Overall the first draft seems to be shaping up well. The report is well written and well organized. Scientific questions have been answered with proper descriptive and inferential statistical methods. The interpretation of the statistical results is clear and correct. Anticipating problems such as missing data and sparse data have also been properly discussed. The following are suggestions to improve the report:

General Comments:

- One of the most important discussions between collaborators is articulating which of the many potential measured variables you chose to include in the model and why. In your models with adjusted analyses, how did you decide which variables to include and why? You indicate you adjusted for "risk factors." It is important to clearly specify which variables you choose to include in your definition of "risk factor" and why.
- Professor Emerson requested that the memo should be clear enough for a non-specialist. There is a good pedagogical rationale for this. Breaking things down for a non-specialist demonstrates your understanding of the definitions of concepts and techniques. This draft – especially the methods section – definitely seems pitched to experts in a specialized review. It's fine for most of us specialists well-versed in the health and methods concepts but for the non-specialist it would be quite dense.

Methods Section:

- State what makes the given levels of CRP and fibrinogen clinically relevant. Also, you never state the fibrinogen divisions in the methods section.
- "a proportional hazards regression model was chosen, since it is much more informative for this association than any other regression would have been, especially those that categorize the sample by those who died in certain time intervals."
  - Could you elaborate on this in as simple language as possible? Similar to the comment above, this is supposed to be directed at a non-specialist.
- For the proportional hazards regression, the method used for computing confidence intervals and p values should be consistently mentioned (robust?).
- The risk effect of CRP and fibrinogen is more likely to be multiplicative. So it would be better if both variables were log-transformed.

Results Section:

- It was not clear how inference was calculated for ratios of Hazard Ratios. I think that method could be more clearly elaborated. Is it just being looked at as a covariate in addition to another in the model or are you running a test ie to test that the ratio hazard ratios per 10 unit increase in CRP or fibrinogen is not equal to 1.
- It would be clearer if the results could be connected with the related table or figure (when you describe your results, it would be better mention the related table or figure to illustrate the results).
- The Kaplan-Meier curve figure lacks a title and it has not been discussed in the results. It would be better if Kaplan-Meier estimates for CVD caused death could also be presented.

- o Additionally, you can only show the upper range of survival probabilities on the curve (y-axis: range from 0.5-1.0) this would make it easier to compare the curves.
- A table for the statistical results of associations between CRP or fibrinogen and mortality or CVD mortality should be presented.
- It would also be better to present a table of statistical results comparing association between inflammatory biomarkers and mortality modified by time (short term or long term survival), and a table of statistical results comparing association between inflammatory biomarkers and mortality modified by sex.
- At page 4, the fourth and sixth paragraph, lack the direction of comparing the hazard (higher or lower?).
- At page 5, the 11th line of the second paragraph, should be "CRP" but not fibrinogen.
- It sounds awkward when you say relatively x% higher or lower. Maybe try a different wording.