

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	The association between physical activity over a 10-year period and current insomnia symptoms, sleep duration and daytime sleepiness – A European population-based study
<b>AUTHORS</b>	Bjornsdottir, Erla; Thorarinsdottir, Elin; Lindberg, Eva; Benediktsdottir, Bryndis; Franklin, Karl; Jarvis, Debbie; Demoly, Pascal; Perret, Jennifer; Garcia Aymerich, Judith; Dorado-Arenas, Sandra; Heinrich, Joachim; Torén, Kjell; Garcia Larsen, Vanessa; Jögi, Rain; Gislason, Thorarinn; Janson, Christer

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Cohen , Zachary L. The University of North Carolina at Chapel Hill, Psychiatry
<b>REVIEW RETURNED</b>	20-Nov-2022

<b>GENERAL COMMENTS</b>	<p>Abstract conclusion: I don't think it's somewhat misleading to say "physically active people have a lower risk of insomnia symptoms." Should say lower risk of SOME insomnia symptoms, or list the specific symptoms. For example there was no relationship between physical activity and maintaining sleep, for example. So it's misleading to imply insomnia symptoms in general. This would also apply to this terminology as used in the discussion.</p> <p>Line 21: The phrase "doctor diagnosis" is awkward and excludes non-physician providers. Would say "no sleep disorder diagnoses from medical providers, or objective assessments, were available."</p> <p>Wouldn't use the term "the elderly" - would say "in older adults" or specify the age range ("adults older than __ years old")</p> <p>Is there a standard definition for "middle aged?"</p> <p>"In conclusion, physical activity over time is associated with lower prevalence of insomnia symptoms and a more likelihood of sleeping the recommended 6-9 hours per night." -Should be "was associated with sleeping 6-9 hours per night." -"A more likelihood" doesn't make sense - Unclear and too broad to say "the recommended 6-9 hours." Say earlier in paper that it is what is recommended by the American Academy of Sleep Medicine, for example (I don't know if that's the case), to show why this amount of sleep is relevant. And then just refer to sleeping 6-9 hours later (not "the recommended 6-9 hours")</p>
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<b>REVIEWER</b>	Wang, Feifei Eötvös Loránd University
<b>REVIEW RETURNED</b>	22-Nov-2022

<b>GENERAL COMMENTS</b>	<p>General comments:</p> <p>The topic of this study is interesting, my effort is to sort out some ambiguations and strengthen the quality of this manuscript. Detailed comments are discussed below. I hope the authors find them useful.</p> <p>Specific comments that I would like the author(s) to respond:</p> <ol style="list-style-type: none"> <li>1. Introduction: I would recommend to add a heading sentence for each paragraph, which allows readers to follow the theme of each paragraph and be focused.</li> <li>2. Introduction: "Finally, no studies have tested at the same time the effect of physical activity on sleep length, daytime sleepiness, and insomnia symptoms." This is sentence can be misleading.</li> <li>3. Material and methods: "Briefly, participating centers first randomly selected samples of 20 to 44-year-old subjects." Please explain why subjects aged only 20 to 44-year-old were selected?</li> <li>4. Results: I wonder whether it is propriate enough to categorize the four PA groups "persistently non-active (non-active at both baseline and follow up), became inactive (active at baseline and non-active at follow up), became active (non-active at baseline and active at follow up) and persistently active (active at both baseline and follow up)" in this way. Although, the authors mentioned it as a limitation. Could the author(s) find previous literature which has similar categorizing method?</li> <li>5. page9,line60: "(0.78 (0.65-0.94))", please add OR to the numbers. Same as page 10, line 52.</li> <li>6. Discussion: the third paragraph seems non relevant to the results.</li> <li>7: page 12,line17: what does "(9, 10)," mean? Is it a reference quote?</li> <li>8. page13, line36: "Under these circumstances physical activity data would only have shown very limited association with sleep." Could the author better explain it?</li> <li>9. "Physical activity is associated with improved cognitive function but the association of sleep and cognitive function seems to be U-shaped, as too much or too little sleep is negatively associated with cognitive function.34 It would therefore be interesting for future studies to explore how cognitive function is affected by the association of physical activity and sleep." Again, these statements are out of the research scope of the present study.</li> <li>10. "Also, the questions included only vigorous physical activity and the effect of moderate or low intensity activity could not be tested." It is better to state it in the "Assessment of physical activity" section.</li> </ol>
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<b>REVIEWER</b>	Al-Sallakh, Mohammad Swansea University Medical School
<b>REVIEW RETURNED</b>	23-Jan-2023

