Author’s response to reviews

Title: Exercise, or exercise and diet for the management of polycystic ovary syndrome: a systematic review and meta-analysis

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Editor's comments:

1. As the study is very likely to focus on the changes of the cardiovascular risk factors rather than the fertility outcomes, the title of the study may be revised and study objectives could be stated more clearly.

We have revised the title according to the relevant comment by reviewer 2. We have not revised the title further to include study outcomes as we did not include outcomes in the eligibility criteria of our protocol because we wanted to look at all outcomes that were measured in this population. We did, however, select cardiovascular risk factors as our primary measures, and fertility-related factors as our secondary outcomes. The title also reflects our PROSPERO registration.

2. For reports with overlapping populations, the paper with the largest population and/or the longest follow-up duration should be included in the analysis.

With regard to this observation, Line 159 acknowledges that “Where multiple publications for the same trial were retrieved, they were linked together, and the earliest paper of the trial was used as the primary reference” – For clarity, we have also added the following sentence: “the
earliest paper was used as the reference only, data were extracted from all papers with the most comprehensive available data included for each outcome.”

3. It is great if the authors can summarize the current major evidence gap based on their findings.

We thank again the editor for this suggestion, and this information is now included in Section 4.5: “Future Directions”.

Reviewer #1:

1. Abstract

Conclusions: State only what your study found; do not include extraneous information not backed up by the results.

We thank the reviewer for this comment. An introductory sentence has been added to the abstract, summarising the key findings as follows:

“Conclusion: Statistically beneficial effects of exercise were found for a range of metabolic, anthropometric and cardiorespiratory fitness related outcomes. However, caution should be adopted when interpreting these findings since many outcomes present modest effects and wide CIs, and statistical effects in many analyses are sensitive to the addition/removal of individual trials. Future work should focus on rigorously designed, well-reported trials that make comparisons involving both exercise and diet.”

2. Discussion

Compare and contrast your study with others in the most relevant world literature, particularly the recent literature.

We thank again the reviewer for this comment. We have followed this in the following points of our discussion and we would be happy to further include and cite any additional studies/publications that the reviewer feels would be beneficial to our discussion:

Line 806 – surrogate markers of IR compared to two recent systematic reviews (Domecq et al. 2013; Moran et al. 2011) and contrasts between exercise only, or lifestyle are made.
Lipid profile findings have been compared to previous reviews (Haqq et al 2015; Moran, 2011) and key differences highlighted; we have also attempted to explain why changes did/or did not occur.

VO2 max – recent studies drawn upon to highlight not only the decreased values in women with PCOS (Dona et al 2017; Orio et al. 2006; Bacchi et al 2015), but also the importance of CRF in capability to exercise, perform activities of daily living, and overall quality of life (Blair et al 1989; Kodama et al 2009). Our findings are also compared to those of previous reviews (Haqq et al 2015)

we also report non-significant findings, contrast these to recent reviews in PCOS, and in healthy populations (Enea et al 2011; Ennour-Idrissi et al 2015), and we attempt to explain why we observed no effect.


• Moran LJ, Hutchison SK, Norman RJ, Teede HJ. Lifestyle changes in women with polycystic ovary syndrome. The Cochrane Library. 2011.


What new information is sufficient to modify existing clinical practice?

We thank again the reviewer for this comment, and have added an additional section (Section 4.5: Future Directions) which highlights the gaps in knowledge that this review has identified and future research directions that can address these. From the findings of our systematic review, we identified that the current evidence is not sufficient to modify existing clinical practice, and we feel that this is also implied in the grading of evidence as being very low or low quality.

And finally, the conclusions and implications for current practice, and particularly for future research that may have a significant impact on clinical decisions

We again thank the reviewer for this comment, and as mentioned above we have added a section (Section 4.5: Future Directions) which discusses the gaps in knowledge that this systematic review has identified and the future research directions that may be beneficial.

