PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	SLEEP DURATION AND MULTIMORBIDITY IN LUXEMBOURG. RESULTS FROM THE EUROPEAN HEALTH EXAMINATION SURVEY IN LUXEMBOURG, 2013-2015
AUTHORS	Ruiz-Castell, Maria; Makovski, Tatjana; Bocquet, Valéry; Stranges, Saverio

VERSION 1 – REVIEW

REVIEWER	Chighaf Bakour University of South Florida, USA
REVIEW RETURNED	20-Oct-2018

GENERAL COMMENTS	This population-based cross-sectional study examined the association between sleep duration and multimorbidity in Luxembourg, using the European Health Examination Survey. The authors found that short sleep duration was linearly associated with the number of chronic conditions. The topic is significant and relevant, and the study has many strengths including the large representative sample and the novelty of looking at sleep duration and sleep problems in this population and their relationship with many chronic diseases. However, there are many methodological issues that overshadow the strengths. My specific comments are below: Major issues • In the introduction, the authors mention the recommended amount of sleep in adults (at least 7 hours), however in their methods they choose two different cut-points for normal sleep during worknights (<6 hours) and non-worknights (<7 hours). No justification was provided for this choice, no reference, and no discussion of the rationale whatsoever. Although different studies have selected different definitions of adequate/short/long sleep, this is the first time that I have encountered a study that used two different cut-points for sleep duration according to work/no work the next day. Very few studies, if any, would consider 6 hours of sleep to be adequate, and more than 7 hours to be considered long. This is a serious flaw in the study, given that biological effect of inadequate sleep does not differ based on work status or day of the week. The authors should either use one definition of “adequate/short/long” sleep durations, or provide a credible reference to justify their choice. • In the methods section, the authors discuss BMI, Smoking, alcohol, and other variables that were collected and presented in the descriptive analysis. However, these variables were not included in the logistic regression model, although they were significantly different among sleep groups and are important risk factors for many chronic diseases. It is unclear why these important potential confounders were unadjusted for, as the

	authors did not explain this omission, which may have biased the odds ratio estimates. • The authors present descriptive statistics related to diagnosis of sleep disorders, trouble falling asleep, sleepiness, and use of sleep medications. However, these variable were not used in the main analysis (logistic regression). They were neither separately analyzed as predictors of multimorbidity, nor controlled for in the analysis of sleep duration and multimorbidity. These are important variables that were excluded from the analysis without explanation or justification. • The discussion section was poorly organized and severely lacking. The first paragraph focuses on sleep problems, which were not the main focus of analysis. Most of this section was a summary of results, with the whole first page summarizing descriptive results, including those related to covariates, rather than focusing on the main findings of the study (results from the logistic regression model). Main results were not mentioned until the second page • The focus of most of the discussion section was on sleep problems, rather than sleep duration which was the focus of the analysis. Most cited studies in this section were also related to sleep problems. Are the authors using "sleep problems" as a blanket term that included sleep duration? This is unclear and quite confusing. • The discussion of possible mechanisms of the association was very deficient. More details are needed. It's unfortunate that the authors mentioned behavioral risk factors (page 11, line 35), which they missed the opportunity to control for, and to discuss this pathway using evidence from their study. Minor issues • Table 3: Presenting the sleep categories in an ordinal manner (starting with the short category) would make the table easier to read • Chronic conditions included two related measures of cardiovascular disease (coronary heart disease, heart attack). These two are better combined. • Last paragraph of the results section (page 9, lines 35-42) does not match the results in table S1: The table did not include the use of sleep medications. • According to page 7, lines 16-17, use of sleep medications was determined by the answer to the question "in the past 2 weeks, have you used other types of medicines that were prescribed to you, such as sleeping tablets?". Was that question specifically related to sleep medications? Or could it include other types of medications. • In the discussion section, page 10, lines 24-25: The authors mention "some studies… while others", giving the impression of 3+ studies in each direction, while only 2 studies were cited. • Also on page 10, line 40 "In our study, long sleep duration more common in women". This statement is a misrepresentation of the findings. As was written in the results and table 3, only work-night sleep displayed this pattern, which was reversed on non-work nights. No comment was made regarding this discrepancy.

REVIEWER	Catia Reis ISAMB- Faculdade de Medicina, Universidade de Lisboa, Portugal; CENC - Sleep Medicine Center, Lisboa, Portugal
REVIEW RETURNED	25-Mar-2019

GENERAL COMMENTS	Some good data and the paper is well written although I do not agree with the categories of sleep differently established according to work or off days. It is well known that people usually sleep less during work days due to their social/work commitments, but that does not make you doing different categories for short sleep duration. I leave my comments on the pdf page 7 line 6 "...in line with most of previously published studies." Which studies? To my knowledge there is no study categorising differently for work and free days considering short, normal or long sleep duration. If you know them you need to give the respective reference. Page 7 line 10 The international recomendations for normal sleep duration for adults are 7- 9h. Long sleep duration is given by >9h of sleep. You can see it at the American National Sleep Foundation publication. https://doi.org/10.1016/j.sleh.2015.10.004 Page 10 line 7 Since you have a group of Portuguese people in your study you should also add a recent population based study reporting the prevalence of short sleep duration for Portugal, it is very high since it was 20.4% but for a a lower cut-off value (<=5h of sleep) for short sleep duration, since it were included also people > 65 years. Page 10 line 38 You could try to calculate the time sleep difference between work and free days for the all groups to try to find if it is a matter of sleep deprivation, if the Portuguese are the ones more sleep deprived during the work days or if they really sleep less than the other groups. Page 21 Its easier to read the table if you have it in a gradient <6h/night; 6-7h/night; >7h/night

VERSION 1 – AUTHOR RESPONSE

Responses to Reviewer #1
Reviewer Name: Chighaf Bakour
Institution and Country: University of South Florida, USA Please state any competing interests or state ‘None declared’: None declared
This population-based cross-sectional study examined the association between sleep duration and multimorbidity in Luxembourg, using the European Health Examination Survey. The authors found that short sleep duration was linearly associated with the number of chronic conditions. The topic is significant and relevant, and the study has many strengths including the large representative sample and the novelty of looking at sleep duration and sleep problems in this population and their relationship with many chronic diseases. However, there are many methodological issues that overshadow the strengths. My specific comments are below:

Major issues

- In the introduction, the authors mention the recommended amount of sleep in adults (at least 7 hours), however in their methods they choose two different cut-points for normal sleep during work nights (<6 hours) and non-work nights (<7 hours).
    - No justification was provided for this choice, no reference, and no discussion of the rationale whatsoever.

- Although different studies have selected different definitions of adequate/short/long sleep, this is the first time that I have encountered a study that used two different cut-points for sleep duration according to work/no work the next day.
- Very few studies, if any, would consider 6 hours of sleep to be adequate, and more than 7 hours to be considered long. This is a serious flaw in the study, given that biological effect of inadequate sleep does not differ based on work status or day of the week. The authors should either use one definition of "adequate/short/long" sleep durations, or provide a credible reference to justify their choice.

Response: We agree that this is a critical issue needing to be addressed. The main reason why two different cut points were used in our study was due to the marked difference observed between sleep hours during work nights (mean: 6.95hrs, SD: 0.97) and non-work nights (mean: 7.86hrs, SD:1.30), approximately one-hour difference. As such, the number of participants who were at both extremes (< 6hrs during the days when not having to work the following day and > 8hrs during workdays) had a very small sample size. We agree with the reviewer that considering "long sleep duration" for more than 7 hours is incorrect and have used the threshold 8 hours during workdays. However, in cases of not having to work the following day, we continued to consider the value ≤6hrs/night instead of <6hrs/night because of the sample size (and the wider confidence intervals observed in the final model). In spite of this, and as a sensitivity analysis, we have included as supplementary material the tables using the same cut points showing similar values, and observing the same trend concerning the association of short sleep duration with the number of chronic conditions.

We have now clarified the above in the manuscript, p.7, Method section, as follows: "Responses to the first question were categorized in short sleep duration (<6hrs/night), medium sleep duration (6-8hrs/night), and long sleep duration (>8hrs/night), in line with previously published studies. Responses to the second question were categorized in short sleep duration (≤6hrs/night), medium sleep duration (7-8hrs/night), and long sleep duration (>8hrs/night). The main reason why we used two different cutoffs was due to the marked difference observed between sleep hours during workdays and non-work days (approximately one-hour difference). As such, the number of participants who were at the extremes (e.g. < 6 hours during the days when not having to work the next day) had a very small sample size."

