

## **Comments on the Paper Authored by Group 02 as Refereed by Group 01**

### ***Comments for Summary:***

- When reporting results from the Cox proportional hazards regression, authors interpret the ratio, but then report confidence intervals that lack interpretation. It does not feel consistent otherwise.
- You do not present the p-values for the cox proportional hazard models.
- The summary is long-winded and requires focusing. Authors need to decide what aspects of their analysis are truly the highlights, and summarize instead of itemize other questions answered.
- Possible limitations or implications of study are not hinted in the summary.

### ***Comments for Background:***

- Good. Gives informative context for the statistical analysis.

### ***Comments for Questions of Interest:***

- The prompt had asked for a list of questions posed by the collaborators, and a separate list of questions you intended to answer in your analysis, and for you to discuss any discrepancies between the two groups of questions. You only provided only one set of questions, with no discussion of the expectations of the collaborators or the limited scope of the analysis.

### ***Comments for Source of Data:***

- Nicely done. You mention in this section that mortality is your primary endpoint, but the summary suggests there are many different endpoints of interest. If mortality is of prime importance, perhaps the summary could focus on presenting those results, with only an abbreviated mention of other outcomes.

### ***Comments for Statistical Methods:***

- “The reason to log-transform CRP and fibrinogen is that we believe the effect of risk factors on the biomarkers is multiplicative instead of additive.” Why do the authors believe this?
- Can authors provide evidence that log transformed provides better fit than linear?
- Make sure to include that you are looking at 2-sided p-values

### ***Comments for Results- Descriptive Statistics:***

- Good work. You could probably leave this section just as it is.

### ***Comments for Results- Linear Regression:***

- Overall pretty good, but perhaps a mention of p-values and comparison with your chosen alpha level for statistical significance would be good to add.
- I think the subheadings should not include the method (linear regression) but rather the predictor of interest and outcome you're examining

### ***Comments for Results- Hazard Ratios:***

- Author's suggest often that "mortality risk is just x% higher," however, reasoning against clinical relevance is not considered.

***Comments for Results- Short Term and Long Term Associations:***

- TBC.

***Comments for Results- Effect Modification by Sex:***

- Can effect modification by sex with C reactive protein be represented graphically?
- Same applies to effect modification by age and cholesterol.
- Did you include a model with sex\*biomarkers to test for significant effect modification? This is unclear
- Generally speaking the model for effect modification is done simply to check the p-value to see if the ratio is statistically significant and the estimate is not presented. If the p-value is significant than you present the stratified model, however if it is not significant you don't need to present the stratified model.
- Be careful about using the word predictable, you are looking at associations but predictive value

***Comments for Discussion:***

- Was the log transformation something considered a priori? Was it considered a linear term?
- Although a number of possible effect modifications are considered, is it possible that correlations amongst those modifiers themselves could reduce the number of effect modifiers?
- In checking for confounding and effect modification, it is implied that the variables cannot be trusted as independent, yet author's state the variables are assumed independent.

***Tables and graphs:***

- *Overall good*
- *Do not need to present Z statistic in 4-6*
- *In tables 5 and 6 it is unclear if you are looking at the HR or a ratio of the HR, I am not sure what the latter would do*