

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Effects of Placebos without Deception compared with no treatment: protocol for a systematic review and meta-analysis
AUTHORS	Petkovic, Grace; Charlesworth, James; Kelley, John; Miller, Franklin; Roberts, Nia; Howick, Jeremy

VERSION 1 - REVIEW

REVIEWER	Howard Maibach Department of Dermatology University of California San Francisco United States of America
REVIEW RETURNED	31-Jul-2015

GENERAL COMMENTS	The reviewer completed the checklist but made no further comments.
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REVIEWER	Christopher Dowrick University of Liverpool, UK
REVIEW RETURNED	04-Aug-2015

GENERAL COMMENTS	<p>This proposal to undertake a systematic review and meta-analysis comparing non-deception placebos with no treatment is unique and important. As the authors note, clinicians frequently prescribe placebos in routine practice, yet we do not have adequate knowledge of whether or how they may work. They plan a rigorous systematic review to address questions related to effectiveness and delivery, following standard Cochrane methodologies. The proposal is clear and well presented, and the authors have strong expertise in this field.</p> <p>I have two related queries:</p> <ol style="list-style-type: none">1. Scope of the review. The authors propose to include a wide range of studies, covering both clinical topics and also research topics (e.g. placebo alcohol studies). This will lead to considerable heterogeneity and hence complexity of analysis, as they acknowledge. Are the authors confident that they can find meaningful comparative results from across such a broad field of inquiry? Might restricting to clinical studies only, or even certain common conditions, be more fruitful?2. The answer to this may in part relate to a parallel problem: it is not clear how large the pool of studies will be, and hence how wieldy or unwieldy the analysis will prove. Have the authors conducted a scoping review? For example, I have done simple PubMed searches based on some of their key search strategy terms: [Placebo +
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	<p>without deception] gives 159 hits, whereas [Placebo + non blind] gives 53,658 hits. The former looks somewhat limited in scope, while the latter would need considerable further filtering before any analysis could be considered.</p> <p>Also some minor points.</p> <p>The abstract page 4 line 32 is missing the word 'compare; and on line 44 the words 'no' and 'and' are the wrong way round.</p> <p>page 7 line 1-2, parenthesis would be better after 'administration'</p> <p>page 10 line 26, it is not clear what the word 'language' refers to: language as in key terms, or language as in English?</p>
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VERSION 1 – AUTHOR RESPONSE

DETAILED RESPONSES:

I) REVIEW SCOPE:

We agree that the scope of the review is broad, and, as the reviewer points out, this will present problems when and if we pool the results.

To address the issue we have added several subgroup analyses. This will reduce the scope (within the subgroup analyses). We have modified the text so it now reads:

“Amongst trials that meet our eligibility criteria we will carry out the following sub-group analyses

1. Trials that used random allocation (described below). This will be to test whether the effects of open label placebos might have arisen due to bias.
2. Amongst those with a blinded or deceived placebo group, we will look for a dose-response. This will be to help gather data about a causal effect of non-deceptive placebos. {Howick, 2009 #1148}
3. Trials conducted in a clinical (as opposed to laboratory) settings. This is to test the clinical relevance of our results.
4. Conditions investigated in three or more trials. This is to measure the condition-specific effects of open label placebos.”

II) SCOPING REVIEW

This is an excellent point, and we have indeed conducted a scoping review, and we anticipate between 7 and 15 studies.

It is also relevant that the terminology in this area is not well defined so the search strategy is necessarily somewhat ‘fuzzy’. We based our search strategy on the 5 studies that we knew about of nondeceptive placebos. It is our hope that this systematic review encourages the use of a common terminology.

(Aside: the term ‘nonblind’ is included in our search strategy, as you can see in the appendix.)

III) RESPONSE TO "MINOR POINTS"

Thank you for pointing these out; we have made the relevant change to the text.