We have also included a supplementary table and a paragraph in the manuscript, p.8, methods section as follows: «We performed sensitivity analyses using the same categories for sleep duration for working days and days when not having to work the following day (<6hrs/night; 6-8hrs/night;>8hrs/night)."

and on p.10, result sections, as follows: «Sensitivity analyses examining the association between sleep duration and chronic conditions/diseases are presented in Table S2. We observed the same trend as in Table 4 with consistent associations of short sleep duration with the number of chronic conditions." Overall, results were consistent although with wider confidence intervals.

- In the methods section, the authors discuss BMI, Smoking, alcohol, and other variables that were collected and presented in the descriptive analysis. However, these variables were not included in the logistic regression model, although they were significantly different among sleep groups and are important risk factors for many chronic diseases. It is unclear why these important potential confounders were unadjusted for, as the authors did not explain this omission, which may have biased the odds ratio estimates.

Response: Thank you for the suggestion. We did not include the variables because there was no effect in the final model. As suggested, and for clarification we have now included the variables in the model.

- The authors present descriptive statistics related to diagnosis of sleep disorders, trouble falling asleep, sleepiness, and use of sleep medications. However, these variables were not used in the main analysis (logistic regression). They were neither separately analyzed as predictors of multimorbidity, nor controlled for in the analysis of sleep duration and

multimorbidity. These are important variables that were excluded from the analysis without explanation or justification.

Response: Thank you for the suggestion. We have now accounted for these additional sleep measures by adjusting the model with the variables diagnosis of sleep disorder, trouble falling asleep, sleepiness, and use of sleep medications.

- The discussion section was poorly organized and severely lacking. The first paragraph focuses on sleep problems, which were not the main focus of analysis. Most of this section was a summary of results, with the whole first page summarizing descriptive results, including those related to covariates, rather than focusing on the main findings of the study (results from the logistic regression model). Main results were not mentioned until the second page

Response: As suggested, we have restructured the discussion, focusing first on sleep duration and then on the main findings from the logistic regression model.

- The focus of most of the discussion section was on sleep problems, rather than sleep duration, which was the focus of the analysis. Most cited studies in this section were also related to sleep problems. Are the authors using “sleep problems” as a blanket term that included sleep duration? This is unclear and quite confusing.

Response: In the text, the term "sleep problem" is used at different places, using references that include, among others, sleep deprivation / duration. We have included a note in the section methods, p.7 to clarify this.

- The discussion of possible mechanisms of the association was very deficient. More details are needed. It is unfortunate that the authors mentioned behavioral risk factors (page 11, line 35), which they missed the opportunity to control for, and to discuss this pathway using evidence from their study.

Response: As suggested, we have restructured the discussion and mentioned results from our study on behavioral risk factors.

Minor issues

- Table 3: Presenting the sleep categories in an ordinal manner (starting with the short category) would make the table easier to read

Response: Thank you for the comment. We have now presented the sleep categories in an ordinal manner

- Chronic conditions included two related measures of cardiovascular disease (coronary heart disease, heart attack). These two are better combined.

Response: Thank you for the comment. We have now used the term “cardiovascular diseases” for coronary heart disease, heart attack and stroke. The text now reads:

“Participants were asked if they ever had a chronic disease or condition diagnosed by a medical doctor (e.g., hypertension, high cholesterol, diabetes, cardiovascular diseases, stomach or duodenal ulcer, cirrhosis or other liver disease, urinary incontinence, kidney problems, chronic back or neck disorder, rheumatoid arthritis, arthrosis, osteoporosis, cancer, severe headache as migraine or chronic anxiety). Cardiovascular diseases included coronary heart disease or angina pectoris, heart attack or its chronic consequences, stroke or its chronic consequences.”

- Last paragraph of the results section (page 9, lines 35-42) does not match the results in table S1: The table did not include the use of sleep medications.

Response: Thank you for the comment. We have removed this information from the results section.

