

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

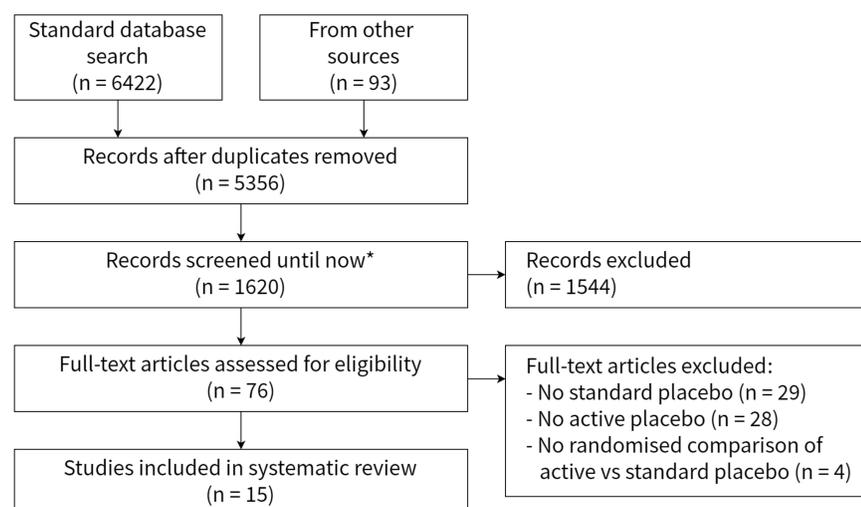
To investigate the impact on treatment effect estimates in randomised trials when active placebo control groups are used instead of standard placebo control groups.

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.



Characteristics of the 15 included trials	n (%)
Design	
Crossover	8 (53%)
Parallel	7 (47%)
Conditions	
Clinical pain	2 (13%)
Experimental pain	7 (47%)
Psychiatric, for example schizophrenia	5 (33%)
Irritable bowel syndrome	1 (7%)
Type of active placebo	
Atropine	4 (27%)
Diphenhydramine	2 (13%)
Phenobarbital	2 (13%)
Phenobarbital and atropine	1 (7%)
Other, for example caffeine, midazolam	6 (40%)

* 3736 records still being screened. References: 1. Storebø CDSR 2018. 2. Jensen J Clin Epi 2017. 3. Moncrieff Int J Meth Psych Res 2003. Acknowledgments: Images by OpenClipart-Vectors and by Clker-Free-Vector-Images from Pixabay (partly modified).



Active placebo versus standard placebo control interventions in pharmacological randomised trials: a systematic review

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Project link where the future publication will be available.

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