Reviewer’s report

Title: Predicting mortality with biomarkers: a population-based prospective cohort study for elderly Costa Ricans

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Reviewer: Bernardo Hernández Prado

Reviewer's report:

Major Compulsory Revisions

The article aims to determine the prognostic value of biomarkers with respect to total and cardiovascular mortality in an elderly population in Costa Rica. It poses a relevant and well defined question, even more when the analysis is conducted with a middle income population. The article is well written, and both abstract and title accurately refer to the content of the study.

The authors describe the source of information used for this analysis (CRELES), and even conduct a validity analysis to test its quality. They also refer funding, details on specimen storage and web site documentation of this survey.

The paper describes in detail the methods employed in the analysis. However, the section “Biomarkers studied and their definitions” should include more information on them, at least the measurement units (that will be only mentioned in table 1), and especially the cut-off points to declare outliers (also just mentioned in a note in Table 1). In the case of medications that affect biomarkers, is it possible to know since when were they taking them?

The manuscript describes the study and results following scientific standards in the field. However, it is a long paper (38 pages) describing a full set of analysis on 22 outcomes. The paper has 3 tables and 6 figures (2 of them with 2 charts each, another one with 4). Although the detail on the analysis is very rich, it becomes difficult to follow. I would recommend to simplify the presentation as follows:

a) The introduction can be reduced from 3 to 2 pages eliminating some details, and without losing its original meaning.

b) In the section of results, mention only the CRELES mortality validity check, and move details and figure 1 (CRELES and Costa Rica life table) to an appendix (an option that PHM allows as additional material).

c) Refer the main results of figure 3 only in the text (as it is in lines 397-405, page 19), and move figure 3 to an appendix

d) In figure 5, it is not clear to me the difference between the left and right charts, but I think the text refers to the one on the right. Keep only that.

Results are really interesting and can generate a lot of discussion. I think it is
important to reinforce in the discussion 3 points that are crucial for the interpretation of this study:

1. What is the meaning of the biomarkers? Biomarkers may reflect a health condition, and in some cases they do not reflect a potential problem itself, but are indicators of a problem. The authors tackle this point in lines 446-452 (p. 21), talking about the interpretation, but I think it can be reinforced in the final discussion.

2. We should keep in mind that it is a population of elderly people with special characteristics, as mentioned in pages 30 and 31. What is the meaning of this indicators for elderly people? Having an excessive BMI is a risk factors the same way it is in early ages, or does it suggest a better present state of health?

3. The baseline measure was collected in 2005, and follow-up in 2010. But we have little information on biomarkers or risk factors for cardiovascular disease before that. Could it be a confounder? I think the possible role of health conditions (reflected in different biomarkers) earlier in time is worthy to be discussed.

Minor Essential Revisions

Some formal points to be considered:

1. Page 11, line 207: write complete DHEAS the first time, as all other acronyms are presented.

2. Page 19, lines 401-402, present correlation coefficients as numbers between -1 and 1 (e.g. r=0.95 instead of r= 95%). Same in figure 3.

3. Page 25, line 530. “figure 6 compares the death RR estimated with the model for CV mortality (full, red dots) with those obtained in all-cause mortality (hollow, blue symbols). From which of the all-cause mortality models were there obtained? Specify.

4. Table 2, some numbers are in red. Do they have a special meaning or was it a printing issue?

5. Figure 2. Set label of Y axis (I think death RR)

6. Figure 5, labels are missing in left chart (see comment d above).

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests