Efficacy of Adderall for attention-deficit/hyperactivity disorder: a meta-analysis
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Authors' objectives
To perform a meta-analysis using data from studies of Adderall in the treatment of people with attention-deficit hyperactivity disorder (ADHD).

Searching
PubMed, PsycINFO, Current Contents, EMBASE and PsycLIT were searched. The keywords were stated, but the dates for which the search was conducted were not.

Study selection
Study designs of evaluations included in the review
Studies with at least 2 weeks' follow-up were eligible for inclusion; the inclusion criteria were not defined otherwise in terms of study design. The included studies were parallel-group or crossover randomised controlled trials (RCTs).

Specific interventions included in the review
Studies that compared Adderall with placebo were eligible for inclusion. Where the drug dosage used in the included studies was reported, doses of Adderall were 12.5 mg, 0.13 to 0.3 mg/kg twice daily, and up to 30 mg twice daily (1 study of adults). The drug regimens consisted of fixed doses and a titrated dose to optimise the effect. The duration of treatment, where stated, ranged from 3 to 7 weeks. In some studies treatment was allocated on a daily basis.

Participants included in the review
The inclusion criteria were not explicitly defined in terms of the participants. Studies of children, adolescents and adults with ADHD were included.

Outcomes assessed in the review
Studies in which the outcomes were assessed using structured measures for ADHD symptoms, aggressive or defiant symptoms, or global rating of behaviour were eligible for inclusion if the outcome assessors were blinded to the treatment group and if the outcomes scores were presented as means with standard deviations. In the included studies, parents, teachers and psychiatrists assessed the outcomes using the following measures: Iowa Conner's Teachers Rating System; Connor's Global Index; Clinical Global Impression Improvement Scale; ADHD Rating Scale; global improvement assessed using a 10-point scale; ADD-H Comprehensive Teacher's Rating Scale; rating of ADHD symptoms; motor activity; and performance on simple maths problems.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Some information on the individual studies was presented in the text of the review. The standardised mean difference (SMD) and 95% confidence interval (CI) between Adderall and placebo was calculated for each study.

Methods of synthesis
How were the studies combined?
Pooled SMDs and 95% CIs were calculated using methods described by Hedges and Olkin. Publication bias was assessed by first considering the symmetry or otherwise of a funnel plot, and second, by replacing the asymmetrical data points in the funnel plot with a mirror image and reanalysing the data using the original data plus the input data ('trim and fill' method).

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared statistic. The influence of individual studies was explored by reanalysing the data after excluding each study in turn. A subgroup analysis was used to explore the influence on the results of the dosing regimen (fixed dose and optimal dosing regimens), type of rater (parent, teacher, clinician) and type of measure (ADHD symptoms, aggressive symptoms and global ratings).

Results of the review
Six studies (384 children and adults) were included.

All of the included RCTs found that Adderall significantly improved all measures in comparison with placebo. The pooled SMD was 1.00 (95% CI: 0.91, 1.10). Significant heterogeneity was found (P<0.001).

Subgroup analysis: heterogeneity was not accounted for by differences between fixed dose and optimal dosing regimens. The type of rater influenced the results: clinician ratings showed significantly larger effect sizes than teachers (P=0.01) or parents (P=0.004). There was no significant difference between teacher- and parent-rated effect sizes (clinician SMD 1.41; parent SMD 0.83; teacher SMD 0.94). There was no significant difference between ADHD and aggressive symptoms ratings of effect size (P=0.4). Global measures were significantly higher than ADHD measures of effect size (P=0.005).

Publication bias: the funnel plot was asymmetrical indicating the potential for publication bias. A meta-analysis after 'trim and fit' adjustment found that Adderall was significantly better than placebo (SMD 0.84, 95% CI: 0.67, 1.0).

Authors' conclusions
Adderall significantly improved outcomes for people with ADHD in comparison with placebo, regardless of the type of dosing, type of rater and type of measure.

CRD commentary
The review question was clear in terms of the intervention and outcomes. The inclusion criteria were not explicitly defined in terms of the participants or study design. Several relevant sources were searched and search terms were given, but the dates for the search were not provided. It was not stated whether any language limitations had been applied and the lack of an attempt to locate unpublished studies raises the possibility of publication bias. There were no details of the methods used to select the studies or extract the data, hence the potential for bias cannot be assessed. Study validity was not assessed, thus it is not possible to assess the quality of the evidence on which the conclusions were based. Some relevant characteristics of the included studies were described in the text of the review, but details of the criteria used to diagnose ADHD were not given and the drug dosage and treatment duration were not reported consistently. It was not reported whether the data were extracted on an intention-to-treat basis, nor whether the order effect was analysed in crossover trials.

A meta-analysis was performed, statistical heterogeneity was assessed and potential sources of heterogeneity were explored. However, it was unclear which outcomes were combined in the main meta-analysis and, in view of the significant statistical heterogeneity, a meta-analysis may not have been appropriate. There were insufficient details on the methods used to conduct this review to comment on the adequacy of the review methodology. In view of the limitations highlighted, caution is advised when interpreting the conclusions of the review.

Implications of the review for practice and research
The authors did not state any implications for further research and practice.
Bibliographic details

PubMedID
12142863

Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Amphetamines /therapeutic use; Attention Deficit Disorder with Hyperactivity /drug therapy; Central Nervous System Stimulants /therapeutic use; Child; Child, Preschool; Humans; Randomized Controlled Trials as Topic

AccessionNumber
12002006724

Date bibliographic record published
31/03/2004

Date abstract record published
31/03/2004

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.