Author's response to reviews

Title: Child maltreatment and hypertension among young adults

Authors:

Shakira F Suglia (sfs2150@cumc.columbia.edu)
Cari J Clark (cjclark@umn.edu)
Renee Boynton-Jarrett (Renee.BoyntonJarrett@bmc.org)
Nancy Kressin (nkressin@bu.edu)
Karestan Koenen (kck5@columbia.edu)

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Author's response to reviews: see over
Dear Prof Latkin,

We very much appreciate the interest in our manuscript and the opportunity to respond to the comments from the reviewers. As requested we have responded to the reviewers comments and provide details of our point-by-point response below, showing the reviewers comments in *italics* followed by our response in normal font.

**Reviewer : Jodi Ford**

**Major revisions**

1. *The prevalence of hypertension among the young adults in the Add Health study is considerably higher than what has been found in other nationally representative studies of young adults conducted around the same time frame. (See Yoon SS, Burt V, Louis T, Carroll MD. Hypertension among adults in the United States, 2009-2010. NCHS Data Brief. 2012:107:1-8.). To avoid critique from others, the researchers should address the disparate prevalence in hypertension between the two national samples --- two studies have been published examining potential reasons for the differences, which may be helpful. (1) Nguyen QC, Tabor JW, Entzel PP, Lau Y, Suchindran C, Hussey JM, Halpern CT, Harris KM, Whitsel EA. Discordance in national estimates of hypertension among young adults. Epidemiology 2011;22:532-541 and (2) Chyu L, McDade TW, Adam EK. Measured blood pressure and hypertension among young adults: A comparison between two nationally representative samples. Biodemography Soc Bio. 2011; 57: 184-199.*

   We agree with the reviewer and have now added the two mentioned references in the discussion section as well as acknowledgement of the high prevalence of hypertension in this sample compared to other national samples, page 12 first paragraph. As differences have been previously noted by Nguyen et al and Chyu et al we do not highlight the prevalence of hypertension as a finding of this study but do acknowledge it in the discussion section, page 12.

2. *The authors found significant associations between sexual abuse and hypertension for females but not for males. They discuss potential measurement error in the section with respect to differences between their overall findings and prior research. However, sex differences in stress-related health outcomes have been found in extant studies, which researchers hypothesize may be attributed to biological and/or social (e.g. gender norms) factors. The disparate findings in this study for males and females in response to sexual abuse adds to this growing body of research. A discussion of potential reasons for the sex differences would further highlight this important finding and the significance of this study.*
In the introduction, we expanded the rationale for examining sex differences to include potential behavioral responses as well as differential physiological mechanisms, such as HPA dysregulation and inflammation in response to stress; we have also added several citations to support this argument, page 4. Furthermore, we have acknowledged in the discussion gender differentials may be due to differential responses to stress. Noting existing literature on gender differences between job strain and hypertension, page 10.

3. The researchers mention that activation of the autonomic nervous system as a consequence of the chronic stress associated with abuse may be a mediator linking abuse to hypertension. I think it would be useful to include a little more discussion on what activation of the ANS means, particularly for readers who may not be familiar with its role in hypertension.

We have moved this discussion to the discussion section adding a few sentences regarding the current evidence of mechanistic studies on the relation between stress and hypertension. The section now reads “A more direct pathway through which stress can affect health is through its activation of the autonomic nervous system. Animal studies have demonstrated that hypertension following social stress is associated with increased norepinephrine turnover, with other mechanistic studies providing evidence for the role of inflammatory responses and renal mechanisms.[28] Chronic stress has also been shown to induce a chronic and systemic state of mild inflammation (i.e., C-reactive protein and interleukin-6) a key mechanism in the development of cardiovascular disease. [29], page 11.

4. The researchers discuss sample attrition in their limitation section, but they don’t include a discussion about missing data from their study. Specifically, it would be useful to include the results of analyses that examine how those participants who were listwise deleted from their study due to missing data differ from those included in their final analytic sample, particularly with respect to exposure to abuse and hypertension.

The number of participants listwise deleted due to missing data was small, 7%, the largest lost of participants comes from those who did not complete the wave 4 assessment or did not complete the wave 3 assessment and are thus missing blood pressure and abuse information. We have noted in the methods section that participants who were included in the final sample differ from the full sample size based on race/ethnicity. We used longitudinal sampling weights, available for participants followed to Wave 4, which adjust the sample to be representative of sample characteristics at baseline, we have noted this in the methods section page 5.

Minor revisions:
1. In the methods section- the last sentence of the measurement of hypertension: “Hypertension was defined as having an elevated systolic blood pressure >= 140mmHg or diastolic >= 90mmHg or reported using use of antihypertensive medications (N=379)” Also I recognize the N=379 refers to the number of participants on antihypertensive medications, but a reader could misconstrue that to be the number who have hypertension according to the study’s definition.
To avoid confusion we have now included the N for participants with high SBP or high DBP (N=2121) as well as the N for those using antihypertensive medications (N=379).

2. In the results section, second sentence of second paragraph... “No statistically significant differences were noted on the relation between child Men who experienced neglect (31% vs. 28%), sexual abuse (30% vs. 28%) or whose families were investigated by social services (32% vs. 28%) had a higher prevalence of hypertension compared to those who did not endorse those experiences, however these were not statistically significant differences.” This sentence is a bit confusing.

We apologize for the confusion, this sentence now reads: "Men who experienced neglect (31% vs. 28%), sexual abuse (30% vs. 28%) or whose families were investigated by social services (32% vs. 28%) had a higher prevalence of hypertension compared to those who did not endorse those experiences, however these were not statistically significant differences”, second paragraph page 9.

Reviewer: David Benett

Major Compulsory Revisions
Methods:
1. The authors state that participants’ medications were recorded, but it is not clear what was done with this information – were participants on BP medication included in the high BP group? Excluded from the data analysis?

Yes, participants on BP medications were included in the hypertension group. As noted in the methods section, page 6 “Hypertension was defined as having an elevated systolic blood pressure >= 140mmHg or diastolic >= 90mmHg (N=2121) or reported using antihypertensive medications (N=379)."

2. The frequency of maltreatment items appears to cover a fairly broad range (e.g., 0 = never to 5 = more than 10 times). Can the authors provide a rationale as to why they used dichotomous variables rather than the more continuous measures of maltreatment (especially since, in addressing how findings differ from their study and that of Riley and colleagues in the Discussion section they note that Riley et al. found abuse frequency to be associated with a higher risk of hypertension)?

Child maltreatment was characterized similar to previous studies using this data. [1] Furthermore, the frequency of some of the outcomes was too small to characterize as occurring more than once, for example the frequency of sexual abuse occurring more than once was 1.5%, we have noted this in the methods section page 7.

3. Similarly, covariates (e.g., current smoking; physical activity; alcohol use; obesity; depressive symptoms) were dichotomized rather than examined as continuous variables. Given that dichotomizing continuous variables often reduces predictive power, a rationale for doing so is needed.
We wanted to adjust for clinically meaningful covariates known to be associated with hypertension as well as maltreatment. While it is correct that continuous variables would have more predictive power they would not represent the risk factors we wanted to adjust for. Furthermore, we re-ran our models adjusting for continuous measures of depression, BMI and alcohol use and noted no differences on the relation between the child maltreatment measures and hypertension when using the continuous vs the dichotomized health behaviors. In addition, the significance of the relation between the health behaviors and hypertension did not change, for example, BMI was the only health behavior associated with hypertension in both men and women.

Minor Essential Revisions
Introduction:
1. On page 4, the authors emphasize the importance of examining gender differences in the relationship between maltreatment and high BP due to differences in prevalence of child maltreatment as a function of gender. A more relevant rationale, however, would be citing any research that might indicate different physiological outcomes of maltreatment as a function of gender.

   As noted in our response to reviewer Jodi Ford, we have expanded in the introduction section the rationale for examining sex differences to include potential behavioral responses as well as differential physiological mechanisms in response to stress.

2. The authors state on p. 4 that prior research has not examined “whether health behaviors or depression, both of which are well documented outcomes related to childhood maltreatment and risk factors for hypertension, explain the relation between child maltreatment and hypertension.” Given that “health behaviors” is a very broad construct, it would be useful if the authors could be more specific (e.g., focusing on the specific health behaviors assessed in the NLSAH). In addition, inclusion of citations for this sentence would be helpful.

   Given that we are not formally testing for mediation and simply adjusting for health behaviors as confounders we have removed this sentence from the introduction.

