

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Bed sharing when parents do not smoke: Is there a risk of SIDS? An individual level analysis of five major cases-control studies.
AUTHORS	Carpenter, Robert; McGarvey, Cliona; Mitchell, Edwin; Tappin, David; Vennemann, Mechtild; Smuk, Melanie; Carpenter, James

VERSION 1 - REVIEW

REVIEWER	Professor Rosemary Horne NHMRC Senior Research Fellow Deputy Director The Ritchie Centre Monash Institute of Medical Research Monash University, Melbourne, Australia
REVIEW RETURNED	01-Dec-2012

GENERAL COMMENTS	<p>Despite the dramatic decline in the Sudden Infant Death Syndrome (SIDS) in western countries following the identification that the practice of sleeping babies on their tummies or prone significantly increased the risk for SIDS, SIDS remains the largest cause of postneonatal death, contributing to around 50% of all deaths in infants aged 1 month to 1 year. Recently there has been concern raised in a number of countries about the finding that half of infants who die from SIDS are found in a bed sharing situation. This has been very prominent in Australia where coroners from at least three states have been vocal in urging governments to ensure that parents are aware of the risk of sleeping with their infant. In the USA several states have launched "fear campaigns" with graphic advertising to try to alert parents to the dangers. Despite a number of meta-analyses of SIDS case studies there is still resistance from most countries to actively advocate that parents do not bed share. Only the Netherlands and American Academy of Pediatrics have advertised clear messages. Parents seem generally confused about the messages given by most SIDS prevention organisations believing that if they do not smoke, drink alcohol or take drugs and breast feed there is no risk to their infant.</p> <p>This is an extremely important paper which has found that bed sharing with an infant significantly increases the risk of SIDS five fold even if the parents do not smoke and the infant is breast fed. The risk is further dramatically increased if parents do smoke, drink alcohol or take drugs and this is particularly the case in infants under 3 months of age. The paper is well written and combines data from 5 previous studies in the UK, New Zealand and Germany and a large multicentre European study with 1472 SIDS cases and 4679 controls. The statistical analysis is extremely comprehensive and exhaustive and although not an expert in this field all the assumptions made have been extensively justified. A strength of the paper is that three of the authors are senior statisticians. The findings are extremely important as many parents take their infants into bed believing that if they do not smoke the baby will be</p>
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	<p>safe. Bed sharing is now the biggest risk for SIDS and there is strong pressure from the breast feeding lobby including the UNICEF baby friendly hospital initiative that bed sharing should be promoted to encourage breast feeding. The paper discusses this and provides new evidence from the Netherlands that despite a significant decrease in the incidence of bed sharing following their “safe sleeping” campaign to alert parents to this risk, the breast feeding rate has increased.</p> <p>It is critical that parents and health care professionals are provided with the most up to date and correct information to make informed choices based on the best scientific evidence. It is also critical that this message gets out to midwives and infant welfare nurses as there has been an alarming increase of infant deaths whilst on the neonatal ward when mothers have been encouraged to breast feed their infant in bed whilst exhausted and under the influence of pain reducing medication.</p> <p>The Tables are clear and Figures informative.</p> <p>Minor comments</p> <p>There are a few minor comments mainly on grammar.</p> <p>Abstract page 2 line 17 add potential confounding factors. Line 28 AOR is not defined Article summary line 49 How is SIDS risk; line 52 increase the risk of SIDS; line 57 replace It with This is</p> <p>Background page 4 line 4 add the Sudden Infant.. Line 18 relace or with but Line 28 add to the different ways Line 35 perhaps state what “the most important risk predictors” are</p> <p>Material and Methods page 4 Line 43 define ECAS Line 51 add when one or both Line 56 add partially or completely breastfed Page 5 line 8 “ and position the infant was last placed” Line 11 add the mother’s alcohol Line 12 delete “of” sixteen</p> <p>Statistical analysis Line 20 the number of control was per case? Line 27 replace children with infants The first table mentioned is Table 3</p> <p>Figure 1 it is unclear exactly what Density is can unit be provided?</p> <p>Page 6 line 33 add “SIDS” risk Line 46 should see appendix be in brackets?</p> <p>Page 7 line 57 Table 2 “also” shows</p> <p>Page 8 line 2 increases “the” risk Line 12 replace groups with group Line 15 add average “risk” for the first 3 months Line 24 add “the” baby Line 51 replace in with is</p> <p>Page 9 line 10 mother aged Discussion line 32 and does not co-sleep</p>
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	<p>Line 34 The review by Mitchell was unable to quantify these risks, suggest but they were not quantified be changed to reflect this. Line 40 replace relating with related Line 44 Replace it may be objected with It could be suggested that or something similar. Line 47 replace of with pertaining to mother's alcohol</p> <p>Page 10 Tot strengthen the first sentence In particular could be replaced with Of importance Line 17 add mother's alcohol "consumption Line 27 It is unusual to have a footnote in a scientific paper and the footnote could simply be added here to the main text. ONS should be defined. Line 30 Table Line 34 add this "rate" is Line 42 NHS needs to be defined as all readers will not be in the UK.</p> <p>Page 11 Line 14 prone should be added after front</p> <p>Page 15 under consistent it would be good to add the number of studies being referred to here.</p> <p>Appendix: Statistical methods Page 20 Line 38 it is unclear what centres are, are these the different studies? Line 46 define MAR.</p> <p>Page 22 line 4 Model 2 requires a capital for consistency and replace children with infants. Line 18 Model Line 31 bed sharing Line 32 replace 1st with first.</p>
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REVIEWER	<p>Rachel Moon, MD Professor of Pediatrics Children's National Medical Center/George Washington University School of Medicine and Health Sciences USA</p> <p>Statement of competing interests: I am a SIDS researcher. I declare no conflict of interest.</p>
REVIEW RETURNED	13-Dec-2012

GENERAL COMMENTS	<p>This is an excellent, well-written paper that helps to answer a question that has been debated for years. I have a few suggestions for clarification:</p> <ol style="list-style-type: none"> 1) Abstract, Results: "Bedsharing risk decreased with infant age." Suggest alternative wording: "Bedsharing risk decreased with INCREASING infant age." 2) Material and Methods, Notes on explanatory variables, Breast fed: Change to "infant was being partially OR completely breast fed..." 3) Materials and Methods, para 3: Please clarify the sentence about how babies who were sofa-sharing were handled. Were they included as cases? As controls? Were they excluded from the analyses? 4) Materials and Methods, para 3, last sentence: This sentence needs to be clarified: "In total of 16 variables..." 5) Results, Calculation of AORs for other risk groups, line 4: please correct sentence to "Thus at 2 weeks the AOR..."
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	<p>6) Results, Calculation of AORs for other risk factors, first line after AOR calculation: please clarify sentence. Should this read: "If, using Table 2 we replace 65.1 WITH 2.9...."</p> <p>7) Results, Calculation of AORs for other risk factors, last line: please change to "...infants will multiple risk factors are likely to be at far greater risk than IS generally supposed."</p> <p>8) Table 4: please clarify, either in text or in table: For what age infants are these analyses appropriate? Less than 3 months or older than 3 months?</p> <p>9) Discussion, para 8, first line: Please change to "...suggests that the promotion OF breast feeding..."</p> <p>10) Discussion, para 9, line 7: "place" should be "placed"</p> <p>11) Discussion, para 9, line 11: change "loosing" to "losing"</p> <p>12) Discussion, para 10, line 1: please change to "being placed on the front for sleep..." ("Put down", in the US, is the term that is used for animal euthanasia)</p>
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REVIEWER	Blair, Peter University of Bristol, Community Based Medicine
REVIEW RETURNED	30-Dec-2012

THE STUDY	More clarity is needed regarding how the differences in the data from the 5 studies were resolved, how missing data was checked and whether data can be imputed when whole studies did not ask certain questions. Interpretation of the findings also needs more clarity especially in terms of the reference groups used. the emphasis placed on teh findings is also questionable.
RESULTS & CONCLUSIONS	The message is clear but does not necessarily fully reflect the findings presented. Perhaps my review needs to be read to understand why I responded 'No' to some of these questions.
GENERAL COMMENTS	<p>I have reviewed this manuscript previously and still find the major points I raised have not been addressed by the authors. The primary focus of this paper, stated in the article summary, is to answer the question "Is there a risk of SIDS due to bed-sharing when baby is breast fed, the parents do not smoke and the mother does not use alcohol or illegal drugs?" This question cannot be addressed when only two of the five studies collected data on maternal alcohol consumption, none of them collected data on the use of illegal drugs prior to bed-sharing and the question is confined to one co-sleeping parent when there are often two .</p> <p>The success of SIDS research in the last few decades has been an iterative process focussing closer and closer on the potential risks within the infant sleep environment prior to death. We have been able to utilise this cumulative knowledge in our latest UK case-control SIDS study in 2003-6 (BMJ 2009;339:b3666) and asked (what now seem obvious questions) who exactly was sleeping next to the baby for the last sleep and how much alcohol or drugs had they consumed. We found a significant interaction and nearly a third of the deaths occurred in these circumstances. The potential role of parental alcohol and drugs in these bed-sharing deaths may also go some way in explaining the increased risk of bed-sharing amongst smokers in that this may act as a proxy if questions regarding alcohol and drugs were not asked.</p> <p>The over-arching argument is thus whether bed-sharing in itself poses a risk to infants or whether the risk is within the hazardous circumstances in which we bed-share. These older studies (data collected between 1987 and 2003) do not have the data to resolve this argument.</p>

	<p>I'm sure it is a difficult task trying to combine data from different studies conducted in different countries at different time periods but there seems additional complexity in the way the data has been analysed in terms of the reference groups chosen and the interpretation placed upon them. I'm also a little perplexed that the authors seem to be advocating a ban on bed-sharing when their own findings seem to indicate a massive interaction with the hazardous circumstances in which these infants were found.</p> <p>Major Points</p> <p>i) Different studies used different definitions for bed-sharing. The Scottish study for instance denoted an infant bed-shared even if they bed-shared some time during the last sleep but were then placed back and found in the cot. Also the New Zealand study had no reference sleep for the control infants and thus (from memory) defined a bed-sharing infant as one that usually bed-shared in the two weeks before the last sleep. How have these differences been reconciled? Stating in the material and methods section (Page 4, line 54) that 'equivalent questions' were used does not provide enough detail.</p> <p>ii) The authors also state (page 9, lines 46 to 51) that for studies where questions on maternal alcohol use and drug use were not included they have "gone back to the original records of breast fed bed-sharing cases when both the mother and partner were non-smokers and established that neither alcohol nor drug use contributed in any way to any of these deaths." Firstly if this could be done it should be done for all cases and controls where possible not just a small subgroup and secondly what do the authors actually mean by this? If questions regarding parental alcohol and drug use were not asked in a detailed research investigation it is unlikely they would have been asked consistently or at all during the coronial investigation. Absence of these pertinent factors could mean that alcohol and drugs were not used but just as likely this could also mean these questions were not asked.</p> <p>iii) None of the studies collected data on parental drug consumption prior to the last sleep of the SIDS infant or the reference sleep of the controls (usually within 24 hours of the interview). Using maternal use of illegal drugs after birth is a poor proxy of the circumstances surrounding the final event. We have shown in our previous larger SIDS study conducted in the 1990's that data on routine use for any factor is a poor marker for what actually happens in the last 24 hours. The authors need to acknowledge that they simply have not got the data to adjust for this important factor.</p> <p>iv) None of the studies collected data on paternal alcohol consumption preceding the last sleep. The authors need to acknowledge that the risk to the infant could come from one or both parents and data on what each parent consumed and the exact sleeping arrangements needs to be collected to properly assess whether a co-sleeping environment is hazardous. Specifically any analysis needs to take into account which parent or parents were sleeping next to the infant.</p> <p>v) Maternal alcohol consumption prior to the last sleep was collected but only for 38.7% of the mothers in the study. Imputing values for parental and alcohol drug consumption on a particular night from a single study when more than 50% of the data is missing requires a fairly homogeneous population and good predictors of 'missingness'. Imputing values from a group of 5 studies, 3 of which did not even ask the question is surely making unreasonable equivalence assumptions across studies conducted in different countries with different cultures in different time periods. In fact one of the two</p>
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studies where some of this data was collected was a multi-centre study of 20 regions across Europe; cultures with different drinking and drug habits. Just how one randomly selects a potential catastrophic event such as a parent drinking too much alcohol or taking drugs (cannabis, methadone, heroin, etc) before bed-sharing on the final night seems an impossible task.

vi) In Table 3 and the abstract much is made of the risk associated with bed-sharing in the absence of other factors (AOR=5.1 (2.3-11.4)) but more clarity is needed to describe what this means? According to the Table the reference group seems to be infants < 3 months old who are room-sharing with parents who did not smoke or drink alcohol but the text also suggests these infants were also breastfed, female and placed supine (page 8, line 11 to 15). If so, then should the fivefold risk be attributed to bed-sharing on its own or is there a combined risk including bottle fed infants, male gender and those placed prone. If these factors (gender, mode of feeding and sleeping position) are adjusted for in this analysis (it is not made clear) then does not using such a low risk reference group inflate the risk of the other factors? For instance although there is a 5-fold risk for bed-sharing there is a 13-fold risk when the infants sleeps in the cot next to the bed of parents who smoke and have drunk alcohol. I would have also thought more emphasis would have been put on the finding in the same table that when the parents smoked and bed-shared the risk increased to 21.8 (11.2-42.6) and when the parents also drank alcohol the risk increased to 151.0 (50.6-450.7)! In fact perhaps the most surprising finding in this table is that although the risk associated with bed-sharing in the absence of alcohol and smoking was unity amongst infants aged 3 months or older it was 243.8 (76.1-781.4) when smoking parents drank alcohol and bed-shared which should surely be the finding to emphasise in any abstract.

vii) The authors argue that in itself the act of an infant lying next to a sleeping adult is causal but this argument using the Bradford Hill criteria is fairly weak. The data cannot really be adjusted for recent alcohol and drug consumption so the contention that there is a strength of association in the absence of known factors does not really stand up. The consistency of findings amongst case-control studies is not comprehensive and there is certainly ecological data suggesting low SIDS rates amongst some populations that often bed-share (see point viii). The evidence of a dose response effect and an analogous example are weak at best but perhaps the argument for coherence is the most surprising. Given this study shows a 10 fold greater risk of bed-sharing amongst smokers (Fig 2), a 90 fold risk of bed-sharing when alcohol was involved (at 2 weeks) and an 'inestimably large' risk associated with stronger drugs than cannabis surely causality is more soundly argued on the basis of potential overlaying for many of these bed-sharing deaths in hazardous circumstances rather than weakly asserting it is the bed-sharing itself and not the way we bed-share that puts infants at risk.

viii) The authors in the discussion (page 10, lines 35 to 40) suggest bed-sharing in the Netherlands has fallen whilst the breastfeeding rates have slightly risen. What they don't say is whether the SIDS rate has changed in this period (I don't think it has) or whether there is any published evidence supporting a relationship between bed-sharing and breastfeeding in the other direction. Ecological data suggest there are several countries or cultures where bed-sharing and breastfeeding are quite prevalent and the SIDS rate fairly low (Sweden, Hong Kong, Japan, Brazil, Hispanic families in the US, Asian families in the UK). We have also shown an interdependent relationship between bed-sharing and breastfeeding (Blair PS,

	<p>Heron J, Fleming PJ. Relationship between bed sharing and breastfeeding: longitudinal, population-based analysis. <i>Pediatrics</i> 2010;126(5):e1119-26) and any discussion of this relationship surely needs to be more balanced.</p> <p>ix) It is not clear but Figure 2 appears to be a subgroup analysis of bed-sharers across age involving only those who breastfeed and bed-share and only those families where either both parents smoke or neither. Further, both the legend and the text suggest the odds ratios have been adjusted for alcohol and drug use. Given the limitations of what has been collected I don't think this can be stated and given alcohol and drug use is probably more common amongst bottle feeding mothers it is important to include all the data split by any smoking/no smoking (rather than drop data where one parent smokes) and adjust for mode of feeding (rather than drop the data on bottle feeders completely).</p> <p>x) The lack of any analysis on sofa-sharing is disappointing, the New Zealand study did not ask about sofa-sharing but the other 4 studies did. The results suggest a much stronger risk with sofas than parental beds and a strong interaction with alcohol or drugs. The data on co-sleeping on a sofa should either be handled as a separate group or analysed together with bed-sharing to evaluate the risk of co-sleeping in general; combining this group with infants who slept in a cot (Table 1) or ignoring this group altogether (Tables 2,3 and 4) makes the interpretation of the risk associated with bed-sharing difficult.</p> <p>xi) In their conclusion the authors suggest the campaign used to reduce prone sleeping, which halved the SIDS rate, could be adopted to reduce bed-sharing claiming a potential further drop in SIDS rates of 88%. This is a poor analogy, prone sleeping was foisted onto parents in the 1950's and thus easier for them to relinquish as an infant care practice whilst bed-sharing has been practiced for thousands of years, is culture specific and potentially related to an increased duration of breastfeeding. I'm not sure how they derive an 88% reduction (half of SIDS infants are found co-sleeping up to a third of which are found on a sofa) but current campaigns do not support their contention. In the US the indication is that bed-sharing rates have increased, despite the American Academy of Pediatrics advising against bed-sharing for the last 6 years and State-specific aggressive campaigns depicting mothers as meat cleavers sleeping next to the child and parental bed-headboards as tombstones, yet the SIDS rate has remained static.</p> <p>More Minor Points</p> <p>i) In the background the authors suggest the UNICEF baby friendly website (reference 13) and NCT website (reference 14) actively promote bed-sharing. The UNICEF website page quoted no longer seems available. However the current UNICEF page related to this http://www.unicef.org.uk/BabyFriendly/Resources/Resources-for-parents/Caring-for-your-baby-at-night/) shows published evidence of a link between breastfeeding and bed-sharing and seems to acknowledge that bed-sharing is a recognised infant care practice but does not tell parents to bed-share. Again on Page 10 (lines 42-44) suggest UNICEF promotes bed-sharing which it doesn't. Similarly the NCT website acknowledges the SIDS evidence and that bed-sharing can occur (both intentionally and unintentionally) but does not actively promote bed-sharing. These references either need removing or rephrasing.</p> <p>ii) The claim by the authors that "the results from analysis of the completed data will primarily depend on the observed data, and only slightly on the imputed data" (Page 9, lines 54-55) seems incongruous to the fact that over 60% of the maternal alcohol data</p>
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	was missing and was therefore imputed.
REVIEWER	Prof Ruth Gilbert Professor of Clinical Epidemiology, UCL Institute of Child Health, UK. No competing interests.
REVIEW RETURNED	14-Jan-2013

GENERAL COMMENTS	<p>This is an really excellent, thorough and carefully presented paper reporting unique results that are extremely important for policy and practice.</p> <p>Minor comments</p> <ol style="list-style-type: none"> 1. Abstract: results: The fact that the absolute risk is not directly derived from the study but estimated would be clearer if described as 'estimated absolute risk'. 2. It would assist assessment of the implications for individual women if the number needed to harm (NNTH) by bed sharing vs not could be derived from the estimated absolute risk difference for some illustrative examples (and mentioned in the abstract). 3. Abstract- conclusion: The wording should be changed to indicate that a substantial reduction could be achieved if parents avoided bed sharing. It is not at all clear how effective discouraging bed sharing might be (wording also relevant to key messages). 4. The conclusion could give more guidance about how the findings inform policy and individual decision making. The clear evidence of harm associated with bed sharing means that policy that advocates bed-sharing cannot be justified. The results support health promotion messages to all parents to avoid bed sharing. Given the low risk of SIDS however, some parents with strong preferences for bed sharing may choose to accept the very small increased risk of SIDS. 5. The conclusion includes the figure of 50% - which is worded as the population attributable fraction. It would be helpful if the authors could briefly mention how this was calculated in the discussion. 6. Background para2 last line: It would be clearer to write "some do not discourage bed sharing but actively promote it" 7. Discussion. The shift from 22% of SIDS bedsharing in the study to 50% now may represent a population shift towards more bedsharing or a change in the risk profile of SIDS. Could the authors comment on the explanation and whether this is likely to change their adjusted odds ratios? For instance, the risk of SIDS associated with front sleeping increased as health promotion messages to avoid front sleeping SIDS were adopted more by low risk than by high risk parents.
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VERSION 1 – AUTHOR RESPONSE

Response to Dr. Alison Walker's and Referees' Comments

In this comment and response section the referees comments are in Tahoma italics script, and the responses are in Times New Roman.

From the managing editor, and Dr Alison Walker, associate editor:

Regarding the Horne, Moon and Gilbert reviews: please do respond to these reviewer comments. In particular the comment regarding the number needed to harm (NNTH) by bed sharing vs not as suggested by Ruth Gilbert (and mentioned in the abstract).

NNTH is a poor statistic and often incorrectly interpreted – see response to Professor Gilbert's comments. The estimated rates and rate ratios, together with their confidence limits present the results clearly and in a manner that can readily be understood.

Please also be much more cautious about the causality message; we suggest you remove this from the conclusion in the Abstract. The title also needs to state the study design and research question. We much prefer titles that frame a research question and study design as this is much more useful when researchers find articles via search engines and indexes. 'Headlines' could be to comment, editorials, news items, press releases, etc.

We have replaced the title, as requested. Now reads: "Bed sharing when parents do not smoke: Is there a risk of SIDS? Findings of a combined analysis of five case-control data sets."

The conclusions in the abstract have been amended as follows: "Bed sharing for sleep when the parents do not smoke or take alcohol or drugs increases the risk of SIDS. Risks associated with bed sharing are greatly increased when combined with parental smoking, maternal alcohol consumption and/or drug use. A substantial reduction of SIDS rates could be achieved if parents avoided bed sharing."

There is also a review from Dr Blair. We accept the potential for dispute here. However we would appreciate your response (some of which will duplicate your response to his review at the BMJ which was not provided to BMJ Open at the time of these reviews) and specifically we would like you to respond to Blair's point vii and the arguments saying B-Hill's causality criteria are weak, in the manuscript.

In response to your request we have amended the panel to make clear that, in our view, it establishes bed sharing as a cause of SIDS in the absence of smoking, alcohol or drugs. We have also added a few sentences to the text.

We have responded to Dr. Blair in detail below. Dr. Blair refuses to accept that bed sharing in itself is carries a risk of SIDS, which includes suffocation because the two are generally indistinguishable. We believe that the data show that it is.

We appreciate the favourable comments by Professor Rosemary Horne and Professor Rachel Moon, and we have accepted their corrections to our text, which are most helpful. Some of Professor Ruth

Gilbert's thoughtful minor comments require two additional short paragraphs at the end of the discussion.

Response to Dr. Ruth Gilbert's minor comments

1. *Abstract: results: The fact that the absolute risk is not directly derived from the study but estimated would be clearer if described as 'estimated absolute risk'.*

Accepted

2. *It would assist assessment of the implications for individual women if the number needed to harm (NNTH) by bed sharing vs not could be derived from the estimated absolute risk difference for some illustrative examples (and mentioned in the abstract).*

We do not think that it would be helpful to report NNTH. We note that like its companion statistic, NNT, it is seldom correctly understood, is biased, and reliable confidence intervals cannot be provided. (Hutton JL. Misleading Statistics. The problems Surrounding Number Needed to Treat and Number needed to Harm. 2012 Pharm. Med. 24; 143-9). We report estimated Absolute Risk and Risk Ratios, together with their confidence limits for a number of representative groups, and in the appendix show how absolute risks may be calculated for other groups.

3. *Abstract- conclusion: The wording should be changed to indicate that a substantial reduction could be achieved if parents avoided bed sharing. It is not at all clear how effective discouraging bed sharing might be (wording also relevant to key messages).* Accepted

4. *The conclusion could give more guidance about how the findings inform policy and individual decision making. The clear evidence of harm associated with bed sharing means that policy that advocates bed-sharing cannot be justified. The results support health promotion messages to all parents to avoid bed sharing. Given the low risk of SIDS however, some parents with strong preferences for bed sharing may choose to accept the very small increased risk of SIDS.*

5. *The conclusion includes the figure of 50% - which is worded as the population attributable fraction. It would be helpful if the authors could briefly mention how this was calculated in the discussion.*

6. *Background para2 last line: It would be clearer to write "some do not discourage bed sharing but actively promote it"*

See revised text.

7. *Discussion. The shift from 22% of SIDS bedsharing in the study to 50% now may represent a population shift towards more bedsharing or a change in the risk profile of SIDS. Could the authors comment on the explanation and whether this is likely to change their adjusted odds ratios? For instance, the risk of SIDS associated with front sleeping increased as health promotion messages to avoid front sleeping SIDS were adopted more by low risk than by high risk parents.*

Two paragraphs have been included at the end of the discussion in response to points 4 to 7.

Response to Reviewer 3's comments

We welcome Dr. Peter Blair's comments because, despite the major contributions that he and his colleagues have made to SIDS research, he is a sceptic of the evidence that bed sharing under 3 months in itself carries a risk of SIDS. Dr. Blair was the first author of the most widely quoted paper on this topic 'Babies sleeping with their parents: case-control study of factors influencing the risk of

sudden infant death syndrome' (Blair PS, Fleming PJ, Ward Platt M et al. 1999 BMJ 319: 1457-62.). In Table 3 of that paper the authors report that the multivariate OR for bed shares at the end of sleep is 9.78 (4.12 to 23.83). The base line for comparison is room sharers. This OR is adjusted for all 23 other significant factors, including parental smoking and smoke exposure. The analytical process for calculating a multivariate OR ensures that cases and controls are comparable in respect of *all* the other variables in the model, In particular this adjusted OR, by controlling for other risk factors leaving only bed sharing as a risk factor, is the estimated OR, all other actors being equal, and in particular, *when no other risk factors are present*. However, after reporting the fully adjusted OR for bed sharing, the authors then note that "Some factors in the multivariate model predominantly involved infants sleeping in a cot rather than the parental bed, such as infants put down in the prone sleeping position (20.8% deaths in a cot v 2.5% deaths in a shared bed), placed on a pillow (11.6% v 1.2% or infants being found with heads covered (19.0% v 6.9%)). Removal of these three variables halved the strength of the association with being found in a shared bed (multivariate odds ratio 4.62 (2.34 to 9.09))." The suggestion appears to be that these readily modifiable risk factors may largely be avoided by bed sharing. Of course the OR for bed sharing is reduced because the bed sharers with a comparatively low proportion of infants exposed to the risk factor are being compared with groups with a much larger proportion of infants of these risk factors, but the OR now no longer estimates the independent risk of bed sharing, all other things being equal. By further selective comparisons the authors conclude that "There is no evidence that bed sharing is hazardous for infants of parents who do not smoke." This is in direct contradiction of the results of their analysis presented in their Table 3.

In the meta analysis of the risks associated with bed sharing [Bed Sharing and the Risk of Sudden Infant Death Syndrome: Can We Resolve the Debate? J. Pediatr. 2012 160(1) 44 – 8.e2] the multivariate OR for bed sharing in the CESDI study is correctly taken as 9.78. (A figure of 21.77 is quoted for Blair PS, 2009 includes sofa sharing). Nevertheless Dr Blair continues to raise every possible objection to our evidence that bed sharing in itself carries a risk of SIDS, and we welcome the opportunity to answer them.

Reviewer 3

More clarity is needed regarding how the differences in the data from the 5 studies were resolved, how missing data was checked and whether data can be imputed when whole studies did not ask certain questions. Interpretation of the findings also needs more clarity especially in terms of the reference groups used. the emphasis placed on teh findings is also questionable.

Responses to identical questions were provided from each of the five datasets, when available. Significant differences between the multivariate adjusted ORs for bed sharing were resolved by the use of multi-level models in which bed sharing was taken as random across studies, thereby giving an average AOR across studies with corresponding CI which includes the variation across studies, as stated in the Appendix: statistical methods, *Calculation of univariate and multivariate odds ratios*, paragraph 1.

Imputation was carried out separately for cases and controls. Because of the extreme sparseness of the alcohol and especially the drug use data, it was not possible to impute using a multilevel model, nor was it possible to use a binary imputation model for drug use or

alcohol, nor was it possible, after including in the imputation model all the main effects of variables in the substantive model, to adjust for study in the imputation model.

Thus drug use and alcohol, both coded 0/1, were imputed as continuous, and then rounded to the nearest of 0, 1. The reference imputation probability for alcohol and drug use, respectively, was therefore the reference baseline probability of alcohol and drug use

over the studies with these observed.

After imputation, the average imputed rates of alcohol and drug use were checked in the cases and controls and found to be close to those in the observed data. Imputation for a variable missing in a study in this setting is valid provided the imputation model is appropriate. See, for example, the discussion in Carpenter and Kenward, (2013), p222.

Also, in the current version the base line for any AOR is clearly specified.

I have reviewed this manuscript previously and still find the major points I raised have not been addressed by the authors. The primary focus of this paper, stated in the article summary, is to answer the question "Is there a risk of SIDS due to bed-sharing when baby is breast fed, the parents do not smoke and the mother does not use alcohol or illegal drugs?" This question cannot be addressed when only two of the five studies collected data on maternal alcohol consumption, none of them collected data on the use of illegal drugs prior to bed-sharing and the question is confined to one co-sleeping parent when there are often two .

Imputation provides a valid unbiased analysis of the data – see references in the statistical appendix. For the key group of cases bed sharing non-smokers our data sets either give details of alcohol and drug use of both the mother and her partner, or we have checked the original case records – see below.

The success of SIDS research in the last few decades has been an iterative process focussing closer and closer on the potential risks within the infant sleep environment prior to death. We have been able to utilise this cumulative knowledge in our latest UK case-control SIDS study in 2003-6 (BMJ 2009;339:b3666) and asked (what now seem obvious questions) who exactly was sleeping next to the baby for the last sleep and how much alcohol or drugs had they consumed. We found a significant interaction and nearly a third of the deaths occurred in these circumstances. The potential role of parental alcohol and drugs in these bed-sharing deaths may also go some way in explaining the increased risk of bed-sharing amongst smokers in that this may act as a proxy if questions regarding alcohol and drugs were not asked.

The over-arching argument is thus whether bed-sharing in itself poses a risk to infants or whether the risk is within the hazardous circumstances in which we bed-share. These older studies (data collected between 1987 and 2003) do not have the data to resolve this argument.

The claim that the older studies did not collect data on the amount of alcohol consumed or on who was sleeping next to the baby is not correct. The amount of alcohol consumed by both parents was recorded in the ECAS and the Irish data set; the New Zealand study and the recent German study also asked potentially relevant but different questions on maternal alcohol consumption; also the position of those bed sharing was recorded in great detail in some of the data sets. While claiming the superior quality of their data, when calculating multivariate ORs, they grouped bed sharing with sofa sharing, as noted by Professor Goerge B. Haycock in his comment on the Bradford study (http://pediatrics.aappublications.org/content/129/3/e673/reply#pediatrics_el_53902).

The authors of the study cited also claim in the text that the data are superior to other studies because the responses to the questionnaire were checked against the narrative report. However, checking the questionnaire responses against the narrative report is nothing new. RGC clearly recalls

doing exactly this in the 1960s for the first case-control study. With regard to the latest revision of our report, for the crucial bed sharing cases where neither parent smoke and questions on alcohol or drug use were not included in the questionnaire, **we have, gone back to the narrative records and established that neither alcohol nor drug use contributed in any way to any of these deaths.** see paragraph 3 of the discussion and the Appendix.

I'm sure it is a difficult task trying to combine data from different studies conducted in different countries at different time periods but there seems additional complexity in the way the data has been analysed in terms of the reference groups chosen and the interpretation placed upon them. I'm also a little perplexed that the authors seem to be advocating a ban on bed-sharing when their own findings seem to indicate a massive interaction with the hazardous circumstances in which these infants were found.

In our view, the analysis establishes beyond reasonable doubt that in the first three months bed sharing is a risk factor for SIDS in the absence of other risk factors. We present SIDS rates for room sharers and bed sharers for selected groups and show how rates for other groups may be calculated, thereby enabling informed choice. The increased risk of SIDS associated with bed sharing when combined with smoking, alcohol and other hazardous factors have been known for many years and have been included in SIDS prevention messages (E.g. FSID's Baby Zone leaflet). However, this messages does not appear to be getting through We note the rising proportion of SIDS occurring in bed often in hazardous circumstances, and the substantial proportion of the cases predicted by our data to be attributable to bed sharing. As scientists, that is as far as we can go. As parents we ask why take unnecessary risks.

Major Points

i) Different studies used different definitions for bed-sharing. The Scottish study for instance denoted an infant bed-shared even if they bed-shared some time during the last sleep but were then placed back and found in the cot. Also the New Zealand study had no reference sleep for the control infants and thus (from memory) defined a bed-sharing infant as one that usually bed-shared in the two weeks before the last sleep. How have these differences been reconciled? Stating in the material and methods section (Page 4, line 54) that 'equivalent questions' were used does not provide enough detail.

The Scottish study asks 'At what time did you last see your baby alive?', 'At what time did you find your baby dead?' and 'Did any one share the same bed, couch or chair with the baby during that sleep?'. Then 'Specify which' with 'bed' as the first option. If the baby was put back in the cot, this would be the last time the baby was seen alive, and so the baby would not be bed sharing during the terminal interval. Thus, the possibility that the baby had been put back in a cot is excluded. With regard to the New Zealand data, Professor Mitchell writes 'This is incorrect. Although we did measure usual sleep location in the last two weeks we also used a nominated (or reference) sleep for the control infants. The specific question was: Did baby share a bed with another person during the nominated sleep (controls)/at the time of death (cases)? That is the data we used in the analyses.'

The questions are specific. 'equivalent questions' deleted.

ii) The authors also state (page 9, lines 46 to 51) that for studies where questions on maternal alcohol use and drug use were not included they have "gone back to the original records of breast fed bed-sharing cases when both the mother and partner were non-smokers and established that neither alcohol nor drug use contributed in any way to any of these deaths." Firstly if this could be done it should be done for all cases and controls where possible not just a small subgroup and secondly what do the authors actually mean by this? If questions regarding parental alcohol and drug use were not asked in a detailed research investigation it is unlikely they would have been asked consistently or at

all during the coronial investigation. Absence of these pertinent factors could mean that alcohol and drugs were not used but just as likely this could also mean these questions were not asked.

We do not have the resources to go back to all the case records, nor is this necessary. Furthermore there is no comparable narrative data for the controls. The question is, when neither parent smokes, can the cases of SIDS which occurred while bed sharing have been due to alcohol or drugs? This is unlikely especially at time before the bans on smoking in a public place. This is confirmed by our data. When neither parent smoked, of 125 cases only 2.4 % of mothers had taken alcohol and only 2.9% of 726 controls and none of the case or control mothers were drug users. It should also be noted that both the large New Zealand and German studies asked pertinent questions about alcohol use. We have therefore modified the text to read 'We have gone back to the original records, [most of which included pertinent questions on maternal alcohol use](#), and established that neither alcohol nor drug use contributed in anyway to any of these deaths. If imputation had underestimated the use of alcohol or drugs among the corresponding controls this would have resulted in an underestimate of the risk associated with bed sharing in this group.

iii) None of the studies collected data on parental drug consumption prior to the last sleep of the SIDS infant or the reference sleep of the controls (usually within 24 hours of the interview). Using maternal use of illegal drugs after birth is a poor proxy of the circumstances surrounding the final event. We have shown in our previous larger SIDS study conducted in the 1990's that data on routine use for any factor is a poor marker for what actually happens in the last 24 hours. The authors need to acknowledge that they simply have not got the data to adjust for this important factor.

iv) None of the studies collected data on paternal alcohol consumption preceding the last sleep. The authors need to acknowledge that the risk to the infant could come from one or both parents and data on what each parent consumed and the exact sleeping arrangements needs to be collected to properly assess whether a co-sleeping environment is hazardous. Specifically any analysis needs to take into account which parent or parents were sleeping next to the infant.

These two points are taken together. The premise is incorrect. The ECAS studies used in in this analysis and the Irish study all collected data on the partner's alcohol consumption in the last 24 hours and partner's drug use after the baby was born. Further, when neither parent smoked, for 41% of the cases and their controls the original records also includes drug use in the last 24 hours. Analysis of the data show that when both partners were non-smokers none of the case or control mothers used drugs after birth or, when known, on the last night. However, in the 873 records of the corresponding partners, one partner of an 8 month old control baby did use illegal drugs, but not marihuana or hard drugs, both after birth and on the last night; he also had 4 alcoholic drinks; the baby was fully breast fed up to the time of interview, slept in a cot in the parents' room but not in the parents' bed. This record does not affect our conclusions.

Also in the key sub group of babies < 3 months who were breast fed whose parents did not smoke and whose mother took less than 2 units of alcohol in the last 24 hours who either bed shared or room shared – we find that in both the bed sharing and room sharing groups the control partners had taken slightly *more* alcohol in the last 24 hours than the cases partners. For this key subgroup the OR for bed sharing, unadjusted for other factors is 5.6 (1.6 – 20.3), $p = 0.009$. After adjusting for partner's alcohol consumption in the last 24 hours, the OR is 7.7 (1.8 – 32.3), although the OR for partner's alcohol is not significant; OR = 0.73 (0.41 – 1.27), $p = 0.265$.

We know of no study which takes account of the *exact sleeping arrangements* and *which parent or parents were sleeping next to the infant* in the analysis. Certainly not his own.

v) *Maternal alcohol consumption prior to the last sleep was collected but only for 38.7% of the mothers in the study. Imputing values for parental and alcohol drug consumption on a particular night from a single study when more than 50% of the data is missing requires a fairly homogeneous population and good predictors of 'missingness'. Imputing values from a group of 5 studies, 3 of which did not even ask the question is surely making unreasonable equivalence assumptions across studies conducted in different countries with different cultures in different time periods. In fact one of the two studies where some of this data was collected was a multi-centre study of 20 regions across Europe; cultures with different drinking and drug habits. Just how one randomly selects a potential catastrophic event such as a parent drinking too much alcohol or taking drugs (cannabis, methadone, heroin, etc) before bed-sharing on the final night seems an impossible task.*

We disagree. Define the key sub group as babies < 3 months who were breast fed whose parents did not smoke and whose mother took less than 2 units of alcohol in the last 24 hours who either bed shared or room shared. Then we note that for the key sub group the OR based on complete records is 5.6 (1.6 – 20.3). For further details see paragraph of the discussion and the second section of the appendix.

vi) *In Table 3 and the abstract much is made of the risk associated with bed-sharing in the absence of other factors (AOR=5.1 (2.3-11.4)) but more clarity is needed to describe what this means? According to the Table the reference group seems to be infants < 3 months old who are room-sharing with parents who did not smoke or drink alcohol but the text also suggests these infants were also breastfed, female and placed supine (page 8, line 11 to 15). If so, then should the fivefold risk be attributed to bed-sharing on its own or is there a combined risk including bottle fed infants, male gender and those placed prone. If these factors (gender, mode of feeding and sleeping position) are adjusted for in this analysis (it is not made clear) then does not using such a low risk reference group inflate the risk of the other factors? For instance although there is a 5-fold risk for bed-sharing there is a 13-fold risk when the infants sleeps in the cot next to the bed of parents who smoke and have drunk alcohol. I would have also thought more emphasis would have been put on the finding in the same table that when the parents smoked and bed-shared the risk increased to 21.8 (11.2-42.6) and when the parents also drank alcohol the risk increased to 151.0 (50.6-450.7)! In fact perhaps the most surprising finding in this table is that although the risk associated with bed-sharing in the absence of alcohol and smoking was unity amongst infants aged 3 months or older it was 243.8 (76.1-781.4) when smoking parents drank alcohol and bed-shared which should surely be the finding to emphasise in any abstract.*

The titles makes clear that the ORs in Tables 2 & 3 are fully adjusted, in that no other risk factors are present. To avoid possible misunderstanding I have set this out for each table. Some other corrections have been made.

vii) *The authors argue that in itself the act of an infant lying next to a sleeping adult is causal but this argument using the Bradford Hill criteria is fairly weak. The data cannot really be adjusted for recent alcohol and drug consumption so the contention that there is a strength of association in the absence of known factors does not really stand up. The consistency of findings amongst case-control studies is not comprehensive and there is certainly ecological data suggesting low SIDS rates amongst some populations that often bed-share (see point viii). The evidence of a dose response effect and an analogous example are weak at best but perhaps the argument for coherence is the most surprising. Given this study shows a 10 fold greater risk of bed-sharing amongst smokers (Fig 2), a 90 fold risk of bed-sharing when alcohol was involved (at 2 weeks) and an 'inestimably large' risk associated with stronger drugs than cannabis surely causality is more soundly argued on the basis of potential*

overlaying for many of these bed-sharing deaths in hazardous circumstances rather than weakly asserting it is the bed-sharing itself and not the way we bed-share that puts infants at risk.

First, we have shown that the OR for the key group i.e., neither parent smoked mother did not use drugs and only one room sharing partner used drugs, and the baby was < 3 months and breast fed based on the observed data is significant and almost identical to the AOR for this group. The OR was not explained by the partner's alcohol consumption because control partners had taken more alcohol than the partners of cases Only one case partner had 4 units of alcohol in the last 24 hours.

Second, we are presenting the argument that bed sharing is causal for SIDS in the absence of smoking, alcohol or drugs. The Title of the panel has been changed to make this clear. The case for consistency makes sense in this context. Further, in a recent meta-analysis 3 studies have reported the ORs for bed sharing in infants of non-smoking mothers (reference number #26). The ORs were 0.98, 2.55 and 2.20.

