

# Accepted Manuscript

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PII: S1389-9457(18)30187-4

DOI: [10.1016/j.sleep.2018.04.013](https://doi.org/10.1016/j.sleep.2018.04.013)

Reference: SLEEP 3699

To appear in: *Sleep Medicine*

Received Date: 25 December 2017

Revised Date: 26 March 2018

Accepted Date: 11 April 2018

Please cite this article as: Vancampfort D, Stubbs B, Smith L, Hallgren M, Firth J, Herring MP, Probst M, Koyanagi A, Physical activity and sleep problems in 38 low- and middle-income countries, *Sleep Medicine* (2018), doi: [10.1016/j.sleep.2018.04.013](https://doi.org/10.1016/j.sleep.2018.04.013).

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**Sleep Medicine****Physical activity and sleep problems in 38 low- and middle-income countries**

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**Highlights**

- The prevalence of sleep problems is higher among those with low physical activity.
- Sleep problems are associated with low physical activity from adulthood to old age.
- This association is found irrespective of mental and physical health problems.

ACCEPTED MANUSCRIPT

**Abstract**

*Objective:* Although physical activity (PA) is associated with a reduction of a wide range of sleep problems, it remains uncertain whether complying with the international guidelines of 150 min of moderate to vigorous PA per week can reduce sleep problems in adults. This research investigated the relationship between compliance with the PA recommendations of the World Health Organization and sleep problems in 38 low- and middle-income countries (LMICs).

*Methods:* Cross-sectional, community-based data from the World Health Survey were analyzed. Adjusted logistic regression analyses were undertaken to explore the relationship between PA levels using the International Physical Activity Questionnaire and self-reported sleep problems (such as difficulties falling asleep, waking up frequently during the night or waking up too early in the morning) in the last 30 days

*Results:* Across 204,315 individuals (38.6±16.1 years; 49.3% males), the overall prevalence (95%CI) of low PA and sleep problems were 29.9% (29.1-30.8%) and 7.5% (7.2-7.9%), respectively. After adjusting for socio-demographics, obesity, chronic physical conditions, depression, and anxiety, not complying with PA recommendations was associated with higher odds for sleep problems overall [odds ratio (OR)=1.23; 95%CI=1.10-1.38] and across the entire age range: 18-34 years (OR=1.26; 95%CI=1.02-1.57); 35-64 years (OR=1.17; 95%CI=1.01-1.35); age ≥65 years (OR=1.40; 95%CI=1.11-1.76).

*Conclusions:* Not complying with international PA recommendations is associated with higher odds of sleep problems, independently of depression and anxiety in LMICs. Future longitudinal and interventional studies are warranted to assess whether increasing PA levels may improve sleep problems in this setting.

**Keywords:** sleep; insomnia; physical activity; exercise

## 1. Introduction

Sleep disturbances are among the most commonly reported health problems in the general population [1], with rates of insomnia ranging from 6% to 30% depending on the definition adopted [2]. There is emerging evidence pointing to a globally increasing prevalence of insomnia and other sleep problems; women [3], older people [3] and those living in urban environments [4] were at the highest risk. Sleep problems are a major public health concern as they are strongly associated with a wide range of somatic and mental health conditions as well as increased risk for premature mortality [5]. Most notable is their potential causal link with cardiovascular diseases [6] and depression [7] which are also among the leading global causes of acute and chronic diseases. [8]. The nature of the association between chronic conditions and sleep problems is still not clear, although increased activation of the autonomic nervous system might be an underlying mechanism, as evidenced by sleep deprivation-related elevations in heart rate and heart rate variability, body temperature, metabolic rate, norepinephrine secretion, and altered activity of the hypothalamic-pituitary-adrenal axis [9, 10]. In addition to the personal burden, the societal costs of sleep disturbances due to reduced school or work productivity and increased school or work absenteeism are high [11, 12]. Currently benzodiazepine-receptor agonists and cognitive-behavioural therapy are supported by the strongest empirical evidence for treating sleep problems [13]. Benzodiazepine-receptor agonists are readily available and effective in short-term management of insomnia, but evidence for long-term efficacy is scarce; as well, most hypnotic drugs are associated with potential adverse effects such as dependency. Cognitive-behavioral therapy is an effective alternative for chronic insomnia, but is more time consuming and not readily available in most settings in LMICs [13].

Given the high prevalence and burden of sleep problems, it is critical that potentially modifiable correlates are identified so that targeted prevention and treatment of sleep problems can be developed [14, 15]. Furthermore, there is an urgent need for novel interventions that may help prevent or alleviate sleep problems at a population level. From a public health perspective, promoting physical activity might be a low-cost and efficacious strategy. There is evidence that physical activity reduces sleep apnea [16], improves both overall sleep quality and subjective sleep, and diminished sleep latency [17, 18]. Although it is generally accepted now that physical activity is associated with reduction of a wide range of sleep problems [18, 19], it remains to be explored in more detail whether complying with the international guidelines of 150 min of moderate to vigorous physical activity per

week [20] can potentially reduce sleep problems among adults. The only published study to date on this topic assessed adults aged 65 years and older ( $n=926$ ) [21]. This UK study demonstrated that walking at or above the internationally recommended threshold of at least 150 min per week was significantly associated with a lower likelihood of reporting insomnia symptoms ( $OR=0.67$ ,  $95\%CI=0.45-0.91$ ). At 4-year follow-up ( $n=577$ ), higher walking levels at baseline significantly predicted a lower likelihood of reporting sleep onset ( $OR=0.64$ ,  $95\%CI=0.42-0.97$ ,  $p<0.05$ ) or sleep maintenance ( $OR=0.63$ ,  $95\%CI=0.41-0.95$ ,  $p<0.05$ ) problems [21].

A number of other biases and gaps exist in the literature. First, there is a lack of multinational studies exploring the association between physical activity and sleep problems [22]. The current focus on specific clinical populations within specific countries may have limited utility from a public health perspective. Second, there is no data on this association from low- and middle-income countries (LMICs), despite the high prevalence and increasing rates of sleep problems [3] and physical inactivity (defined as not meeting the physical activity guidelines) [23] in this part of the world. It is well known that LMICs are undergoing rapid demographic and epidemiologic transition. In addition, these countries are facing a rapid ageing of the population, and an emerging burden of non-communicable diseases [24]. Furthermore, the results of previous studies on low physical activity levels and sleep problems may not be generalizable to LMICs given that the underlying factors of sleep problems (e.g., more stressful and poor living conditions often involving noise pollution, light exposure, uncomfortable sleeping surfaces, lack of temperature control, and occupational stress) may differ [25, 26]. Next to this, the continuing dearth of physical activity studies in LMICs highlights the gap between where research is conducted and where the largest public health impacts of increasing PA can potentially occur [27].

Given the current gaps within the literature, this study investigated the association between compliance with physical activity recommendations and sleep problems using predominantly nationally representative, community-based data from 38 countries which participated in the World Health Survey (WHS).

## Materials and methods

### 1.1. The survey

The WHS cross-sectional survey was carried out in 70 countries in 2002-2004. Survey details are available here <http://www.who.int/healthinfo/survey/en/>. Briefly, single-stage random sampling and stratified multi-stage random cluster sampling was conducted in 10 and 60 countries respectively. Eligible participants were  $\geq 18$  years old with a valid home address.. One individual was randomly chosen from the household with the use of Kish tables. Standard translation procedures were applied to questionnaires to ensure comparability between countries. Face-to-face interviews were conducted by trained interviewers. The overall individual response rate was 98.5% [28]. To adjust for non-response, sampling weights were generated using the population distribution as reported by the United Nations Statistical Division. Ethical approval for the survey was provided by ethical boards at each study site. All participants gave their informed consent.

Data were publically available for 69 countries. We excluded 10 countries as they lacked sampling information. A further 10 high-income countries were deleted as the focus of the study was on LMICs. Countries which either lacked or were missing  $>25\%$  of the information on physical activity and/or sleep problems were also deleted from the analysis ( $n=11$ ). Thus, the final sample included participants from a total of 38 countries ( $n=204,315$ ), of which 16 ( $n=83,905$ ) and 22 ( $n=120,410$ ) were low-income countries (LICs) and middle-income countries (MICs), respectively, at the time of the survey (2003) according to the World Bank. .

### 1.2. Sleep problems (outcome)

Sleep problems were assessed by the question "Overall in the last 30 days, how much of a problem did you have with sleeping, such as falling asleep, waking up frequently during the night or waking up too early in the morning?" with answer options none, mild, moderate, severe, and extreme. Those who answered severe and extreme were considered to have sleep problems. This definition has been used in previous publications using the same survey question on sleep problems [29-31].

### 1.3. Physical activity (exposure)

In order to assess if participants completed the recommended physical activity levels of 150 min of moderate to vigorous physical activity per week [32], we used the International Physical Activity

Questionnaire [33]. The total amount of moderate to vigorous physical activity over the last week was calculated based on self-reported (time spent physically active and frequency) moderate and vigorous physical activity combined. Those scoring  $\geq 150$  min of moderate to vigorous physical activity were classified as meeting the recommended guidelines (coded 0), and those scoring  $< 150$  min (low physical activity) were classified as not meeting the recommended guidelines (coded 1).

#### *1.4. Control variables*

Based on previous research, we controlled for a wide range of socio-demographic variables: age [3], sex [3], wealth quintiles [34, 35], employment status (unemployed or not), educational status (highest level: no formal, primary, secondary, tertiary) [36], and living in rural versus urban areas [4]). Principal component analysis based on 15-20 assets was performed to establish country-wise wealth quintiles. Additionally, we controlled for several physical and mental health parameters: body mass index (BMI), the presence of chronic physical conditions [37, 38], anxiety [39, 40], and depression [37]. BMI was based on self-reported weight and height. Seven chronic physical conditions (angina, arthritis, asthma, chronic back pain, diabetes, visual impairment, hearing problems) were assessed and those having at least one of the conditions were considered to have a chronic condition. Arthritis, asthma, and diabetes were based solely on self-reported lifetime diagnosis. For angina, in addition to a self-reported diagnosis, a symptom-based diagnosis based on the Rose questionnaire was also used [41]. Chronic back pain was defined as back pain (including disc problems) every day during the last 30 days. Visual impairment was defined as extreme difficulty in seeing and recognizing a person that the participant knows across the road (i.e., from a distance about 20 meters) [42]. Hearing problems were based on interviewer's impression at the conclusion of the survey. Anxiety was assessed by the question 'Overall in the past 30 days, how much of a problem did you have with worry or anxiety' with answer options being none, mild, moderate, severe, and extreme. Those who answered severe and extreme were considered to have anxiety [31, 43]. Depression was defined using the DSM-IV algorithm and was based on duration and persistence of depressive symptoms in the past 12 months [44, 45].

### 1.5. Statistical analysis

Descriptive analysis was conducted to characterize the study sample. Multivariable logistic regression analyses were used to estimate the association between low physical activity (exposure) and sleep problems (outcome). Two models were constructed to assess the effect of the inclusion of different variables in the models: Model 1 - Adjusted for sociodemographic variables (age, sex, wealth, educational and employment status, rural/urban area, country), obesity, and chronic conditions; Model 2 - Adjusted for factors in Model 1 and mental health (depression and anxiety). Since 27.9% of the values on BMI were missing, we included a missing category only for BMI in order to avoid the loss of a large number of observations from the regression analyses. Analyses using the overall sample, and by country income level (i.e., LICs and MICs) were conducted. In addition, using the overall sample, we performed analyses stratified by age groups (18-34, 35-64, and  $\geq 65$  years) while adjusting for variables in Model 2 to assess whether the association between low physical activity and sleep problems are similar across different age groups.

Next, in order to assess whether the association between low physical activity and sleep problems is consistent across countries, we conducted a country-wise logistic regression analysis adjusting for age and sex. The estimates for each country were also combined into a random-effect meta-analysis with the Higgins'  $I^2$  statistic being calculated. The Higgins'  $I^2$  represents the degree of heterogeneity between countries that is not explained by sampling error; a value of <40% is typically considered as negligible and 40-60% as moderate heterogeneity [46].

Adjustment for country was conducted by including dummy variables for each country as in previous WHS publications [47, 48]. All variables were included in the models as categorical variables with the exception of age. All analyses were done using Stata statistical software version 14.1 (Stata Corp LP, College Station, Texas). The sample weighting and the complex study design were taken into account in all analyses using Taylor linearization methods. Results from the logistic regression models are presented as ORs with 95% confidence intervals (95% CIs). The level of statistical significance was set at  $P < 0.05$ .

### 3. Results

The final sample consisted of 204,315 individuals aged  $\geq 18$  years (full list of countries and their sample sizes are provided in **eTable 1** of the Appendix). The mean (SD) age was 38.6 (16.1) years and 49.3% were males (**Table 1**). The overall prevalence (95%CI) of low physical activity and sleep problems were 29.9% (29.1-30.8%) and 7.5% (7.2-7.9%), respectively. The prevalence of sleep problems was higher among those with low physical activity in the overall sample as well as in both LICs and MICs (**Figure 1**). The results of the multivariable logistic regression analysis examining the association between low physical activity and sleep problems are shown in **Table 2**. After adjustment for sociodemographic factors, obesity, and chronic conditions, the ORs (95%CI) of low physical activity for sleep problems were 1.26 (1.14-1.41), 1.30 (1.10-1.54), and 1.23 (1.08-1.40) in the overall, LIC, and MIC samples, respectively (Model 1). These figures were slightly attenuated after the inclusion of mental health conditions (anxiety and depression) in the models (Model 2) in the overall and LIC samples but the ORs remained significant [Overall OR=1.23 (95%CI=1.10-1.38); LIC OR=1.20 (95%CI=1.01-1.43); MIC OR=1.27 (95%CI=1.09-1.48)]. The age-stratified analysis using the overall sample showed that low physical activity was significantly associated with sleep problems across the entire age range: age 18-34 (OR=1.26; 95%CI=1.02-1.57); age 35-64 (OR=1.17; 95%CI=1.01-1.35); age  $\geq 65$  (OR=1.40; 95%CI=1.11-1.76). The results of the country-wise associations between low physical activity and sleep problems are illustrated in **Figure 2**. Low physical activity was associated with significantly higher odds for sleep problems in 13 countries with particularly high ORs observed in Kenya (OR=2.76), Sri Lanka (OR=2.13), and Estonia (OR=2.01). The pooled OR (95%CI) based on a meta-analysis was 1.27 (1.16-1.40) with a moderate level of heterogeneity being observed ( $I^2=57.1$ ).

## 4. Discussion

### 4.1. General findings

To the authors' knowledge, this is the first study in LMICs examining the link between compliance with international physical activity recommendations (i.e., 150 min per week of moderate to vigorous activity) and the presence of sleep problems. This is also the first study to date exploring this association across all income and age groups in adulthood. After adjustment for a wide range of sociodemographic factors and physical and mental health variables, those not complying with the international physical activity standards still had higher odds (OR=1.23; 95%CI=1.10-1.38) for having sleep problems. The associations were similar across country, income level and age groups. The inclusion of depression and anxiety attenuated the association slightly in some samples but did not fully explain the association. Finally, a moderate level of between-country heterogeneity in the association between low physical activity and sleep problems was observed.

### 4.2. Interpretation of findings

The exact mechanisms linking sleep problems to lower physical activity levels remain unclear. We hypothesize that the relationship between physical activity and sleep is influenced by underlying neurobiological mechanisms which were not assessed in the current study. For example, it is known that exercise, or a structured form of physical activity, is implicated in a range of physiological changes, including potential alterations of circadian rhythms [49, 50]. Several studies have observed that moderate to vigorous intensity exercise may acutely (i.e., within minutes) alter melatonin levels and result in a shift of the onset of nocturnal melatonin. The presence and nature of both acute and delayed effects appear to be dependent on the timing of exercise [51]. While morning exercise enhances parasympathetic activity as indicated by heart rate variability, evening exercise increases heart rate following nocturnal sleep and delays the circadian rhythm by about one hour [52]. A national sleep survey in the US demonstrated that morning vigorous exercisers report the most favorable sleep outcomes, including greater likelihood of reporting good sleep quality (OR=1.88,  $p<0.001$ ) and lower likelihood of waking unrefreshed (OR=0.56,  $p=0.03$ ) while evening moderate or vigorous exercisers did not differ in any of the reported sleep metrics compared to non-exercisers

[53]. Other factors to consider include time spent outdoors [50] and light exposure [54] as potentially moderating the association between physical activity levels and presence of sleep problems via circadian-driven aspects of sleep. However, to the best of our knowledge no previous study on the effects of a physical activity intervention on sleep outcomes has tested, or controlled for, increased exposure to light arising from increased time spent being physically active outdoors. Future longitudinal and intervention research exploring these pathways is needed to clarify the associations between being physically active and sleep problems.

