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Title	The relative contribution of maternal adverse childhood experiences for understanding child externalizing and internalizing behaviour at age 5? Findings from the All Our Families cohort
Authors	Erin Hetherington PhD, Nicole Racine PhD, Sheri Madigan PhD, Sheila McDonald PhD, Suzanne Tough PhD
Reviewer 1	Dr. Ivan Barry Pless
Institution	Community Pediatric Research, Montreal Children's Hospital, Montréal, Que.
General comments (author response in bold)	<p>This paper set out to "... to examine the association between maternal ACEs and child behaviour (internalizing and externalizing) at age 5 in the context of other factors". I assume it did so either because the authors were convinced that all the related studies were seriously flawed or that they believed they could provide a new perspective on this issue. It is evident that their analysis revealed few important such relationships. They concluded that not ACEs but some of the 'other factors' were far more important. I agree with the conclusion although there are several issues related to the scientific aspects of the study that merit attention.</p> <p>For example, I could not determine the size of the initial cohort. This is important because it would put the response rate into a clearer perspective. We are told that 231 mothers had 4+ ACEs (and that this is 16.4% of the respondents) but that number needs to be related to the original total, not just the respondents. As well, a distribution of those with 1,2, or 3 ACEs might help the reader what the 4+ cut-off means.</p> <p><b>We have clarified the response rate, sample size (pg 8) and numbers including adding a flow chart (in the supplementary files). We have expanded table 1 to include more granularity on how many women reported how many ACES.</b></p> <p>It seems there were no statements describing the validity and reliability of some of the key measures, especially the BASC. Apart from not being included in the text I searched the web for references to the BASC that were not behind a pay wall. For that matter it seems something should be said about the properties of all the measure use. I am familiar with most, but not all readers will be</p> <p><b>We have clarified what the BASC is and how it is used. We are unable to provide a lot of details about the BASC questions or how it is calculated, as this is considered proprietary information. We are licensed by Pearson (developer of the BASC) to use the tool, but not distribute it. We have calculated a reliability coefficient for each of the scales. (page 5)</b></p> <p>I was surprised to see both confidence intervals and p values in the tables. Generally, CIs are preferred, and p values are often misinterpreted, redundant or both.</p> <p><b>We agree that these are somewhat redundant. However the journal requirements ask for both confidence intervals and p-values, so we have provided both.</b></p> <p>Some statements need clarification, such as "high levels of negative child affect is associated with a two fold increased odds of both externalizing and internalizing behaviours" but I assume that these behaviours are, in a sense, part of affect.</p> <p><b>We agree with the reviewer. High negative affectivity is considered a precursor for later internalizing and externalizing difficulties. At younger</b></p>

ages (e.g. age 3 in the current study), negative affectivity captures affective responses such as fear, anger, sadness, and discomfort. Similar behaviours are noted and measured at 5 years of age and called Externalizing and Internalizing difficulties. In essence, emotional difficulties at age 3 are related to emotional difficulties at age 5. We have removed this statement and clarified our results to indicate there are many things associated with child externalizing and internalizing behaviours.

The authors do a good job of identifying limitations but may have glossed over problems with the sample itself. As shown in table 1 nearly 70% of the families responding had incomes of \$100,000 or more. Even in oil-rich Alberta, this suggests a sample that is unlikely to be representative of the province, let alone the nation. **We agree that we overstated the generalizability. We have provided more information on the representativeness of the sample, and limited our generalizability to middle and upper income families, and noted that these results may not be applicable to more vulnerable families. We have also added a section in the limitations on the likelihood of bias by our response rate and how this might affect our point estimates and generalizability (pg 11). We expect that this would render our findings conservative given the generally protective influence of higher income.**

Unfortunately, the goal is compromised by several difficulties, both stylistic and substantive. The inclusion of the ACE acronym in the title may discourage readers who are not familiar with this topic. As well I am not convinced that a good rationale for this study stems from the “growing interest” in this topic. It seems many recent papers focus heavily on child abuse (physical or sexual) experienced by the parents and not on the broader elements in the original ACE “test”. A fundamental question is why should we be interested in this topic? If a strong relationship were found, it is not evident what the authors might propose should be done to prevent those undesired behaviours at age 5? Is there solid evidence any interventions are feasible and effective? Consequently, the concluding sentence of this report is surprising and possibly misleading: “Considering the busy nature of pediatric visits, physicians can be reassured that information on the proximal and relevant risk factors, such as child affect, parent mental health and parenting practices, will identify those most at risk for child behaviour problems.” This is not merited by the study’s findings nor was the intent of the study to provide reassurance to pediatricians.

**We have removed the ACE acronym from the title and included more recent literature pointing to the growing practice among family physicians to ask about both child and parental ACES as part of routine visits. (page 3)**

**We are motivated by concern for this, especially since there is no good evidence around interventions that are feasible and effective.**

**This research is part of a larger ongoing study that broadly examines determinants of child development and behaviour over the life course, which we have clarified in the methods.**

**We have removed the concluding sentence of the report and have softened the interpretation of the findings.**

Similarly, the conclusion in the Abstract was troubling and puzzling: “Focusing on more proximal factors, such as parental mental health and parenting behaviours may be a more influential and less stigmatizing way of identifying children at risk of

behavioural problems at age 5.” This suggests the authors believe the ACS approach may be stigmatizing, which has not been shown, but this concern raises an ethical question that may have been overlooked in the ethical review. In many respects the idea behind this study was to provide a rationale for screening (or case-finding) without having a proven intervention to offer those judged to be at risk. I realize that the negative findings make this issue moot, but it is nonetheless a concern.

**We agree that this issue is complex and that asking about sensitive topics can cause distress. We were motivated due to our concern that there is a growing practice of routinely asking about ACES in general practice settings without appropriate follow-up and we have provided additional evidence that this is occurring (see page 3). While there is no definitive evidence that asking about ACES is stigmatizing there is evidence that it causes discomfort to patients (see new references on page 10) A potential unintended consequence of ongoing repeated screening could potentially stigmatize patients. We have modified the introduction to better highlight the challenges around screening and concerns with this practice.**

**We would like to reassure the reviewer that our study underwent rigorous ethical review. We provide referral information in our questionnaires for any woman who might find any of our questions troubling and our research assistants are trained in providing this information to any woman who calls in with questions. Also, all questions are voluntary, and participants may skip any question they do not wish to answer.**

I was surprised there were no references to any of the literally hundreds of reports from the British Birth Cohort Studies. In these, which I regard as exemplary and which addressed the basic question being pursued in this study, there are none with which I am familiar that found the kind of relationship being sought here other than perhaps with parents who experienced abuse. So the negative findings don't surprise me. Either these were overlooked or viewed by the authors as uninformative. If the authors are not familiar with these studies, they may wish to use Helen Pearson's book, *The Life Project*, as an introduction. A quote written by Pearson in reference to the book describes the studies as “a remarkable series of scientific studies that have tracked generations of children growing up in Britain since the end of the war. The results fed into the foundation of the NHS, changed the way women give birth in Britain and established much of the advice given to expectant parents, as well as changing the way we are educated, parent our children and how we understand our employment, health, illness and death.”

**We agree that many of reports from the British Birth Cohort Studies have provided a fundamental understanding of early influences on child development and behaviour. We have added a reference to this study on the impact of lower income in childhood on development in our background section.**

**We suggest that our study adds to the understanding of contemporary factors that influence child behaviour and provides evidence for early identification of risk and points of intervention.**

A few small points the authors may wish to consider when revising:

1. The title suggests child behaviour broadly but the study is about undesirable (abnormal) behaviour
2. The title uses the phrase 'longitudinal cohort' which seems tautological; all

	<p>cohorts are longitudinal  <b>We have changed the title to include specific reference to internalizing and externalizing behaviour and removed the word “longitudinal”.</b></p> <p>References 1-5 do not all support the statement made in the opening sentence  <b>We have removed 2 references and reviewed the others to ensure that they better capture our intended meaning.</b></p> <p>The notion that the findings might be ‘provide clarity on where physicians should focus their efforts in the context of pediatric visits’ may seem to some as wishful thinking  <b>We have removed this conclusion.</b></p> <p>I am not convinced reference 27 convincingly addresses precursors for psychopathology in later childhood  <b>We have added additional references to support our claim.</b></p> <p>In the Methods section it would be preferable to be clear that the questionnaire was first sent to the eligible women  <b>We have reworded the methods and added a figure in the supplemental material to cover the flow of the study to clarify the full scope of the overall program of research.</b></p> <p>A 69% response rate in 1994 may warrant a comment in the Discussion as a Limitation  <b>We agree. We have considerably expanded the discussion to limit the generalizability of our findings and estimate how the response rate may bias our findings.(page 11)</b></p> <p>I found the sentence beginning Among other child level covariates puzzling  <b>We have reworded this.</b></p> <p>Reference 41 is incomplete. I am uncertain if this and reference 23 support the statement “our study is consistent with’4  <b>Thank you for pointing out the incomplete reference. We have removed both references and added additional references to support our claim.</b></p> <p>The last sentence of this paragraph needs to be rewritten to clarify the dangling final phrase  <b>We have rephrased.</b></p> <p>As may be evident from the preceding comments I believe this study had many more limitations than the few listed  <b>We have expanded our limitations section. (page 11)</b></p>
<b>Reviewer 2</b>	Dr. John Charles LeBlanc
Institution	Pediatrics, IWK Health Centre, Halifax, NS
General comments (author response in bold)	<p>Page 4: "data was" should be "data were".  <b>We apologize for the error, we have changed this sentence.</b></p> <p>It's difficult to make sense of the response rates since you provide different denominators. In your description of the "All Our Families" cohort, you should</p>

provide the total number enrolled. That will allow you to calculate a more realistic response rate based on the initial size. It's excellent to have a longitudinal cohort as you have here. Nevertheless, the response rate and whether those missing are missing at random or otherwise, is going to be critical to interpreting the results. I don't see how you got your final sample size of 1682. It is this number divided by the total number enrolled that would properly indicate response rate. You briefly discussed this in your limitations paragraph but simply acknowledging it as a limitation and not addressing it is a different matter. You could easily look at sample characteristics of the 30 or 40% not in your final sample and compare this with the total cohort.

**We appreciate that our original description was unclear. We have substantially restructured this section, and provided a flow chart in the supplementary material to indicate the overall participation. We have added details on the number of cases analyzed, as well missingness in variables. (page 4 and Table 1) We have also included a sentence about responders and non-responders on page 8.**

**We have also added a section to the discussion to underscore the limited generalizability of our results. Moreover, we appreciate the potential for bias due to non-response. We attempt to address how this bias might impact our results and limit the generalizability of our findings in the discussion. (page 11)**

Modified ACE Score: it's fair enough to modify the instrument as there are some problems with its initial formulation. Nevertheless, you should briefly summarize those changes from the original and also specify whether your modified instrument has been validated.

**We have clarified how the original ACE instrument was modified (very minimally). Please see the response to a similar comment above, as well as the new wording on page 5. We have added a figure with the ACE questions.**

Dichotomized version of ACE outcome: I appreciate that you checked whether simplifying covariates through a information by checking with continuous variables. However, I'm also concerned with the dichotomization of outcome itself. Felitti nicely showed dose-response relationships of ACE scores with many adverse outcomes and it seems a shame to throw away this dose-response information by dichotomizing the ACE outcome. Have you checked ordinal or perhaps linear regression models to see if you are throwing away too much information by dichotomizing this outcome? You could, for example, stratify the ACE score by quintile, and do an ordinal regression on that.

**We appreciate that additional adversity may follow a dose-response relationship (as shown by Felitti's original work). Our supplemental table includes the estimates for each additional ACE score, using ACES as a continuous predictor of child behaviour outcomes. Our results with the ACEs score as continuous are consistent.**

Family Income: the unusual creation of this variable with \$10,000 increments followed by \$25,000 increments will make odds ratios difficult to interpret.

**We agree we have collapsed the categories to be \$50,000 increments to make the intervals more consistent.**

Ethnicity: should "self-reported white" be altered to "self-reported

Caucasian/European descent”?

**We are motivated to use the term “white” by two factors. First, this was one of the response categories that women could choose to self-identify their ethnicity. Second, we are guided by work showing that the use of the term Caucasian can be problematic in biomedical research. (Kaplan, Judith B., and Trude Bennett. "Use of race and ethnicity in biomedical publication." *Jama* 289.20 (2003): 2709-2716.)**

Results: I find it hard to believe that 70% of mothers had no mental health symptoms. Most people endorse something on mental health instruments. I could understand if you meant that there were no mental health disorders or no symptoms beyond a certain threshold. Perhaps this is what you meant since you do talk about thresholds when you describe the outcomes

**We have removed this section for space and clarified the interpretation in our tables. The reviewer is correct that we meant to indicate that 70% of women had not symptoms beyond predetermined clinically relevant thresholds. We appreciate that our previous wording was unclear and have worked to clarify our language throughout.**

Table 1: RCBQ needs to be defined. Also, I’m puzzled that you report family income in different strata than you defined in your methods section. Also, you have an unnecessary 5 after “100,000”. It would be useful to tell the reader how representative this cohort is to the same age-sex cohort in Alberta using perhaps some provincial or national survey data on a few key variables.

**Thank you for identifying these typos and inconsistencies. We have fixed these, we have reframed our generalizability statements to better reflect how our sample compares to the general population.**

In terms of take away messages, influencing modifiable risk factors early in childhood would be potentially useful to readers. Ineffective hostile parenting is a good candidate for potential intervention. However, it is measured at the same time as externalizing and internalizing behaviour and it is therefore difficult to tease out whether ineffective parenting led to behaviour problems, vice versa, or some interactive interplay between the two. I don’t think this is well addressed in the interpretation. For example, the sentence “Specifically, proximal factors including child affect in early childhood, parenting practices, and parent mental health are more strongly associated with the children’s risk of externalizing and/or internalizing behaviours at age 5” is not followed by a discussion or a reminder to the reader that these are all measured at the same age. No question that measuring these factors will help identify needs that are amenable to intervention but these needs e.g. behaviour problems, hostile parenting) can be assessed without any recourse to measurement of ACEs.

**We agree with the reviewer’s comments. We have removed this sentence and rephrased subsequent sections to more clearly indicate that there is very likely some interplay between child behaviour and parenting. (pg 11) We were not trying to establish causality and have reworded our interpretation to indicate that our purpose was to establish what could be potential points for early intervention and prevention for child internalizing and externalizing behaviours.**

