Reviewer's report

Title: INfluence of Successful Periodontal Intervention in Renal Disease (INSPIRED): study protocol for a randomised controlled pilot clinical trial.

Version: 0 Date: 01 Aug 2017

Reviewer: Natasha Wiebe

Reviewer's report:

The authors have drafted a lengthy trial protocol that is closely aligned to what they have submitted to the NIHR registry. The background is well-written and the question worthwhile however the methods have redundancies that should be eliminated, making the piece a shorter easier read.

Major Essential Revisions

1. Shorten the methods by removing all or most repeat information. One example, "60 patients with CKD and periodontitis will be randomised into one of two equal arms using a parallel group RCT design" shows up 6 times.

2. "At least 80% of patients recruited with full follow-up" would have been a good singular primary objective for any pilot trial. The term primary should probably be removed from the protocol as it encompasses all the pilot's objectives. Moreover, how does the "success criteria for INSPIRED" and its primary aim fit with the broad primary objective and pilot objects mentioned earlier? These sections contradict each other.

3. The measurements at month 15 and 18 should be more clearly describe as post-trial follow-up for both arms.

4. On page 10, the authors state that the protocol is subject to change as the trial progresses. This is troublesome as the trial was not described as adaptive.

5. Will participants from both groups be supported similarly as it relates to anticipated compliance issues?

6. The statistical analysis section contains many elements that are not related strictly to analysis. The information about reporting (e.g., CONSORT), data management (privacy, confidentiality, data storage), and aims/objectives (i.e., to inform suitability of outcome measures, provide the data necessary for a sample size collection) do not belong in the statistical analysis section.
7. Will you look for differences between the groups on dichotomous outcomes as well? How will report them? I'm also not sure what you mean when you say that the mean differences will determine sensitivity to change. Change in what?

8. Will CRP and IL-6 not be measured?

Minor Essential Revisions

9. The term high-risk CKD is puzzling. It is used a few times before it is defined. It begs the question high-risk for what specifically. The term advanced (stage) or severe CKD would be better understood.

10. The last sentence on page 7 needs references: "To date only a limited number of underpowered, non-randomised interventional studies have investigated the effect of periodontal therapy on renal function."

11. Under inclusion criteria, criteria 4iii) should be described as non-dialysis CKD stage 4 or 5. Not all CKD patients will receive dialysis at a later point in time.

12. Remove the first and second exclusion criteria as they are redundant given the inclusion criteria.

13. Add the term permuted to the description of block randomization. Also give the variable block sizes.

14. Why can not the assessor of general health be blind to each patient's treatment allocation?

15. In figure 2, Agree to participate, should be replaced with Agree to be approached as they have not yet consent according to the diagram. Also the last 6 months should be described similarly for both groups - they are post-trial follow-up periods for both treatment groups.

Comments

16. In the write-up of the results, the authors will need to be clear that the results do not generalize to all patients with stage 1-3 CKD, only those with declining eGFRs or albuminuria.

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