

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

## ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Migraine, tension-type headache and medication-overuse headache in a large population of shift working nurses - a cross-sectional study in Norway
<b>AUTHORS</b>	Bjorvatn, Bjørn; Pallesen, Ståle; Moen, Bente; Waage, Siri; Kristoffersen, Espen Saxhaug

## VERSION 1 – REVIEW

<b>REVIEWER</b>	Kirsten Nabe-Nielsen Department of Public Health, University of Copenhagen, Denmark
<b>REVIEW RETURNED</b>	12-Apr-2018

<b>GENERAL COMMENTS</b>	<p>Review of “Migraine, tension-type headache and medication-overuse headache in a large population of shift working nurses”</p> <p>Dear authors Thank you for your manuscript which addresses an important public health problem—headache—which despite its prevalence has received surprisingly little attention.</p> <p><b>Relevance</b> It is indeed relevant to address the effect of working condition with the prevalence of headache, and the major strength of this study mainly lies in its use of a thorough assessment of subtypes of primary headache. Due to the scarcity of studies on this issue, this study can be of some relevance. I would suggest, though, that the authors referred to all the published studies on the area in order to draw a more complete picture of the current knowledge. Below, I have listed the studies that I am aware of on the topic. The authors of the manuscript under review are obviously not obliged to refer to specific papers, but I think that their study as a whole would be more relevant if it was presented and discussed in the context of strengths and limitations of these previous studies (all cross-sectional).</p> <ul style="list-style-type: none"><li>• Jensen et al. The impact of shift work on intensive care nurses’ lives outside work: A cross-sectional study. <i>J Clin Nurs</i>. 2018; 27:e703–e709.</li><li>• Molarius A, Tegelberg Å, Öhrvik J. Socio-economic factors, lifestyle, and headache disorders - A population-based study in Sweden. <i>Headache</i>. 2008;48(10):1426–37.</li><li>• Portela LF, Rotenberg L, Waissmann W. Self-reported health and sleep complaints among nursing personnel working under 12 h night and day shifts. <i>Chronobiol Int</i>. 2004;21(6):859–70.</li></ul>
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- Ho KH, Ong BKC. Perceived headache associations in Singapore. Results of a randomized national survey. *Headache*. 2001;41(2):164–70. Parkes et al. 1999
- Chan OY, Gan SL, Yeo MH. Study on the health of female electronics workers on 12 hour shifts. *Occup Med (Chic Ill)*. 1993; 43(3):143–8.
- Alfredsson L, Akerstedt T, Mattsson M, Wilborg B. Self-reported health and well-being amongst night security guards: a comparison with the working population. *Ergonomics*. 1991 May;34(5):525–30.

#### **Confounders**

In the objective (p.6) the authors include the statement “...after adjusting for relevant confounders.” However, as far as I can see, the authors completely omit any argumentation for what are relevant confounders here. Thus, 1) the introduction does not provide any knowledge about what would be potential confounders (e.g. addressed in the context of a description of weaknesses of previous studies), 2) it is not clear to the reader why this is brought up specifically in the aim of the study (isn't it quite obvious that relevant confounders should be adjusted for?), 3) it is not clear to me, why marital status, children living at home, and percentage of full-time equivalent are “relevant confounders” when a range of other risk factors for headache, which are also associated with shift work, is not even discussed. I think that the authors should engage even more in the argumentation for the choices regarding covariates that might play a role as confounders in the observed associations.

#### **Definition of the outcome**

Regarding the definition of the outcome, it is described that the diagnoses of migraine and TTH are mutually exclusive. But wouldn't it be possible for the participants to suffer from both migraine and TTH? In fact, don't these conditions often co-occur? What consequences do this have for the findings?

Regarding the categories of frequent and chronic headache, do these categories disregard the type of headache, i.e. whether they are caused by migraine or TTH?

Generally, I am lacking an argument (preferable physiological or behavioral mechanisms) for an association between specific features of the work schedule and the different types of headache. I am also wondering whether there is a dose-response association between the number of night shifts (as continuous variable) and TTH.

#### **Interpretation of the findings**

I think it is quite surprising that SWD and insomnia disorder is not associated with TTH. If you agree that this finding contradict what is generally known about risk factors for TTH, I would suggest to elaborate more on the validity of this finding. For instance, I am wondering whether this finding could be due to the two diagnoses (migraine vs. TTH) being mutually exclusive (if I understood you correctly). Furthermore, as far as I understand your argumentation (p.10 l.57-p.11 l. 6) sleep play an important role in TTH. But then, no association is seen with quick returns and any of the outcomes, and TTH is not associated with insomnia disorders. Overall, it would be appreciated if the authors guided the reader somewhat more in the process of understanding these (apparently) contradictory results. Preferably, with a particular focus on differentiating between observed associations that are mainly due

	to methodological limitations (cross-sectional design, selection, unadjusted confounding...) and potentially true (surprising) causal effects.
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<b>REVIEWER</b>	Rosaria Di Lorenzo Psychiatrist, Psychiatric Intensive Treatment Facility, Department of Mental Health and Drug Abuse, AUSL Modena, Modena, Italy
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<b>REVIEW RETURNED</b>	09-Jun-2018
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<b>GENERAL COMMENTS</b>	<p>The study is a good example of cross sectional research implemented in a large and homogeneous sample with the clearly defined aim of evaluating the association between headache disorders and shift works.</p> <p>In the Introduction, at page 5, line 17, I suggest to add the following detail with a new citation: "risk of health complaints, sick leave and fatigue.4-7"</p> <p>The new citation has to be reported in the References: 7 Ferri P, Guadi M, Marcheselli L, Balduzzi S, Magnani D, Di Lorenzo R. The impact of shift work on the psychological and physical health of nurses in a general hospital: a comparison between rotating night shifts and day shifts. Risk Manag Healthc Policy. 2016 Sep 14;9:203-211.</p> <p>The limitations reported are clearly stated. One of the strengths, not completely highlighted by the authors, is the significant association between headache disorders and the presence of sleeping disorders in shift working nurses. Therefore, I suggest to modify the Conclusion in order to put in evidence it: "We found a significant association between headaches and sleeping disorders in shift working nurses. This result suggests that sleepiness problems induced by shift work modality can act as a trigger for headache disorders. In fact, nurses with SWD reported higher prevalence of frequent headache, migraine, and chronic headache compared to nurses not having SWD. Similarly, nurses with insomnia disorder, compared to those without, reported higher prevalence of all types of headache, except TTH. Although we did not find any association between different types of headache and work schedule or quick returns, we highlighted that TTH was associated with high number of night shifts. Future longitudinal research should be implemented in order to deepen the causality/directionality of association between headaches and work variables."</p> <p>I suggest to consistently modify the Conclusion of the Abstract: "We did not find any association between different types of headache and work schedule, but we highlighted a significant association between headaches and sleeping disorders in shift working nurses. This result suggests that sleepiness problems induced by shift work modality can act as a trigger for headache disorders."</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Kirsten Nabe-Nielsen

Institution and Country: Department of Public Health, University of Copenhagen, Denmark

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

Dear authors

Thank you for your manuscript which addresses an important public health problem—headache—which despite its prevalence has received surprisingly little attention.

Relevance

It is indeed relevant to address the effect of working condition with the prevalence of headache, and the major strength of this study mainly lies in its use of a thorough assessment of subtypes of primary headache.

Due to the scarcity of studies on this issue, this study can be of some relevance. I would suggest, though, that the authors referred to all the published studies on the area in order to draw a more complete picture of the current knowledge.

Below, I have listed the studies that I am aware of on the topic. The authors of the manuscript under review are obviously not obliged to refer to specific papers, but I think that their study as a whole would be more relevant if it was presented and discussed in the context of strengths and limitations of these previous studies (all cross-sectional).

- Jensen et al. The impact of shift work on intensive care nurses' lives outside work: A cross-sectional study. *J Clin Nurs*. 2018; 27:e703–e709.
- Molarius A, Tegelberg Å8, Öhrvik J. Socio-economic factors, lifestyle, and headache disorders - A population-based study in Sweden. *Headache*. 2008;48(10):1426–37.
- Portela LF, Rotenberg L, Waissmann W. Self-reported health and sleep complaints among nursing personnel working under 12 h night and day shifts. *Chronobiol Int*. 2004;21(6):859–70.
- Ho KH, Ong BKC. Perceived headache associations in Singapore. Results of a randomized national survey. *Headache*. 2001;41(2):164–70.
- Parkes et al. 1999
- Chan O Y, Gan SL, Yeo MH. Study on the health of female electronics workers on 12 hour shifts. *Occup Med (Chic Ill)*. 1993; 43(3):143–8.
- Alfredsson L, Akerstedt T, Mattsson M, Wilborg B. Self-reported health and well-being amongst night security guards: a comparison with the working population. *Ergonomics*. 1991 May;34(5):525–30.

ANSWER: We have now added and referred to most of the references in the introduction, as suggested. The text reads: “Many of the existing studies suffer from methodological limitations, such as low number of participants (<300) (Alfredsson, 1991; Portela, 2004; Jensen, 2018) and not using validated headache questions (Alfredsson, 1991; Portela, 2004; Jensen, 2018; Ho, 2001; Molarius, 2008).”

Confounders

In the objective (p.6) the authors include the statement “...after adjusting for relevant confounders.” However, as far as I can see, the authors completely omit any argumentation for what are relevant confounders here. Thus, 1) the introduction does not provide any knowledge about what would be potential confounders (e.g. addressed in the context of a description of weaknesses of previous studies), 2) it is not clear to the reader why this is brought up specifically in the aim of the study (isn't it quite obvious that relevant confounders should be adjusted for?), 3) it is not clear to me, why marital status, children living at home, and percentage of full-time equivalent are “relevant confounders” when a range of other risk factors for headache, which are also associated with shift work, is not even discussed. I think that the authors should engage even more in the argumentation for the choices regarding covariates that might play a role as confounders in the observed associations.

ANSWER: We agree that we have not addressed the issue of confounders in the introduction. We have therefore deleted “after adjusting for relevant confounders”, when stating the objective of the study (last paragraph in introduction). Furthermore, we agree with the reviewer regarding the issue of confounders. Thus, we have now added a short discussion about the choice of confounders in the limitation section of the discussion. It reads: “We adjusted for several confounders known to influence shift work and headache, however, many other relevant factors were not adjusted for, e.g. physical

inactivity, stress, and psychological disturbances. Lack of such adjustment should be taken into consideration when interpreting the results.”

#### Definition of the outcome

Regarding the definition of the outcome, it is described that the diagnoses of migraine and TTH are mutually exclusive. But wouldn't it be possible for the participants to suffer from both migraine and TTH? In fact, don't these conditions often co-occur?

ANSWER: The reviewer raises a valid point. Migraine and tension-type headache often co-exist in the same person. However, as is common in headache questionnaire studies, the participants report the overall worst and most disabling headache. In this way, we avoid over-counting/reporting. However, the shortcoming of this approach is clearly that we can only differentiate between those who suffer mostly from migraine and those who suffer mostly from tension-type headache. Migraine is hierarchically more important in the International Classification of Headache Disorders. Thus, migraine and TTH are mutually exclusive in the questionnaire used in the present study. Those who report migraine may still have co-existing TTH, and some of those who report TTH may have a very low frequency migraine. Most likely, possible differences between migraine and TTH are underestimated owing to the presence of people with TTH in the migraine group and vice versa, making the two groups more similar than they actually are.

This shortcoming leads to a possible underestimation of TTH in almost all questionnaire studies, also reflected by the fact that the prevalence of TTH is varying between 15 and 90% in different prevalence studies across the world. However, misclassification may not be a big problem as the prevalence of migraine, TTH and medication-overuse headache in the present study is consistent with other population-based studies.

The gold standard in terms of diagnosis is a three months diagnostic headache diary followed by a clinical headache interview by a trained headache expert. However, this is not feasible in larger studies such as the present one. Based on this, we decided to use a well renowned (within the headache epidemiology field) and validated headache questionnaire specifically designed for population-based studies.

We have now elaborated more on this in the limitation section: “A limitation of the headache questionnaire is that migraine and TTH are mutually exclusive, i.e. the questionnaire only allows the participant to be diagnosed with the most bothersome headache subtype even though some might suffer from both migraine and TTH (Linde, 2011). It is possible that differences between migraine and TTH are underestimated owing to the presence of people with TTH in the migraine group and vice versa, making the two groups more similar than they actually are. Thus, some caution is needed when interpreting the results. As migraine is hierarchically more important in the headache classification (Headache Classification Committee of the International Headache Society, 2013) than TTH, it is possible that there is an underestimation of TTH in the sample. However, the prevalence of the different headaches reported in the present study is similar to those reported previously,(Jensen, 2008; Linde, 2011; Jonsson, 2011; Wang, 2015; Grande, 2008) strengthening the assumption of representativeness of the study population.”

What consequences do this have for the findings?

ANSWER: See answer above. We have added that caution is needed when interpreting the results.

Regarding the categories of frequent and chronic headache, do these categories disregard the type of headache, i.e. whether they are caused by migraine or TTH?

ANSWER: Yes, in the present paper they do. As co-existing headache types are even more common in chronic headaches we have not classified the headaches into chronic tension-type headache or chronic migraine. However, the diagnosis of MOH is independent of the underlying primary headache

so MOH could be correctly diagnosed and classified only on the basis on the headache and medication frequency. In the methods, we now state: "Frequent headache was defined as headache >1 day per month, and chronic headache was defined as headache >14 days per month, independently of the underlying subtype of headache."

Generally, I am lacking an argument (preferable physiological or behavioral mechanisms) for an association between specific features of the work schedule and the different types of headache. I am also wondering whether there is a dose-response association between the number of night shifts (as continuous variable) and TTH.

ANSWER: It is well known that lack of sleep or disrupted sleep may trigger TTH and that both lack of sleep, but also too much sleep may trigger and/or alleviate migraine attacks. The exact underlying pathophysiological mechanisms for this are currently unknown. Depending on the sleep-wake rhythm and sleep pattern of the different work schedules, this may at least partly explain an association between subtypes of headache and work schedules. We have included this issue in the introduction. In the tables, the number of night shifts is split into three groups, suggesting a dose-response association with TTH (Table 3). We believe such a split communicates better than reporting number of night shifts as a continuous variable.

Interpretation of the findings

I think it is quite surprising that SWD and insomnia disorder is not associated with TTH. If you agree that this finding contradict what is generally known about risk factors for TTH, I would suggest to elaborate more on the validity of this finding. For instance, I am wondering whether this finding could be due to the two diagnoses (migraine vs. TTH) being mutually exclusive (if I understood you correctly). Furthermore, as far as I understand your argumentation (p.10 l.57-p.11 l. 6) sleep play an important role in TTH. But then, no association is seen with quick returns and any of the outcomes, and TTH is not associated with insomnia disorders. Overall, it would be appreciated if the authors guided the reader somewhat more in the process of understanding these (apparently) contradictory results. Preferably, with a particular focus on differentiating between observed associations that are mainly due to methodological limitations (cross-sectional design, selection, unadjusted confounding...) and potentially true (surprising) causal effects.

ANSWER: We agree with the reviewer that it was surprising that SWD, insomnia disorder and number of quick returns were not associated with TTH. Since lack of sleep is known to trigger TTH, we expected to find such associations. We do not have an obvious explanation for this. In line with the reviewer's suggestion, we have tried to elaborate more on this unexpected finding several places in the discussion.

Reviewer: 2

Reviewer Name: Rosaria Di Lorenzo

Institution and Country: Psychiatrist, Psychiatric Intensive Treatment Facility, Department of Mental Health and Drug Abuse, AUSL Modena, Modena, Italy

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

Please leave your comments for the authors below

The study is a good example of cross sectional research implemented in a large and homogeneous sample with the clearly defined aim of evaluating the association between headache disorders and shift works.

In the Introduction, at page 5, line 17, I suggest to add the following detail with a new citation: "risk of health complaints, sick leave and fatigue.4-7"

The new citation has to be reported in the References:

7 Ferri P, Guadi M, Marcheselli L, Balduzzi S, Magnani D, Di Lorenzo R. The impact of shift work on the psychological and physical health of nurses in a general hospital: a comparison between rotating night shifts and day shifts. *Risk Manag Healthc Policy*. 2016 Sep 14;9:203-211.

ANSWER: This new reference is now added and referred to, as suggested. As fatigue is a health complaint, we decided not to change the sentence, but keep "risk of health complaints and sick leave".

The limitations reported are clearly stated. One of the strengths, not completely highlighted by the authors, is the significant association between headache disorders and the presence of sleeping disorders in shift working nurses. Therefore, I suggest to modify the Conclusion in order to put in evidence it:

"We found a significant association between headaches and sleeping disorders in shift working nurses. This result suggests that sleepiness problems induced by shift work modality can act as a trigger for headache disorders. In fact, nurses with SWD reported higher prevalence of frequent headache, migraine, and chronic headache compared to nurses not having SWD. Similarly, nurses with insomnia disorder, compared to those without, reported higher prevalence of all types of headache, except TTH. Although we did not find any association between different types of headache and work schedule or quick returns, we highlighted that TTH was associated with high number of night shifts. Future longitudinal research should be implemented in order to deepen the causality/directionality of association between headaches and work variables."

ANSWER: Thank you for pointing out this important finding. We have accordingly modified the conclusion. However, we think the reviewer's statement "This result suggests that sleepiness problems induced by shift work modality can act as a trigger for headache disorders." is not substantiated by our findings. This statement implies causality, however, the present study is cross-sectional, which prevents us from drawing such conclusions (we do not know for sure that sleep problems are induced by shift work). Our conclusion now reads: "We found a significant association between headaches and SWD and insomnia disorder in our cohort of nurses. In fact, nurses with SWD reported higher prevalence of frequent headache, migraine, and chronic headache compared to nurses not having SWD. Similarly, nurses with insomnia disorder, compared to those without, reported higher prevalence of all types of headache, except TTH. Although we did not find any association between different types of headache and work schedule or quick returns, TTH was associated with high number of night shifts. Future longitudinal research should be conducted in order to investigate the causality/directionality of association between headaches and work variables."

I suggest to consistently modify the Conclusion of the Abstract:

"We did not find any association between different types of headache and work schedule, but we highlighted a significant association between headaches and sleeping disorders in shift working nurses. This result suggests that sleepiness problems induced by shift work modality can act as a trigger for headache disorders."

ANSWER: We have now modified the conclusion of the abstract. However, as mentioned above, we omitted the last sentence because it implies causality. The text now reads: "We did not find any association between different types of headache and work schedule. However, tension-type headache was associated with high number of night shifts. Nurses with sleep disorders (insomnia disorder and shift work disorder) reported higher prevalence of frequent headache, migraine, chronic headache and medication-overuse headache (only insomnia) compared to nurses not having insomnia disorder and shift work disorder, respectively."

FORMATTING AMENDMENTS (if any)

Required amendments will be listed here; please include these changes in your revised version:  
 - We have implemented an additional requirement to all articles to include 'Patient and Public Involvement statement' within the main text of your main document. Please refer below for more information regarding this new instruction:

Authors must include a statement in the methods section of the manuscript under the sub-heading 'Patient and Public Involvement'.

This should provide a brief response to the following questions:

How was the development of the research question and outcome measures informed by patients' priorities, experience, and preferences?

How did you involve patients in the design of this study?

Were patients involved in the recruitment to and conduct of the study?

How will the results be disseminated to study participants?

For randomised controlled trials, was the burden of the intervention assessed by patients themselves?

Patient advisers should also be thanked in the contributorship statement/acknowledgements.

If patients were not involved please state this.

ANSWER: We have now added a "Patient and public involvement"-statement in the method section. It reads: "The questionnaire was developed by a group of researchers experienced with shift work and shift work related problems. The participating nurses were not involved in the design, recruitment or conduct of the study. The results will be disseminated to the study participants in the yearly report we send to the journal of the Norwegian nurses. Here we address last year's published data from the cohort study. In addition, the results will appear on a designated website – [www.sussh.no](http://www.sussh.no) (after publication)."