Paragraph two on page 10 concludes: “Our results are consistent with other

	<p>findings that the influence of maternal ACEs on child outcomes is relatively small compared to other factors”. However, there is a risk of a type II error here, especially given the simplification of the ACEs score into a dichotomy. The dose-response information that was discarded by dichotomization may show a stronger influence of ACEs on externalizing and internalizing behaviour.</p> <p><b>We agree that the interpretation of the dichotomized ACEs score may be oversimplified. We have attempted to address the possibility of a type II error by showing the adjusted association between one additional ACE and each behavioural outcome (results available in the supplementary file). One additional ACE is associated with an adjusted OR 1.19 (1.08, 1.32) for externalizing behaviours and adjusted OR 1.02 (0.94, 1.10) for internalizing behaviours. We do not wish to indicate we think this is a null finding (for externalizing), only that other factors are potentially more useful either for screening or intervention.</b></p> <p>Influence of maternal mental health: pages nine and 10 “Screening tools for depression and anxiety are widely available, and can result in more efficiencies in service utilization.” There is no evidence from randomized control trials that formal screening programs for depression in primary care settings is effective. (I don’t know about screening for anxiety but I would be surprised if there were). The citations for this sentence do not support your contention that these tools can result in more efficiencies. They may well do the opposite by wasting clinicians’ precious time. I strongly suggest that unless you can provide randomized controlled trial evidence for this, that you remove this conclusion. Physicians need to be vigilant about the mental health of their patients but they don’t necessarily need to use a screening tool to do so.</p> <p><b>We have removed this sentence.</b></p> <p>I agree with your conclusion that rather than focusing on maternal ACE scores, primary care clinician should focus on parental mental health (and also parenting practices).</p> <p><b>Thank you.</b></p>
<b>Reviewer 3</b>	Dr. Catherine S. Birken
Institution	Paediatric Medicine, Hospital for Sick Children, Toronto, Ont.
General comments (author response in bold)	<p>With increasing attention to intergenerational transmission of the effects of childhood adversity, this study uses the All Our Families Cohort to measure associations between maternal adverse childhood experiences (ACEs) and offspring externalizing and internalizing, adjusting for more proximal child, family and social risk factors. The study found that while maternal ACEs were associated with higher odds of both externalizing and internalizing behavior, the associations were somewhat attenuated after adjustment. The authors point out that other factors have greater magnitude of association with behavior than ACEs (including maternal mental health and negative parenting style). Based on these findings, the authors conclude that focusing on these proximal findings may be more meaningful for clinical screening.</p> <p>The manuscript is well-written and the study is well designed with appropriate sample size and measures to answer their questions. The study findings are interesting and potentially very meaningful to both research and clinical practice addressing the consequences of childhood adversity. Our comments are focused around the interpretation of these findings and that may exceed what can be inferred using the study design.</p>

Abstract:  
Clear and well-written  
**Thank you.**

Introduction:  
The authors provide a clear conceptual model and identify a meaningful gap in the literature to justify their study. The authors identify the benefits of clinical screening as a key motivator for their study, and this is very important for interpretation of findings  
**Thank you.**

Methods:  
As this is data from a cohort study, clearly describing the study design for this analysis from the outset would be helpful.  
**We have clarified that this study is a secondary data analysis of a cohort study in Calgary, Alberta**

Given that ACES are asking about childhood experiences of adults, what is the value in ensuring the temporal precedence in this study? Is this needed?  
**We agree that there is no need to ask this question earlier, as it is retrospective for adults. However, this just happens to be the timepoint at which it was asked in this overall cohort.**

Overall, variables are clearly defined. We think differentiating between persistent and periodic maternal depressive symptoms is a strength.  
**Thank you.**

We suggest the authors include all of the ACE questions in the methods section of the manuscript. This information is important for interpretation of the findings and is more accessible in the text than as supplementary material. A small table or figure may be helpful if you do not wish to list them all in the text.  
**We have included a figure in the methods with the exact ACEs questions (though not the formatting of our questionnaire).**

“White” and “minority” definitions of ethnicity represent a very limited way to measure cultural variability in parenting styles, and we are not certain this is what this variable reflects. We believe that this variable could also be meaningful as it may more directly address discrimination, potential immigration status, and other socioeconomic factors related to child behavior. These factors should be mentioned as well

**We agree that these represent a limited way of measuring cultural variability, and have removed mention of this in the manuscript. While it is true that being part of a minority ethnicity is likely associated with forms of discrimination and other socio-economic factors, we felt that exploring this was beyond the scope of the current paper.**

Did the authors consider adjusting for maternal age?  
**We have added maternal age as a covariate.**

Did the authors consider any formal causal analysis? Their conclusions rest to



some degree on an inference of mediation, so they could consider even a simple path model to show the reader relationships between variables.