Third, we do not deny that certain factors make bed sharing more hazardous. However the focus of this paper was to answer the question as to whether bed sharing is a risk when parents do not smoke or take alcohol or drugs. We have clearly shown that it is.

viii) The authors in the discussion (page10, lines 35 to 40) suggest bed-sharing in the Netherlands has fallen whilst the breastfeeding rates have slightly risen. What they don't say is whether the SIDS rate has changed in this period (I don't think it has) or whether there is any published evidence supporting a relationship between bed-sharing and breastfeeding in the other direction. Ecological data suggest there are several countries or cultures where bed-sharing and breastfeeding are quite prevalent and the SIDS rate fairly low (Sweden, Hong Kong, Japan, Brazil, Hispanic families in the US, Asian families in the UK). We have also shown an interdependent relationship between bed-sharing and breastfeeding (Blair PS, Heron J, Fleming PJ. Relationship between bed sharing and breastfeeding: longitudinal, population-based analysis. Pediatrics 2010;126(5):e1119-26) and any discussion of this relationship surely needs to be more balanced.

SIDS rates fell during this period, see revised text. We don't think further discussion of the well known relationship is necessary at this point.

ix) It is not clear but Figure 2 appears to be a subgroup analysis of bed-sharers across age involving only those who breastfeed and bed-share and only those families where either both parents smoke or neither. Further, both the legend and the text suggest the odds ratios have been adjusted for alcohol and drug use. Given the limitations of what has been collected I don't think this can be stated and given alcohol and drug use is probably more common amongst bottle feeding mothers it is important to include all the data split by any smoking/no smoking (rather than drop data where one parent smokes) and adjust for mode of feeding (rather than drop the data on bottle feeders completely).

This appears to be a misunderstanding from a previous review. Following the description of Fig 2, the text states explicitly that 'These values are predicted by the overall model of the whole data set.' The title of Fig.2 states that the AORs are adjusted for all other risk factors, as are the corresponding figures shown in Table 2. It is much more powerful to fit an overall model to the whole data, than to embark on subgroup analysis. We have checked both the overall fit of the model to the data and also the fit of the model in the area of special interest – see the appendix.

x) The lack of any analysis on sofa-sharing is disappointing, the New Zealand study did not ask about sofa-sharing but the other 4 studies did. The results suggest a much stronger risk with sofas than parental beds and a strong interaction with alcohol or drugs. The data on co-sleeping on a sofa

should either be handled as a separate group or analysed together with bed-sharing to evaluate the risk of co-sleeping in general; combining this group with infants who slept in a cot (Table 1) or ignoring this group altogether (Tables 2,3 and 4) makes the interpretation of the risk associated with bed-sharing difficult.

The New Zealand study did examine sofa sharing, but it has not been reported as only 5 (1.3%) of the 393 deaths occurred on a sofa while bed sharing with another person. In the publications from the New Zealand Cot Death Study they have been included as bed sharing deaths. However, in the present study sofa sharing is not included with bed sharing. Sofa sharing was not categorised as bed sharing in the NZ dataset, because we only accepted a code of bed sharing when 'Room baby found' was 'parents' bedroom'; otherwise a code of 'bed sharing' was recoded as 'not bed sharing' and 'sleeping elsewhere'. In retrospect, we might have re-examined the risks of sofa sharing, but from the start the question was is bed sharing safe?

xi) In their conclusion the authors suggest the campaign used to reduce prone sleeping, which halved the SIDS rate, could be adopted to reduce bed-sharing claiming a potential further drop in SIDS rates of 88%. This is a poor analogy, prone sleeping was foisted onto parents in the 1950's and thus easier for them to relinquish as an infant care practice whilst bed-sharing has been practiced for thousands of years, is culture specific and potentially related to an increased duration of breastfeeding. I'm not sure how they derive an 88% reduction (half of SIDS infants are found co-sleeping up to a third of which are found on a sofa) but current campaigns do not support their contention. In the US the indication is that bed-sharing rates have increased, despite the American Academy of Pediatrics advising against bed-sharing for the last 6 years and State-specific aggressive campaigns depicting mothers as meat cleavers sleeping next to the child and parental bed-headboards as tombstones, yet the SIDS rate has remained static.

The analysis shows that in our data, 88% of the bed sharing deaths are attributable to bed sharing. The discussion now includes a brief discussion on prevention.

More Minor Points

i) In the background the authors suggest the UNICEF baby friendly website (reference 13) and NCT website (reference 14) actively promote bed-sharing. The UNICEF website page quoted no longer seems available. However the current UNICEF page related to this

<http://www.unicef.org.uk/BabyFriendly/Resources/Resources-for-parents/Caring-for-your-baby-at-night/> shows published evidence of a link between breastfeeding and bed-sharing and seems to acknowledge that bed-sharing is a recognised infant care practice but does not tell parents to bed-share. Again on Page 10 (lines 42-44) suggest UNICEF promotes bed-sharing which it doesn't. Similarly the NCT website acknowledges the SIDS evidence and that bed-sharing can occur (both intentionally and unintentionally) but does not actively promote bed-sharing. These references either need removing or rephrasing.

Rephrased – see the text and new reference. On Page 10 it does not say that UNICEF advocates bed sharing but that **if** bed sharing is promoted to improve breast feeding rates, then it is likely to be counter productive.

ii) The claim by the authors that “the results from analysis of the completed data will primarily depend on the observed data, and only slightly on the imputed data” (Page 9, lines 54-55) seems incongruous to the fact that over 60% of the maternal alcohol data was missing and was therefore imputed.

We are sorry if this was unclear.

Since study is the primary cause of missing alcohol and drug data, and study is adjusted for in the substantive model, we expect the complete records analysis to give essentially unbiased coefficients (Carpenter and Kenward, 2013, p28).

Further, it seems very plausible that alcohol and drug use are missing at random, given study, which is included both in the model of interest and in the imputation model.

Thus our multiple imputations, which is performed under the missing at random assumption, is expected mostly to recover information, rather than correct bias. The majority of this information comes from including in the analysis records whose alcohol and drug data are missing. In this respect, this example is similar to that discussed by Carpenter and Kenward (2013) p 220. As in that setting, most of the information will accrue to the estimates of parameters whose covariates form the observed part of the partially observed records (which are included after multiple imputation).

To put it another way, the imputation process generates random values conditional on the observed associations in the data. Ten data sets were imputed, in each of which the observed data are the same and the imputed data may vary. The analysis combines the analysis of these 10 data using the same model and takes account of the variation between them due to the variation in the imputed values. Thus, the observed data receives much more weight than the imputed values.

Reference:

Carpenter JR and Kenward MG (2013) Multiple Imputation and its Application, Chichester: Wiley