Author's response to reviews

Title: Physical activity for the prevention and treatment of major chronic disease: an overview of systematic reviews study protocol

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Author's response to reviews: see over
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Dear Editor(s),

This cover letter contains a point-by-point response to the editorial and reviewer comments for our manuscript entitled: Physical activity for the prevention and treatment of major chronic disease: an overview of systematic reviews study protocol’.

1. The inclusion of our PROSPERO number has been added to the abstract as per the editorial request.

Response to reviewer comments:

1. We thank the reviewer for their timely and thorough review of our protocol paper. We note that the reviewer has marked their comments/suggestions as ‘discretionary revisions’. Therefore, in giving our response we mainly discuss some of the issues raised by the reviewer without necessarily making changes to the manuscript. Where changes to the manuscript have been made based on reviewer comments, these have been indicated with track changes as requested by the editors.

2. We agree with the reviewer’s comments regarding the issue over the time-period needed for physical activity in preventing chronic diseases and the ‘impossible’ nature of an RCT in these circumstances. The reviewer states “.a few such trials exist)” and ‘interventions usually consist of RCTs of perhaps up to a year’s duration, and then mostly for a chronic condition.” The aim of our study is provide in one place the totality of the evidence he eludes to, even if “one of the results is almost certainly predictable from the start” as suggested. It is entirely plausible that we will find little high-level evidence (systematic review of RCTs, RCTs) to reach conclusions around the preventative effect of physical activity in the prevention of most major chronic diseases, but there may be some conditions (e.g. diabetes mellitus, obesity, osteoarthritis) for which there is some evidence of an effect. Moreover, most healthcare guidelines for the major chronic diseases contain recommendations for physical activity as part of a lifestyle prevention and/or management strategy. We think it would be interesting to see whether the evidence from this could be supported better by evidence from RCTs rather than the observational data currently cited. If the answer is no, then this would indicate where gaps in the evidence base lies. Where there is evidence from RCTs, this could be used to inform trials for conditions where high-level evidence is lacking and that would be suitable to an RCT design (e.g. secondary prevention of myocardial infarction, heart failure, stroke).

3. We acknowledge the reviewer’s concern about reinforcing a “nihilistic approach to physical activity”. We certainly do not wish or intend for this and aim to avoid such a scenario by not stating that there is ‘no evidence’ should we find a lack of high-level evidence for a particular
condition. In such cases we will state that the evidence is still based on observational studies and that suitable RCT evidence is lacking.

4. We thank the reviewer for pointing out or use of the I2 statistic to assess heterogeneity. We have overlooked the fact that some reviews may not include pooled data (probably due to heterogeneity and/or number of eligible studies). We have therefore edited this section of our manuscript so that it indicates the I2 statistic will be used to assess heterogeneity where reviews have included pooled outcomes that generate an I2 statistic.

5. We acknowledge the reviewer’s concern regarding the number of primary outcomes. We understand that consideration of 42 primary outcomes appears illogical in terms of scale and scope. However, the nature of overviews of systematic reviews lend themselves to this issue and there are examples of this type of review that include an even greater number of primary outcomes (Singh et al. 2011. Cochrane Database of Systematic Reviews 2011, Issue 2. Art. No.: CD008794). Moreover, we do not anticipate eligible reviews for all the conditions we have listed, therefore we are unlikely to report 42 primary outcomes.

6. The reviewer indicates that it is “very unlikely” for our goal of generalising findings such as type, intensity, volume, duration etc by disease condition to be realised. If this is the case then it is in itself an important and noteworthy finding. When you compare the evidence related to pharmacological interventions for prevention/treatment of chronic conditions, it would not be difficult to find answers to these type of specific questions (e.g. dosage (amount), frequency (when/when not to take), time to effect (minutes/hours), adverse effects, etc). Why should this not be the same for physical activity interventions? If it is not reported adequately, then this is methodological flaw within the PA research community and one that would need highlighting.

7. We agree that a public health approach is intrinsic to the physical activity/inactivity problem. However, and particularly in the UK, healthcare providers are being increasingly targeted as key deliverer’s of policies to improve lifestyle management of their patients. In the UK context, this is driven by the fact that over 80% of the population will visit their GP at least once in any one year. GPs are therefore seen as key to aiding their patients, and by implication the general public/population, in achieving a healthier lifestyle, including physical activity. In fact this is the main reason why we are conducting this review. When we have asked GPs why they do not routinely prescribe exercise the responses we get are along the lines of “To whom should I prescribe it?”; “What PA should I prescribe?”; “How do I prescribe it?” “How do I measure it?” “What is the follow up period?” We feel that by conducting this overview we will hopefully be able to provide some answers to these questions or demonstrate that they cannot currently be answered by the use of high-level evidence.

We hope our responses above are satisfactory and demonstrate that we have considered the reviewer’s comments carefully.

Kind regards,

David