Reviewer's report

Title: Need for Exercise among Patients with Hypertension and Renal Disease (NEPHROS Trial): Randomized Controlled Trial

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Reviewer: Kevin C Abbott

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Barcellos et al present a proposed protocol of a RCT comparing regular exercise among patients with non-diabetic CKD and outcomes, most esp eGFR and quality of life, at 16 weeks.

Because the exclusion of diabetic patients, who comprise ~50% of CKD patients, is so important, this should be included in the title and methods section of the abstract.

Why did the authors exclude diabetic patients?

The other mean issue is the choice of change in eGFR as an outcome and the use of their internal population to estimate sample size. Because the authors will be assessing longitudinal changes, use of a cross sectional population to estimate sample size is likely not the best choice. The authors cite the MDRD study and use that formula (they need to specify exactly which one since there are several; the four variable formula is most commonly used).

Using data from the MDRD study, how many patients would have been required to see a difference of 10% in eGFR at 16 weeks? Is this difference an absolute difference between the two groups or is it a "delta delta", namely the difference in CHANGE between baseline and 16 week eGFR, between the two groups? It is possible that at 16 weeks, acute hemodynamic changes might be seen rather than persistent changes in kidney function.

The authors mention medications as covariates, but will any specific medications be considered causes for exclusion (warfarin, for example, or beta blockers, or digoxin?) If not how will the authors assure random distribution between groups (ie does the sample size analysis account for this?)

How are the groups to be randomized? By computer random number assignment, or some other scheme? We need to be sure the groups are not alternating, which can introduce bias.

In addition to the exclusionary criteria, are there criteria for assessing that exercise would not be safe for patients, since it is assumed most patients have been sedentary? Will there be an "acclimation period" to allow patients to work up to a reasonable exercise schedule?

How will patients be contacted in their homes? Might this be considered
intrusive?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.