male	Intervention type Interventions compared	Long Term Follow Up Length of F/U	Results		Notes
				Child Behavior	Parent Competence	
Webster-Stratton, 2011 <sup>10</sup>	N-Tx: 49, WLC: 50 <b>Mean Age</b> - Tx: 64.1m, WLC: 64.4 m <b>Male</b> - Tx: 73%, WLC: 78%	<b>Type:</b> RCT <b>Comparisons:</b> Incredible Years vs. WLC	<b>LT F/U:</b> None <b>LF/U:</b> NA	Significant treatment effects for children's emotion vocabulary and problem solving ability.	Significant treatment effects for appropriate and harsh discipline, use of physical punishment and monitoring in mothers. Both mothers and fathers reported treatment effects for children's externalizing, hyperactivity, inattentive and oppositional behaviors, and emotion regulation and social competence.	3 dropped out
Day, 2012 <sup>18</sup>	N-Tx: 59, WLC: 57 <b>Mean Age</b> - Tx:4.7y , WLC: 4.8y <b>Male</b> -Tx: 56%, WLC: 63%	<b>Type:</b> RCT <b>Comparisons:</b> "Empowering Parents, Empowering Communities" training vs. no training	<b>LT F/U:</b> None <b>LF/U:</b> NA	Significant improvement in child behavior of parents in the treatment group as measured by the Eyberg Child Behavior Inventory's intensity, problem, and "concerns about my child" subscales.	Significant improvement in positive parenting practices as measured by the Arnold O'Leary's parenting scale.	Improvements in child behavior were seen in only one of the two measures used.

**Evidence Table Key Question 1. Among children younger than 6 years of age with ADHD or DBD, what are the effectiveness and adverse event outcomes following treatment?**

**Diet**

Study	N Mean Age % Male	Intervention type Interventions compared	Long Term Follow Up Length of F/U	Child Behavior	Notes
Pelsser, 2011 <sup>4</sup>	<b>N</b> - Tx:50, Ctrl: 50 <b>Mean Age</b> - Tx: 6.8y, Ctrl: 7.0y <b>Male</b> : Tx: 88%, Ctrl: 84%	<b>Type</b> : RCT <b>Comparisons</b> : Restricted elimination diet vs. healthy food advice	<b>LT F/U</b> : No <b>LF/U</b> : NA	Significant difference in ADHD symptoms (mean 23.7, 95% CI 18.6- 28.8) and on the Conner Scale (mean 11.8, 95% CI 9.2- 14.5) between treatment and control group at the end of week 9. Between weeks 10- 13, there was a relapse in the ADHD symptoms of 63% of subjects who underwent restricted (high-IgG or low- IgG) food challenges.	This study has 3 phases: Baseline (weeks 1-3), Phase 1 (weeks 4-9) and Phase 2 (weeks 10- 13). Phase 1 had masked ADHD symptoms assessments by a pediatrician. Phase 2 was a double blind crossover food challenge for the treatment group.

**Evidence Table Key Question 2. 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?**

**Medication**

Study	Design	N Age % Male	Intervention compared	Long Term Follow Up Length of F/U	Results		Notes
					Effectiveness	Safety	
Powell, 2011 <sup>6</sup>	Observational	<b>N:</b> 410 <b>Age:</b> All ages <b>Male:</b> 90%	Ritalin, Ritalin Uno, Concerta, dexamphetamine, or Strattera	<b>LTFU:</b> Yes <b>LFU:</b> 6y (approx)	Age at start and comorbidity influenced dosage and end status was significantly associated with time spent at minimum and maximum dosages.		
Barnard-Brak, 2011 <sup>8</sup>	Prospective Cohort	<b>N:</b> 783 <b>Age:</b> 3-10y (approx) <b>Male:</b> 74%	Pharmacotherapy	<b>LTFU:</b> Yes <b>LFU:</b> 7y (approx)	Non significant association between pharmacological treatment and academic achievement among children with ADHD.		ECLS-K data followed children from Kindergarten-5th grade. Age is not specifically mentioned.

