Author's response to reviews

Title: Unemployment and ill health: a connection through inflammation?

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KUOPIO UNIVERSITY HOSPITAL 27 August 2009
Department of Psychiatry

Andrea Bucceri PhD
Scientific Editor
BMC-series Journals
BioMed Central

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Unemployment and ill health: a connection through inflammation?

Dear Editor,

I submit the revised version of our manuscript “Unemployment and ill health: a connection through inflammation?”. We thank the Editor and the Reviewers for your interest in our manuscript. We have made several revisions and hope that the paper now is worth of publishing in BMC Public Health.

Our detailed responses to the Reviewers are as follows:

Reviewer: Nicolas Rohleder

Major Compulsory Revisions

1 General methodological point: the authors measure IL-6 and CRP in plasma and dichotomize participants into having low-grade inflammation or not based on
specific cut-offs. No attempt is made to use continuous values of IL-6 and CRP. … The authors cite two papers (Capuron and Yaffe) that have successfully used median splits. … In summary, while I agree that the strategies by Yaffe and Capuron are a valid approach, and might be used on this sample, I disagree that it is sufficient to do so. … It might turn out that the authors’ approach is better suited, but I think it is absolutely necessary to use the continuous distribution of the inflammatory variables.

We thank the reviewer for this valuable comment and constructive criticism. We have now used IL-6 and hs-CRP as continuous variables in several analyses. Our new methodology has been presented in the methods section (p. 8) and findings in the results section (p. 9). Both methodology and findings have been discussed in the discussion section (p. 11-12).

2 Methods - IL-6 is measured using a multiplex assay. Usually, multiplex assays do not have a sensitivity high enough for detecting unstimulated plasma concentrations of IL-6; or if they do, they yield strangely elevated levels. … This is a limitation that needs to be thoroughly discussed…

The reviewer is correct in pointing out that multiplex assays frequently provide values below the detection level when examining naïve (unstimulated) samples. However, we did not observe pronouncedly elevated values, either. In line with previous studies using the same methodology, the examined unstimulated samples provided somewhat low levels of inflammatory markers (Hoge et al. 2009). However, regardless of the observed overall levels of IL-6 and hs-CRP, an elevated inflammatory status associated independently with unemployment. The above-described issues, as well as further discussion on the methodological issues related to utilizing multiplex assays and the Luminex method in particular, have now been added to the Discussion section.

Minor Essential Revisions

3 P4 - I would remove the bracketed (March 2009) from the first line of the background section. You could say “In March 2009, approximately…” It is now “In June 2009, approximately…”.

4 P5 - is the sole paragraph on top of page 5 a summary of the literature summarized previously? Or is it a hypothesis? Please make that more clear. The text has been rewritten to be more clear.

5 P6, second paragraph – “I suggest rephrasing “…were assessed to have...”” This has been rephrased.

6 P6/7 – “ it would help the reader if the structure of the methods section would be improved…”
The structure of the methods section has been reorganized as suggested by the reviewer.

7 P7—“specify the units of CVs (percentages?)”
The units (percentages) have been added.

Reviewer: Kaki M. York

Major Compulsory Revisions:

1. “I am concerned about the decision to artificially dichotomize immune marker values rather than analyzing the data continuously.”
   See our first response to reviewer Nicolas Rohleder.

Minor essential revisions

2. “You mentioned that you controlled for “economic hardship” in the multivariate model but it isn’t clear how that was operationally defined?”
   This is now explained in the methods section.

3. In the statistical methods section, it would be helpful if you explained which tests were used for which analyses instead of simply stating that chi square, t-test and Mann Whitney U’s were used for univariate analyses. The test should be paired with a specific hypothesis.
   We now explain in the methods section which tests were used for which analyses.

4. “Also, you mentioned that you controlled for alcohol consumption. How was alcohol consumption measured?”
   This is now explained in the methods section.

5. “In the discussion section, you conclude that “the association was even stronger after adjustments for several possible confounders….It would be more correct to say that the model remained significant even after controlling covariates…”
   This has been corrected.

Discretionary:

6. “Consider replacing the term “subject” throughout with “participant” or “individual” as appropriate”
   This has been done throughout the text.

7. “You used the expression “pilot study” several times throughout the paper. You may wish to change this term also.”
The expression “pilot study” has been removed.

8. “On page 6, paragraph 3, you stated that you calculated BMI from height and weight. This is a common, but I think imprecise use of language. I believe that it would be more correct to say that you obtained an estimated BMI…”
This has been corrected as suggested by the reviewer.

9. “It would help the reader if you repeat the names of the covariates in the results section when you provide the results of that analysis.”
The names of the covariates have been repeated in the results section.

Yours sincerely,

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