### VERSION 2 – REVIEW

<b>REVIEWER</b>	Kirsten Nabe-Nielsen Department of Public Health, University of Copenhagen, Denmark
<b>REVIEW RETURNED</b>	09-Jul-2018

<b>GENERAL COMMENTS</b>	<p>Dear authors, I have now completed the second peer-review. I found some small inconsistencies that you might want to address and I have a comment regarding the response to my previous comments about the rationale for confounder adjustment. Good luck with resubmission.</p> <p>Best regards, Kirsten Nabe-Nielsen</p> <p><b>KEY MESSAGES:</b>          "Tension-type headache was associated with high number of night shifts, but neither migraine, tension-type headache, nor medication-overuse headache were associated with work schedule."          It seems counterintuitive that "TTH is associated with a high number of night shifts" but "migraine, TTH etc were NOT associated with work schedule". I guess it is because your use of the term "work schedule" and "number of night shifts" as two very distinct variables, despite that the latter term may obviously be a characteristic related to the first term. But it might confuse the new reader, maybe consider reformulation.</p> <p><b>ABSTRACT:</b></p>
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	<p>I think you need to indicate that what you present after OR are the 95% confidence intervals, i.e. OR 2.05, 95% CI: 1.62-2.59). This comment also applies to the remaining manuscript.</p> <p><b>METHODS:</b> I didn't notice during my previous review that work schedule, number of night shifts and quick returns, i.e. some of the main variables, are described under the heading "Demographics". It may be somewhat misplaced here and even presented as part of a list of covariates.</p> <p>In my previous review, I noticed that it was not clear to me, why marital status, children living at home, and percentage of full-time equivalent are denoted relevant confounders when a range of other risk factors for headache, which are also associated with shift work, is not even discussed. I think that the authors should engage even more in the argumentation for the choices regarding covariates that might play a role as confounders in the observed associations.</p> <p>The response to this request was: "We adjusted for several confounders known to influence shift work and headache, however, many other relevant factors were not adjusted for, e.g. physical inactivity, stress, and psychological disturbances. Lack of such adjustment should be taken into consideration when interpreting the results."</p> <p>As I see it, the authors do still not argue for their choice of covariates (in the discussion it says that these are known to influence shift work and headache, but this is not addressed/documentated elsewhere in the manuscript. Furthermore, in the light of the lack of association between shift work (and related variables) and headache-related outcomes, extensive adjustment for confounding may not be necessary. Still the authors argue that these (e.g. physical inactivity, stress etc.) as "relevant factors" and mention that "lack of such adjustment should be taken into consideration when interpreting the results". Thus, I wonder why they are not included if they are deemed relevant, and I am wondering how "lack of such adjustment should be taken into consideration when interpreting the results"?</p> <p><b>DISCUSSION:</b> These two sentences seem contradictory: "Insomnia disorder was associated with all headache types, except TTH, which is in line with the findings from several other studies" and "Surprisingly, TTH was not associated with insomnia disorder in our study, in contrast to two other population-based studies." Maybe "all headache types" should just be specified.</p>
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<b>REVIEWER</b>	Rosaria Di Lorenzo Mental Health Department, AZUSL Modena, Italy
<b>REVIEW RETURNED</b>	14-Jul-2018
<b>GENERAL COMMENTS</b>	Your manuscript has been revised according to editotr's and reviewers' suggestions and can be published.

## VERSION 2 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Kirsten Nabe-Nielsen

Institution and Country: Department of Public Health, University of Copenhagen, Denmark

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

Please leave your comments for the authors below

Dear authors, I have now completed the second peer-review. I found some small inconsistencies that you might want to address and I have a comment regarding the response to my previous comments about the rationale for confounder adjustment.

Good luck with resubmission.

Best regards,

Kirsten Nabe-Nielsen

### KEY MESSAGES:

“Tension-type headache was associated with high number of night shifts, but neither migraine, tension-type headache, nor medication-overuse headache were associated with work schedule.”

It seems counterintuitive that “TTH is associated with a high number of night shifts” but “migraine, TTH etc were NOT associated with work schedule”. I guess it is because your use of the term “work schedule” and “number of night shifts” as two very distinct variables, despite that the latter term may obviously be a characteristic related to the first term. But it might confuse the new reader, maybe consider reformulation.

ANSWER: We agree that this may be confusing. We have now removed/deleted these key messages, as suggested by the editor.

### ABSTRACT:

I think you need to indicate that what you present after OR are the 95% confidence intervals, i.e. OR 2.05, 95% CI: 1.62-2.59). This comment also applies to the remaining manuscript.

ANSWER: We agree and 95% confidence intervals (95% CI) are now included the first time confidence intervals are mentioned in the abstract. We have also changed this in the remaining text.

