Reviewer’s report

Title: The Low Indexes of Metabolism Intervention Trial (LIMIT): Design and baseline data of a randomized controlled clinical trial to evaluate how alerting primary care teams to low metabolic values, could affect the health of patients aged 75 or older

Version: 2 Date: 08 May 2017

Reviewer: Maya Vadiveloo

Reviewer’s report:

Overall, the manuscript is improved, but there remain a few additional issues that require clarification.

1. Introduction: The flow in the introduction remains awkward and the rationale for study difficult to follow. Some specific comments:

   - Line 27-28 is awkwardly phrased and lacks a necessary justification regarding the both the biologic plausibility of why low BMI, HbA1c, and serum cholesterol require more attention and some evidence of the numbers of elderly adults currently who are not flagged by low values and who may experience higher morbidity and mortality as a result.

2. Line 39- when the authors refer to nutritional intervention trials, it is not clear what the outcomes are in those trials, making the interpretation of the sentence difficult.

3. Transitions are needed between lines 45 and 46. Something like, "Similar to BMI, the correlation between xxx and xxx is U-shaped for both HbA1c and total cholesterol..."

4. A bit more discussion on HbA1c targets in the elderly would help the reader understand if the issue that needs to be addressed in the elderly is over-treatment or A1c targets that are too aggressive- especially because the authors specifically focus on patients taking 2 antidiabetic medications- do the criteria change for 1 medication or for individuals who are pre-diabetic?

5. Line 18 (2nd page of introduction)- can the authors please define low-risk

6. A transition is needed between the discussion of cholesterol and screening malnourished patients- the authors move from talking primarily about population statistics and then move to clinical populations (e.g. hospitalized), and it is not clear how the 2 are connected.

7. Line 22-24 ("made significant effect" is awkwardly phrased- additionally, using numbers to show the effect would be more convincing.
8. Can the authors add two additional sentences/ideas somewhere in the introduction: 1) It is not clear to a non-expert in this area that healthcare practitioners are "missing" these individuals--adding some numbers to let the reader know that x% of hospitalized patients meet these risk criteria yet only x% are referred for additional counseling. The "so what" of the problem still seems missing from the introduction. Additionally, could the authors please try to add a bit more detail about the intervention in the Introduction--e.g. After the authors mention the previous success of the previous family medicine intervention, they could indicate something about the current intervention (i.e. is it a single email that the nurse or MD receives? Is it upon enrollment?).

Objectives:
- It may be valuable to indicate that the primary objective is to see if the intervention improves patient survival across 7 groups of high risk patients.
- Line 50-51- what are the authors referring to when they say "the number needed to treat" (the number of patients?)

Table 1:
- The authors state that the effect on mortality will be analyzed for each LIMIT subgroup, but subgroup G only has 8 participants. Based on the power calculations, it does not seem that the authors are powered to detect subgroup differences without combining some subgroups.

Methods:
- The authors discuss controlling for confounding, but it would be useful to know what confounding variables are being considered and how they are being measured
- As with the introduction, a bit more description of when and how frequently a reminder email was sent would be helpful to better understand the intervention.
- -How are the authors handling the automatic emails that were sent but not opened by the physician or healthcare practitioner?
General

Could the authors consider some kind of flow diagram to show how the >40,000 in the Southern and Northern districts moved to 8,584 study participants and 7 subgroups (e.g. just the first row of numbers for each of the 7 subgroups in Table 5)

Table 3:

- For criteria "c" the word "all" should be changed to "both"

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

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