

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Anticipatory guidance to prevent infant sleep problems within a randomised controlled trial: infant, maternal and partner outcomes at 6 months of age.
AUTHORS	Galland, Barbara; Sayers, Rachel; Cameron, Sonya; Gray, Andrew; Heath, Anne-Louise; Lawrence, Julie; Newlands, Alana; Taylor, Barry; Taylor, Rachael

VERSION 1 - REVIEW

REVIEWER	Lauren Philbrook Auburn University, USA
REVIEW RETURNED	21-Nov-2016

GENERAL COMMENTS	<p>This study examined the effectiveness of intervention program aimed at improving infant sleep, settling and safe sleep practices, and parent mental health and sleep across the transition to a new baby. Strengths of the study include a large sample size and advanced statistical methodologies to evaluate study hypotheses. Furthermore, the intervention includes a session delivered prior to the birth of the infant; as described by the authors, little work has explored the utility of prevention programming to improve infant sleep and therefore this is an important empirical question. The manuscript is well-written and the introduction nicely frames the results. My concerns are minor and mostly are regarding the methods and the interpretation of the results.</p> <p>Introduction</p> <p>1. If space requirements allow, I think the authors could consider briefly highlighting mechanisms via which poor sleep in infancy may translate into increased risk for obesity in childhood, particularly because the overall intervention program was aimed at reducing obesity outcomes.</p> <p>2. I found the first sentence of paragraph 3 on page 5 to be a little confusing. It is stated that prior interventions focused on improving infant sleep have shown small to medium effects on infant nocturnal sleep time and small impacts on infant sleep- are those two pieces of information distinct from one another?</p> <p>Method</p> <p>3. As noted in the Study Design section, data from baseline and 6 months of age are reported in the current paper. I wonder if perhaps the authors will be more likely to see significant effects later in the infant's life, when night wakings are less normative. Table 3 shows that on average parents were aware of 1-2 infant night wakings per night, suggesting that only a small minority of babies were sleeping throughout the night on their own. Is it possible that greater intervention effects will be seen when a larger percentage of infants</p>
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	<p>develop a capacity for self-regulated sleep? Perhaps then the intervention will result in decreased likelihood of problematic sleep problems.</p> <p>4. Were there any missing data? If so, how was it accounted for?</p> <p>5. I think it would be helpful to know how many days of actigraphy information infants had on average. (Did all infants have between 5-7 days?) Did any infants have fewer than 5 days of data, and if so, was their data included in the analyses?</p> <p>6. Was whether the infant was sick or on medication during the sleep assessments accounted for in the analyses?</p> <p>7. I think it would be helpful to include the full name of the EPDS in the manuscript text. I apologize if I missed this.</p> <p>Results & Discussion</p> <p>8. I agree with the authors that a potential explanation for fewer significant effects than expected could be due in part to the sample being relatively low-risk and well-educated. However, since there is some variability in education and family income, I wonder if it might be possible to examine whether the intervention was more effective in improving infant and parent sleep, parental well-being, and safe sleep and settling practices for the more at-risk families in the sample?</p> <p>9. I am curious about the extent to which the authors believe the results could be impacted by parental leave policies in New Zealand. If one or both parents is able to stay home with the baby for an extended period, might they be less likely to rate the infant's sleep as problematic, and perhaps less concerned about the infant quickly learning to develop self-regulated sleep?</p> <p>10. I thought it was notable that the authors observed that parents were only slightly more likely to put the infant to sleep awake in the intervention compared to control groups. Since a similar minority of participants continued to lay the baby down asleep regardless of intervention, I wonder if there might be barriers to putting the baby down awake (e.g., "I can't listen to the baby cry; the baby always falls asleep feeding") that could be integrated into the intervention in the future, if they are not already.</p>
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REVIEWER	Dr Brian Symon Australian Family Care Australia
REVIEW RETURNED	12-Feb-2017

GENERAL COMMENTS	<p>This is an elegantly written paper which adds to knowledge in this area.</p> <p>This is a very well written study with an excellent design structure. There are some issues that I feel would allow publication with minor revisions.</p> <p>These are mentioned in the order of appearance in the text.</p> <ol style="list-style-type: none"> 1. Page 7, line 32 (7/32) <ul style="list-style-type: none"> ◦ the text "iii" is absent
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2. 9/5:

- ... “delaying the introduction of complementary foods until around 6 months of age.”
 - this point does not need revision as it reflects the teaching utilised in the study.
 - My reason for mentioning this is that latest research suggests that earlier introduction of allergenic proteins decreases the risk of food allergy particularly with peanuts.
 - Du Toit G, Katz Y, Sasieni P, et al. Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy. J Allergy Clin Immunol 2008;122: 984-991.
 - as a clinician it is my experience that early introduction of complementary foods has a major positive impact on sleep performance particularly in boys and even more particularly boys who are genetically destined to be tall.
 - The intervention as studied has shown no significant improvement in sleep performance at 6 months. As a clinician working in the field I believe that one of the reasons for failed impact is that complementary feeding was delayed by the teaching protocols and that the maintenance of relative hunger delays the development of good sleep patterns. I do not write this as a criticism of the paper.

3. 12/52

- The data shows increases in a perception of a sleep problem for both mothers and partners when comparing 4 to 6 months. For mothers there is a 30% increase in reports of infant sleep problems and for partners 42% increase. My point is that by 6 months an increasing proportion of families saw their infant's sleep as a problem compared to 4 months. I am unable to see analysis of that data. While 80.1% of mothers at 6 months were not reporting a sleep problem the proportion of mothers reporting a problem was increased. This might be worthy of a small comment.
- At 6 months mothers were significantly more likely to report a sleep problem than partners ($p = 0.050$). This probably reflects that the mothers are taking primary responsibility for the waking child.

4. 18/5

- remove the word 'expectantly' as it adds little to the meaning of the sentence or if the authors prefer if could possibly read ... “practices that were expected to be

common ..”

5. 18/10

- “.. there is still much benefit to be gained from....services delivering sleep education.”
- I can only agree with the authors. As this paper clearly describes these sleep issues are common in our society with significant consequences. Seeking effective, low cost support services is important.
- This study was so well designed and the described information given to the patients of such clarity I have been surprised at a lack of provable efficacy.

6. 18/47

- “.. infant night waking in the first 6 months is considered to be normal, ..”
- the authors are very complete in mentioning such alternative paradigms but I strongly disagree with the alternative. To do so is simply stating that we, as caring professionals, are having trouble proving methods which improve infant sleep we should accept defeat and redefine the problem as normal.
- I do not recommend any revision to the paper as I feel that it is clearly written and an honest statement of competing philosophies.

7. 38/41

- 'Allow 2-3 minutes of self settling in the first month and five minutes at three months'.
- No revision is recommended as this is a correct reporting of the recommendations of the study.
- My professional work is focused on the care of neonates with feeding and sleep problems. My experience is that parental responsiveness which is as rapid as 2-5 minutes is too fast. That even quite young babies can rapidly learn behaviours of distress as the parents will respond within a few minutes. It is my experience that self settling can take longer, particularly if the infant is over tired or hungry or both, and that a slower parental response is needed to assist in the development of truly independent and high quality self settling sleep skills. In fact such rapid responses can, in a behavioural sense, increase parent seeking behaviour by the infant.

Conclusion.

I found the paper extremely well written. The study is easy to comprehend and the data is presented in a manner that it can be easily understood. The authors also highlight the social importance of this problem in our society.

	<p>I recommend publication as it adds to the literature in the field.</p> <p>I can add my hypothesis on why the intervention failed.</p> <ol style="list-style-type: none"> 1. The parent response times recommended were too rapid. My experience is that this in fact can amplify rather than decrease parent seeking by the infant. As a result the excellent information given to the parents about infant sleep hygiene was possibly counterbalanced by encouraging a response time which was too short. 2. Complementary feeding was not encouraged until 6 months and exclusive breast feeding was encouraged for that time. Again it is my experience that large number of infants need additional nutrition long before 6 months. If a proportion of the infants were truly hungry then they, as babies, have no choice but to increase night time feeds to attempt to maintain an appropriate velocity of growth.
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Lauren Philbrook

Institution and Country: Auburn University, USA

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

This study examined the effectiveness of intervention program aimed at improving infant sleep, settling and safe sleep practices, and parent mental health and sleep across the transition to a new baby. Strengths of the study include a large sample size and advanced statistical methodologies to evaluate study hypotheses. Furthermore, the intervention includes a session delivered prior to the birth of the infant; as described by the authors, little work has explored the utility of prevention programming to improve infant sleep and therefore this is an important empirical question. The manuscript is well-written and the introduction nicely frames the results. My concerns are minor and mostly are regarding the methods and the interpretation of the results.