**We agree that exploring the intergenerational transmission of ACEs through a formal causal analysis would be interesting and informative. However, this was beyond the scope of the current paper as the interpretation of mediation analyses can be complex, and we wanted to provide clear indicators of potential child behavioural problems. We have suggested a formal causal analysis as a potential future direction in the discussion.**

Results:

Clearly written and well organized

**Thank you.**

Discussion:

Placing these results in the context of other studies would be a strength; including any previous studies on the more proximal factors such as hostile parenting.

Including strengths compared to the AVON study referenced.

**We have restructured the discussion, added additional references to better contextualize our findings.**

While the OR for externalizing is slightly attenuated after adjustment, without any causal analysis, it is difficult to attribute this to mediation. Perhaps the maternal ACEs add additional information that is useful? We would appreciate hearing the authors' thoughts on this alternate possibility

**We have restructured our discussion in this area. We speculate on possible mediation and potential pathways, and suggest further formal causal analysis of these issues.**

We often like to avoid making statements around the effect estimates of covariates in the models, as these models weren't designed to answer questions about the covariates. Can the authors reframe the discussion around the effect estimates of the covariates?

**We have reframed the discussion to reflect that other covariates also have associations with the outcome, and that these are potentially easier and less stigmatizing to assess. We do not wish to overinterpret covariate estimates, only draw attention to the fact that our findings are consistent with the literature and may provide a more useful discussion area for clinicians.**

There is a striking difference in the degree to which adding covariates attenuates the strength and magnitude of association for internalizing symptoms vs externalizing symptoms. What do the authors make of this?

**Thank-you for this comment. We agree that this is an interesting result likely due to the differences in the magnitude of bivariate associations across combinations among maternal ACEs, covariates, and child outcomes. Maternal mental health was measured in terms of depression and anxiety (both internalizing symptoms), which may suggest a potential biological or psychosocial pathway for transmission of risk. We have noted this in the discussion**

Do children have comorbid internalizing disorders and externalizing disorders?  
How would this be addressed?

**While it is possible for these disorders to be comorbid, this was not the case for any of the children in our sample. We have clarified this in the results.**

Though the authors indicate that their results are broadly generalizable, we wonder about generalizability with respect to family income, minority ethnicity and single parent families. Who are higher risk groups? Would there be value in examining whether income is a moderator in this relationship – perhaps several of these factors may have differential impact depending on income

**We have considerably reworded our claims of generalizability, and added additional information on how we believe our results may be impacted by differential attrition.**

The final sentence of the conclusion provides relatively strong clinical direction that is not directly supported by the study findings, and may be overstated.

**We have removed this conclusion.**

Do the authors think that a high report of maternal adversity or even report of a major life trauma should or could influence the approach that a clinician takes to addressing the proximal factors identified as meaningful in this study? Could trauma affect the way that a parent responds to a parenting intervention? These may be important points to mention for future consideration. Is there any therapeutic value in screening for parental ACES in the context of screening for mental health or other proximal problems. Do adults tend to make the connection between their ACES and mental health or parenting behaviours?

**We agree that the report of maternal adversity may impact the approach a clinician takes or recommendations they make for treatment. A trauma-informed approach to assessment and treatment as a universal precaution, regardless of a high ACE score or not, is critical. While it is possible that previous trauma may have an influence on how a parent responds to intervention, we contend that a comprehensive evaluation of current maternal mental health and proximal factors may be more informative. This has been added to the discussion section.**

We suggest rearranging the order of table 1 or excluding outcome from table 1 altogether.

**We have restructured Table 1 and added a Table 2 with internalizing and externalizing behaviours.**