

Comments on the paper authored by Group 10 as Refereed by Group 09:

General comments:

- Please correct basic spelling and grammatical errors
- Please keep consistent font size. There is plenty of variation on this aspect.
- Abbreviations for variables should be defined at the first instance and their use should be consistent throughout the paper
 - note: C-reactive protein (CRP) is defined in the background and methods section, but the acronym is used previously in the summary
 - Fibrinogen is referred as FIB in the report but the acronym is not formally defined
- Always provide the appropriate units. In the second sentence of the summary, it is not clear what (>65) is referring to. I assume it's age
- Always provide all four values: estimate, CI (upper limit and lower limit), and p-value when reporting inference in results and summary section of document

Suggested corrections:

- In Methods part 1), is “ankle and arm systolic blood pressure (AAI)” referring to ankle and arm index?
- Table 3 refers to “systematic blood pressure” - should this be “systolic blood pressure”?

Comments regarding tables and figures:

- Conventionally title of tables is placed above table and title of a figure below the figure
- Remember sig figs when presenting data in table (currently shows 4-5)
- Table 1: It is not clear what the asterisk is referring to next to SD in the first row
- Tables 1 and 3 appear to be way outside the margins. It may be appropriate that you consider reducing the size of the columns
- Consider combining tables 4 and 5
- Change scale on KM curves so that it is easier to view, especially figure 2

Comments regarding analytic approach:

- I think your summary portion contains a lot of results that should otherwise be in the results section. It may be appropriate to just report the part that answers your main question of interest in this portion and leave the rest of the findings for other sections

- In the summary, when the final model (adjusted proportional hazards regression model) refers to the hazard ratio, is the endpoint all-cause mortality or cardiovascular death? I can't find this point estimate of the hazard ratio in tables 4 or 5. Also, the summary states the hazard ratio is significantly higher, though the confidence interval for the point estimate (-0.31% to 1.53%) clearly overlaps 0. Is this the case?
- Explain to researchers your assumptions/reasoning in log transforming inflammatory markers CRP and fibrinogen
- Is there a rationale for computing the geometric mean ratio for CRP and FIB given the various risk factors?
- How were AAI and systolic BP found to be in the causal pathway?
- For methods sections 3 and 5, you may want to make it clear which question of interest is being addressed
- For the results of the analysis section: I think all variables in the model are of interest and not just the significant ones. Presenting a table with all the parameter estimates, CI's and P-values may be a lot more informative. You may want to provide interpretation of a few of the estimates.
- The wording for the section comparing the predictive capabilities of FIB and CRP in males and females is a bit tricky to follow. Is the Z-test computing the difference in estimated hazard ratios for FIB and CRP across gender?
- How are the time periods "short term" and "long term" defined? How are the predictive capabilities for each biomarker compared between these time periods?
- Was there any consideration given to controlling the overall type I error rate? Even if the overall type I error rate was not explicitly controlled, perhaps stating this in the discussion would be good.