Introduction

1. If space requirements allow, I think the authors could consider briefly highlighting mechanisms via which poor sleep in infancy may translate into increased risk for obesity in childhood, particularly because the overall intervention program was aimed at reducing obesity outcomes.

A brief coverage of this has been added to the Introduction (Page 6 para 2) stating: "In exploratory analyses, the trial found a protective effect for obesity among groups receiving the sleep intervention.[31] The exact mechanisms by which sleep could influence obesity in early life are unclear, although the ability of an infant to learn to self-regulate his/her own sleep is considered one of the earliest biological markers of self-regulatory behaviours.[32] This enhanced sleep self-regulation could conceivably help shape other self-regulatory behaviours linked to healthy weight. Other potential mechanisms linked to insufficient sleep in children and adults include changes in

neurohormonal control of appetite regulation, impacts on dietary intake, and increased sedentary activity –all favouring weight gain.[33]

2. I found the first sentence of paragraph 3 on page 5 to be a little confusing. It is stated that prior interventions focused on improving infant sleep have shown small to medium effects on infant nocturnal sleep time and small impacts on infant sleep- are those two pieces of information distinct from one another?

We agree this was confusing. The section has been amended to make a clearer distinction between the findings of the two interventions (Page 5 last para).

Method

3. As noted in the Study Design section, data from baseline and 6 months of age are reported in the current paper. I wonder if perhaps the authors will be more likely to see significant effects later in the infant's life, when night wakings are less normative. Table 3 shows that on average parents were aware of 1-2 infant night wakings per night, suggesting that only a small minority of babies were sleeping throughout the night on their own. Is it possible that greater intervention effects will be seen when a larger percentage of infants develop a capacity for self-regulated sleep? Perhaps then the intervention will result in decreased likelihood of problematic sleep problems.

We agree with the reviewer that this is a valid proposition. However, these data were analysed for our paper on the main outcomes from our RCT and indicated that no differences were apparent in the number of night wakings at 1-2 years of age. Ref # 31.

4. Were there any missing data? If so, how was it accounted for?

Yes there were missing data. No formal treatment was made for missing data (the magnitude of missing data is indicated by the sample size for each model reported in the tables). This assumes that the missing data were missing completely at random or missing at random conditioning on the stratification variables (family SES and parity). Education and income effects on missing data are likely to be partially incorporated via the small area (meshblock) NZ Deprivation categories, which are also based on other measures likely to be associated with missing data including transport, employment, and Internet access.

5. I think it would be helpful to know how many days of actigraphy information infants had on average. (Did all infants have between 5-7 days?) Did any infants have fewer than 5 days of data, and if so, was their data included in the analyses?

The footnote to Table 3 indicates the data were from a mean of 3-7 days of actigraphy, with a median of 4 days. Children had to provide at least 3 days of data to be included in analyses – this has been added to the footnote.

6. Was whether the infant was sick or on medication during the sleep assessments accounted for in the analyses?

Information on frequency of medication use over the last 2 weeks was asked at the 4 month and 6 month assessments. The prevalence of infants taking medication (almost exclusively paracetamol) on 5-6 nights or more over the last two weeks was small (1.1% at 4 months and 2.7% at 3 months). Given these small percentages and the fact that paracetamol is commonly given in this population, medication was not taken into account in the analyses. Assessments of infants unwell at the time of data collection were postponed until the infant had recovered.

7. I think it would be helpful to include the full name of the EPDS in the manuscript text. I apologize if I missed this.

Thank you for pointing this out. The full name was included, but we had omitted the abbreviation the first time EPDS appeared in full. The abbreviation has been added (Page 10, Para 1).

Results & Discussion

8. I agree with the authors that a potential explanation for fewer significant effects than expected could be due in part to the sample being relatively low-risk and well-educated. However, since there is some variability in education and family income, I wonder if it might be possible to examine whether the intervention was more effective in improving infant and parent sleep, parental well-being, and safe sleep and settling practices for the more at-risk families in the sample?

