PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

| TITLE (PROVISIONAL) | Familial factors and child characteristics as predictors of injuries in |
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| | toddlers: A prospective cohort study |
| AUTHORS | Mia Cathrine Myhre, Siri Thoresen, Jens Grøgaard, Grete Dyb |

VERSION 1 - REVIEW

| REVIEWER | David C. Schwebel, PhD Professor of Psychology Associate Dean for Research in the Sciences College of Arts and Sciences University of Alabama at Birmingham, USA |
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| | I have no competing interests. |
| REVIEW RETURNED | 29/12/2011 |

| THE STUDY | No major concerns. |
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| GENERAL COMMENTS | This is a strong paper that will contribute nicely to the literature. Many of the findings are replications, but this paper replicates those results with a large sample and strong methodology. A few findings are novel to the literature – in particular, I find the findings concerning motor development to be fascinating and important to the field. I have several comments for the authors to consider. |
| | The issue of intentional (abusive) injuries seems to be thrown into the manuscript as a bit of an afterthought, and doesn't come across cleanly. In the introduction, there is just one sentence on the topic and it isn't integrated well with the rest of the presentation. The feel in the discussion is similar. I'm not sure a lot can be said given the data available, but the authors might consider how to address the issue a bit more carefully. Cronbach's alphas are presented for some scales, but not all. It's hard to get "adequate" alphas (> .70) with scales having only a few |
| | items and categorical response options, but presenting alphas or other internal consistency measures for other scales (e.g., ASQ, CBCL) might be sensible. |
| | less than or greater than 12 years? Why not use a continuous measure of some sort (e.g., years of education)? I don't expect it will make much difference in the results, however. |
| | 4. I gather gestational age was used as a continuous measure. I wonder, however, if the key issue is premature birth versus full term. Is differentiating short and longer gestation within a full-term period meaningful? Would results be different if this measure was categorized into pre-term vs. full term? |
| | 5. Older siblings may act as supervisors, but also as models of risky behavior. This possibility might be added to the second paragraph of the discussion. 6. The finding on aggression is interesting, but not entirely surprising |

| to me. Most previous research linking aggression and injuries have examined children who were slightly older. There may be significant |
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| changes in the expression of aggression between 18 and 60 months, and the discussion of the results in this study might be |
| couched in the developmental aspects involved. |

| REVIEWER | Anders Hjern, MD, Adjunct Professor of Paediatric epidemiology, Centre for Health Equity Studies, Karolinska Institutet/Stockholms |
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| | Universitet, Sweden. |
| REVIEW RETURNED | 31/01/2012 |

| REPORTING & ETHICS This study investigates risk factors for injuries in children between 18 and 36 months of age in an interesting data set based on a large birth cohort. This data has a potential to generate new knowledge about risk factors for injuries in this age group that can be addressed in interventions by child health services that serve this age group. Considering the potential and limitations of this data there are, however, some major issues that need to be addressed. 1. The dropout rate in this cohort is large (58%) which needs to be considered in the study design since this probably has different implications for different kinds of variables. One would expect that the child oriented data regarding development, temperament etc would be least affected by this dropout since these factors were completely unknown when the cohort was recruited during gestation, while socio-economic variables are much more problematic with a probable selection of advantaged parents into the study. Thus the |
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| major research question posed in this paper seems poorly chosen. |
| comparing these two kinds of risk factors. I think the authors should |
| consider a research design with a firm focus on child characteristics, |
| treating the family risk factors as confounders. In my opinion this |
| would be a better way of exploiting the particular strengths of this |
| conort data. After all, there are quite a few studies of familiar risk |
| specific risk factors of the kind available in this data set |
| 2 It seems a little odd to use hospital attended injuries as the |
| outcome variable in an interview study. Most authors that use this |
| outcome do it because that's what's available in hospital registers. |
| Many minor injuries are equally attended in medical care outside of |
| hospitals and could well have been included in the definition of the |
| outcome variable here as well, if they were asked for. Now the |
| authors have a hospital outcome with the recall bias associated with |
| interview data as well as the geographical bias associated with using |
| discussed a little better |
| 3 The authors interpretation of Table 1 that child related risk factors |
| are less important than familial risk factors because of the way they |
| were attenuated in the multivariate analysis is questionable to say |
| the least. First of all, the design of the statistical analysis is not well |
| suited for drawing this kind of conclusions. A more appropriate |
| design here would be an analysis in several steps where we can pin |
| out the effect of the familial risk factors from other confounders and |
| other child specific factors in separate steps. Secondly, there is no |
| injury fine motor development and gross motor development in the |
| multivariate analysis. |

VERSION 1 – AUTHOR RESPONSE

Responses to the reviewer's comments We would like to thank both reviewers for the valuable, constructive critique.

Responses to reviewer 1

1. The issue of intentional (abusive) injuries seems to be thrown into the manuscript as a bit of an afterthought, and doesn't come across cleanly. In the introduction, there is just one sentence on the topic and it isn't integrated well with the rest of the presentation. The feel in the discussion is similar. I'm not sure a lot can be said given the data available, but the authors might consider how to address the issue a bit more carefully.

We agree that this is a very important aspect when investigating injuries in children, but the available data did unfortunately not allow assessments or analyses of the influence of intentional injuries or neglect. Due to this limitation we have omitted the discussion of child maltreatment in the introduction (page 41-45).

2 Cronbach's alphas are presented for some scales, but not all. It's hard to get "adequate" alphas (> .70) with scales having only a few items and categorical response options, but presenting alphas or other internal consistency measures for other scales (e.g., ASQ, CBCL) might be sensible.

As stated under statistics, scales with internal consistency of Cronbach's α <0.60 were transformed into categorical variables. (Page 9, line 32)

To avoid misunderstandings the Cronbach's alphas are now given for all scales, and it is described which variables (CBCL and ASQ) were analyzed as categorical variables due to poor internal consistency. (Page 8, line 12-16 and line 56)

3. What's the advantage of dichotomizing maternal education into less than or greater than 12 years? Why not use a continuous measure of some sort (e.g., years of education)? I don't expect it will make much difference in the results, however.

Unfortunately there was no continuous measure of education available. Maternal education was originally recorded as 7 predefined categories. Preliminary analysis including all the 7 categories did not make any difference on the results presented in the paper, and a simplification was reasonable. In Norway youths are entitled to 12 years of education, which guided the choice of cut-off in this sample.

4. I gather gestational age was used as a continuous measure. I wonder, however, if the key issue is premature birth versus full term. Is differentiating short and longer gestation within a full-term period meaningful? Would results be different if this measure was categorized into pre-term vs. full term?

We understand the reviewer's concern. However, the effect was found across all gestational ages with no-clear cut-off. To avoid any confusion, we have added the univariate association between preterm birth and injuries to Results. (Page 10, line 30)

The definition of preterm birth has also been added to Methods. (Page 7, line57) The continuous measure is maintained in the model to make the adjustment as accurate as possible.

5. Older siblings may act as supervisors, but also as models of risky behavior. This possibility might be added to the second paragraph of the discussion.

We have added this good point as suggested. (Page 13, line 22)

6. The finding on aggression is interesting, but not entirely surprising to me. Most previous research linking aggression and injuries have examined children who were slightly older. There may be significant changes in the expression of aggression between 18 and 60 months, and the discussion of the results in this study might be couched in the developmental aspects involved.

We agree, and a paragraph to elaborate this important point is added to the discussion. (page 15, line 17)

Responses to reviewer 2

1 The dropout rate in this cohort is large (58%) which needs to be considered in the study design since this probably has different implications for different kinds of variables. One would expect that the child oriented data regarding development, temperament etc. would be least affected by this dropout since these factors were completely unknown when the cohort was recruited during gestation, while socio-economic variables are much more problematic with a probable selection of advantaged parents into the study. Thus the major research question posed in this paper seems poorly chosen, comparing these two kinds of risk factors. I think the authors should consider a research design with a firm focus on child characteristics, treating the family risk factors as confounders. In my opinion this would be a better way of exploiting the particular strengths of this cohort data. After all, there are quite a few studies of familiar risk factors for injuries, but very few that have been able to include child specific risk factors of the kind available in this data set.