Previous studies have also shown that anxiety [55] and depression [56] are associated with low physical activity levels, while sleep problems are core features of depression. Despite this, the mental health status (anxiety and depression) did not have a major influence in the low physical activity - sleep problem relationship observed in our study. This could mean that addressing mental health problems may only have a minimal effect in improving sleep in people who engage in low levels of physical activity. However, given the established benefits of physical activity for impaired mental health, this could also mean that increased physical activity may be a viable alternative therapy to improve both impaired mental health and sleep disturbances.

Finally, a moderate level of between-country heterogeneity in the association between physical activity and sleep problems was observed. This may reflect, for example, differences in types of physical activity or availability of treatment for sleep problems between countries; the underlying reason is only speculative and should be explored in future research.

#### *4.2. Limitations*

The current findings should be interpreted in the light of several limitations. First of all, there are no standard epidemiological definitions for sleep problems nor insomnia [2]. We used the extreme categories based on a single-item question that assessed three aspects of insomnia (i.e., problems falling asleep, waking up often during the night, and waking up too early in the morning) to determine the presence of sleep problems. The specificity of the definition is likely to have been enhanced by the use of extreme categories. It is reassuring that in our study, sleep disturbances were more frequent with increasing age and more frequent in women, which mirrors a well-known distribution [57, 58]. Nevertheless, we were unable to undertake more detailed analyses related to the type, severity or chronicity of the sleep problems. Second, physical activity was assessed with a self-report

measure. The accuracy of self-report physical activity instruments has been questioned [59, 60]. Relevant to this concern, across our entire sample only 29.9% of participants were classified as being insufficiently active, which is lower than expected based on previous research [61]. Therefore, the relationship between sleep problems and low physical activity in our study may be underestimated. Moreover, the IPAQ captures only physical activity over the past 7 days [33]. Future research may wish to consider physical activity over typical 7-day periods [62]. In addition, future research should explore whether different subtypes of physical activity (e.g. time spent in work-related physical activity, active travel, leisure time physical activity) are differently related to the presence of sleep disturbances. Although we included a wide variety of important chronic conditions, we lacked data on other chronic conditions such as migraine [63] and Parkinson's disease [64], which could have been associated with both sleep problems and altered levels of physical activity. Other factors such as pregnancy [65] or medication use, which may contribute to sleep disturbances or affect levels of physical activity was not considered due to lack of data. Thus, we cannot preclude the possibility of residual confounding. Institutionalized patients were not included in the current study. Thus, our study results may not be generalizable to this population which may have a higher prevalence of severe medical conditions. Our study was cross-sectional, therefore the directionality of the relationships cannot be deduced with certainty. For example, it is also possible that sleep problems lead to low physical activity via associated fatigue. Although our data provides some potential hypotheses to address the relationship between adhering to international physical activity recommendations and the presence of sleep problems, longitudinal studies are required to better disentangle the relationships we observed. Nonetheless, the strengths of the current study include the large sample size (over 204,000), the multi-national scope, and the use of predominantly nationally representative data. Most of the research in the domain of physical activity and sleep problems has been conducted in Western countries; little is known about these associations in regions across which there are multiple economic, cultural or social stress factors or differences in health systems.

In conclusion, the current study demonstrates that not complying with international physical activity recommendations is associated with higher odds for having sleeping problems irrespective of the presence of mental and physical health problems. Considering the social and occupational costs of sleep problems, physical activity initiatives should be promoted more widely in LMICs. To this end, policy makers and budget holders should invest in strategies that promote and facilitate physical

activity opportunities as part of a national public health strategy. Finally, (inter)national agencies should increase public health awareness of the importance of complying with the international physical activity standards across all people due to the established benefits, but with special focus on those with sleep problems who are at particular risk of inactivity. Providing the financial resources for these awareness campaigns may prove cost-effective by reducing the economic burden associated with work absenteeism and lower productivity due to sleep deprivation.

### **Acknowledgements**

AK's work is supported by the Miguel Servet contract financed by the CP13/00150 and PI15/00862 projects, integrated into the National R + D + I and funded by the ISCIII - General Branch Evaluation and Promotion of Health Research - and the European Regional Development Fund (ERDF-FEDER). BS is part funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. BS is also supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care South London at King's College Hospital NHS Foundation Trust. The views expressed are those of the author[s] and not necessarily those of the NHS, the NIHR or the Department of Health. JF is supported by a Blackmores Institute Fellowship.

### **Conflict of interest statement**

The authors confirm that there are no financial conflicts of interest associated with this paper.

### **References**

- [1] Singleton N, Bumpstead R, O'Brien M, Lee A, Meltzer H. Psychiatric morbidity among adults living in private households, 2000. *International Review of Psychiatry*. 2003;15:65-73.
- [2] Roth T. Insomnia: definition, prevalence, etiology, and consequences. *Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine*. 2007;3:S7.
- [3] Stranges S, Tigbe W, Gómez-Olivé FX, Thorogood M, Kandala N-B. Sleep problems: an emerging global epidemic? Findings from the INDEPTH WHO-SAGE study among more than 40,000 older adults from 8 countries across Africa and Asia. *Sleep*. 2012;35:1173-81.

- [4] Tang J, Liao Y, Kelly BC, Xie L, Xiang Y-T, Qi C, et al. Gender and Regional Differences in Sleep Quality and Insomnia: A General Population-based Study in Hunan Province of China. *Scientific Reports*. 2017;7.
- [5] Liu T-Z, Xu C, Rota M, Cai H, Zhang C, Shi M-J, et al. Sleep duration and risk of all-cause mortality: a flexible, non-linear, meta-regression of 40 prospective cohort studies. *Sleep Medicine Reviews*. 2017;32:28-36.
- [6] He Q, Zhang P, Li G, Dai H, Shi J. The association between insomnia symptoms and risk of cardio-cerebral vascular events: A meta-analysis of prospective cohort studies. *European Journal of Preventive Cardiology*. 2017:2047487317702043.
- [7] Li L, Wu C, Gan Y, Qu X, Lu Z. Insomnia and the risk of depression: a meta-analysis of prospective cohort studies. *BMC Psychiatry*. 2016;16:375.
- [8] Vos T, Barber RM, Bell B, Bertozzi-Villa A, Biryukov S, Bolliger I, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *The Lancet*. 2015;386:743-800.
- [9] van Dalen JH, Markus CR. The influence of sleep on human hypothalamic-pituitary-adrenal (HPA) axis reactivity: a systematic review. *Sleep Medicine Reviews*. 2017; doi: 10.1016/j.smr.2017.10.002.
- [10] Bonnet MH, Arand DL. Hyperarousal and insomnia: state of the science. *Sleep medicine reviews*. 2010;14:9-15.
- [11] van Mill JG, Vogelzangs N, Hoogendijk WJ, Penninx BW. Sleep disturbances and reduced work functioning in depressive or anxiety disorders. *Sleep Medicine*. 2013;14:1170-7.
- [12] Bauducco SV, Tillfors M, Özdemir M, Flink IK, Linton SJ. Too tired for school? The effects of insomnia on absenteeism in adolescence. *Sleep Health*. 2015;1:205-10.
- [13] Morin CM, Benca R. Chronic insomnia. *The Lancet*. 2012;379:1129-41.
- [14] Freeman D, Sheaves B, Goodwin GM, Yu L-M, Nickless A, Harrison PJ, et al. The effects of improving sleep on mental health (OASIS): a randomised controlled trial with mediation analysis. *The Lancet Psychiatry*. 2017;4:749-58.

- [15] Christensen H, Batterham PJ, Gosling JA, Ritterband LM, Griffiths KM, Thorndike FP, et al. Effectiveness of an online insomnia program (SHUTi) for prevention of depressive episodes (the GoodNight Study): a randomised controlled trial. *The Lancet Psychiatry*. 2016;3:333-41.
- [16] Aiello KD, Caughey WG, Nelluri B, Sharma A, Mookadam F, Mookadam M. Effect of exercise training on sleep apnea: A systematic review and meta-analysis. *Respiratory Medicine*. 2016;116:85-92.
- [17] Kelley GA, Kelley KS. Exercise and sleep: a systematic review of previous meta-analyses. *Journal of Evidence-Based Medicine*. 2017;10:26-36.
- [18] Kredlow MA, Capozzoli MC, Hearon BA, Calkins AW, Otto MW. The effects of physical activity on sleep: a meta-analytic review. *Journal of Behavioral Medicine*. 2015;38:427-49.
- [19] Lang C, Kalak N, Brand S, Holsboer-Trachsler E, Pühse U, Gerber M. The relationship between physical activity and sleep from mid adolescence to early adulthood. A systematic review of methodological approaches and meta-analysis. *Sleep Medicine Reviews*. 2016;28:32-45.
- [20] World Health Organization. Physical Activity Factsheet. 2014.
- [21] Hartescu I, Morgan K, Stevinson CD. Sleep quality and recommended levels of physical activity in older people. *Journal of Aging and Physical Activity*. 2016;24:201-6.
- [22] Koyanagi A, Stubbs B, Vancampfort D. Correlates of low physical activity across 46 low-and middle-income countries: A cross-sectional analysis of community-based data. *Preventive Medicine*. 2018; 106:107-113.
- [23] Vancampfort D, Koyanagi A, Ward PB, Rosenbaum S, Schuch FB, Mugisha J, et al. Chronic physical conditions, multimorbidity and physical activity across 46 low-and middle-income countries. *International Journal of Behavioral Nutrition and Physical Activity*. 2017;14:6.
- [24] Vos T, Allen C, Arora M, Barber RM, Bhutta ZA, Brown A, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet*. 2016;388:1545-602.
- [25] Stamatakis KA, Kaplan GA, Roberts RE. Short sleep duration across income, education, and race/ethnic groups: population prevalence and growing disparities during 34 years of follow-up. *Annals of Epidemiology*. 2007;17:948-55.
- [26] Grandner MA, Patel NP, Gehrman PR, Xie D, Sha D, Weaver T, et al. Who gets the best sleep? Ethnic and socioeconomic factors related to sleep complaints. *Sleep Medicine*. 2010;11:470-8.

- [27] Sallis JF, Bull F, Guthold R, Heath GW, Inoue S, Kelly P, et al. Progress in physical activity over the Olympic quadrennium. *The Lancet*. 2016.
- [28] Nuevo R, Chatterji S, Verdes E, Naidoo N, Arango C, Ayuso-Mateos JL. The continuum of psychotic symptoms in the general population: a cross-national study. *Schizophrenia Bulletin*. 2012;38:475-85.
- [29] Stranges S, Tigbe W, Gomez-Olive FX, Thorogood M, Kandala NB. Sleep problems: an emerging global epidemic? findings from the INDEPTH WHO-SAGE study among more than 40,000 older adults from 8 countries across Africa and Asia. *Sleep*. 2012;35:1173-81.
- [30] Koyanagi A, Garin N, Olaya B, Ayuso-Mateos JL, Chatterji S, Leonardi M, et al. Chronic conditions and sleep problems among adults aged 50 years or over in nine countries: a multi-country study. *PLoS One*. 2014;9:e114742.
- [31] Koyanagi A, Stickley A. The Association between Sleep Problems and Psychotic Symptoms in the General Population: A Global Perspective. *Sleep*. 2015;38:1875-85.
- [32] Vancampfort D, Hert MD, Skjerven LH, Gyllenstein AL, Parker A, Mulders N, et al. International Organization of Physical Therapy in Mental Health consensus on physical activity within multidisciplinary rehabilitation programmes for minimising cardio-metabolic risk in patients with schizophrenia. *Disability and Rehabilitation*. 2012;34:1-12.
- [33] Craig C, Marshall A, Sjostrom M, Bauman A, Booth M, Ainsworth B, et al. International physical activity questionnaire: 12-country reliability and validity. *Medicine & Science in Sports & Exercise*. 2003;35:1381-95.
- [34] Garfield V, Llewellyn CH, Kumari M. The relationship between physical activity, sleep duration and depressive symptoms in older adults: The English Longitudinal Study of Ageing (ELSA). *Preventive Medicine Reports*. 2016;4:512-6.
- [35] Sedigh G, Devlin RA, Grenier G, Armstrong CD. Revisiting the relationship between wages and sleep duration: The role of insomnia. *Economics & Human Biology*. 2017;24:125-39.
- [36] Kim W-H, Kim B-S, Kim S-K, Chang S-M, Lee D-W, Cho M-J, et al. Prevalence of insomnia and associated factors in a community sample of elderly individuals in South Korea. *International Psychogeriatrics*. 2013;25:1729-37.

