Author’s response to reviews

Title: The relationship of health care use with the persistence of insomnia: a prospective cohort study

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Author’s response to reviews: see over
Dear Sonia

MS:  6101475434379514
The relationship of health care use with the persistence of insomnia: a prospective cohort study
Richard A Hayward, Kelvin P Jordan and Peter R Croft

Thank you for your email dated 18th November 2010. We were pleased by the generally positive and thoughtful comments of the referees. Below we have stated in italics how we have addressed each of their comments:

Editor

1. Ethics - Experimental research that is reported in the manuscript must have been performed with the approval of an appropriate ethics committee. Research carried out on humans must be in compliance with the Helsinki Declaration (http://www.wma.net/en/30publications/10policies/b3/index.html), and any experimental research on animals must follow internationally recognized guidelines. A statement to this effect must appear in the Methods section of the manuscript, including the name of the body which gave approval, with a reference number where appropriate.

We apologise for the omission of this statement. We have now added it to the start of the Methods (p.4).

2. Copy-edit - We recommend that you ask a native English speaking colleague to help you copyedit the paper. If this is not possible, you may need to use a professional copyediting service. Examples are those provided by the Manuscript Presentation Service (www.biomedes.co.uk), International Science Editing (http://www.internationalscienceediting.com/) and English Manager Science Editing (http://www.sciencemanager.com/). BioMed Central has no first-hand experience of these companies and can take no responsibility for the quality of their service.

The paper has been written by native English speakers.

3. Abstract - We recommend you to elaborate on the background section of the abstract of your manuscript.

Thank you. We have added to the background.

Reviewer 1

1. The title of this article is “The relationship of health care use with persistence of insomnia: a prospective cohort study.” The authors defined “Health care use” as medical consultations and hospital admissions, and also as encompassing more accidents at work and greater use of medication (compared to those without insomnia). However, the authors addressed only medication use and mood consultation and not hospital admission or accident rate in this study. The authors should reconsider the definition of “health care use”.

We included medical consultations and hospital admissions as examples of health care use. Accident rates etc were not meant to be examples of health care use and we apologise for the
fact the sentence was poorly phrased. We have amended it. We have also changed the title to refer to primary health care to be clear.

2. The authors report that prescription of hypnotics appeared most “strongly associated” with persistence of insomnia at follow-up (OR 3.18; 95%CI 0.93-10.92). This wording is misleading and not acceptable, given that association with use of hypnotics did not, ultimately, achieve statistical significance. The authors may be able to say “Hypnotic use tended to be associated with persistence of insomnia symptoms at 12 month”. P-value should also be reported to further strengthen this assertion.

In common with many researchers nowadays, we feel that there is an over-reliance on p-values and their significance at an (arbitrary) level of 5%. The odds ratio (OR) of 3.18 is our best estimate of the association with persistence and is a high value for an OR. We have been careful not to suggest the results are statistically significant, and the size of the estimated OR does suggest that hypnotics may be associated with persistence. Please see also referee 2’s 6th point. We feel the confidence interval gives far more information than a p-value and we have ensured we always report the confidence interval alongside the OR estimate to allow the reader to see the extent of uncertainty around this estimate. We have however toned down the statement the referee refers to.

3. The authors assessed anxiety and depression using the Hospital Anxiety and Depression Scale (HADS), however, did not provide these results. As mentioned in the manuscript, insomnia is closely linked to anxiety and depression and it apparently has a stronger association with persistence of insomnia than prescribed medication use. In this manuscript, the objective is to determine the association of persistence and remission of insomnia using a longitudinal study. If so, these results should be provided.

The objective of the study as stated on p.3 was to assess the relationship of primary health care for either insomnia or anxiety and depression with the persistence of insomnia symptoms. However, we agree this is would be an interesting finding and have now added the results for association of baseline anxiety/depression with persistence on p.7. Anxiety and depression had a similar relationship with persistence of insomnia as health care use had (OR 1.39; 95% CI 0.87, 2.22).

4. There are various factors which cause insomnia symptoms including anxiety, medication, alcohol, tobacco, and obesity (including its relationship to sleep apnea). The authors should provide more detailed information about patient characteristics related to these related insomnia factors.

This is a follow-up study of a group who already had sleep problems. Our objective was to determine the relationship of prescribed medication and consultations for insomnia or anxiety and depression with persistence of insomnia symptoms rather than to assess factors that might be associated with onset of insomnia. The baseline characteristics of this group in terms of age, gender, and anxiety and depression are described on p.6/7.

5. The authors should include a section on limitations of this study.

There is a section on limitations of the study starting on p.9.

Discretionary revisions
6. Did author address the question of patient self-treatment? Many people turn to OTC drugs such as melatonin or valerian for insomnia symptoms, foregoing prescribed medicine. When the authors analyze the association of persistence and remission of insomnia, information about self-treatment may be important and should be included.

*This is a good point. Whilst we do not have information on self-medication, we have commented on this in the discussion (p.10).*

Minor Essential Revisions
7. The footnote in Table 2 should read “baseline” not “baselin.”

*Thank you for spotting this. We have corrected it.*

8. Please provide page numbers.

*We have added page numbers.*

Reviewer 2
1. It is ashamed to discard such large amount of data by just focusing on those who reported insomnia at baseline. One would argue that we are not seeing the full picture. The authors need to justify why weren’t the four combinations of insomnia taken into account: those with no insomnia at the 2 time points; insomnia at baseline but not at follow-up; insomnia at follow-up but not at baseline; and insomnia at both time points. To increase the power of the study, the authors could define insomnia as those who gave a positive answer to any of the 4 questions. It is also worthwhile to investigate the severity of sleep problems i.e the people who experienced all the four aspects of sleeping difficulties.

*This is an interesting point but the purpose of the study is specifically to investigate the persistence of insomnia in those who had insomnia at baseline (which would encompass 2 of the 4 groups noted by the referee) and its relationship with primary health care use for insomnia, anxiety or depression. It is difficult to know what the interpretation would be of identifying health care use for the other 2 groups who started without insomnia, and assessing its relationship with onset of insomnia given we would not know when the insomnia began. The definition of insomnia is as the referee stated (a positive answer to any of the 4 questions), and is described on p.5. We have adjusted for “severity” in our final models by counting the number of symptoms and whilst again we agree it would be interesting and valuable to learn more about those with multiple symptoms, the number with all four symptoms was too low to make a separate analysis feasible.*

2. The literature review could be improved substantially. The authors seemed to have missed some key reviews and papers such as the one mentioned above and the work Byles JE et al (Sleep. 2005 Aug 1;28(8):972-9) that described the longitudinal experience of insomnia among older women.

*Thank you for this reference. It has now been added along with other references.*

3. The definition of insomnia should be up front in the introduction section.

*We have added this to the introduction.*
4. A flow diagram to explain the study design in the methods section would be more useful than a verbal description in the results section.

We have now added a flow diagram

5. As 64% of those with sleep problems at baseline responded to follow-up. Could this be due to them having more health problems than the non-respondents? The authors should provide the percentage of women with sleep problems at baseline and who did not respond to follow-up.

We are not quite sure what extra information the referee wishes for here. It may be that non-responders have different levels of health problems however we have stated (p.6) that those who responded had similar levels of anxiety and depression, and a similar number of areas of pain as those who did not respond. There was also no difference by gender.

6. The odds ratio was 1.98 which was quite high and so instead of placing too much weight on ‘p-value’ I would suggest that the authors say that “although the result was not statistically significant”, it was “suggestive” of...

Thank you for the this suggestion. We have followed your advice.

Minor comments:
7. Tables 1 & 2 - were the adjusted and unadjusted analyses based on the same n?

For the main adjusted analysis, there were 12 less cases than for the unadjusted (474 v. 462)

8. Table 1 – there was hardly anyone with took hypnotics and who did not have a sleep problem (n)

That is correct.

9. The analyses in tables 1 & 2 should be done in a stepwise manner –
   OR for age + age
   OR for age + sex + insomnia at baseline
   OR for age + sex + insomnia at baseline + pain + depression.

Thank you for the suggestion but we are not sure this adds to our main objective of determining relationship of health care use with persistence of insomnia and so have left the structure of the analyses as they are.

10. The use of prospective cohort in the title is misleading as at this stage the study just has a one follow-up – 12 months apart.

We would argue that this is still a prospective cohort study, defined as following a group of individuals over time.

Reviewer3
1. As I see it, the main message is that use of health care is associated with chronic insomnia (both at baseline and 1 yr FU), which the authors interpret as treatment for mood disorders does not help to alleviate insomnia symptoms. My main concerns are related to
the issues of insomnia severity and comorbidity. In my view, it may very well be that the insomniacs treated for a mood disorder have more severe insomnia to start with, or at least they have more comorbidity? As such, the two groups (consultation vs no consultation) are too different to compare using remission as an outcome. The authors appropriately address this issue by adjusting for baseline insomnia, pain and anx + dep, which indeed leaves all the findings non-significant! Therefore, I don’t see how the authors’ interpretations and conclusions are valid. Although the authors to some extent acknowledge this, my impression is that the high effect-sizes (ORs) are too strongly interpreted, especially since they are non-significant when adjusted. The crude analyses are not that interesting.

As the referee points out, we have adjusted for baseline severity and comorbidity. As the referee also points out, some of the results were non-significant which is of interest in itself and should not make the study of less importance or interest. Our conclusions are that insomnia persists regardless of health care use, that some people with persistent insomnia do not seek health care, and that hypnotic prescriptions may be associated with persistence. These do not appear to us to be invalid conclusions from the data presented, nor too strong an interpretation. Please note also our response to referee 1’s 2nd point, and please also note referee 2’s 6th point. The current focus is to move away from reliance on p-values and to include confidence intervals around the OR estimates which is what we have done.

2. Also, I find that the manuscript covers the existing literature a bit superficially. There are several very central papers about e.g. the natural history of insomnia (eg. Morin: Arch Gen Psych) which are left out, as is also the case for the literature on insomnia and health care use, as well treatment practices of insomnia among GPs

Thank you for the reference. The paper by Morin and several others have now been included.

We look forward to hearing from you.

Yours sincerely

Richard Hayward