Reviewer’s report

Title: Allostatic load amplifies the effect of blood lead levels on elevated blood pressure among middle-aged U.S. adults: -a cross-sectional study

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Reviewer: Jane Clougherty

Reviewer’s report:

Thank you for the opportunity to review this paper. It presents a very thorough cross-sectional analysis of Pb effect son blood pressure, as modified by a measure of allostatic load, across 5 waves of NHANES data.

I do recommend publication, but have several persistent concerns about the paper:

1) In the introduction, the authors need to do a better job of contextualizing & caveating their measure. AL is not “stress.” AL is – as the authors state on page 18 -- “a measure of physiologic dysregulation.” Here, because neither stressors nor perceived stress are measured (and, indeed, psychological stress is inherently about perception), the authors are merely assuming that the primary driver of this AL measure in the NHANES sample is psychological stress – which may or may not be true. Even if AL is tightly inversely correlated with indicators of SES, SES is such an enormously complex composite of social and physical exposures impacting systemic regulation, that it is impossible here to know what portion of AL actually proxies for “stress.”

2) Methods: It is not shown how this 7-item metric compares to the original & more commonly-used 10-item validated AL measures(i.e., Seeman and McEwen). It would be helpful to understand the correlation between these composites in NHANES (if possible), and their relative internal consistency (i.e., Chronbach’s alphas).

3) Relatedly, for utility as an indicator, one would want to see consistency between the 7- and 10-item AL scales. BUT – in this case, because the authors have removed their primary outcome (BP) from the AL scale (and, indeed, SBP and DBP were the first 2 items included in the original scale), their analysis requires that the remaining AL components NOT be overly collinear with BP. Proving that the AL measure does not inherently proxy for BP – and testing the consequent effects on observed main effects and interactions for AL and Pb – has not been adequately tackled here.

Can the authors offer a better theoretical or epidemiologic justification than utilitarian clinical thresholds for emphasizing the dichotomous over continuous BP results? Though the results are reasonably consistent (and I am convinced that there is something different going on in the “high AL” population), there is a suggestion here of cherry-picking those results which support the hypothesis.
What is the potential impact of the excluded subjects having higher average BP and lower AL? This suggests a main effect among excludeds which is opposite to hypotheses & opposite to observed association in the retained subjects. Can the authors explain this?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

'I declare that I have no competing interests'