- [37] Poole L, Jackowska M. The Epidemiology of Depressive Symptoms and Poor Sleep: Findings from the English Longitudinal Study of Ageing (ELSA). *International Journal of Behavioral Medicine*. 2017;1-11.
- [38] Skarpsno ES, Nilsen TI, Sand T, Hagen K, Mork PJ. Do physical activity and body mass index modify the association between chronic musculoskeletal pain and insomnia? Longitudinal data from the HUNT study, Norway. *Journal of Sleep Research*. 2017.
- [39] Vancampfort D, Stubbs B, Herring M, Hallgren M, Koyanagi A. Sedentary behavior and anxiety: Association and influential factors among 42,469 community-dwelling adults in six low-and middle-income countries. *General Hospital Psychiatry*. 2018;50:26-32.
- [40] Vancampfort D, Stubbs B, Koyanagi A. Physical activity correlates in people with anxiety: Data from 46 low-and middle-income countries. *General Hospital Psychiatry*. 2017;49:26-31.
- [41] Rose GA. The diagnosis of ischaemic heart pain and intermittent claudication in field surveys. *Bulletin of the World Health Organization*. 1962;27:645-58.
- [42] Freeman EE, Roy-Gagnon MH, Samson E, Haddad S, Aubin MJ, Vela C, et al. The global burden of visual difficulty in low, middle, and high income countries. *PloS One*. 2013;8:e63315.
- [43] Wong KO, Hunter Rowe B, Douwes J, Senthilselvan A. Asthma and wheezing are associated with depression and anxiety in adults: an analysis from 54 countries. *Pulmonary Medicine*. 2013;2013:929028.
- [44] Loerbroks A, Herr RM, Subramanian S, Bosch JA. The association of asthma and wheezing with major depressive episodes: an analysis of 245 727 women and men from 57 countries. *International Journal of Epidemiology*. 2012;41:1436-44.
- [45] Cifuentes M, Sembajwe G, Tak S, Gore R, Kriebel D, Punnett L. The association of major depressive episodes with income inequality and the human development index. *Social Science & Medicine (1982)*. 2008;67:529-39.
- [46] Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistical Medicine*. 2002;21:1539-58.
- [47] Koyanagi A, Oh H, Stubbs B, Haro JM, DeVylder JE. Epidemiology of depression with psychotic experiences and its association with chronic physical conditions in 47 low- and middle-income countries. *Psychological Medicine*. 2017;47:531-42.

- [48] Stubbs B, Koyanagi A, Veronese N, Vancampfort D, Solmi M, Gaughran F, et al. Physical multimorbidity and psychosis: comprehensive cross sectional analysis including 242,952 people across 48 low- and middle-income countries. *BMC Medicine*. 2016;14:189.
- [49] Aoyama S, Shibata S. The Role of Circadian Rhythms in Muscular and Osseous Physiology and Their Regulation by Nutrition and Exercise. *Frontiers in Neuroscience*. 2017;11.
- [50] Murray K, Godbole S, Natarajan L, Full K, Hipp JA, Glanz K, et al. The relations between sleep, time of physical activity, and time outdoors among adult women. *PLoS One*. 2017;12:e0182013.
- [51] Buxton OM, L'Hermite-Balériaux M, Hirschfeld U, Van Cauter E. Acute and delayed effects of exercise on human melatonin secretion. *Journal of Biological Rhythms*. 1997;12:568-74.
- [52] Yamanaka Y, Hashimoto S, Takasu NN, Tanahashi Y, Nishide S-y, Honma S, et al. Morning and evening physical exercise differentially regulate the autonomic nervous system during nocturnal sleep in humans. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*. 2015;309:R1112-R21.
- [53] Buman MP, Phillips BA, Youngstedt SD, Kline CE, Hirshkowitz M. Does nighttime exercise really disturb sleep? Results from the 2013 National Sleep Foundation Sleep in America Poll. *Sleep Medicine*. 2014;15:755-61.
- [54] Joo EY, Abbott SM, Reid KJ, Wu D, Kang J, Wilson J, et al. Timing of light exposure and activity in adults with delayed sleep-wake phase disorder. *Sleep Medicine*. 2017;32:259-65.
- [55] Vancampfort D, Koyanagi A, Hallgren M, Probst M, Stubbs B. The relationship between chronic physical conditions, multimorbidity and anxiety in the general population: A global perspective across 42 countries. *General Hospital Psychiatry*. 2017;45:1-6.
- [56] Schuch F, Vancampfort D, Firth J, Rosenbaum S, Ward P, Reichert T, et al. Physical activity and sedentary behavior in people with major depressive disorder: A systematic review and meta-analysis. *Journal of Affective Disorders*. 2017;210:139-50.
- [57] Mazzotti DR, Guindalini C, Sosa AL, Ferri CP, Tufik S. Prevalence and correlates for sleep complaints in older adults in low and middle income countries: a 10/66 Dementia Research Group study. *Sleep Medicine*. 2012;13(6):697-702.
- [58] Morin CM, LeBlanc M, Daley M, Gregoire JP, Merette C. Epidemiology of insomnia: prevalence, self-help treatments, consultations, and determinants of help-seeking behaviors. *Sleep Medicine* 2006;7:123–130.