We appreciate the remark on this issue. However, as family factors are known to be strongly associated with injury risk in children and some of them were among the strongest predictors in our model, our suggestion is to keep both child and family factors in the model. In addition this dataset offered an opportunity to study interesting familial variables not so often assessed in connection with injury risk in children, such as maternal mental distress.

As discussed under limitation the selection of mothers in the study may have been the reason why other risk factors such as maternal education, unemployment and single parenthood were not predicting injury in this sample. However, even in this advantaged sample other familial factors were found to be important predictors, and these associations are likely to be generalizable.

2. It seems a little odd to use hospital attended injuries as the outcome variable in an interview study. Most authors that use this outcome do it because that's what's available in hospital registers. Many minor injuries are equally attended in medical care outside of hospitals and could well have been included in the definition of the outcome variable here as well, if they were asked for. Now the authors have a hospital outcome with the recall bias associated with interview data as well as the geographical bias associated with using hospitals care only to create the outcome variable. This nees to be discussed a little better .

We have given the outcome variable a lot of consideration. There were only two injury questions available in the Norwegian Mother and Child Cohort study 36 months form (see methods page 7). We decided not to use the self-reported" any injury or accident", as this would probably include a large proportion of insignificant events.

We thank the reviewer for this important comment. We have added the implication of injuries treated in outpatient clinics, and discussed the possibility of geographical biases under limitations.(page 15,

line 39)

3. The authors interpretation of Table 1 that child related risk factors are less important than familial risk factors because of the way they were attenuated in the multivariate analysis is questionable to say the least. First of all, the design of the statistical analysis is not well suited for drawing this kind of conclusions. A more appropriate design here would be an analysis in several steps where we can pin out the effect of the familial risk factors from other confounders and other child specific factors in separate steps. Secondly, there is no attenuation at all of two of the major child-specific determinants of injury, fine motor development and gross motor development, in the multivariate analysis. **

We agree that the interpretations and conclusions drawn in the paper were questionable and that division into familial and child related factors have been a simplification that does not have sufficient support in the data. In the revision of the paper we have modified the text abstract (page 2, line 6-9 and line 50-57), article focus (page3, line 9-16), key messages (page 3I line 22-29), introduction (page 5 line 47-57) and discussion (page 13, line7-16 and page 15 line 10-14) to simply describe which factors were associated with injuries.

The effects sizes were rather small, and we think analysis in more steps will enhance the danger of over interpret the results.

VERSION 2 – REVIEW

| REVIEWER | Anders Hjern, MD, PhD. Centre for Health Equity Studies. |
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| REVIEW RETURNED | 10/02/2012 |

| THE STUDY | This is now a purely descriptive paper, without any real research questions. The p-level is too low for a paper with this many independent variable |
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| RESULTS & CONCLUSIONS | This paper lacks research questions, and the questions above are |
| | thus irrelevant |
| GENERAL COMMENTS | This has now developed into a purely descriptive article without any real research questions at all. The authors seem to believe that the large number of independent variables is an advantage, while in the statistical analysis it is actually a major problem, that make random effects more than probable with the p-level set at 0.05. I suggest that the authors try to find some more pointed research questions to answer with this rich data material. |

| REVIEWER | David C. Schwebel, PhD Professor of Psychology Associate Dean for Research in the Sciences University of Alabama at Birmingham, USA |
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| REVIEW RETURNED | I have no competing interests to report. 13/02/2012 |

| GENERAL COMMENTS | The authors have done a nice job of responding to the previous |
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| | reviews. I have no other concerns and believe this manuscript is a |
| | nice contribution to the literature. |