3. At the end of the Discussion, under the subheading "Limitations," review the limitations of your study.

We welcome this suggestion, and although not under the sub-heading “limitations” we have already reported this within our paper; Sections 4.2: Overall completeness and applicability of findings, and 4.3: Quality of the evidence describe factors of the included studies which may limit the importance of the findings. Then Section 4.4: Potential biases in the review process summarises methodological limitations. This has now been highlighted at the start of section 4.2 by the addition of a sentence which says ‘However, there are limitations to this systematic review’ to aid the reader in identifying this analysis. Furthermore, we have renamed Section 4.4. as “Limitations and potential biases in the review process”, and have alluded to further potential limitations.

4. At the end of the limitations, under the subheading "Future directions".
As suggested, we have added this section as: “Section 4.5: Future Directions”, as discussed above

5. Conclusion

Take special care to draw your conclusions only from your results and verify that your conclusions are firmly supported by your data

We thank again the reviewer for this suggestion. Our conclusion draws together the key findings from our meta-analysis, describes the quality of these findings as measured by GRADE, and urges the reader to interpret our findings with caution due to the methodological issues in the eligible studies. We would be happy to add any further clarification that the reviewer feels necessary to the conclusion section.

6. I would recommend to add also funnel plots and a meta-regression analysis.

According to the recommendations within the Cochrane Handbook (Deeks, Higgins and Altman, 2011), meta-regression has not been completed because all (apart from BMI) meta-analyses include fewer than 10 studies. Similarly, funnel plots have not been included because when there are fewer studies, the power of tests is too low to distinguish chance from real asymmetry. We have, however, provided the funnel plot for the BMI analysis within the Supplementary Figures (Supplementary Figure 4) and added a sentence (line 242) explaining the rationale for this.


7. References

References have been amended to reflect the changes.
Reviewer #2:

1. The title "Exercise and diet for the management of polycystic ovary syndrome: a systematic review and meta-analysis" is somewhat misleading since the manuscript was focused on the effect of exercise with or without diet on PCOS.

We acknowledge this request and have amended the title to “Exercise, or exercise and diet for the management of PCOS…”

2. The authors included the earliest paper of a trial if multiple publications were found. Are there papers that included more comprehensive data but published later?

We thank the reviewer for this comment, where multiple publications were evident, all were included within the review; we simply cited the earliest paper for the reference. Where new outcomes, or larger sample sizes were present, data was extracted from the most comprehensive paper. And we’ve added this information: “The earliest paper was used as the reference only, data were extracted from all papers with the most comprehensive available data included for each outcome.” (line 160)

3. Please explain the clinical importance of reporting immediately post-intervention values in the results section.

We thank the reviewer for this request and have added a relevant explanation into the methodology – “immediately post-intervention analysis was also included so as to nullify the effect of selective reporting, but also to better indicate whether there was a treatment effect regardless of baseline values.” (line 202).

4. The authors reported that 27 papers from 18 trials were included. It may be unnecessary to include multiple papers from one trial if data were only extracted from one paper. Besides, in line 276, the authors said they were sent one additional article after requesting information from another author, does this mean they actually included 28 papers?

We thank the reviewer for this comment, in answer 27 papers from 18 trials were included in this review. This is demonstrated by the PRISMA flow diagram we present (Fig. 1). For reader clarity, the sentence from line 276 about the additional paper has been moved up to line 264.
5. Starting from line 306, the authors mentioned that trials included women who were overweight and obese based on different BMI values. For women in a trial that was categorized as overweight, was the mean BMI 25-29.9 or the range of BMI 25-29.9?

We acknowledge the importance of this point, and thank the reviewer for raising it. The mean BMI of participants fell within the respective BMI categorisation. For example, “seven trials included women who were overweight” – that is the mean BMI fell between 25-29.9 kg/m2.

6. The authors had very detailed description of the features of included studies that were included in table 2. This part should be shortened.

We acknowledge this request and this section has been shortened – please see track changes in the revised manuscript.

7. References should be included in table 3.

An additional column has been added to Table 3 containing the references for the studies included in each analysis. Two columns with trial numbers have been deleted from Table 3 as can be calculated from new column.