**Evidence Table Key Question 2. 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?**

**Behavioral**

Study	N Mean Age % Male	Intervention type Interventions compared	Long Term Follow Up Length of F/U	Results	Notes
Safren, 2010 <sup>3</sup>	<b>N</b> -CBT: 43, Relaxation: 43 <b>Mean Age</b> -CBT: 42y, Relaxation: 44y <b>Male</b> -CBT: 56%, Relaxation: 56%	<b>Type:</b> RCT <b>Comparisons:</b> CBT vs. Relaxation+Education	<b>LTFU:</b> Yes <b>LFU:</b> 6- and 12-m	Treatment using CBT led to improved ADHD outcomes (as measured by the Clinical Global Impressions Scale and the ADHD Rating Scale) compared to treatment using relaxation and education. Gains made through CBT were sustained at the 12 month follow up.	CBT=Cognitive Behavioral Therapy

**Evidence Table Key Question 2. Adverse events of ADHD medications in patients > 6 years old**

Study	Study Type N	Med	General AE	Nervous System	Gastrointestinal	Respiratory	Cardiovascular
Cooper, 2011 <sup>2</sup>	<b>Type:</b> Retrospective Cohort <b>Age:</b> 2-24y <b>N:</b> 1,200, 438	Methylphenidate, dexamethylphenidate, dextroamphetamines, amphetamine salts, atomoxetine, pemoline	NR	NR	NR	NR	Rate per 100,000 person-yr Sudden cardiac death: 0.80 Actual myocardial infraction: 0 Stroke: 1.07
Habel, 2011 <sup>3</sup>	<b>Type:</b> Retrospective Cohort <b>Age:</b> 25-64y <b>N:</b> 150359 (drug users), 292839 (non users)	Methylphenidate, dexamethylphenidate, dextroamphetamines, amphetamine salts, atomoxetine, pemoline	NR	NR	NR	NR	Crude incidence rates in current users, per 1000 person-yr Myocardial infraction: 1.34 Sudden cardiac death: 0.30 Stroke: 0.56

**Evidence Table Key Question 3. 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?**

<b>Study Prevalence (%)</b>	<b>Geography</b>	<b>Population and Ethnicity</b>	<b>Age</b>	<b>Sex</b>	<b>Data Source</b>	<b>Socioeconomic Status</b>	<b>Comment</b>
No author, 2010 <b>Overall Prevalence:</b> 9.5%	United States Northeast: 9.4% Midwest: 9.9% South: 10.9% West: 7.0%	<b>Population:</b> Children <18y in the US <b>Ethnicity:</b> Hispanic/Latino: 5.6% Non-Hispanic/Latino: 10.5%	4-10y: 6.6% 11-14y: 11.2% 15-17y: 13.6%	Male: 13.2% Female: 5.6%	National Survey of Children's Health, 2007	Poverty level <=100%: 11.6% >100%-<=200%: 10.3% >200%: 8.6%	
Coghill, 2008 <sup>9</sup> <b>Prevalence of ADHD children per household:</b> 1 child: 73% >1 child: 27%	10 European countries: Belgium, France, Germany, Netherlands, Norway, Poland, Spain, Sweden, Switzerland, and UK	<b>Population:</b> Children age 6-18y <b>Ethnicity:</b> NR	NR	Male: 76% Female: 24%	Survey of 910 families of children with ADHD and 995 families of children w/o ADHD. Sample drawn from Harris Interactive's Pan European panel which is representative of general population within Europe	NR	Receiving stimulant medication: 38% 6-8 hour medication: 40% 12-hour medication: 60% Not receiving medication: 62%  Time on meds: 3-6 m: 8% 6-12m: 15% >1y: 77%

Study Prevalence (%)	Geography	Population and Ethnicity	Age	Sex	Data Source	Socioeconomic Status	Comment
Zoega, 2011 <sup>14</sup>  <b>Prevalence of ADHD medication use in Nordic countries: 2.76 per 1000 people</b>	Nordic countries: Denmark (2.41 per 1000), Finland (1.23 per 1000), Iceland (12.46 per 1000), Norway (4.73 per 1000), and Sweden (2.52 per 1000)	<b>Population:</b> all ages <b>Ethnicity:</b> NR	In men, use peaked at age 11-15y in Iceland (72.04 per 1000), Norway (33.97 per 1000), Sweden (17.93 per 1000) and at age 7-10y in Finland (11.30 per 1000)  In women, use peaked at 11-15y in Iceland (26.29 per 1000) and Sweden (4.63 per 1000) and 7-10y in Finland (1.90 per 1000), and 16-20y in Norway (10.92 per 1000)	Nordic men were 2 times more likely than Nordic women to have used ADHD drugs. Among children 7-15y, boys were over 4 times more likely than girls to have dispensed an ADHD drug. The gender ratio gap closed in adulthood (Prev Ratio: 1.24, CI: 1.21-1.27)	Data on dispensed ADHD drugs from 1 January 2007 to 31 December 2007 were retrieved from nationwide prescription databases. The number of inhabitants in each country at the end of 2007, used as a dominator for prevalence, was based on publicly available statistics from national population registers. Information on marketing authorisations, indications and reimbursement status of ADHD drugs was obtained from the national agencies for medicines control and institutions of national health insurance	NR	The overall prevalence of ADHD drug use in the Nordic area (2.76 per 1000) is considerably lower than the reported use in the United States between 2000 and 2005. Iceland is the only Nordic country where use of ADHD drugs approximates the United States rates.