### METHODS:

I didn't notice during my previous review that work schedule, number of night shifts and quick returns, i.e. some of the main variables, are described under the heading "Demographics". It may be somewhat misplaced here and even presented as part of a list of covariates.

ANSWER: We have now changed the heading to "Demographics and work-related factors" to make it clearer to the reader that this paragraph includes information about work schedule etc. Furthermore, in the statistics section, it is clearly stated that these work-related factors were analyzed in relation to the prevalence of different types of headache.

In my previous review, I noticed that it was not clear to me, why marital status, children living at home, and percentage of full-time equivalent are denoted relevant confounders when a range of other risk factors for headache, which are also associated with shift work, is not even discussed. I think that the authors should engage even more in the argumentation for the choices regarding covariates that might play a role as confounders in the observed associations.

The response to this request was:

"We adjusted for several confounders known to influence shift work and headache, however, many other relevant factors were not adjusted for, e.g. physical inactivity, stress, and psychological disturbances. Lack of such adjustment should be taken into consideration when interpreting the results."

As I see it, the authors do still not argue for their choice of covariates (in the discussion it says that these are known to influence shift work and headache, but this is not addressed/documentated elsewhere in the manuscript. Furthermore, in the light of the lack of association between shift work (and related variables) and headache-related outcomes, extensive adjustment for confounding may not be necessary. Still the authors argue that these (e.g. physical inactivity, stress etc.) as "relevant factors" and mention that "lack of such adjustment should be taken into consideration when interpreting the results". Thus, I wonder why they are not included if they are deemed relevant, and I am wondering how "lack of such adjustment should be taken into consideration when interpreting the results"?

ANSWER: The decision about which confounders to adjust for and which not to include in the analyses is often complex. We acknowledge the reviewer's concern. However, in Table 2 we report the results from the chi-square tests (unadjusted analyses), and in Table 3 we report logistic regressions with adjustment for sex, age, percentage of full-time equivalent, marital status and children living at home. Thus, we have both unadjusted and adjusted analyses, and both show similar findings, strengthening our conclusions. We believe it is appropriate and common to adjust for variables like sex and age, and also the other confounders in our analyses. However, the choice of confounders is often influenced by which ones are available. Other possible and relevant confounders, like physical inactivity and stress, were not available in this study, and are therefore not included. We still think it is appropriate to state "lack of such adjustment should be taken into consideration when interpreting the results", but we do not want to speculate how this influenced the results. Also, as the reviewer states, extensive adjustment for confounding may not be necessary. However, in order to engage some more in the argumentation for our choices, as the reviewer recommends, we have now changed our previous response from "We adjusted for several confounders known to influence shift work and headache, however, many other relevant factors were not adjusted for, e.g. physical inactivity, stress, and psychological disturbances. Lack of such adjustment should be taken into consideration when interpreting the results" to "In the logistic regressions we adjusted for several relevant confounders, like sex, age, percentage of full-time equivalent, marital status and children living at home, because such factors are known to influence shift work tolerance and headache (Molarius et al. 2008, Flo et al. 2012). However, other possible and

relevant factors were not adjusted for, e.g. physical inactivity, stress, and psychological disturbances (Molarius et al. 2008, Houle et al. 2012), since data on these variables were not available. Lack of such adjustment should be taken into consideration when interpreting the results.”

#### DISCUSSION:

These two sentences seem contradictory: “Insomnia disorder was associated with all headache types, except TTH, which is in line with the findings from several other studies” and “Surprisingly, TTH was not associated with insomnia disorder in our study, in contrast to two other population-based studies.” Maybe “all headache types” should just be specified.

ANSWER: Thank you for this comment. In order to make the statements less contradictory, we have specified “all headache types”, as suggested. The first sentence now reads: “Insomnia disorder was associated with frequent headache, migraine, chronic headache, and medication-overuse headache, which is in line with the findings from several other studies.”

Reviewer: 2

Reviewer Name: Rosaria Di Lorenzo

Institution and Country: Mental Health Department, AZUSL Modena, Italy

Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below

Your manuscript has been revised according to editor's and reviewers' suggestions and can be published.

ANSWER: Thank you for this nice comment.