- According to page 7, lines 16-17, use of sleep medications was determined by the answer to the question “in the past 2 weeks, have you used other types of medicines that were prescribed to you, such as sleeping tablets?”. Was that question specifically related to sleep medications? Or could it include other types of medications.

Response: Thank you for the comment. The question “in the past 2 weeks, have you used other types of medicines that were prescribed to you” had two possible answers: “1) Sleeping tablets and 2) Antibiotics”. This means that participants only answered for “sleep medication” and could not include other type of medication.

In the past 2 weeks, have you used other types of medicines **that were prescribed to you**, such as …?

Sleeping tablets	☐ Yes	☐ No
Antibiotics (such as penicillin for example)	☐ Yes	☐ No

We have now clarified the above in the manuscript, p.7, Methods section, as follows:"
"Sleep medications were assessed using the question "In the past 2 weeks, have you used other types of medicines that were prescribed to you?". The question was aimed at gathering information about several medications, including sleep tablets."

- In the discussion section, page 10, lines 24-25: The authors mention "some studies… while others", giving the impression of 3+ studies in each direction, while only 2 studies were cited.

This is due to the limitation to the number of references we can include in the manuscript. In the previous version, we had also included the following references:
Villarroel N, Artazcoz L. Immigration and Sleep Problems in a Southern European Country: Do Immigrants Get the Best Sleep? Behavioral medicine (Washington, DC). 2017; 43 (4): 233-241.
Sano Y, Antabe R, Kyeremeh E, Kwon E, Amoyaw J. Immigration as a social determinant of troubled sleep in Canada: some evidence from the Canadian Community Health Survey-Mental Health.Sleep Health. 2019;5(2):135-140.

We have removed this information and the text now reads:" The relationship between immigration status and sleep patterns remains unclear, possibly related to (…)"

- Also on page 10, line 40 "In our study, long sleep duration more common in women". This statement is a misrepresentation of the findings. As was written in the results and table 3, only work-night sleep displayed this pattern, which was reversed on non-work nights. No comment was made regarding this discrepancy.

Response: Thanks you for this remark. We have observed that in Table 3, although not statistically significant, the categories were inversed, with women sleeping more than 8h compared to men. In the new models with the multivariate adjustment and new categories, we observed a trend for women to be more likely long sleepers compared to men in both work and not working days (Table 4). The text now reads:
"In our study, there was a trend for women to be more likely long sleepers compared to men."

Reviewer: 2
Reviewer Name: Catia Reis
Institution and Country: ISAMB- Faculdade de Medicina, Universidade de Lisboa, Portugal; CENC - Sleep Medicine Center, Lisboa, Portugal
Please state any competing interests or state 'None declared': Nothing to declare
See file attached.

- Some good data and the paper is well written although I do not agree with the categories of sleep differently established according to work or off days. It is well known that people usually sleep less during workdays due to their social/work commitments, but that does not make you doing different categories for short sleep duration.

Response: We agree with the reviewer that it would be interesting and relevant to use the same categories in both cases. We decided to distinguish two categories because the sample size across categories was significantly reduced. As the difference between the total sleeping hours between both nights when having and not having to work the next day (6.95hrs±0.97 and 7.86hrs±1.30 respectively) was approximately one hour (a remarkable difference), we considered that this would justify the use of two distinct categories. Nevertheless, to improve the quality of the present study, we have analyzed the models again, using the same categories in both cases as a sensitivity analysis (supplementary table S2).

- I leave my comments on the pdf page 7 line 6 "...in line with most of previously published studies. "Which studies? To my knowledge there is no study categorizing differently for work and free days considering short, normal or long sleep duration. If you know them you need to give the respective reference.

Response: This phrase referred to the use of sleep categories (<6h; 6-7 and>7h), not intended to differentiate between working days and not working days. We agree that this is a critical issue needing to be addressed. The main reason why two different cut points were used in our study was due to the marked difference observed between sleep hours during workdays and non-work days (approximately one-hour difference). As such, the number of participants who were at both extremes (< 6hrs during the days when not having to work the following day and > 8hrs during workdays) had a very small sample size. We agree with the reviewer that considering "long sleep duration" for more than 7hrs is incorrect and have used the threshold 8hrs during workdays. However, in cases of not having to work the following day, we continued to consider the value ≤6hrs/night instead of <6hrs/night because of the sample size (and the wider confidence intervals observed in the final model). In spite of this, and as a sensitivity analysis, we have included as supplementary material the tables using the same cut points, and observing the same trend concerning the association of short sleep duration with the number of chronic conditions.

We have also included the following references in the text using the categorization <6h, 6-8h, and >8h:

  - Stranges, S., et al. (2008). "Correlates of short and long sleep duration: a cross-cultural comparison between the United Kingdom and the United States: the Whitehall II Study and the Western New York Health Study." Am J Epidemiol 168(12): 1353-1364.
  - Whinnery, J., et al. (2014). "Short and long sleep duration associated with race/ethnicity, sociodemographics, and socioeconomic position." Sleep 37(3): 601-611.

- Page 7 line 10. The international recommendations for normal sleep duration for adults are 7-9h. Long sleep duration is given by >9h of sleep. You can see it at the American National Sleep Foundation publication.

Response: Thank you for this comment. Although the international recommendation for long sleep duration is defined as sleep duration >9hrs we did not have enough participants in this category for the analysis. Only eight individuals (1.18%) reported sleeping >9hrs when working the following day. This could be in part explained by the fact that recommendations are for the total hours of sleep per day, and that our study did not include naps. We have included this information in the limitations section and used the cutoff >8hrs.

The text now reads: «In our study, we only included the number of sleep hours during the night, without including nap times. For this reason, the categories used here are slightly different from the recommendations of daily sleep hours."

- Page 10 line 7. Since you have a group of Portuguese people in your study you should also add a recent population based study reporting the prevalence of short sleep duration for Portugal, it is very high since it was 20.4% but for a lower cutoff value (<=5h of sleep) for short sleep duration, since it were included also people > 65 years.

Response: Thank you for the suggestion. We have included the reference of the reviewer in the text. Now the text reads:" Results are similar to those observed in other countries, although in countries such as Brazil the prevalence of short sleep duration was of nearly 22%, and in Portugal and the United States values reached up to 20% in 2015-2016 and 34.8% in 2014, respectively.

Reference included:

  - Reis, C., et al. (2018). "Sleep duration, lifestyles and chronic diseases: a cross-sectional population-based study." Sleep Sci 11(4): 217-230.

- Page 10 line 38. You could try to calculate the time sleep difference between work and free days for the all groups to try to find if it is a matter of sleep deprivation, if the Portuguese are

the ones more sleep deprived during the workdays or if they really sleep less than the other groups.

Response: We calculate the time sleep difference between work and non-working days for all groups and we did not observed any difference. As observed in Table 3 Portuguese were those sleeping less hours in both working and non-working days. In the new model in Table 4, the effect was only significant when not having to work the following day.

Mean time sleep difference by immigration

Immigration	N	Mean time sleep difference (SD)	P value
Luxembourg	607	1.05 (1.08)	0.286
Portugal	166	1.17 (1.29)	
Other	376	1.15 (1.19)	

Regression model

	Time sleep difference	
	Coef (SE)	(95% CI)
Immigration		
Luxembourg	1.00	
Portugal	0.101 (0.10)	(-0.09, 0.30)
Other	1.082 (0.07)	(-0.07, 0.23)

- Page 21. It's easier to read the table if you have it in a gradient <6h/night; 6-7h/night; >7h/night

Response: Thank you for the comment. We have now presented the sleep categories in an ordinal manner

VERSION 2 – REVIEW

REVIEWER	Chighaf Bakour University of South Florida USA
REVIEW RETURNED	28-Jun-2019

