Reviewer’s report

Title: Supervised exercise training and increased physical activity to reduce cardiovascular disease risk in women with polycystic ovary syndrome: study protocol for a randomized controlled feasibility trial

Version: 1 Date: 31 May 2019

Reviewer: Stephen Burns

Reviewer's report:

Summary:
This manuscript describes a protocol for a randomised controlled trial (RCT) comparing the effects of 12 weeks of lifestyle physical activity (LPAG) and structured exercise (EG) with no exercise (Control) on oxidised LDL, blood lipids and other metabolic risk markers for cardiovascular disease (CVD) in pre-menopausal adult (≥18 years) women with polycystic ovary syndrome (PCOS). The research is positioned as a feasibility study using an exploratory RCT with the primary outcomes listed as acceptability and feasibility of procedures for recruitment, allocation, measurement and retention for the intervention.

Comments:
Thank you for allowing me to review this demanding protocol. Please could you help clarify the comments below:

1. The main issue with this study is how it is positioned. The primary outcomes are recruitment rate, attrition rate, compliance, reasons for drop-out and completions rates of the exercise programmes. This suggests that the study is therefore looking at the suitability of the exercise interventions in these women. However, the title is clear in stating the effect on oxidised LDL and cardometabolic profile in women with PCOS which are secondary outcomes. Supporting this, the introduction focuses on oxidised LDL, and the Discussion (Lines 390-1) states that the study, "aims to measure the feasibility of analysing oxidised LDL in PCOS, including whether concentrations can be reduced through structured exercise training.’ Firstly, oxidised LDL can be measured in PCOS - a study is not needed to determine the feasibility of this. Secondly, as stated in Lines 372-373, there is no formal sample size to determine whether oxidised LDL concentrations can be reduced through structured exercise training. Based on the primary outcomes, this study should be re-positioned as a mixed-methods study to examine the feasibility of structured versus lifestyle exercise interventions in women with PCOS. A mix of quantitative and qualitative barriers to exercise can be described. If the study aims to look at oxidised LDL then that needs to be the primary outcome measure and powered to do so.

2. A second issue is the LPAG. One aim is to reduce sedentary behaviour (Introduction and Line 394). Physical activity will be monitored and tracked using a smartphone fitness application but there is no measure of sedentary behaviour taken. Increasing physical activity does not
necessarily reduce sedentary time and the two concepts are not synonymous. How is sitting time (the main marker of sedentary activity) assessed?

3. Please can you provide more details on how the intensity is determined for the EG participants? Line 228 states that exercise sessions should be 50-70% of maximum oxygen uptake (VO2max) but only a single stage Astrand test is being used to predict VO2max so workload cannot be set from this for walking or cycling. Lines 241-3 state that ACSM recommend individuals to work at 57-74% of maximum heart rate and that participants will progress to this 74% over 4 week increments. Please state how workload is initially determined and achieved and how it is controlled - it is unclear? Is predicted maximum heart rate used?

4. Line 174: Please state how eligibility criteria (iii) is determined. Self-report or objectively measured? Is it only structured exercise, leisure-time physical activity, or total physical activity?

5. Line 175: Please confirm inclusion criteria (iv). Individuals must have been taking metformin for &gt;3 months to participate. So individuals not on metformin are ineligible?

6. Line 180: Inclusion criteria (vii) - current CVD means clinically defined?

7. Line 186: Please define where waist and hip measurements are taken.

8. Line 251: Please state which smartphone fitness application.

9. Line 326: Please state how many individuals will be completed. This should be determined prospectively. Please can you submit a copy of the guiding interview questions (semi-structured) with the protocol.

Level of interest
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