- [59] Soundy A, Roskell C, Stubbs B, Vancampfort D. Selection, use and psychometric properties of physical activity measures to assess individuals with severe mental illness: a narrative synthesis. *Archives of Psychiatric Nursing*. 2014;28:135-51.
- [60] Stubbs B, Firth J, Berry A, Schuch FB, Rosenbaum S, Gaughran F, et al. How much physical activity do people with schizophrenia engage in? A systematic review, comparative meta-analysis and meta-regression. *Schizophrenia Research*. 2016; 176(2-3):431-440.
- [61] Sallis JF, Bull F, Guthold R, Heath GW, Inoue S, Kelly P, et al. Progress in physical activity over the Olympic quadrennium. *The Lancet*. 2016;388:1325-36.
- [62] Rosenbaum S, Ward PB. The Simple Physical Activity Questionnaire. *The Lancet Psychiatry*. 2016;3:e1.
- [63] Fernández-de-Las-Peñas C, Fernández-Muñoz JJ, Palacios-Ceña M, Parás-Bravo P, Cigarán-Méndez M, Navarro-Pardo E. Sleep disturbances in tension-type headache and migraine. *Therapeutic Advance in Neurological Disorders*. 2017;. doi: 10.1177/1756285617745444.
- [64] Albers JA, Chand P, Anch AM. Multifactorial sleep disturbance in Parkinson's disease. *Sleep Medicine*. 2017;35:41-48.
- [65] Juulia Paavonen E, Saarenpää-Heikkilä O, Pölkki P, Kylliäinen A, Porkka-Heiskanen T, Paunio T. Maternal and paternal sleep during pregnancy in the Child-sleep birth cohort. *Sleep Medicine*. 2017;29:47-56.

**Table 1** Sample characteristics (overall and by country income level)

Characteristic	Category	Total (38 countries)	Low-income (16 countries)	Middle-income (22 countries)
Sleep problems	Yes	7.5	7.0	8.2
Low physical activity <sup>a</sup>	Yes	29.9	28.3	32.0
Age	Mean (SD)	38.6 (16.1)	36.9 (15.4)	40.8 (16.7)
Sex	Male	49.3	50.8	47.3
Education	No formal	23.8	38.2	5.2
	Primary	31.5	34.3	28.0
	Secondary	34.8	20.8	52.9
	Tertiary	9.9	6.7	13.9
Employment status	Unemployed	42.3	42.3	42.4
Setting	Rural	55.6	74.8	30.1
	Urban	44.4	25.2	69.9
Obesity	Yes	8.6	5.2	12.1
Chronic condition <sup>b</sup>	Yes	31.1	30.4	32.1
Depression	Yes	6.8	6.8	6.9
Anxiety	Yes	11.7	9.2	15.0

Abbreviation: SD Standard deviation

Data are % unless otherwise stated.

Estimates are based on weighted sample.

<sup>a</sup> The total amount of moderate-to-vigorous physical activity over the last week was calculated and those scoring <150 minutes were considered to have low physical activity.

<sup>b</sup> Presence of at least one of these: angina, arthritis, asthma, chronic back pain, diabetes, visual impairment, hearing problems.

**Table 2** Association of low physical activity and other covariates with sleep problems (outcome) estimated by multivariate logistic regression (overall and by country income level)