3. On a minor note, the authors state that “We focus on abuse that occurred early in childhood, prior to age 11” but I believe their focus is on the broader construct of maltreatment given that they examine neglect.

   We thank the reviewer for pointing this out, we have changed the sentence to read: "We focus on maltreatment that occurred early in childhood, prior to age 11”.

4. A sentence explicitly stating that high BP in early adulthood is a risk factor for later cardiovascular disease is needed.

   We have added the following sentence to the introduction, page 4: “Hypertension in young adulthood is a known risk factor for cardiovascular disease in adulthood.”
Methods:
5. The authors state that the mean participant age at wave 4 is 29; inclusion of the range and SD would be of interest (p. 5).
   We have provided the SD (1.7) and range (25 – 34) of the study participants in the text, page 8.

6. Are definitions of child maltreatment (e.g., child neglect = having parents or adult caregivers not taken care of their basic needs such as keeping you clean or providing food or clothing) summations of the actual questions or the verbatim text presented to participants (in which case putting the definitions in quotes would be helpful to identify it as the verbatim wording).
   We thank the reviewer for bringing this to our attention; we have revised the text to reflect the actual questions asked of participants and have added quotes to denote this, methods section page 6-7.

7. Can the authors present any data as to whether participants who were included in the wave 4 follow-up differed from those who did not participate on any of the earlier demographic or predictor variables?
   We have noted in the methods section that participants who were included in the final sample differ from the full sample size based on race/ethnicity. We used longitudinal sampling weights, available for participants followed to Wave 4, which adjust the sample to be representative of sample characteristics at baseline, we have noted this in the methods section page 5.

Results:
8. The sentence (p. 8) reading “No statistically significant differences were noted on the relation between child Men who experienced neglect...” is confusing.
   We apologize for the confusion, this sentence now reads: “Men who experienced neglect (31% vs. 28%), sexual abuse (30% vs. 28%) or whose families were investigated by social services (32% vs. 28%) had a higher prevalence of hypertension compared to those who did not endorse those experiences, however these were not statistically significant differences.”

9. The authors present a number of findings in describing Figure 1, sometimes stating that a relation was significant, sometimes that differences were not statistically significant (but perhaps were trends?) (p. 8). Inclusion of p values would be helpful for readers to more fully interpret the study findings.
   As noted on the results section, none of the bivariate associations presented in Figure 1 were statistically significant, we have added a note to the figure to avoid confusion. Given that we are not using ordinal variables, only dichotomized ones, the use of trend analyses is not useful.

10. A brief, more explicit statement as to what the authors mean by “limited violence assessment” would be helpful (p. 10). Likewise, on p. 11 the authors refer again to “violence exposure” in the limitations section, though throughout the rest of the
manuscript they refer to “physical maltreatment” - are the authors suggesting that their measure of physical maltreatment was limited in scope as a measure of physical maltreatment, or that it would also have been helpful to include a measure of violence exposure (which typically includes witnessing violence, not necessarily being a direct target of the violence)?

We apologize for the confusion; we meant to state that the assessment of child maltreatment is limited in that it relied on one question for physical abuse and one question for sexual abuse. We have changed the sentence to read: “This discrepancy of results can be attributed to the limited single item child maltreatment assessment, which prevented us from characterizing child maltreatment, by severity and frequency.”, page 11-12.

11. A brief discussion of clinical implications for the study findings would be of interest.

We have included a brief discussion of clinical implications for our study findings, noting that ‘Detection of child abuse early in the life course, coupled with appropriate psychological counseling and health behavior management may prevent the development of hypertension among women along with numerous adverse health conditions.’ page 12-13.

Discretionary Revisions

Discussion:

1. The equal prevalence of sexual abuse (5% for both genders) is somewhat inconsistent with most studies, which find a greater prevalence among females. Do the authors have any suggestions as to why the prevalence did not differ as a function of gender in their study?

   It is difficult to speculate on why the prevalence of sexual abuse does not differ by gender, it could potentially be due to the measurement issues, (single item assessment) which we have already addressed in the limitations section.

2. I would suggest replacing “can” with “might”, etc., in the statement “…lack of an association in our study among men … can be attributed to the difference in outcome measurements.”

   We have made this change.

