Active placebos
Impact on effect estimates in randomised trials

Background
In randomised placebo-controlled trials, bias due to unblinding may be an issue when experimental drugs have perceptible adverse and psychotropic effects. For example, patients treated with methylphenidate for attention deficit hyperactivity disorder (ADHD) may experience adverse effects such as mild euphoria, nausea, sleep problems and decreased appetite (1).

Some trials have attempted to address this problem by using active placebo controls that mimic such adverse effects. However, active placebos are infrequently and inconsistently used (2), and previous empirical comparisons of active placebos versus standard placebos are rare and mostly based on observational studies (3).

Objective
To investigate the impact on treatment effect estimates in randomised trials when active placebo control groups are used instead of standard placebo control groups.

Methods
A methodological systematic review of trials randomising participants to either active placebo or standard placebo interventions, with planned meta-analyses.

Results
The 15 included trials with direct randomised comparisons of active and standard placebos constitute a unique material in methodological research. Meta-analyses are not yet finalised.