We acknowledge the point but feel it is beyond the scope of this particular manuscript to include separate analyses of data from high-risk families. Furthermore such analyses were not pre-specified and the study was not powered for investigating intervention effects in these high-risk groups.

9. I am curious about the extent to which the authors believe the results could be impacted by parental leave policies in New Zealand. If one or both parents is able to stay home with the baby for an extended period, might they be less likely to rate the infant's sleep as problematic, and perhaps less concerned about the infant quickly learning to develop self-regulated sleep?

There are many factors influencing mothers', and indeed fathers', perception of their infant's sleep as problematic and as such a much larger study would be required to tease out this aspect. However it is worthy of consideration for future studies, given that some of the stresses around sleep loss and early start times may be alleviated for the non-working parent. This assumes of course that nocturnal sleep rather than daytime napping is the most problematic.

10. I thought it was notable that the authors observed that parents were only slightly more likely to put the infant to sleep awake in the intervention compared to control groups. Since a similar minority of participants continued to lay the baby down asleep regardless of intervention, I wonder if there might be barriers to putting the baby down awake (e.g., "I can't listen to the baby cry; the baby always falls asleep feeding") that could be integrated into the intervention in the future, if they are not already

Thank you. Anecdotally it was not uncommon for the mothers to express concerns about not wanting to let their infant cry to sleep. This could have been a potential barrier and reason why uptake of "putting baby to sleep awake" was low. We did educate parents regarding the normalisation of infant crying but perhaps more emphasis was required. For future studies it would be worth considering the commitment and acceptance theory that forms the basis of the Possum program as proposed by Whittingham & Douglas (Infant Ment Health J 2014;35:614-23) for managing infant sleep problems. A further consideration is to encourage another caregiver (not so emotionally impacted by the crying) to take over some of the responsibility for laying the baby down to sleep whilst still awake.

Reviewer 2

Dr Brian Symon

This is a very well written study with an excellent design structure. There are some issues that I feel would allow publication with minor revisions.

These are mentioned in the order of appearance in the text.

1. Page 7, line 32 (7/32)

◦ the text "iii)" is absent

The missing numeral has been inserted (page 7 last para).

2. 9/5:

- 7 “delaying the introduction of complementary foods until around 6 months of age.”
- this point does not need revision as it reflects the teaching utilised in the study.
- My reason for mentioning this is that latest research suggests that earlier introduction of allergenic proteins decreases the risk of food allergy particularly with peanuts.
- Du Toit G, Katz Y, Sasieni P, et al. Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy. *J Allergy Clin Immunol* 2008;122: 984-991.
- as a clinician it is my experience that early introduction of complementary foods has a major positive impact on sleep performance particularly in boys and even more particularly boys who are genetically destined to be tall.
- The intervention as studied has shown no significant improvement in sleep performance at 6 months. As a clinician working in the field I believe that one of the reasons for failed impact is that complementary feeding was delayed by the teaching protocols and that the maintenance of relative hunger delays the development of good sleep patterns. I do not write this as a criticism of the paper.

Thank you. Your comments have been noted. The protocol for delaying complementary foods followed the recommendations of the New Zealand Ministry of Health (Food and nutrition guidelines for healthy infants and toddlers (aged 0–2): a background paper. 4th ed. Wellington (New Zealand): New Zealand Ministry of Health; 2008), and recommendations in many other industrialized countries (including the US, UK, and Australia), that complementary foods should be introduced at around 6 months of age, and that parents should be guided by their infant’s developmental readiness.

3. 12/52

- The data shows increases in a perception of a sleep problem for both mothers and partners when comparing 4 to 6 months. For mothers there is a 30% increase in reports of infant sleep problems and for partners 42% increase. My point is that by 6 months an increasing proportion of families saw their infant’s sleep as a problem compared to 4 months. I am unable to see analysis of that data. While 80.1% of mothers at 6 months were not reporting a sleep problem the proportion of mothers reporting a problem was increased. This might be worthy of a small comment.

We acknowledge the reviewer’s point that more mothers and partners appeared to indicate their child had a sleep problem (16.1% and 19.9% of mothers at 4 and 6 months respectively, and 11.7% and 16.6% of fathers at the same time points) but have not included any comment on this in the paper given this was not a pre-specified analysis and given the word constraints.

