ARTICLE DETAILS

<table>
<thead>
<tr>
<th>TITLE (PROVISIONAL)</th>
<th>Sleep problems, behavioural problems and respiratory health in children born extremely preterm. A parental questionnaire study</th>
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<tr>
<td>AUTHORS</td>
<td>Stangenes, Kristine; Hysing, Mari; Elgen, Irene; Halvorsen, Thomas; Markestad, Trond; Bjorvatn, Bjørn</td>
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VERSION 1 – REVIEW

<table>
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<tr>
<th>REVIEWER</th>
<th>Reviewer name: Rosemary SC Horne</th>
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<tbody>
<tr>
<td>Institution and Country</td>
<td>Monash University Australia</td>
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<tr>
<td>Competing interests</td>
<td>None</td>
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| REVIEW RETURNED | 28-Jun-2019 |

| GENERAL COMMENTS | This paper highlights the importance of screening for sleep problems in children born extremely preterm. The study showed that sleep problems – difficulty falling asleep, waking during the night, snoring daytime sleepiness and short sleep were all associated with higher scores on the Strengths and Difficulties Questionnaire which is a general behavioural screening questionnaire. Respiratory health was also assessed and daytime sleepiness and disturbed sleep were associated with increased respiratory problems. The paper is well written and the data appropriately analysed. |

Major comments:
- It is not stated until the discussion that this sample of extremely preterm children included those with severe developmental delay. This should be highlighted in the methods and results sections and the number with severe disability added to the demographics table.
- As highlighted by the authors in the introduction children with neurological problems often have sleep problems. It is important to separate out those with severe neurological problems in addition to extreme prematurity.
- It should also be presented the differences between the parents of children who responded and those that didn’t – simply mentioning that this has been reported previously does not help the reader of the current paper and this information should be summarised.
- It has been well reported that children born preterm are at increased risk for sleep disordered breathing and sleep problems and these papers should be included for completeness as sleep disordered breathing affects behaviour and attention in typically developing children.

It is not described what questions the parents were asked other than their education level and smoking history. Were questions asked about socioeconomic status and the child’s sleep environment as this can also affect sleep.

Minor comments:
Page 4 line 35 delete time “how long the child was awake”
Page 5 what was the clinical cut off score for the SDQ?
Page 5 statistical analysis it is not clear exactly what “the groups” were as in the Tables there are more comparisons than listed in this section.
How did the parental report and teacher report compare for the SDQ?
Had any of the children been treated for snoring or their sleep problems?
Were there any differences in symptoms between boys and girls?

REVIEWER
Reviewer name: Emmanouil Bagkeris
Institution and Country: University College London
Competing interests: No competing interests

REVIEW RETURNED 07-Jul-2019

GENERAL COMMENTS
Dear authors, this is a very interesting piece of work. Please address my points below:

1. Perhaps consider changing the objective of the abstract to address the conclusion, e.g. “To explore whether EPT children with different types of sleep problems had more mental and respiratory health problems than EPT children without sleeping problems”.

2. Please change “sub-analyze” to British English sub-analyse.

3. The results section for sleep problems and mental health and sleep problems and respiratory health have no numerical expression of the differences and the associations claimed to exist. Please consider adding the relevant estimates to support the statements for the significant differences and associations.

4. The discussion states that a strength of the study is the large national population-based sample. However, none of the multivariable models included more than 200 children. It could be a representative sample, however not a large sample.

5. Considering that several models have been fitted, have you considered correction for multiple testing?

6. The manuscript does not indicate the months when the study was conducted. Was it during winter or summer or both? Have you considered whether seasonality was a factor that may be associated with sleep problems? If not, why? Perhaps consider adding this as a limitation of the study.
1. This paper highlights the importance of screening for sleep problems in children born extremely preterm. The study showed that sleep problems—difficulty falling asleep, waking during the night, snoring daytime sleepiness and short sleep were all associated with higher scores on the Strengths and Difficulties Questionnaire which is a general behavioural screening questionnaire. Respiratory health was also assessed and daytime sleepiness and disturbed sleep were associated with increased respiratory problems. The paper is well written and the data appropriately analysed.

Comment: Thanks to the reviewer for this positive feedback.

Major comments:

2. It is not stated until the discussion that this sample of extremely preterm children included those with severe developmental delay. This should be highlighted in the methods and results sections and the number with severe disability added to the demographics table. As highlighted by the authors in the introduction children with neurological problems often have sleep problems. It is important to separate out those with severe neurological problems in addition to extreme prematurity.

Comment: We thank the reviewer for this feedback. This is now specified in the methods section, and results are included in Table 1 as well as the results section.

The new text in the methods section: "EPT children with severe disability were included. (The degree of neurodevelopmental disability was assessed by clinical examination when the children were 5 years old (ref.).)"

The new text in the results section: "Of the 216 participating children, 6 had severe disability at age 5 years (ref.)."

3. It should also be presented the differences between the parents of children who responded and those that didn’t—simply mentioning that this has been reported previously does not help the reader of the current paper and this information should be summarised.

Comment: We thank the reviewer for this feedback. The text in the results section and in the discussion section has been changed to point this out.

The new text in the result section: "Participants and non-participants did not differ regarding gestational age or the ratio of SGA, bronchopulmonary dysplasia or retinopathy of prematurity, but there was a tendency for less severe disability among the participants (3.3 % (n=6) vs. 9.8 % (n=12))."

The new text in the discussion section: "The limited response rate at follow-up was a weakness. However, we found that for most variables the assessed children were representative of all survivors at the age of 11 years."

4. It has been well reported that children born preterm are at increased risk for sleep disordered breathing and sleep problems and these papers should be included for completeness as sleep disordered breathing affects behaviour and attention in typically developing children.


Comment: We thank the reviewer for this feedback. The fact that previous studies have shown that children born prematurely have an increased risk of sleep disordered breathing is now included in the discussion section and the suggested articles are used as references.

The new text in the discussion section: “Snoring is a common symptom of sleep disordered breathing (SDB) and previous studies have shown that children born prematurely have an increased risk of SDB (ref). The prevalence SDB during childhood in children born EPT is unknown. In general, SDB in childhood is a risk factor for behavioral problems, externalizing symptoms and inattention. More studies are needed to map the association between SDB and behavioural problems in children born EPT.”

5. It is not described what questions the parents were asked other than their education level and smoking history. Were questions asked about socioeconomic status and the child’s sleep environment as this can also affect sleep.

Comment: Unfortunately, we lack detailed information about socioeconomic status and the child’s sleeping environment. Both these factors are now listed as weaknesses in the discussion section.

The new text: “Other limitations were lack of detailed information about socioeconomic status, the child’s sleep environment, what season the parents answered the questionnaires, and whether the children had been treated for snoring or for sleep problems.

Minor comments:

6. Page 4 line 35 delete time “how long the child was awake”

Comment: This has been changed in the manuscript, as suggested.

7. Page 5 what was the clinical cut off score for the SDQ?

Comment: We did not use cut off score for the SDQ. People with and without the specified sleep problems were compared by average SDQ scores.

8. Page 5 statistical analysis it is not clear exactly what “the groups” were as in the Tables there are more comparisons than listed in this section.

Comment: The manuscript has been revised according to the point raised by the reviewer. We wish to thank for the valuable comment.

The new text: "For each specific dichotomized sleep outcome variable, the groups were compared according to the results on the SDQ, ISAAC, current asthma vs. no asthma, use vs. no use of inhaled corticosteroids or oral leukotriene modifiers, and use vs. no use of inhaled bronchodilators.”
9. How did the parental report and teacher report compare for the SDQ?

Comment: We have not explored how the parent-reported SDQ and teacher-reported SDQ compare at the individual level. At group level, this largely coincides, as shown in the result section.

10. Had any of the children been treated for snoring or their sleep problems?

Comment: The parents were not asked if their children had been treated for snoring or their sleep problems. This is a weakness and is now added as a limitations.

The new text: "Other limitations were lack of detailed information about socioeconomic status, the child’s sleep environment, what season the parents answered the questionnaires, and whether the children had been treated for snoring or for sleep problems."

11. Were there any differences in symptoms between boys and girls?

Comment: There were no significant sex differences regarding the prevalence of the specified sleep problems. This information is now included in the results. Due to small group sizes, we did not explore sex differences in the associations between sleep and behavior and between sleep and respiratory health.

The new text in the result section: There were no significant sex differences regarding the prevalence of the specified sleep problems.

Reviewer 2:

1. Dear authors, this is a very interesting piece of work. Please address my points below: Perhaps consider changing the objective of the abstract to address the conclusion, e.g. “To explore whether EPT children with different types of sleep problems had more mental and respiratory health problems than EPT children without sleeping problems”.

Comment: The manuscript has been revised according to the points raised by the reviewer. We would like to thank the reviewer for this suggestion.

2. Please change “sub-analyze” to British English sub-analyse.

Comment: This has been changed in the manuscript.

3. The results section for sleep problems and mental health and sleep problems and respiratory health have no numerical expression of the differences and the associations claimed to exist. Please consider adding the relevant estimates to support the statements for the significant differences and associations.

Comment: Thanks to the reviewer for this suggestion. We have considered this but decided not to make any changes to the results section, partly to avoid double-reporting and partly due to the journal’s word limit. All these specified details are found in the tables.

4. The discussion states that a strength of the study is the large national population-based sample. However, none of the multivariable models included more than 200 children. It could be a representative sample, however not a large sample.

Comment: Thanks to the reviewer for this feedback. We agree. Large has been removed.
5. Considering that several models have been fitted, have you considered correction for multiple testing?

Comment:

We considered correcting for multiple testing but chose not to do this mainly due to power issues and risks of type II errors. Because of this, the results must be interpreted with caution. This is now mentioned in the discussion section.

The new text in the discussion section: “We did not correct for multiple testing, and therefore, the results must be interpreted with caution.”

6. The manuscript does not indicate the months when the study was conducted. Was it during winter or summer or both? Have you considered whether seasonality was a factor that may be associated with sleep problems? If not, why? Perhaps consider adding this as a limitation of the study.

Comment: Unfortunately we do not have information about which season the study was conducted. We agree with the reviewer that this may provide interesting information.

This is now added as a weakness in the discussion.

The new text: “Other limitations were lack of detailed information about socioeconomic status, the child’s sleep environment, what season the parents answered the questionnaires, and whether the child had been treated for snoring or for sleep problems.”