<b>GENERAL COMMENTS</b>	This study investigates the association between the 'longitudinal pattern' of physical activity (persistently active, persistently inactive, became active, became inactive) and sleep-related
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	<p>outcomes at follow-up among middle-aged people in 9 European countries using two questionnaires (ECRHS II and ECRHS III) 10 years apart. A main conclusion is that persistent physical activity was associated with a lower risk of insomnia symptoms and extreme sleep duration at follow-up, compared with persistent physical inactivity.</p> <p>The manuscript is well written, and the findings add important insights into the association between physical activity and sleep related outcomes.</p> <p>1. However, as the authors pointed out, a key limitation is the absence of sleep-related measurements at the baseline. I suggest that this methodological limitation deserves more emphasis in the discussion. Although the measurement of physical activity is longitudinal, it may not be entirely appropriate to describe the associations between physical activity and sleep outcomes as longitudinal (as in the title). The term "longitudinal association" may give the impression that sleep outcomes were also measured at the baseline.</p> <p>In addition, in the abstract, the authors concluded: "Physically active people have a lower risk of insomnia symptoms and extreme sleep duration, both long and short" and they mentioned in the first point in the "Strengths and limitations" box that the study design allowed testing the directionality of the association. Although the main findings (associations) in this study are consistent with other studies, with the lack of baseline measurement of sleep outcomes, I am not entirely sure that the *directionality* of association between physical activity and sleep outcomes could be sufficiently tested in this study.</p> <p>2. At the end of the discussion, the authors mentioned that "the questions included only vigorous physical activity". However, in "Material and methods/Assessment of physical activity", the intensity of exercise is not specified.</p> <p>3. In their systematic review (10.1080/21679169.2019.1623314), Wang &amp; Boros 2019 concluded that "moderate exercise showed more promising outcome on sleep quality than vigorous exercise". If you only included 'vigorous' physical activity, it would be useful to compare your findings with this systematic review.</p> <p>4. Please discuss the potential implications of residual confounders that can influence both physical activity and sleep outcomes (e.g., mental health, musculoskeletal disorders/pain, ...) on the study findings.</p> <p>5. In the footer of Table 3, the authors mentioned that the odds ratios were also adjusted for the study centre. Please add this information to the Methods and clarify if the study centre (n = 21) was used as a fixed effect (or random effect).</p> <p>6. Please add p-values to Table 3.</p>
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<b>REVIEWER</b>	Banno, Masahiro Seichiryō Hospital, Department of Psychiatry
<b>REVIEW RETURNED</b>	22-Mar-2023

<b>GENERAL COMMENTS</b>	<p>This study aimed to assess the interrelationship between physical activity based on frequency, duration and intensity and symptoms of insomnia, self-reported sleep duration and daytime sleepiness among middle-aged subjects from 21 centers in 9 countries.</p> <p>The strength of this study was to conduct analysis using a rigorous method of a population-based, multi-center cohort study. However, there were some concerns in this study.</p> <p>First, the authors had better add the data of the effect estimates (odds ratios) and those confidence intervals for the following variables, age, sex, BMI, smoking history, and study center in logistic regression.</p> <p>Second, in the discussion section, they had better add a discussion if any of the variables (sex, age, smoking history, and BMI) are associated with the outcomes of the study.</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Zachary L. Cohen , The University of North Carolina at Chapel Hill

Comments to the Author:

Abstract conclusion: I don't think it's somewhat misleading to say "physically active people have a lower risk of insomnia symptoms." Should say lower risk of SOME insomnia symptoms, or list the specific symptoms. For example there was no relationship between physical activity and maintaining sleep, for example. So it's misleading to imply insomnia symptoms in general. This would also apply to this terminology as used in the discussion.

Thank you for this comment – we have changed the wording of the abstract conclusion in accordance to this.

Line 21: The phrase "doctor diagnosis" is awkward and excludes non-physician providers. Would say "no sleep disorder diagnoses from medical providers, or objective assessments, were available."

Thank you for this comment – we have changed this

Wouldn't use the term "the elderly" - would say "in older adults" or specify the age range ("adults older than \_\_ years old")

Thank you for this comment – we have changed this

Is there a standard definition for "middle aged?"

We have now deleted the words middle aged and put in the age range which is 39-67 years.

"In conclusion, physical activity over time is associated with lower prevalence of insomnia symptoms and a more likelihood of sleeping the recommended 6-9 hours per night."

-Should be "was associated with sleeping 6-9 hours per night."

-"A more likelihood" doesn't make sense

- Unclear and too broad to say "the recommended 6-9 hours." Say earlier in paper that it is what is recommended by the American Academy of Sleep Medicine, for example (I don't know if that's the

case), to show why this amount of sleep is relevant. And then just refer to sleeping 6-9 hours later (not "the recommended 6-9 hours")

Thank you for this comment – we have changed the wording of the conclusion in accordance to this.

Reviewer: 2

Dr. Feifei Wang, Eötvös Loránd University, Fudan University

Comments to the Author:

General comments:

The topic of this study is interesting, my effort is to sort out some ambiguations and strengthen the quality of this manuscript. Detailed comments are discussed below. I hope the authors find them useful.

Specific comments that I would like the author(s) to respond:

1. Introduction: I would recommend to add a heading sentence for each paragraph, which allows readers to follow the theme of each paragraph and be focused.

Thank you for this suggestion – we have now added heading sentences for each paragraph in the introduction.

2. Introduction: "Finally, no studies have tested at the same time the effect of physical activity on sleep length, daytime sleepiness, and insomnia symptoms." This is sentence can be misleading.

Thank you for this comment – we have rephrased the sentence.

3. Material and methods: "Briefly, participating centers first randomly selected samples of 20 to 44-year-old subjects." Please explain why subjects aged only 20 to 44-year-old were selected?

The age – span 20-44 was originally chosen in 1990 (ECRSH I) because the main aim of ECRSH was to follow a general population cohort regarding asthma, allergy, and lung diseases. As described on the web page ([www.ecrsh.org](http://www.ecrsh.org)) this multicentre follow-up study had many different working groups including lifestyle and sleep. This is now described in more detail in the text on page 6, paragraph 3.

4. Results: I wonder whether it is appropriate enough to categorize the four PA groups "persistently non-active (non-active at both baseline and follow up), became inactive (active at baseline and non-active at follow up), became active (non-active at baseline and active at follow up) and persistently active (active at both baseline and follow up)" in this way. Although, the authors mentioned it as a limitation. Could the author(s) find previous literature which has similar categorizing method?

- The decision to categorize the participants was taken after a careful evaluation when analysing these data, a priori for the relationship between physical activity and lung function. Was published in Thorax 2018: "Leisure-time vigorous physical activity is associated with better lung function: the prospective ECRHS study PMID: 29306902" by partly the same authors. In the Thorax paper there is a detailed description in the Method section on how the categorization was done:

- Leisure-time vigorous physical activity was estimated by asking participants how often (frequency) and for how many hours per week (duration) they usually exercised so much that they got out of breath or sweaty (ref 19) using previously validated questions (ref 20, 21). The responses for

frequency were every day, 4–6 times a week, 2–3 times a week, once a week, once a month, less than once a month and never. For statistical analyses, we grouped together the first two categories, the next two categories and the last three categories. The responses for duration were 7 hours or more, about 4–6 hours, about 2–3 hours, about 1 hour, about half an hour and none. For statistical analyses, we grouped together the first two categories, the next two categories and the last two categories. At each time point, individuals were categorised as being active if they exercised with a frequency of two or more times a week ('2–3 times a week' or greater) and with a duration of about 1 hour a week or more, and non-active otherwise (as done previously in the ECRHS (ref 22 and by others 23). Change in activity status was categorised into four groups: non-active at both examinations, became inactive, became active and active at both examinations.

• References 19-23:

19. World Health Organization. Global Strategy on Diet | Physical Activity and Health. What is Moderate-intensity and Vigorous-intensity Physical Activity? [Internet]. [http://www.who.int/dietphysicalactivity/physical\\_activity\\_intensity/en](http://www.who.int/dietphysicalactivity/physical_activity_intensity/en)

20. Rovio S, K reholt I, Helkala EL, et al. Leisure-time physical activity at midlife and the risk of dementia and Alzheimer's disease. *Lancet Neurol* 2005;4:705–11.

21. Washburn RA, Goldfield SR, Smith KW, et al. The validity of self-reported exercise-induced sweating as a measure of physical activity. *Am J Epidemiol* 1990;132:107–13.

22. Shaaban R, Leynaert B, Soussan D, et al. Physical activity and bronchial hyperresponsiveness: European Community Respiratory Health Survey II. *Thorax* 2007;62:403–10.

23. Booth ML, Okely AD, Chey T, et al. The reliability and validity of the physical activity questions in the WHO health behaviour in schoolchildren (HBSC) survey: a population study. *Br J Sports Med* 2001;35:263–7.

Our text on page 7 is now explaining better based on the publication in Thorax.

5. page9,line60: "(0.78 (0.65-0.94)", please add OR to the numbers. Same as page 10, line 52.

Thank you for this comment – this has been added.

6. Discussion: the third paragraph seems non relevant to the results.

We would like to keep this paragraph as we think it is important to compare our results to what others have found regarding insomnia and physical activity.

7: page 12,line17: what does "(9, 10)," mean? Is it a reference quote?

Yes these are references, we have now corrected the format.

8. page13, line36: "Under these circumstances physical activity data would only have shown very limited association with sleep." Could the author better explain it?

Thank you for this comment - we have now removed this sentence

9. "Physical activity is associated with improved cognitive function but the association of sleep and cognitive function seems to be U-shaped, as too much or too little sleep is negatively associated with cognitive function.<sup>34</sup> It would therefore be interesting for future studies to explore how cognitive function is affected by the association of physical activity and sleep." Again, these statements are out of the research scope of the present study.

Thank you for this comment. We have changed the wording of this sentence to make it fit better with the discussion of the results of the current study and future directions.

10. "Also, the questions included only vigorous physical activity and the effect of moderate or low intensity activity could not be tested." It is better to state it in the "Assessment of physical activity" section.

Thank you for this suggestions, we agree and have now removed this sentence.

Reviewer: 3

Dr. Mohammad Al-Sallakh, Swansea University Medical School

Comments to the Author:

This study investigates the association between the 'longitudinal pattern' of physical activity (persistently active, persistently inactive, became active, became inactive) and sleep-related outcomes at follow-up among middle-aged people in 9 European countries using two questionnaires (ECRHS II and ECRHS III) 10 years apart. A main conclusion is that persistent physical activity was associated with a lower risk of insomnia symptoms and extreme sleep duration at follow-up, compared with persistent physical inactivity.

The manuscript is well written, and the findings add important insights into the association between physical activity and sleep related outcomes.

1. However, as the authors pointed out, a key limitation is the absence of sleep-related measurements at the baseline. I suggest that this methodological limitation deserves more emphasis in the discussion. Although the measurement of physical activity is longitudinal, it may not be entirely appropriate to describe the associations between physical activity and sleep outcomes as longitudinal (as in the title). The term "longitudinal association" may give the impression that sleep outcomes were also measured at the baseline.

Thank you for this valuable comment, we agree, and we have now added a sentence regarding this in the last paragraph of the discussion. We have also changed the title of the manuscript accordingly.

In addition, in the abstract, the authors concluded: "Physically active people have a lower risk of insomnia symptoms and extreme sleep duration, both long and short" and they mentioned in the first point in the "Strengths and limitations" box that the study design allowed testing the directionality of the association. Although the main findings (associations) in this study are consistent with other studies, with the lack of baseline measurement of sleep outcomes, I am not entirely sure that the \*directionality\* of association between physical activity and sleep outcomes could be sufficiently tested in this study.

Thank you for this comment, we agree with you, and we have tried to make this more clear in the discussion chapter when going over the limitations of the current study.

2. At the end of the discussion, the authors mentioned that "the questions included only vigorous physical activity". However, in "Material and methods/Assessment of physical activity", the intensity of exercise is not specified.

Thank you for this comment – we have changed the wording to make this more clear

3. In their systematic review (10.1080/21679169.2019.1623314), Wang & Boros 2019 concluded that "moderate exercise showed more promising outcome on sleep quality than vigorous exercise". If you

only included 'vigorous' physical activity, it would be useful to compare your findings with this systematic review.

Thank you for this suggestion – we have now gone thoroughly over this review and added it to our paper and reference list

4. Please discuss the potential implications of residual confounders that can influence both physical activity and sleep outcomes (e.g., mental health, musculoskeletal disorders/pain, ...) on the study findings.

Thank you for this suggestion – we have now added a sentence regarding this in the last paragraph of the discussion chapter.

5. In the footer of Table 3, the authors mentioned that the odds ratios were also adjusted for the study centre. Please add this information to the Methods and clarify if the study centre (n = 21) was used as a fixed effect (or random effect).

All variables in the model were treated as fixed effects. This has been stated more clearly in the methods section (see page 8, paragraph 2).

6. Please add p-values to Table 3.

Of course, we could add p-values, but it would make the table more difficult to read and we think that the 95% confidence intervals of the odds ratios are an even better indicator of significant differences than p-values. We would like to keep the table unchanged, but we have added to the text about significance.

Reviewer: 4

Dr. Masahiro Banno, Seichiryō Hospital, Nagoya University Graduate School of Medicine

Comments to the Author:

This study aimed to assess the interrelationship between physical activity based on frequency, duration and intensity and symptoms of insomnia, self-reported sleep duration and daytime sleepiness among middle-aged subjects from 21 centers in 9 countries.

The strength of this study was to conduct analysis using a rigorous method of a population-based, multi-center cohort study. However, there were some concerns in this study.

First, the authors had better add the data of the effect estimates (odds ratios) and those confidence intervals for the following variables, age, sex, BMI, smoking history, and study center in logistic regression.

We agree and have added an additional table covering this (Table 4). In the table we have adjusted for centre but have not included that variable in the table as this would make the table quite complicated.

Second, in the discussion section, they had better add a discussion if any of the variables (sex, age, smoking history, and BMI) are associated with the outcomes of the study.

Thank you for this comment – we have added a sentence regarding this in the first paragraph of the discussion.



Reviewer: 1  
Competing interests of Reviewer: None

Reviewer: 2  
Competing interests of Reviewer: n/a

Reviewer: 3  
Competing interests of Reviewer: None

Reviewer: 4  
Competing interests of Reviewer: None

### VERSION 2 – REVIEW

<b>REVIEWER</b>	Al-Sallakh, Mohammad Swansea University Medical School
<b>REVIEW RETURNED</b>	13-Aug-2023

<b>GENERAL COMMENTS</b>	<p>Thank you for responding to my comments.</p> <p>In the title, you could replace "longitudinal physical activity" with "... longitudinal change in physical activity ..." or "10-year change in physical activity".</p> <p>Thank you for adding the limitation that the association tested in this study may not be longitudinal, to the discussion section. However, the first point in the "Strengths and limitations of this study" box still reads "The longitudinal study design, with the exposure (physical activity) measured 10 years before the outcome (sleep outcomes) allows testing the directionality of the association." As I pointed out in my previous comments, this may not be a valid statement, since the study design only allows establishing the longitudinal change in physical activity but not in sleep outcomes.</p> <p>In the discussion ("Furthermore, a recent systematic review..."), if you are citing the systematic review by Wang and Boros (10.1080/21679169.2019.1623314) please make sure you include it in the reference list</p>
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<b>REVIEWER</b>	Banno, Masahiro Seichiryō Hospital, Department of Psychiatry
<b>REVIEW RETURNED</b>	31-Jul-2023

<b>GENERAL COMMENTS</b>	The authors have revised the manuscript extensively. I have no additional comments for the manuscript.
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## VERSION 2 – AUTHOR RESPONSE

In the title, you could replace "longitudinal physical activity" with "... longitudinal change in physical activity ..." or "10-year change in physical activity".

Reply: Thank you for these suggestions. We have now rephrased the title to: The association between physical activity over a 10-year period and current insomnia symptoms, sleep duration and daytime sleepiness – A European population-based study.

Thank you for adding the limitation that the association tested in this study may not be longitudinal, to the discussion section.

However, the first point in the "Strengths and limitations of this study" box still reads "The longitudinal study design, with the exposure (physical activity) measured 10 years before the outcome (sleep outcomes) allows testing the directionality of the association." As I pointed out in my previous comments, this may not be a valid statement, since the study design only allows establishing the longitudinal change in physical activity but not in sleep outcomes.

Reply: This sentence in the strengths/limitations has now been changed to make it clear that the study design only makes it possible to investigate what affect longitudinal change in physical activity has on the sleep outcomes that were only measured at follow up.

In the discussion ("Furthermore, a recent systematic review...), if you are citing the systematic review by Wang and Boros (10.1080/21679169.2019.1623314) please make sure you include it in the reference list

Reply: Thank you for pointing this out. We have now added the right reference.