Reviewer Chioun Lee

Literature review:

• There is not clear evidence across studies establishing that men are more likely to experience physical abuse and neglect. Using one citation [10] published in 1997 does not sufficiently support the authors’ argument. I’d like to suggest either including more citations or re-phrasing the sentence.

   We have included other justifications for the exploration of gender differences in the introduction section, page 4, and thus have removed this sentence from the manuscript.
Aims of the study:
• In both the abstract and main text, it is unclear what exactly the authors aimed to investigate. Did this study examine whether each type of childhood maltreatment affects the risk of having hypertension in young adulthood? Did it examine potential mediators, such as health behaviors and depression (as described on page 4)? If so, the authors should describe the mediators more clearly in the abstract and at the end of the introduction.

We apologize for the confusion; we have clarified in the abstract that we are examining the relation between types of child maltreatment and hypertension. In the introduction we have clarified that we are further adjusting the analyses for health behaviors and depression known to be associated with child maltreatment and hypertension to make it clear we are not testing for mediation.

Methods:
• The authors might want to rearrange the measurement section to clarify which covariates are controls (e.g., age, race/ethnicity), moderator(s) (sex), or potential mediators (e.g., smoking, exercise, BMI).

As noted we are not explicitly testing for mediation, we have rearranged the list of covariates to present socio-demographic factors first and the additional covariates second.

• It would be useful if the authors reported correlations between the four variables related to childhood maltreatment, for men and women separately.

We thank the reviewer for this suggestion we have added the correlation of the measures (0.12 to 0.30) in the methods section, page 8.

Data analyses:
• The authors should clarify parts of the sentence: “Given the high prevalence of hypertension in this sample.” It is unclear what percent of respondents meet the criterion of hypertension in the sample and how such (high) prevalence may affect the results of this study.

We have now specified the prevalence of hypertension in this sample. We were alluding to the fact that due to the high prevalence the use of odds ratios would be inappropriate, thus we use binomial regression models which directly calculate prevalence ratios, methods section page 8.

• The authors should clarify how the four independent variables were operationalized. Did the authors recode ordinal variables as dichotomous variables? Why didn’t the authors utilize the original scale to investigate whether the severity of abuse/neglect is important?

As noted in the methods section, page 7. We dichotomized the child maltreatment variables similar to previous analyses of this data. As noted earlier, the low frequency of some of the maltreatment variables prevent us from exploring frequency of the events experienced. For example, the frequency of sexual abuse occurring more than once was 1.5%.
• Given that the authors adjusted for obesity, alcohol use, physical activity, and smoking as well as high depressive symptomatology, I assumed that the authors were aiming to explore potential mediators, but neither the literature review nor the methods section clearly describes potential mediators. The authors might want to elaborate those parts of the paper.

Given that the health factors were measured simultaneously with blood pressure we felt testing for mediation would be inappropriate given that we can not establish with certainty that the health behaviors measured preceded the high blood pressure. Instead we frame our question as whether the effects of child maltreatment and hypertension are evident even after accounting for health behaviors which might also be associated with hypertension (and thus need to be adjusted for). We have thus removed language that suggests mediation effects to avoid reader confusion.

• Until examining Table 2, it is difficult for readers to understand the way that the authors included each type of child maltreatment and having social services in the models. The authors might want to address the following questions in the main text. Did the authors include all four variables of childhood maltreatment in the same model? What would be the theoretical and methodological justifications for such a model? Why didn’t the authors create a summary measure to indicate whether respondents experienced any of the four forms of childhood maltreatment?

Given that previous research has documented a relation with specific types of abuse and hypertension, we examined specific types of maltreatment in relation to hypertension. For example, as noted in the introduction, using the Nurses Health Study II data, Riley and colleagues noted an association between severe and frequent experiences of child maltreatment and self-reported hypertension.[2] An analysis using the World Mental Health Survey demonstrated that experiencing physical abuse during childhood is associated with self-reported hypertension in adulthood.[3] In addition the correlation between the types of maltreatment and neglect was fairly low (.12 to .30), we have made this clear in the data analyses section page 8.

Results:
• Given that there are various gender comparisons in types of childhood abuse and health behaviors, the authors might want to include p-values in Table 1 to show which gender differences were statistically significant.

We thank the reviewer for this suggestion; we have included p-values to Table 1.