Study Prevalence (%)	Geography	Population and Ethnicity	Age	Sex	Data Source	Socioeconomic Status	Comment
Lecendreux, 2011 <sup>15</sup>  <b>Prevalence:</b> ADHD: 3.5-5.6% Treatment: 3.5%	France	<b>Population:</b> Children 6-12y  <b>Ethnicity:</b> NR	NR	Prevalence of ADHD greater among boys than girls (4.7% vs. 2.2%). Higher prevalence of repeated grade in school among boys (7.1%) compared to girls.	Phone survey of 7,912 telephone numbers. Population data from the Institut National de la Statistique et des Etudes Economiques (INSEE).	NR	Children with ADHD were significantly likely to have another family member with ADHD and also have higher prevalence of conduct and oppositional disorders. They also have higher prevalence of learning problems.
de Zwaan, 2012 <sup>16</sup>  <b>Prevalence:</b> 4.7%	Germany  Urban residency: 3.8% Rural residency: 12.1%	<b>Population:</b> Adults 18-64y  <b>Ethnicity:</b> NR	18-24y: 9.8% 25-34y: 3.9% 35-44y: 4.6% 45-54y: 4.5% 55-64y: 3.5%	Female: 4.8% Male: 4.6%	Survey of a nationally representative German population	Married: 3.1% Never married: 6.8% Divorced: 6.6% Widowed: 4.8%  Employed/student/home maker: 3.8% Unemployed: 14.0%	This study did not find any association between ADHD and gender.
Faraone, 2004 <sup>17</sup>  <b>Prevalence:</b> Only 25% of the adults with ADHD had been first diagnosed as having the disorder in childhood or adolescence	US	<b>Population:</b> NR <b>Ethnicity:</b> NR	NR	NR	Review by 50 psychiatrists and 50 primary care practitioners (PCPs) of 537 and 317 medical records, respectively, of adults diagnosed as having ADHD	NR	PCPs were the least aggressive in diagnosing ADHD  In psychiatric and PCP settings, there was a statistical difference in the use of pharmacotherapy (91% vs 78%, respectively) and the proportion of patients taking drug holidays (24% vs 17%, respectively)

**Evidence Table Key Questions 1 and 2. Systematic Reviews**

Study	Purpose	Search Years	Findings
Arkan, 2012 <sup>12</sup>	To evaluate the efficacy of commonly used evidence based parent training programmes for ADHD. To outline the similarities and differences in terms of participants, method of training and long term results in order to find out most appropriate model for training parents in Turkey	1982-2009	The Triple P and Incredible Years the two most commonly used parent training programs. These programs have been associated with increases in positive parenting practices and reductions in problem behaviors in children. These programs offer a multi-disciplinary approach with high evidence standards and yield long term results.
Furlong, 2012 <sup>13</sup>	To assess the effectiveness and cost-effectiveness of behavioral and cognitive-behavioral group based parenting programs in children with conduct problems	1872-Current	Behavioral and cognitive group based parenting interventions are effective and cost effective for improving child conduct problems, and parenting skills in the short term. The cost of these programs are modest (approximately \$2500 per family) when compared to the long term social, educational, health, and legal costs associated with the presence of conduct problems.
Fabiano, 2009 <sup>11</sup>	To assess the effectiveness of behavior modification treatment for children with ADHD. The researchers conducted separate meta-analyses for single-subject research, pre-post studies with no control group, and between-group studies. The latter meet inclusion criteria for the AHRQ CER.	1967-2006	Between group studies of behavioral modification had a mean effect size of 0.83 on measures of behavioral change. Mean age in these studies was 7.1 years.