GENERAL COMMENTS	Thank you for responding to my previous comments. Many of my concerns have been addressed, and the manuscript has improved significantly. However, the concern over the definition of the main exposure (sleep duration) remains. The authors justify their choice of using two different cut points by citing the small sample size, which, in my opinion, is not acceptable. The definition of short sleep duration is based on scientific studies that determine the adequate amount of sleep for adults. This amount does not change based on days of the week or according to available sample size. The authors must select one cut-off, backed by scientific evidence, and report the findings, even if the confidence intervals are wide. One suggestion to deal with the sample size issue is to calculated a weighted average of weekday sleep (when they have work the next day) and weekend sleep (when they don't have work the next day. You may do this by assigning a weight of 2/7 for weekends, and 5/7

	for weekdays (assuming 5 day work weeks). This method has previously been used in multiple studies. Examples can be found in the links below: - Watanabe et al. (2010) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2817903/ - Lauderdale et al. (2018) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2785092/ - Bakour et. al. (2017) https://academic.oup.com/sleep/article/40/11/zsx156/4372126 - Additionally, it is unclear from reading the manuscript whether sleep duration is considered to be the exposure or the outcome. Table 4 presents sleep duration as the outcome, with chronic diseases as the exposure or predictor, while the discussion section includes potential mechanisms that explain the deleterious effects of short sleep duration and their contribution to chronic diseases. This is quite confusing to the reader as the manuscript appears to lack a coherent flow from the introduction to the conclusion. It's true that the cross-sectional nature prevents the determination of direction of association, but the analysis must be based on a clear research question/hypothesis, and the discussion must be based on this same hypothesis as well as the results.

REVIEWER	Cátia Reis ISAMB - Faculdade de Medicina, Universidade de Lisbon, Portugal CENC - Sleep Medicine Center, Lisbon, Portugal
REVIEW RETURNED	03-Jul-2019

GENERAL COMMENTS	The study is interesting but there are some questions regarding sleep that continue not to be addressed in this second revision. It's difficult to have an association with long sleep duration and worse health outcome because >8h is still considered as recommended sleep hours, what is considered long sleep duration for adults are in fact >9h. Being this sample composed by adults only until 64 years this is even more relevant. I do understand that the sample size is the reason why this cut-off value was done, but this need to be discussed in the manuscript. Different cut-off points for work and work-free days does not make any sense. The sensitivity model like the authors done, makes much more sense than two different cut-offs for both conditions. I will now give more detailed comments: - Line 24 page 10 With different cut-off points for work and work-free days the prevalence values statement can't be done; - Line 31 page 10 It needs to be highlighted the fact of having different cut-off points in the other population samples. For the US sample the cut-off point established for short sleep duration was in fact 6h, but for Portugal was 5h; - Line 34 page 11 "However, after adjusting for sleep disorders the association with short sleep duration was only maintained for non-work-days" This makes the all sense and explains that they are only sleeping less on workdays because they need to work and are very likely

	awaken by an alarm clock. Suffering from social jet lag. Once more this explains why two different cut-off points can't be used. The condition short sleep duration must be the same for both conditions. - Line 54 page 11 It's not ciercadian rhythm but circadian rhythm - Line 51 page Sleep deprivation was not measured in the manuscript. Although with the number of working days and the sleep duration for work and for free-days it is possible to calculate sleep dept that is a proxi for sleep deprivation.

VERSION 2 – AUTHOR RESPONSE

Responses to Reviewer #1

Reviewer Name: Chighaf Bakour

Institution and Country: University of South Florida USA

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

Please leave your comments for the authors below

Comment 1

Thank you for responding to my previous comments. Many of my concerns have been addressed, and the manuscript has improved significantly. However, the concern over the definition of the main exposure (sleep duration) remains. The authors justify their choice of using two different cut points by citing the small sample size, which, in my opinion, is not acceptable. The definition of short sleep duration is based on scientific studies that determine the adequate amount of sleep for adults. This amount does not change based on days of the week or according to available sample size. The authors must select one cut-off, backed by scientific evidence, and report the findings, even if the confidence intervals are wide. One suggestion to deal with the sample size issue is to calculated a weighted average of weekday sleep (when they have work the next day) and weekend sleep (when they don't have work the next day. You may do this by assigning a weight of 2/7 for weekends, and 5/7 for weekdays (assuming 5 day work weeks). This method has previously been used in multiple studies. Examples can be found in the links below:

- Watanabe et al. (2010) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2817903/

- Lauderdale et al. (2018) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2785092/

- Bakour et. al. (2017) https://academic.oup.com/sleep/article/40/11/zsx156/4372126

Response: Thank you for the suggestion. We could not calculate, as a first step, a weighted average because we did not have information on the number of days individuals worked. After further consultationwith the coauthors, it was agreed to calculate the weighted average in order to avoid the issue of dealing with sample size. Accordingly, we have now included in the limitations section an additional statement regarding the fact that we assumed participants worked 5 days per week on average. Results are now presented in the revised tables 3 and 4. We also modified table 1. Likewise,

we also explained in the methodology that we calculated the weighted average of sleep hours and included a comment in the limitation section.

Comment 2

Additionally, it is unclear from reading the manuscript whether sleep duration is considered to be

the exposure or the outcome. Table 4 presents sleep duration as the outcome, with chronic diseases as the exposure or predictor, while the discussion section includes potential mechanisms that explain the deleterious effects of short sleep duration and their contribution to chronic diseases. This is quite confusing to the reader as the manuscript appears to lack a coherent flow from the

introduction to the conclusion. It's true that the cross-sectional nature prevents the determination of direction of association, but the analysis must be based on a clear research question/hypothesis,

and the discussion must be based on this same hypothesis as well as the results.

Response: As suggested, we have restructured the discussion and clarified the confusion.

Responses to Reviewer #2

Reviewer Name: Cátia Reis

Institution and Country:

ISAMB - Faculdade de Medicina, Universidade de Lisbon, Portugal CENC - Sleep Medicine Center, Lisbon, Portugal

Please state any competing interests or state ‘None declared’: Nothing to declare

Please leave your comments for the authors below

Comment 1

The study is interesting but there are some questions regarding sleep that continue not to be addressed in this second revision. It's difficult to have an association with long sleep duration and worse health outcome because >8h is still considered as recommended sleep hours, what is considered long sleep duration for adults are in fact >9h. Being this sample composed by adults only until 64 years this is even more relevant. I do understand that the sample size is the reason why this cut-off value was done, but this need to be discussed in the manuscript.

Different cut-off points for work and work-free days does not make any sense. The sensitivity model like the authors done, makes much more sense than two different cut-offs for both conditions.

Response: We appreciate these additional comments and have addressed both issues by calculating the weighted average for sleep as also suggested by reviewer 1. We then used consistent cutoffs <6h, 6-9 and >9h without differentiating work and work-free days. As observed in the previous analysis, long sleep duration (>9h) was not associated with multimorbidity. Results are now presented in the revised tables 3 and 4. We also modified table 1. We have also provided additional explanations in the methodology stating that we calculated the weighted average of sleep hours and included a comment in the limitation section.

I will now give more detailed comments (also see attached):

- Line 24 page 10: With different cut-off points for work and work-free days the prevalence values statement can't be done;

Response: Following the new definition (weighted average of sleep hours) we have corrected the prevalence for Luxembourg.

- Line 31 page 10: It needs to be highlighted the fact of having different cut-off points in the other population samples. For the US sample the cut-off point established for short sleep duration was in fact 6h, but for Portugal was 5h;

Response: Thank you for the remark. We have now clarified the cut-off point used in Portugal. As for the study in the US the cut-off was 7hrs and we have only named the European and Brazilian studies with the same cut-off (<6hrs).

- Line 34 page 11: "However, after adjusting for sleep disorders the association with short sleep duration was only maintained for nonwork-days" This makes the all sense and explains that they are only sleeping less on workdays because they need to work and are very likely awaken by an alarm clock. Suffering from social jet lag. Once more this explains why two different cut-off points can't be used. The condition short sleep duration must be the same for both conditions.

Response: With the weighted average calculated, we have addressed the point.

- Line 54 page 11: It's not ciercadian rhythm but circadian rhythm

Response: We have corrected the misspelling.

- Line 51 page: Sleep deprivation was not measured in the manuscript. Although with the number of working days and the sleep duration for work and for free-days it is possible to calculate sleep dept that is a proxi for sleep deprivation.

Response: We have corrected the term and used sleep duration instead of sleep deprivation.

VERSION 3 – REVIEW

REVIEWER	Chighaf Bakour USA - University of South Florida
REVIEW RETURNED	27-Jul-2019

GENERAL COMMENTS	Thank you for addressing my concerns. The manuscript has improved significantly. I have no further comments