• Interpretations of Table 2 are unclear. Does Model 1 include all four types of childhood maltreatment? If so, the effects of sexual abuse on risk of having hypertension should be interpreted; for example, after controlling for other types of abuse/neglect and having social services, experiencing sexual abuse is significantly associated with risk of developing hypertension.

The reviewer is correct in that all forms of maltreatment and social services visits are included in the model, we have changed the text to note “in models
adjusted for socio-demographic factors and other forms of maltreatment, ...” to clarify that all types of maltreatment are included in the model simultaneously. In addition we explicitly state in the data analyses section that all models are adjusted for other types of maltreatment.

• It is unclear what PR stands for in the text AND what RR stands for in Table 2. Did the authors report relative risk? If so, it should be RR in both Table 2 and the main text.

  We apologize for the confusion, PR stands for prevalence ratio, we have explicitly defined this in the methods section, page 8. The use of RR in the text was incorrect and we have removed this from the text.

• In the discussion section (page 9), the authors mention that health behaviors partially explain the association between sexual abuse and risk of having hypertension. The authors might want to include a percentage change of RR before and after including potential mediators and report whether these mediators significantly reduce the main effects of sexual abuse.

  As we are not formally testing for mediation, we have removed this language from the manuscript.

Discussion:

• On page 9, the authors mentioned that data limitations prevent them from characterizing the severity and frequency of child maltreatment. However, the original scale of childhood maltreatment, which ranges from 0 (= never) to 5 (= more than 10 times), possibly captures the frequency or severity of childhood abuse. The authors should clarify why the original scale was not utilized.

  We have noted that the frequency of abuse was low for some of the types of maltreatment measures, page 7. Specifically, we note that “The frequency of some of the outcomes was too small to characterize as occurring more than once, for example the frequency of sexual abuse occurring more than once was 1.5%, hence physical abuse was defined as endorsing one time or more to the first question and sexual abuse as endorsing one or more times to the second question”.

• The authors also should add some discussion about why there was a significant association between sexual abuse and hypertension for women only. If the link was attributed to health behaviors, which health behaviors? Are some health behaviors particularly harmful for women who experienced sexual abuse?

  We have included a discussion regarding the potential mechanisms behind the gender differentials. The differences may be due to differentials in behavioral responses to stress, though we can’t say with certainty which behaviors may explain the difference. In our analyses behavioral factors were not associated with hypertension in either men or women.

Figure:

• The authors should include a note in Figure 1 that indicates whether the bar graphs (e.g., abuse vs. no abuse) are significantly different.
We have made this change.

Citations and references:
• The authors should double check all references. Some items in the references do not match the citing text. For example, on page 3, the authors write that “…681,000 children were victims of some form of maltreatment in 2011.[2]” BUT the citation number [2] in the list of references was published in 2010.

We apologize for this mistake; we have edited this reference to reflect the correct source of this information (CDC Report on Child Maltreatment 2013). Furthermore we have carefully reviewed all the references in the manuscript.

• The authors should include a citation for the sentence “[a]n estimated 8% of the US population has undiagnosed hypertension,” on page 3.

We have revised this statement based on the latest report from NHANES, the sentence now reads: “NHANES data has demonstrated that only 83% of hypertensive adults over age 18 are aware of their hypertension, thus, use of self-reported hypertension would underestimate the true prevalence of hypertension and potentially bias results toward the null.” and includes the NHANES reports citation.

Discretionary revisions
• The authors should edit the manuscript very carefully. Some parts of the manuscript were hard to follow. There were several typos and the citation format was not consistent—for example, on page 3, there is a different citation format with the reference number 5 (superscript).

We apologize for any grammatical errors; we have carefully revised the manuscript and references for any errors.

Terms:
• The authors inconsistently described the developmental period or age at which the respondents might have experienced child maltreatment. The authors use “prior to 6th grade,” “early childhood,” and “prior to age 11.” In the child developmental perspective, does 6th grade refer to early childhood? Are all 6th graders younger than age 11?

The questions regarding abuse were phrased to participants as ‘prior to entering the 6th grade’ which in the US generally refers to prior to age 11. We have clarified this in the manuscript and now consistently use prior to age 11 and when necessary note that prior to 6th grade refers to 11 years of age.
Reference: