PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Interaction of sleep quality and sleep duration on impaired fasting glucose: A population-based cross-sectional survey in China
AUTHORS	Lou, Peian; Chen, Peipei; Zhang, Lei; Zhang, Pan; Chang, Guiqiu; Zhang, Ning; Li, Ting; Qiao, Cheng

VERSION 1 - REVIEW

REVIEWER	Fei Xu Nanjing Municipal Center for Disease Control and Prevention; Nanjing Medical Univeristy School of Public Health; China
REVIEW RETURNED	18-Dec-2013

GENERAL COMMENTS	Recently there are increasing interests in investigating the association of sleep with blood glucose metabolism and its related influential factors including excess body weight gain. However, the combined effects of sleep duration and quality on diabetes or IFG were less explored. This manuscript, generally well-organized, reported the relationship between sleep duration and impaired fasting blood glucose level with consideration of sleep quality. I think it makes the contribution to present literature and will be of interest for colleagues within this field. However, I have some major concerns waiting for authors' clarification. This is a piece of research that appears to come from an experienced team with considerable knowledge of their area. In this large sample cross-sectional study, the relationship between sleep duration and impaired fasting blood glucose level (IFG) was examined with consideration of sleep quality. The findings suggested that there was a joint influence of sleep duration and its quality on IFG. It will be of help for potential readers within this research field. However, I have several major comments that need authors to pay much attention to. Major compulsory revisions: 1. Participants Authors have stated that the participants were volunteers recruited from a primary-care based cross-sectional study. Due to the nature of cross-sectional study, it is critical to guarantee no or least bias for subjects' selection. Thus, I believe it is necessary for author to describe in detail (1) the sampling approach used to recruit those volunteers in this study; (2) representativeness of the participants to general population in terms of some key variables. Again, what difference between those excluded and included in

analysis regarding major demographic characteristics? And why excluded those volunteers who had received antihypertensive medication, or were suffering from any cardiovascular disease, stroke, neuropathy, psychosis, depression, chronic obstructive pulmonary disease, ache, or any other disease and how to verify those people with the mentioned diseases? What were the inclusion criteria for eligible participants?

2. Definition of sleep quality
The quality was generated from PSQI score, BUT the authors did not demonstrate how to classify participants as with good or poor quality of sleep (the cutoff point value based on PSQI). It is particularly important to clear present the approach used to define this key variable.

Another concern is that sleep duration was also used to construct the global PSQI score and it was also used as an independent variable in the analysis.

Previous studies show that there was a U-shape between sleep time and the risk of developing IFG and diabetes. Thus, it is very important to appropriately use the cutoffs to categorize participants into those with short or prolonged sleep time in such studies. The cutoffs used to categorize sleep duration were 6 and 8. In previous studies, a majority of studies 7and 9 were sued as the cutoffs that sleep time less than 7 was treated as too short while 9 and above as prolonged. So please justify the approach you used in this study.

3. Definition of covariates
3.1 The definition of smoking was not the regular practice.
3.2 What instrument used to measure physical activity, a critical potential influential factor for blood glucose metabolism?
3.3 Why not use the specific recommendations by China Obesity Workforce for Chinese adult BMI cutoffs to define overweight and obesity?

4. Statistical methods
There might be interaction between sleep time and quality on IFG, especially when sleep time was also used to generate the term of sleep quality in this study. However, I really think what they explored was the joint effects of sleep duration and quality on IFG. Thus, the separate influence of sleep time and quality on IFG need to be examined individually, next to test the potential interaction between sleep time and quality, and then to investigate the joint association of sleep duration and quality with IFG. The biological effects in terms of RERI, AP and SI were with little significance in this study with consideration of data from a cross-sectional survey. Please get advices from statisticians and experts in this area.

5. Results
Why not to investigate the association of global PSQI with IFG? In table 2, only PQSI and its each component score was compared between those with and without IFG. It would be better to see the link between PQSI and IFG.

Minor comments:

	1. The sentence (line 5-7 on page 3), "The average annual incidence of diabetes in a cohort of patients with IFG is 11% over a six-year period without intervention." Please clearly indicate the subjects were Chinese or other countries' people.
	2. The word, "increasingly", in line 15 on page 3 was not appropriate, because only two ref. cited here.
	3. The word, "confirmed", in line 34 on page 3 is not appropriate, because your previous study was a cross-section survey. Again, the term "relatively healthy individuals" was a little bit confusing and not strict.
	4. Statistics methods It will be better to describe what specific logistic regression model used in the analysis. Is there any potential cluster effects?
	5.Please add mean sleep duration in RESULTS.
	6. References Please indicate all ref. not published in English.
	7. Tables 7.1 All tables need modification to meet regular format. 7.2 Add another table to show the separate association of sleep time and quality with IFG, individually.
	8. Language I believe a native English speaker with background of public health or epidemiology is needed to closely edit throughout the entire manuscript.

REVIEWER	Zumin Shi University of Adelaide, Australia
REVIEW RETURNED	18-Dec-2013

GENERAL COMMENTS	Main results from Table 3 should be summarized in the abstract. Currently the information is hard to understand by many readers without specific knowledge. This cross-sectional study assessed the interaction between sleep duration and sleep quality in relation to the risk of impaired fasting glucose. It is an interesting study with a large sample size. Major concern: 1. It has been known that long sleep duration is associated with increased risk of mortality. The reasons are not fully clear. The fact that long sleep duration with good sleep quality had the second highest risk of IFG is very interesting (even higher than those long sleep duration with poor sleep quality). Could the author provide some explanation? A thorough analysis of components of PSQI may provide some additional information. 2. Is there any gender difference? If yes, gender specific results should be provided. 3. Abstract-Results from Table 3 should be summarized in the abstract. Minor: 1. Please provide detailed information on the sampling method.

	What is the response rate?
	2. Before excluding participants with chronic diseases, what is the sample size? The prevalence of IFG in the study is much lower than the national data (published in NEJM 2010 and JAMA 2013). If the sampling method is robust, the prevalence of diabetes should be reported in a separate paper. Currently, there is concern on the possible overestimation of the prevalence of diabetes in China.
	3. Table 1- provide percentage in addition to number of participants
	4. Table 2- age adjusted mean is more informative
	5. The question used to assess sleep duration should be described in the method section.

GENERAL COMMENTS	Overall, the manuscript was well-written and well-presented. There were several issues that need to be addressed, however:
	1. How was medical history assessed? Was it just by self-report? If so, this should be mentioned.
	2. The authors state that the PSQI has diagnostic ability, but "good" and "poor" sleep categories are not diagnostic.
	3. The sleep duration categories need to be justified. How were they determined? Also, how was sleep duration assessed? It seems that it was the single item on the PSQI but this is not specified. Also, some justification is needed for using this single-item measure.
	4. The paper does not describe how lifestyle factors were assessed.
	5. How was height and weight measured? (Were these self-reported or objective?)
	6. Why were overweight and obese categories combined? In much of the sleep duration literature, there are clear differences in effects for overweight versus obesity.
	7. Interaction terms should be reported to justify stratification.
	8. The manuscript mentions a relationship with "all PSQI items." However the table (Table 2) notes PSQI subscales, which seem to be what was meant. It should be noted that PSQI subscales are not continuous variables (they are ordinal or at least categorical) and should be evaluated as such.
	9. The discussion section should include some commentary on the literature describing short sleep duration with insomnia. The Penn State group (e.g., Vgontzas, Bixler, Fernandez-Mendoza et al) have published extensively on this concept and more of their work should be cited.
	10. The discussion might also benefit from commentary on the paper by Altman et al 2012, which studies sleep duration in the context of insufficient sleep associated with diabetes and obesity (among other outcomes). This is another example of the relationship between sleep duration and sleep quality.

	References 10 and 42 seem to not be displayed correctly.

VERSION 1 – AUTHOR RESPONSE

Reviewer#1 （Fei Xu）
Institution and Country Nanjing Municipal Center for Disease Control and Prevention; Nanjing Medical University School of Public Health; China
Please state any competing interests or state 'None declared': None declared.

Recently there are increasing interests in investigating the association of sleep with blood glucose metabolism and its related influential factors including excess body weight gain. However, the combined effects of sleep duration and quality on diabetes or IFG were less explored. This manuscript, generally well-organized, reported the relationship between sleep duration and impaired fasting blood glucose level with consideration of sleep quality. I think it makes the contribution to present literature and will be of interest for colleagues within this field.

However, I have some major concerns waiting for authors' clarification.

Comments to authors
This is a piece of research that appears to come from an experienced team with considerable knowledge of their area. In this large sample cross-sectional study, the relationship between sleep duration and impaired fasting blood glucose level (IFG) was examined with consideration of sleep quality. The findings suggested that there was a joint influence of sleep duration and its quality on IFG. It will be of help for potential readers within this research field. However, I have several major comments that need authors to pay much attention to.

Major compulsory revisions:
1. Participants
Authors have stated that the participants were volunteers recruited from a primary-care based cross-sectional study. Due to the nature of cross-sectional study, it is critical to guarantee no or least bias for subjects' selection. Thus, I believe it is necessary for author to describe in detail (1) the sampling approach used to recruit those volunteers in this study; (2) representativeness of the participants to general population in terms of some key variables.

The sampling was selected with probability proportional to size from all of the eleven regions in Xuzhou city. In the first stage, 5 subdistricts/townships in urban/rural areas were selected from each region. In the second stage, 5 communities/ villages were selected from each subdistricts/townships. In the final stage, one person who was at least 18 years old and lived in the current residence for at least 5 years was selected from each household using a Kish selection table. A total of 16500 people were selected assuming an estimation prevalence of diabetes of 5.5% with 90% power and α=0.05 and allowing for a drop-out of 10%.
We have added the sentences in the method part.

Again, what difference between those excluded and included in analysis regarding major demographic characteristics? And why excluded those volunteers who had received antihypertensive medication, or were suffering from any cardiovascular disease, stroke, neuropathy, psychosis, depression, chronic obstructive pulmonary disease, ache, or any other disease and how to verify those people with the mentioned diseases? What were the inclusion criteria for eligible participants?

It had been reported that there were relations between hypertension, cardiovascular disease, stroke, psychosis, depression, chronic obstructive pulmonary disease and diabetes. In addition, neuropathy

and ache affect sleep quality. Those factors above were excluded in this paper to ensure the aim our study whether sleep disorders influence blood glucose levels.
These diseases verified according to medical records which had been added in text.

2. Definition of sleep quality
The quality was generated from PSQI score, BUT the authors did not demonstrate how to classify participants as with good or poor quality of sleep (the cutoff point value based on PSQI). It is particularly important to clear present the approach used to define this key variable.
In this study design, a PSQI score ≤5 was also conventionally defined as 'good sleep quality', and a PSQI score > 5 was defined as 'poor sleep quality'. It had been added in the text.

Another concern is that sleep duration was also used to construct the global PSQI score and it was also used as an independent variable in the analysis.

The PSQI is a validated self-rated questionnaire that assesses sleep quality over a one-month time interval. However, the sleep duration used for interaction analysis mainly assesses habitual sleep duration. The two are independent variables.

Previous studies show that there was a U-shape between sleep time and the risk of developing IFG and diabetes. Thus, it is very important to appropriately use the cutoffs to categorize participants into those with short or prolonged sleep time in such studies. The cutoffs used to categorize sleep duration were 6 and 8. In previous studies, a majority of studies 7and 9 were sued as the cutoffs that sleep time less than 7 was treated as too short while 9 and above as prolonged. So please justify the approach you used in this study.
The classification is consistent with the classifications used in our previous studies (see ref.3,7, 8), and also consistent with other reports (see ref. 5). In a recent meta-analysis, short and long sleep duration were defined as ≤5–6 hours and >8–9 hours, respectively (Cappuccio et al. 2011).

3. Definition of covariates
3.1 The definition of smoking was not the regular practice.
The definition of smoking is accordance with our previous study (Ref. 7)

3.2 What instrument used to measure physical activity, a critical potential influential factor for blood glucose metabolism?
In this study design, regular leisure-time physical activity was defined as participating in moderate or vigorous activity for no less than 30 minutes per day at least three days a week. Using a self-reporting
3.3 Why not use the specific recommendations by China Obesity Workforce for Chinese adult BMI cutoffs to define overweight and obesity?
In this study design, the BMI cutoffs is Chinese adult. We only want to more reference SCI papers.
4. Statistical methods
There might be interaction between sleep time and quality on IFG, especially when sleep time was also used to generate the term of sleep quality in this study. However, I really think what they explored was the joint effects of sleep duration and quality on IFG. Thus, the separate influence of sleep time and quality on IFG need to be examined individually, next to test the potential interaction between sleep time and quality, and then to investigate the joint association of sleep duration and quality with IFG. The biological effects in terms of RERI, AP and SI were with little significance in this study with consideration of data from a cross-sectional survey. Please get advices from statisticians and experts in this area.

Thank you for the suggestion. We have added the results of sleep duration, sleep quality with IFG. Given the positive relationships, we analyzed further the interaction effect.

5. Results

Why not to investigate the association of global PSQI with IFG? In table 2, only PQSI and its each component score was compared between those with and without IFG. It would be better to see the link between PQSI and IFG.

We have analyzed the association between global PSQI with IFG, which have been published (please see ref. 3 and 8). The aim of this study is to examine the combined effects of sleep quality and sleep duration on IFG

Minor comments:

1. The sentence (line 5-7 on page 3), "The average annual incidence of diabetes in a cohort of patients with IFG is 11% over a six-year period without intervention." Please clearly indicate the subjects were Chinese or other countries' people.

The subjects are Chinese. We have added it in the text.

2. The word, "increasingly", in line 15 on page 3 was not appropriate, because only two ref. cited here. It had been deleted.

3. The word, "confirmed", in line 34 on page 3 is not appropriate, because your previous study was a cross-section survey. Again, the term "relatively healthy individuals" was a little bit confusing and not strict.

"confirmed" had been revised "indicated". Please see the text.

4. Statistics methods

It will be better to describe what specific logistic regression model used in the analysis. Is there any potential cluster effects?

A new variable was created to combine sleep duration and sleep quality. Therefore, we do not think there are potential cluster effects.

5. Please add mean sleep duration in RESULTS.

Done.

6. References

Please indicate all ref. not published in English.

Ref.3,8,9 are in Chinese. We have added "in Chinese" at the end of each reference.

7. Tables

7.1 All tables need modification to meet regular format.

We have refreshed the tables.

7.2 Add another table to show the separate association of sleep time and quality with IFG, individually.

We have added a table.

8. Language

I believe a native English speaker with background of public health or epidemiology is needed to closely edit throughout the entire manuscript.

It had been reviewed and improved by EssayStar.

Reviewer #2（Zumin Shi）

Institution and Country University of Adelaide, Australia Please state any competing interests or state 'None declared': None declared

Main results from Table 3 should be summarized in the abstract. Currently the information is hard to

understand by many readers without specific knowledge.

This cross-sectional study assessed the interaction between sleep duration and sleep quality in relation to the risk of impaired fasting glucose. It is an interesting study with a large sample size.
Major concern:
1. It has been known that long sleep duration is associated with increased risk of mortality. The reasons are not fully clear. The fact that long sleep duration with good sleep quality had the second highest risk of IFG is very interesting (even higher than those long sleep duration with poor sleep quality). Could the author provide some explanation? A thorough analysis of components of PSQI may provide some additional information.
Your proposal gives us good suggestion. We want to write another paper to analyze relation of components of PSQI and IFG or diabetes.
The long sleep duration with good sleep quality had the second highest risk of IFG, however, there was no joint effects, which had been discussed in paragraph 7 of discussion.
2. Is there any gender difference? If yes, gender specific results should be provided.
There in no difference in gender
3. Abstract-Results from Table 3 should be summarized in the abstract.
Done.

Minor:
1. Please provide detailed information on the sampling method. What is the response rate?
It had been answered in No 1. question of reviewer Xu. The response rate is 91.3%.
2. Before excluding participants with chronic diseases, what is the sample size? The prevalence of IFG in the study is much lower than the national data (published in NEJM 2010 and JAMA 2013). If the sampling method is robust, the prevalence of diabetes should be reported in a separate paper. Currently, there is concern on the possible overestimation of the prevalence of diabetes in China.
Thanks. We are ready to report the prevalence of diabetes in Xuzhou area.
3. Table 1- provide percentage in addition to number of participants
Done
4. Table 2- age adjusted mean is more informative
Done. See the table 2.
5. The question used to assess sleep duration should be described in the method section.
Done

Reviewer #3 （Michael Grandner ）
Institution and Country University of Pennsylvania, USA
Please state any competing interests or state 'None declared': None declared

Overall, the manuscript was well-written and well-presented. There were several issues that need to be addressed, however:

1. How was medical history assessed? Was it just by self-report? If so, this should be mentioned.
The medical history was assessed according to medical records, it had been added in text.

2. The authors state that the PSQI has diagnostic ability, but "good" and "poor" sleep categories are not diagnostic.

In this study design, a PSQI score ≤5 was also conventionally defined as 'good sleep quality', and a PSQI score＞5 was defined as 'poor sleep quality'. It had been added in the text.

3. The sleep duration categories need to be justified. How were they determined? Also, how was sleep duration assessed? It seems that it was the single item on the PSQI but this is not specified.

Also, some justification is needed for using this single-item measure.
Self-reported sleep measures of chronic sleep. Two variables were used to evaluate degree of "chronic sleep restriction" by estimating average nightly sleep duration: (i) "usual sleep" (from questionnaires) and (ii) "average nightly sleep" (from sleep diaries). It had been added in the text.

4. The paper does not describe how lifestyle factors were assessed.
"Lifestyle variables included cigarette smoking, alcohol drinking and physical activity level. Cigarette smoking was defined as having smoked at least 100 cigarettes in a lifetime. Information was obtained on the amount and type of alcohol that was consumed during the previous year, and alcohol drinking was defined as the consumption of at least 30 g of alcohol per week for one year or more. Regular leisure-time physical activity was defined as participating in moderate or vigorous activity for no less than 30 minutes per day at least three days a week." It had been introduced in the covariates of text. The poor diet which had been reported in the limitation was not assessed

5. How was height and weight measured? (Were these self-reported or objective?)
"Each volunteer's body height (to the nearest 0.1 cm) and weight (to the nearest 0.1 kg) in light indoor clothing were measured". It had been introduced in the covariates of text.

6. Why were overweight and obese categories combined? In much of the sleep duration literature, there are clear differences in effects for overweight versus obesity.
This paper is not focus on overweight or obesity, which only be treated as confounding factors

7. Interaction terms should be reported to justify stratification.
P for interaction is 0.000, which we have reported in the results.

8. The manuscript mentions a relationship with "all PSQI items." However the table (Table 2) notes PSQI subscales, which seem to be what was meant. It should be noted that PSQI subscales are not continuous variables (they are ordinal or at least categorical) and should be evaluated as such.
We have assigned PSQI subscales with scores. Therefore, the variables are continuous.

9. The discussion section should include some commentary on the literature describing short sleep duration with insomnia. The Penn State group (e.g., Vgontzas, Bixler, Fernandez-Mendoza et al) have published extensively on this concept and more of their work should be cited.
We are not quite sure. It seems difficulty to link the literature with our manuscript. Our main objective was to assess the interaction effect of sleep quality and sleep duration on IFG, while the literature suggested insignificant relationship between sleep duration and obesity. Furthermore, we did not include insomnia in our manuscript. Could you please give clearer suggestion to discuss with the literature?

10. The discussion might also benefit from commentary on the paper by Altman et al 2012, which studies sleep duration in the context of insufficient sleep associated with diabetes and obesity (among other outcomes). This is another example of the relationship between sleep duration and sleep quality.

Similarly, Altman et al indicated both sleep duration and insufficiency related to cardiometabolic health outcomes. However, we used PSQI to assess sleep quality. We focused to assess the interaction effect of sleep quality and sleep duration on IFG, rather than relationship between sleep duration and sleep quality. Could you please give clearer suggestion to discuss with the literature?

11.References 10 and 42 seem to not be displayed correctly.
It had been revised in the text.

VERSION 2 – REVIEW

REVIEWER	Fei Xu Nanjing Municipal Center for Disease Control and Prevention; Nanjing Medical University School of Public Health
REVIEW RETURNED	08-Feb-2014

GENERAL COMMENTS	I think the language still needs further editing if possible. Thank you for your positive response and revision. I think your manuscript has been sufficiently improved. However, I still have one discretionary concern for your consideration. 1. I think it is good to cite the original paper reporting BMI cutoffs for Chinese adults and need not cite the second-hand article.

REVIEWER	Zumin Shi University of Adelaide, Australia
REVIEW RETURNED	05-Feb-2014

GENERAL COMMENTS	The revised version and responses are satisfactory. I have one minor comment. One additional table describing the sample chacteristics by the combination of sleep duration and sleep quality may be helpful for readers to better understand the findings.

VERSION 2 – AUTHOR RESPONSE

Reviewer Zumin Shi
The revised version and responses are satisfactory.
I have one minor comment. One additional table describing the sample chacteristics by the combination of sleep duration and sleep quality may be helpful for readers to better understand the findings.

We had done according to your advice, please see the table 2 in the manuscript.

Reviewer Fei Xu
Thank you for your positive response and revision. I think your manuscript has been sufficiently improved. However, I still have one discretionary concern for your consideration.
1. I think it is good to cite the original paper reporting BMI cutoffs for Chinese adults and need not cite the second-hand article.

It was done in the manuscript, please see the Ref 13.