Reviewer’s report

Title: Systematic Review of Pediatric Health Outcomes Associated With Childhood Adversity

Version: 0 Date: 19 Jul 2017

Reviewer: Jeffrey Roth

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Review of BPED-D-17-00319: Systematic Review of Pediatric Health Outcomes Associated With Childhood Adversity

This literature review surveys longitudinal cohort studies that examined the association between the health of children and their exposure to adversity. The survey focuses on two developmental outcomes (physical/reproductive, and cognitive); and nine clinical outcomes (endocrine function, inflammation and immune system function autonomic nervous system function, telomere length, obesity, asthma, Infections and illnesses, somatic complaints, and sleep). The authors conclude that the accumulated evidence is unequivocal: children who experience chronic stress suffer ill health. They concur with the American Academy of Pediatrics that screening for adverse childhood experiences should become a standard of practice and that developing "services and interventions focused on helping children mitigate the effects of toxic stress" will "prevent long-term negative health outcomes across the life course." [P20, L352-357]

The review is comprehensive and well organized. The following comments are intended to increase the value of the paper to readers of BMC Pediatrics.

1. It is not clear what the authors intend by attaching the word "scoping" to their systematic review of the literature on the pediatric health outcomes associated with childhood adversity. There are no references to this variant of the traditional literature review nor to the criteria established by PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses. http://www.prisma-statement.org). For example, the exclusion criteria used to reduce to 24 98 identified longitudinal cohort studies of childhood adversities and biological health outcomes are not stipulated [P8, L92]. PRISMA recommends a flow diagram charting each step of the inclusion and exclusion process.

2. A useful article distinguishes between a systematic review and a scoping study: "First, a systematic review might typically focus on a well-defined question where appropriate study designs can be identified in advance whilst a scoping study tends to address broader topics where many different study designs might be applicable. Second, the systematic review aims to provide answers to questions from a relatively narrow range of quality assessed studies, whilst a scoping study is less likely to seek to address very specific research questions nor,
consequently, to assess the quality of included studies." (Arksey, H. and O'Malley, L. (2005) Scoping studies: towards a methodological framework, International Journal of Social Research Methodology, 8(1), 19-32). Given that the current paper considered only longitudinal cohort studies as its appropriate design and furthermore excluded all studies related to children’s mental health, perhaps scoping might be deleted from the title.

3. Arksey and O'Malley further characterize a scoping study as "a useful way of mapping fields of study where it is difficult to visualise the range of material that might be available." This mapping of the field was recently carried out by members of the Center for Youth Wellness. (See Bucci M, Marques SS, Oh D, Harris NB. Toxic stress in children and adolescents. Advances in Pediatrics. 2016;63(1):403-28. [Reference 8]. This previous publication structured the fields of study surveyed using a nearly identical taxonomy (developmental outcomes followed by clinical outcomes).

4. To the extent that the current paper represents one of the 4 rationales that Arksey and O'Malley give for undertaking a scoping study ("to describe in more detail the findings and range of research in particular areas of study, thereby providing a mechanism for summarising and disseminating research findings to policy makers, practitioners and consumers"), it is disappointing that no guidance is offered to any of three stakeholder groups referenced above about potential strategies for mitigating exposure to childhood adversity.

5. Please provide at least some information about "services and interventions" have proven effective in mitigating toxic stress in childhood. What methods have been shown to be successful in developing "protective mechanisms of resilience" [P20, L356]. Given the seriousness of the diagnosis (adversity in childhood distorts normal development), some specifics about treatment options are warranted.

6. A sentence in the Implications sub-section seems to contradict an earlier sentence in the Discussion section: Compare "childhood adversity can have a profound effect on child's health" [P19, L331-2] to ‘in general, the effect sizes reported across the various studies were small, which could be an accurate reflection of the small differences adversity exerts on the child outcome we captured in this review" [P18, L310-2]. Mention of effect sizes cries out for the authors to next conduct a rigorous meta-analysis which could possibly quantify the degree of harm that each ACE perpetrates, thereby helping all of us concerned about preserving the health of children.

PS: Reference 77 is a duplicate of Reference 18.

**Are the methods appropriate and well described?**

If not, please specify what is required in your comments to the authors.

No
Does the work include the necessary controls?
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Unable to assess

Are the conclusions drawn adequately supported by the data shown?
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Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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