Does stimulant therapy help adult ADHD?

EVIDENCE-BASED ANSWER

Central nervous system stimulants improve symptoms of attention deficit–hyperactivity disorder (ADHD) in adults (strength of recommendation: B, based on an older, inconclusive systematic review, a lesser-quality systematic review, and several newer small randomized controlled trials).

Although not the focus of this question, nonstimulant medications (including buproprion, modafinil, and guanfacine) have also been studied in the treatment of ADHD in adults. Recently, atomoxetine became the only nonstimulant medication to receive approval by the US Food and Drug Administration for the treatment of ADHD.

EVIDENCE SUMMARY

A well-done systematic review of 12 trials assessing the efficacy of stimulant therapy in the treatment of adult ADHD did not find sufficient evidence that stimulants were effective.[1] Significant heterogeneity and poor reporting of methodology was seen among the studies.

The 1 study rated as high-quality was a 7-week randomized controlled trial using a crossover comparison of methylphenidate and placebo.[2] There was a favorable response in 78% (18/23) of subjects while takin methylphenidate, in contrast to 4% (1/23) while taking placebo (number needed to treat [NNT]=1.4; $P<.0001$). A favorable response was assessed by the Clinical Global Impression Scale, a measure of illness severity and improvement, and a >30% reduction in symptoms as measured by the ADHD Rating Scale. A more recent, but less rigorous, systematic review identified 15 studies of stimulant efficacy in adults.[3] Researchers concluded that under controlled conditions, stimulants are efficacious in the treatment of ADHD in adults. The rate of response among the studies ranged from 25% to 78%.

One of the better studies in this review was a randomized, double-blind, 3-phase crossover study of dextroamphetamine, modafinil (a drug used to treat narcolepsy), and placebo.[4] Each phase was 2 weeks long, with a 4-day washout in between. A favorable response was defined as a reduction of ADHD symptoms by at least 30% on the *DSM-IV* ADHD Behavior Checklist for Adults. Dextroamphetamine and modafinil showed the same response rate in 10 of 21 patients. Both treatments had a significant improvement over placebo ($P<.001$). It was unclear from the study what percentage of subjects responded to placebo.

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What are Clinical Inquiries?

Clinical Inquiries answer real questions that family physicians submit to the Family Practice Inquiries Network (FPIN), a national, not-for-profit consortium of family practice departments, residency programs, academic health sciences libraries, primary care practice-based research networks, and other specialists.

Questions chosen are those family physicians vote as most important through a web-based voting system.

Answers are developed by a specific method:

- FPIN medical librarians conduct systematic and standardized literature searches in collaboration with an FPIN clinician or clinicians.
- FPIN clinician authors select the research articles to include, critically appraise the research evidence, review the authoritative sources, and write the answers.
- Each Clinical Inquiry is reviewed by 4 or more peers and editors before publication in JFP.
- FPIN medical librarians co-author each of the Clinical Inquiries that have required a systematic search.
- Finally, a practicing family physician writes an accompanying commentary.

TABLE

Stimulants used to treat ADHD in adults

Drug	Starting dose	Maximum daily dose
Methylphenidate		
Ritalin, Methylin	5 mg twice daily	65 mg*
Ritalin-SR, Methylin ER, Metadate ER, Metadate CR	20 mg every morning	65 mg*
Concerta	18 mg every morning	54 mg
Dextroamphetamine sulfate		
Dexedrine	2.5 mg twice daily	45 mg*
Dexedrine spansules	5 mg every morning	45 mg*
Mixed amphetamine salts		
Adderall	5 mg	40 mg
Adderall XR	10 mg every morning	30 mg

*American Academy of Child and Adolescent Psychiatry Practice Parameter

A similar study compared dextroamphetamine, guanfacine (an antihypertensive agent), and placebo in 17 patients.[5] On the *DSM-IV* ADHD Behavior Checklist for Adults, subjects taking dextroamphetamine or guanfacine reported similar decreases in mean ADHD scores compared with placebo (24 vs 22 vs 30; $P<.05$). They did not report the number of subjects who had a 30% reduction in symptoms. Of note: at the end of the study but prior to unblinding, subjects were asked which medication they preferred. Twelve subjects chose dextroamphetamine, 4 chose guanfacine, and 1 chose placebo. Subjects' stated reason for choosing dextroamphetamine was the positive effect it had on their motivation.

Another study included in this review was a randomized controlled trial of mixed amphetamine salts. Of the 27 adults who completed the study, 19 (70%) responded favorably to mixed amphetamine salts compared with 2 (7.4%) receiving placebo (NNT=1.6; $P<.001$).[6] Favorable response was defined as more than a 30% reduction of symptoms on the ADHD Rating Scale. Not included in either review was a 7-week randomized controlled trial comparing methylphenidate with sustained-release buproprion.[7] Thirty out of 37 subjects completed at least 1 week of the study. The primary indicator of a favorable response was the Clinical Global Impression Scale. The rate of response was 50% for methylphenidate, 64% for sustained-release buproprion, and 27% for placebo ($P<.14$).

RECOMMENDATIONS FROM OTHERS

The American Academy of Child and Adolescent Psychiatry[8] concluded that stimulant medication can be used to treat adults who have been carefully evaluated. They recommend starting methylphenidate, dextroamphetamine, or mixed amphetamine salts according to patient and clinician preference (**Table**). They do not recommend the use of pemoline due to the potential for hepatic failure.

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CLINICAL COMMENTARY

Medication can help even well-adapted adults with ADHD

Stimulant therapy benefits many adult patients with ADHD. While some adults need scheduled dosing, others do well with as-needed dosing.

Adults with ADHD often have made behavioral adaptations that allow success without medication. Drugs help these patients when focused attention is critical for specific tasks. A salesman doing a month-end report may find the improvement in attention helpful, but not needed for most daily tasks. A college student may need medication only for a specific class or project. Physicians can help patients with ADHD through anticipatory guidance in choosing a program of study or career goal and then collaborating in choosing appropriate behavioral and medication therapies.

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REFERENCES

1. Jadad AR, Boyle M, Cunningham C, Kim M, Schachar R. Treatment of attention-deficit/hyperactivity disorder. *Evid Rep Technol Assess (Summ)* 1999; 11:i–viii, 1–341.
2. Spencer T, Wilens T, Biederman J, Faraone S, Ablon S, Lapey K. A double-blind, crossover comparison of methylphenidate and placebo in adults with childhood-onset attention-deficit hyperactivity disorder. *Arch Gen Psychiatry* 1995; 52:434–443.
3. Wilens T, Spencer J, Biederman J. A review of the pharmacotherapy of adults with attention-deficit/hyperactivity disorder. *J Atten Disord* 2002; 5:189–202.
4. Taylor F, Russo J. Efficacy of modafinil compared to dextroamphetamine for the treatment of attention deficit hyperactivity disorder in adults. *J Child Adolesc Psychopharmacol* 2000; 10:311–320.
5. Taylor F, Russo J. Comparing guanfacine and dextroamphetamine for the treatment of adult attention-deficit/hyperactivity disorder. *J Clin Psychopharmacol* 2001; 21:223–228.
6. Spencer T, Biederman J, Wilens T, et al. Efficacy of mixed amphetamine salts compound in adults with attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 2001; 58:775–782.
7. Kuperman S, Perry P, Gaffney G, et al. Buproprion SR vs. methylphenidate vs. placebo for attention deficit hyperactivity disorder in adults. *Ann Clin Psychiatry* 2001; 13:129–134.
8. American Academy of Child and Adolescent Psychiatry. Practice parameter for the use of stimulant medications in the treatment of children, adolescents and adults. *J Am Acad Chil Adolesc Psychiatry* 2001; 41:26S–49S.

Does a high-fiber diet prevent colon cancer in at-risk patients?

EVIDENCE-BASED ANSWER

There is no direct evidence of an effect of dietary fiber on colon cancer incidence. A diet high in fiber has not been shown to be effective in the short-term (2- to 4-year) prevention of recurrent colon polyps (strength of recommendation [SOR]=**A**, based on consistent randomized clinical trials). Furthermore, epidemiological evidence is inconsistent in demonstrating an association between dietary fiber consumption and the occurrence of colon cancer (SOR=**C**).

EVIDENCE SUMMARY

The term "dietary fiber" refers to a heterogeneous group of substances that may vary in their biologic effects. Fiber is thought to reduce the risk of colon cancer through the following proposed mechanisms—decreased gastrointestinal transit time, increased stool bulk, and fermentation of volatile fatty acids. Other aspects of diet such as fat content, red meat, and micronutrients may also play a role in the development of colon cancer.

Additional proposed risk factors include sedentary lifestyle, obesity, tobacco use, and alcohol consumption[1]; while the commonly accepted high-risk groups for colon cancer are those aged >60 years, those with a positive family history of colorectal cancer, and those with familial polyposis syndrome. In summary, it appears that the cause of colon cancer is complex and multifactorial.

No randomized controlled trials of interventions test whether increase dietary fiber affects the development of colon cancer. Recent randomized controlled trials of interventions have used colon polyps as a surrogate endpoint, since it is believed that polyps are precursors to cancer. A Cochrane meta-analysis[2] of 5 trials

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