Reviewer’s report

Title: Allostatic load modifies 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: Junenette Peters

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This paper poses an original question in that it looks at allostatic load instead of psychometric stress measures as a modifier of the effect of blood lead on blood pressure. This paper adds to the interest in the modifying effect of psychosocial factors on environmental exposure-disease relationship.

A. Major Compulsory Revisions

1. The key conceptual concern is that the outcome - elevated blood pressure (systolic and diastolic blood pressure) - is one of the parameters used to operationalize allostatic load (McEwen 2000; Seeman et al. 1997; Sebbah et al. 2008; Allsworth et al. 2005). In reviewing the papers cited, blood pressure was included in the definitions of allostatic load. Allostatic load is based on a number of parameters that reflect activity across a range of regulatory systems (Seeman, 1997; McEwen 2000). For example, blood pressure is thought to index cardiovascular activity. Not sure then how blood pressure relates to the other physiological measures of allostatic load as an outcome modified by these components.

2. Should consider allostatic load as a measure of cumulative psychological dysregulation or biological risk? Allostatic load reflects more than chronic stress also encompassing many aspects of a person life that can affect regulations of physiological systems including genetics and lifestyle choices (such as smoking, diet, etc.) (McEwen & Seeman (Annals of New York Academy of Science. 2006, Vol. 896, Issue 1). Thus allostatic load could be thought of as a mediator of chronic stress (along the pathway) and not necessarily a measure of stress per se.

3. Some studies use either a specific cut-point (Sebbah et al. 2008 or Allsworth et al., 2005) whether based on clinical or other criteria while others use the top quintile versus the other quintiles (Seeman et al., 2001). What was the rationale behind using the median of the scores as opposed to these methods (any references?). One benefit of identifying specific cut points by whatever method is the ability to compare the cut-offs in this study with those in other studies (here the median and range were presented). Additionally, are the results sensitive to the cut-offs/method used (are results similar over various definitions of high allostatic load). At minimum, the Discussion section could include the pros and cons of the method chosen for this paper. It may also help to state what
sensitivity tests were conducted (pg. 15, para 1).

4. Was there truly a modifying affect (two groups – high versus low allostatic load - significantly different)? Would be informative to see the results for the interaction terms particularly the interaction between lead and allostatic load (from pg. 9, para 2). Also, as an added curiosity, were any interactions observed using lead and allostatic load as linear (as opposed to categorical) variables?

B. Discretionary Revisions

1. On pg. 6 the age range of 40-65 was chosen to ‘minimize the effect of confounding by age.’ What was the rationale behind choosing middle-aged versus older adults.

2. A ‘better’ way to test for trend could be to use the median value for each quintile.

3. It would be great for an environmental health audience to say something about what physiological system the different components of allostatic load correspond to. Also what is ‘bad’ for each – some may not be as obvious. Also the reader may not be familiar with or get the implications of ‘primary’ verses ‘secondary’ mediators of chronic stress response (may want to say something about that in the Introduction and state which is being measured here).

4. Given the interrelation of stress, hypertension and allostatic load may want to address the possibility that there may be reverse association - higher blood pressure increasing allostatic load (not sure how it would relate based on #1 of the Major Concerns).

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests,