Comparative efficacy and tolerability of pharmacological interventions for attention-deficit/hyperactivity disorder in children, adolescents and adults: protocol for a systematic review and network meta-analysis

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ABSTRACT

Introduction:
Attention-deficit/hyperactivity disorder (ADHD) is a major public health issue. Pharmacological treatments play an important role in the multimodal treatment of ADHD. Currently, there is a lack of up-to-date and comprehensive evidence on how available ADHD drugs compare and rank in terms of efficacy and tolerability, in children or adolescents as well as in adults. We will conduct a network meta-analysis (NMA), integrating direct and indirect comparisons from randomised controlled trials (RCTs), to rank pharmacological treatments for ADHD according to their efficacy and tolerability profiles.

Methods and analysis:
We will search a broad range of electronic databases, including PubMed, MEDLINE, EMBASE, PsycINFO, ERIC and Web of Science, with no date or language restrictions. We will also search for unpublished studies using international clinical trial registries and contacting relevant drug companies. We will identify and include available parallel-group, cross-over and cluster randomised trials that compare methylphenidate, dexamphetamine, amphetamine derivatives (including lisdexamfetamine), atomoxetine, clonidine, guanfacine, bupropion or modafinil (as oral therapy) either with each other or to placebo, in children, adolescents or adults with ADHD. Primary outcomes will be efficacy (indicated by reduction in severity of ADHD core symptoms measured on a standardised scale) and tolerability (the proportion of patients who left a study early due to side effects). Secondary outcomes will be global functioning, acceptability (proportion of patients who left the study early by any cause) and changes in blood pressure and body weight. NMA will be conducted in STATA within a frequentist framework. The quality of RCTs will be evaluated using the Cochrane risk of bias tool, and the quality of the evidence will be assessed using the GRADE approach. Subgroup and sensitivity analyses will be conducted to assess the robustness of the findings.

Ethics and dissemination:
No ethical issues are foreseen. Results from this study will be published in a peer-reviewed journal and possibly presented at relevant national and international conferences.

Trial registration number: CRD42014008976.