## Appendix C. Questionnaire Matrix

### Surveillance and Identification of Triggers for Updating Systematic Reviews for the EHC Program

**Title: Attention Deficit Hyperactivity Disorder (ADHD): Effectiveness of Treatment in At-Risk Preschoolers; Long-Term Effectiveness in All Ages; and Variability in Prevalence, Diagnosis, and Treatment**

Your Name: \_\_\_\_\_

Your Contact Information (for Honorarium): \_\_\_\_\_

Conclusions From CER Executive Summary	Is this conclusion almost certainly still supported by the evidence?	Has there been new evidence that may change this conclusion?	Do Not Know
<b>Key Question 1: Effectiveness of interventions for ADHD and Disruptive Behavior Disorders (DBD) in children younger than 6 years of age</b>			
<b>Parent Behavior Training:</b> Parent behavioral interventions are an efficacious treatment option for preschoolers with DBD and show benefit for ADHD symptoms. 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.	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<b>Multicomponent Home and School or Daycare-Based Interventions:</b> Evidence is drawn from few reports.		New Evidence:	

<b>Conclusions From CER Executive Summary</b>	<b>Is this conclusion almost certainly still supported by the evidence?</b>	<b>Has there been new evidence that may change this conclusion?</b>	<b>Do Not Know</b>
<p>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 parent behavior training (PBT) sessions. Relative benefits of the school-based intervention diminished over 2 years.</p>	<input type="checkbox"/>		<input type="checkbox"/>
<p><b>Medication (MPH Only):</b> With evidence drawn primarily from the Preschool ADHD Treatment Study (PATS) study, Methylphenidate (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.</p>	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<b>Key Question 2: Long-term (&gt;1 year) effectiveness of interventions for ADHD in people 6 years and older</b>			
<p><b>Other Medication Treatment (SOE low):</b> 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. Atomoxetine (ATX) is effective for ADHD symptoms and well tolerated over 12 months.</p>	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<p><b>Medication Treatment (SOE Insufficient):</b> Only one study of guanfacine extended release (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.</p>	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>

<b>Conclusions From CER Executive Summary</b>	<b>Is this conclusion almost certainly still supported by the evidence?</b>	<b>Has there been new evidence that may change this conclusion?</b>	<b>Do Not Know</b>
<p><b>Combined Psychostimulant Medication and Behavioral Treatment:</b> 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.</p> <p>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.</p>	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<p><b>Behavioral/Psychosocial:</b> There is not enough evidence to draw conclusions for persons 6 years and older with a diagnosis of ADHD.</p>	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<p><b>Parent Behavior Training:</b> There is not enough evidence to draw conclusions for persons 6 years and older with a diagnosis of ADHD.</p>	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<p><b>Academic Interventions:</b> 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.</p>	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<p><b>Key Question 3: Underlying prevalence of ADHD, rates of diagnosis, and treatment by geography, time period, provider type, and sociodemographic characteristics</b></p>			

<b>Conclusions From CER Executive Summary</b>	<b>Is this conclusion almost certainly still supported by the evidence?</b>	<b>Has there been new evidence that may change this conclusion?</b>	<b>Do Not Know</b>
<b>Prevalence (Geography):</b> 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	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<b>Prevalence (Time period):</b> 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.	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<b>Prevalence (SES):</b> Some studies suggest that those of lower SES have a higher prevalence of ADHD, although those of higher socioeconomic status (SES) are more likely to be treated.	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<b>Prevalence (Sex):</b> Most studies illustrate a sex difference in the prevalence of ADHD (males > females).	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<b>Prevalence (Age):</b> The age group $\approx$ 5-10 years appears to experience the highest prevalence. ADHD research detailing prevalence in adults is lacking	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<b>Treatment (Location):</b> Rates of treatment vary considerably due to location and access to providers of health care services, internationally as		New Evidence:	

<b>Conclusions From CER Executive Summary</b>	<b>Is this conclusion almost certainly still supported by the evidence?</b>	<b>Has there been new evidence that may change this conclusion?</b>	<b>Do Not Know</b>
well as regionally or even within the same community, dependent on provider type and availability, provider remuneration, and insurance status of patient.	<input type="checkbox"/>		<input type="checkbox"/>
<b>Treatment (Provider):</b> Family practitioners in many jurisdictions, particularly those with limited access to specialists, report significant pressure from parents and teachers to prescribe stimulant medications.	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<b>Treatment (Informant):</b> 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.	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<b>Treatment (Time):</b> 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 (S-DDD), 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>2</sup>	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<b>Treatment (SES):</b> 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	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>

<sup>2</sup> 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).

<b>Conclusions From CER Executive Summary</b>	<b>Is this conclusion almost certainly still supported by the evidence?</b>	<b>Has there been new evidence that may change this conclusion?</b>	<b>Do Not Know</b>
influence access to specialist providers in the United States.			
<b>Treatment (Sex):</b> Only sparse comparative data are available examining rates of treatment by sex once ADHD is diagnosed.	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<b>Treatment (Age):</b> Medication treatment prevalence is higher for primary school-age children than for adolescents or adults.	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
<b>Are there new data that could inform the key questions that might not be addressed in the conclusions?</b>			