Reviewer’s report

Title: Association between life-course socioeconomic position and inflammatory biomarkers in older age: a nationally representative cohort study in Taiwan

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Reviewer: Dejana Braithwaite

Reviewer’s report:

At the outset of this paper, the authors sought to associate CRP levels with cardiovascular disease. There are several studies that have measured the association between elevated CRP levels and cardiovascular disease risk. However, the authors failed to cite literature to clearly express this point. More information about the etiologic importance of CRP and IL-6 would be helpful in the background to better understand the importance of measuring them.

A really good addition to this paper was an explanation of the three major life-course models: critical period, accumulation and social mobility. Understanding the differences between these three models is crucial to best interpreting the importance of a life-course effect on an outcome. The authors never clearly express which life-course framework they believe SEP fits into. Only near the end of the paper do they mention that the findings of early childhood SEP on CRP reflect critical period effects. A more robust method of assessing this research question would be to a priori specify which framework they believe SEP most clearly aligns with. I think this is a limitation of the study that should be clearly addressed.

A minor concern in the study was the dichotomization of SEP at each timepoint. Without indicating any justification for this method, it seems very restrictive, and takes away the ability to measure intermediate SEP levels. The study seems adequately powered to potential trichotomize the effect to better understand high, moderate, and low SEP levels, compared to simply high and low effects. This might be important to consider in a sensitivity analysis.

Finally, it is worth mentioning in the limitations section the systemic nature of CRP and IL-6. While the goal of this paper is to acknowledge how SEP affects inflammation levels later in life, the use of one measurement has caveats, such as inability to distinguish between acute and chronic inflammation and inability to directly attribute CRP levels to cardiovascular conditions despite adjustment. In essence, I think authors should mention the potential for residual confounding due to the systemic nature of CRP and IL-6.

To recap, I believe the authors should address the following:

1. Etiologic effects of CRP in cardiovascular disease and previous evidence of association between CRP and CVD.
2. Focus on one of the three life-course frameworks, and clear choice of one of the three frameworks, with previous literature support

3. Dichotomization of SEP at each time point, specifically whether trichotomization or other method of measurement was considered. A sensitivity analysis should be considered.

4. Mention of limitations of CRP and IL-6 measurement due to systemic nature in several diseases.

5. Mention of potential for residual confounding due to systemic nature of CRP and IL-6.

In addition, I believe the authors should consider addressing the following:

1. Could you please explain the p-values in Table 1? Are they chi-square and t-test analyses?

2. What is the distinction between a large outlier versus a "non-large" outlier? Were some outliers not trimmed compared to others?

3. Are all of the covariates specified in the methods section? In particular, what other inflammatory markers were considered in model 6? I do not see them in the methods section.

4. Authors specify that higher SEP was inversely associated with adverse health behaviors. I would caution the authors against using such strong language for a non-significant finding.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
I recommend additional statistical review

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