- At 6 months mothers were significantly more likely to report a sleep problem than partners ($p = 0.050$). This probably reflects that the mothers are taking primary responsibility for the waking child.

We agree this is probably the case, but as the question asked “whether their child’s sleep was a problem for them” and was not restricted to problems with night waking, we can’t confidently make that statement.

4. 18/5

- remove the word 'expectantly' as it adds little to the meaning of the sentence or if the authors prefer if could possibly read ... “practices that were expected to be common ..”

This has been changed to read ... “practices that were expected to be common”...(page 18, para 2)

5. 18/10

- “.. there is still much benefit to be gained from....services delivering sleep education.”
- I can only agree with the authors. As this paper clearly describes these sleep issues are common in our society with significant consequences. Seeking effective, low cost support services is important.
- This study was so well designed and the described information given to the patients of such clarity I have been surprised at a lack of provable efficacy.

Thank you for your comments.

6. 18/47

- “.. infant night waking in the first 6 months is considered to be normal, ..”
- the authors are very complete in mentioning such alternative paradigms but I strongly disagree with the alternative. To do so is simply stating that we, as caring professionals, are having trouble proving methods which improve infant sleep we should accept defeat and redefine the problem as normal.
- I do not recommend any revision to the paper as I feel that it is clearly written and an honest statement of competing philosophies.

Thank you for your comments. We feel it is important to acknowledge these alternative paradigms.

7. 38/41

- 'Allow 2-3 minutes of self settling in the first month and five minutes at three months'.
- No revision is recommended as this is a correct reporting of the recommendations of the study.
- My professional work is focused on the care of neonates with feeding and sleep problems. My experience is that parental responsiveness which is as rapid as 2-5 minutes is too fast. That even quite young babies can rapidly learn behaviours of distress as the parents will respond within a few minutes. It is my experience that self settling can take longer, particularly if the infant is over tired or hungry or both, and that a slower parental response is needed to assist in the development of truly independent and high quality self settling sleep skills. In fact such rapid responses can, in a behavioural sense, increase parent seeking behaviour by the infant.

Thank you. Your comments are well noted.

Conclusion.

I found the paper extremely well written. The study is easy to comprehend and the data is presented in a manner that it can be easily understood. The authors also highlight the social importance of this problem in our society. I recommend publication as it adds to the literature in the field. I can add my hypothesis on why the intervention failed.

1. The parent response times recommended were too rapid. My experience is that this in fact can amplify rather than decrease parent seeking by the infant. As a result the excellent information given to the parents about infant sleep hygiene was possibly counterbalanced by encouraging a response time which was too short.

2. Complementary feeding was not encouraged until 6 months and exclusive breast feeding was encouraged for that time. Again it is my experience that large number of infants need additional nutrition long before 6 months. If a proportion of the infants were truly hungry then they, as babies, have no choice but to increase night time feeds to attempt to maintain an appropriate velocity of growth.

Thank you once again, and we will take these comments into consideration when planning future infant sleep interventions.

VERSION 2 – REVIEW

REVIEWER	Lauren Philbrook Auburn University, USA
REVIEW RETURNED	19-Mar-2017

GENERAL COMMENTS	I very much appreciate the authors' thorough and thoughtful responses to all of the points raised by the reviewers. I look forward to seeing the paper published.
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REVIEWER	Dr Brian Symon Kensington Park Medical Practice 84 Shipsters Rd Kensington Park South Australia 5068 Australia
REVIEW RETURNED	24-Mar-2017

GENERAL COMMENTS	I have read all edits in this revised version and feel that both reviewers concerns have been well addressed.
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VERSION 2 – AUTHOR RESPONSE

Thank you for your comments received today (31 March) requesting minor revisions to the manuscript. We have made those minor revisions as outlined in the reviewer response section and look forward to your response.

VERSION 3 – REVIEW

REVIEWER	Lauren Philbrook Auburn University, USA
REVIEW RETURNED	31-Mar-2017

GENERAL COMMENTS	I think the authors have made appropriate changes to the manuscript in response to the editor's feedback.
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REVIEWER	Dr Brian Symon Kensington Park Medical Practice
REVIEW RETURNED	09-Apr-2017

GENERAL COMMENTS	This appears to be the same paper that I have previously reviewed and accepted after minor revisions.
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