	Overall (38 countries)				Low-income (16 countries)				Middle-income (22 countries)			
	Model 1		Model 2		Model 1		Model 2		Model 1		Model 2	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
<b>Low physical activity<sup>a</sup></b>												
Yes vs. No	1.26***	[1.14,1.41]	1.23***	[1.10,1.38]	1.30**	[1.10,1.54]	1.20*	[1.01,1.43]	1.23**	[1.08,1.40]	1.27**	[1.09,1.48]
<b>Age (years)</b>	1.03***	[1.03,1.04]	1.02***	[1.02,1.03]	1.03***	[1.03,1.04]	1.02***	[1.02,1.03]	1.03***	[1.03,1.04]	1.02***	[1.02,1.03]
<b>Sex</b>												
Male vs. Female	0.69***	[0.63,0.76]	0.78***	[0.70,0.86]	0.66***	[0.57,0.76]	0.74***	[0.64,0.85]	0.69***	[0.61,0.79]	0.79***	[0.69,0.91]
<b>Wealth</b>												
Poorest	1.00		1.00		1.00		1.00		1.00		1.00	
Poorer	0.91	[0.82,1.02]	0.92	[0.81,1.04]	0.91	[0.77,1.07]	1.00	[0.83,1.20]	0.91	[0.79,1.05]	0.83*	[0.71,0.97]
Middle	0.82**	[0.73,0.92]	0.89	[0.79,1.02]	0.85*	[0.72,1.00]	0.94	[0.79,1.12]	0.78**	[0.66,0.92]	0.83*	[0.69,1.00]
Richer	0.81**	[0.71,0.94]	0.89	[0.77,1.04]	0.86	[0.70,1.05]	0.98	[0.78,1.22]	0.75**	[0.63,0.91]	0.79*	[0.65,0.96]
Richest	0.69***	[0.58,0.81]	0.78**	[0.65,0.94]	0.70**	[0.56,0.87]	0.82	[0.64,1.06]	0.68**	[0.53,0.86]	0.74*	[0.56,0.97]
<b>Education</b>												
No formal education	1.00		1.00		1.00		1.00		1.00		1.00	
Primary	1.01	[0.90,1.14]	1.05	[0.92,1.19]	1.16*	[1.00,1.34]	1.15	[0.99,1.35]	0.81*	[0.67,0.98]	0.86	[0.68,1.09]
Secondary	0.80**	[0.69,0.93]	0.83*	[0.70,0.98]	0.74**	[0.59,0.93]	0.76*	[0.59,0.98]	0.72**	[0.57,0.91]	0.78	[0.59,1.03]
Tertiary	0.73**	[0.59,0.90]	0.75*	[0.59,0.94]	0.68*	[0.48,0.97]	0.70	[0.47,1.02]	0.66**	[0.49,0.90]	0.72	[0.51,1.01]
<b>Unemployed</b>												
Yes vs. No	1.35***	[1.23,1.49]	1.31***	[1.19,1.45]	1.22**	[1.08,1.37]	1.19**	[1.04,1.35]	1.53***	[1.33,1.76]	1.46***	[1.25,1.72]
<b>Setting</b>												
Urban vs. Rural	1.07	[0.96,1.20]	1.01	[0.90,1.15]	1.09	[0.92,1.30]	1.03	[0.86,1.25]	1.09	[0.93,1.26]	1.02	[0.87,1.19]
<b>Obesity</b>												
Yes vs. No	1.02	[0.87,1.20]	1.06	[0.88,1.27]	0.56**	[0.38,0.82]	0.64*	[0.44,0.94]	1.14	[0.96,1.37]	1.17	[0.94,1.44]
<b>Chronic condition<sup>b</sup></b>												
Yes vs. No	2.84***	[2.59,3.12]	2.18***	[1.98,2.41]	2.97***	[2.59,3.41]	2.28***	[1.97,2.63]	2.67***	[2.36,3.03]	2.05***	[1.79,2.34]
<b>Depression</b>												
Yes vs. No			1.86***	[1.64,2.11]			1.84***	[1.56,2.17]			1.90***	[1.57,2.29]
<b>Anxiety</b>												
Yes vs. No			7.16***	[6.40,8.00]			7.42***	[6.34,8.68]			6.77***	[5.82,7.88]

Abbreviation: OR Odds ratio; CI Confidence interval

Model 1: Adjusted for socio-demographics (age, sex, wealth, education, unemployment, setting, country), obesity, and chronic conditions.

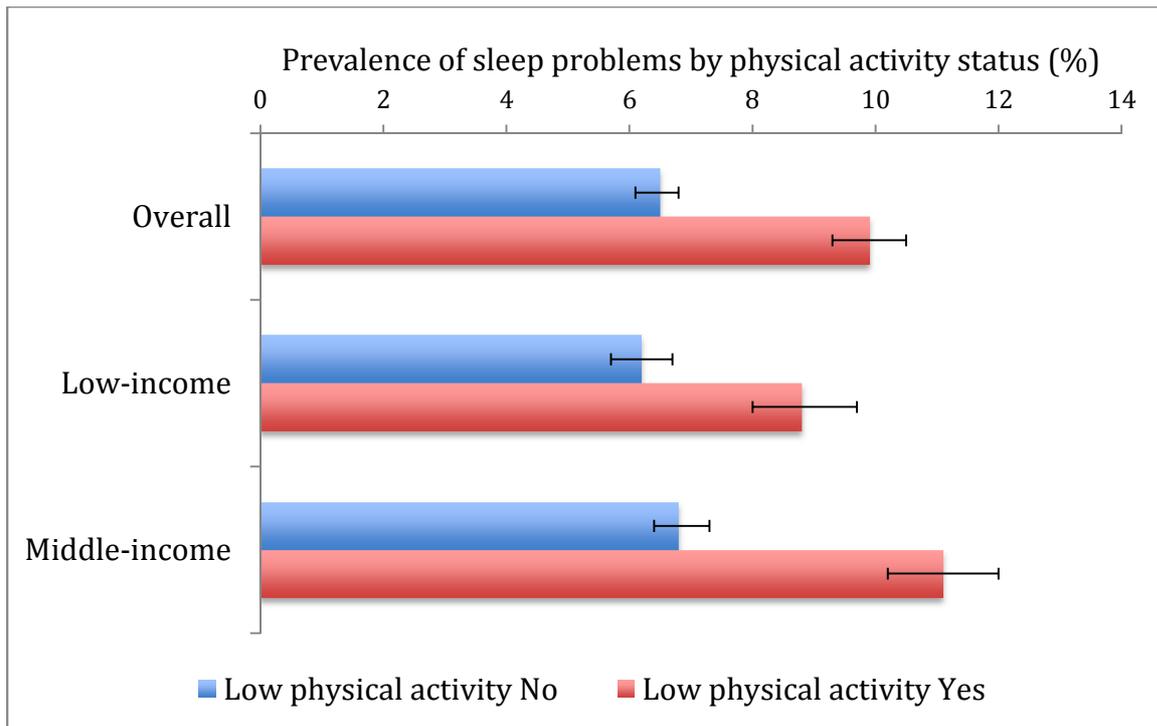
Model 2: Adjusted for factors in Model 1 and depression and anxiety.

<sup>a</sup> The total amount of moderate-to-vigorous physical activity over the last week was calculated and those scoring <150 minutes were considered to have low physical activity.

<sup>b</sup> Presence of at least one of these: angina, arthritis, asthma, chronic back pain, diabetes, visual impairment, hearing problems.

\*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$

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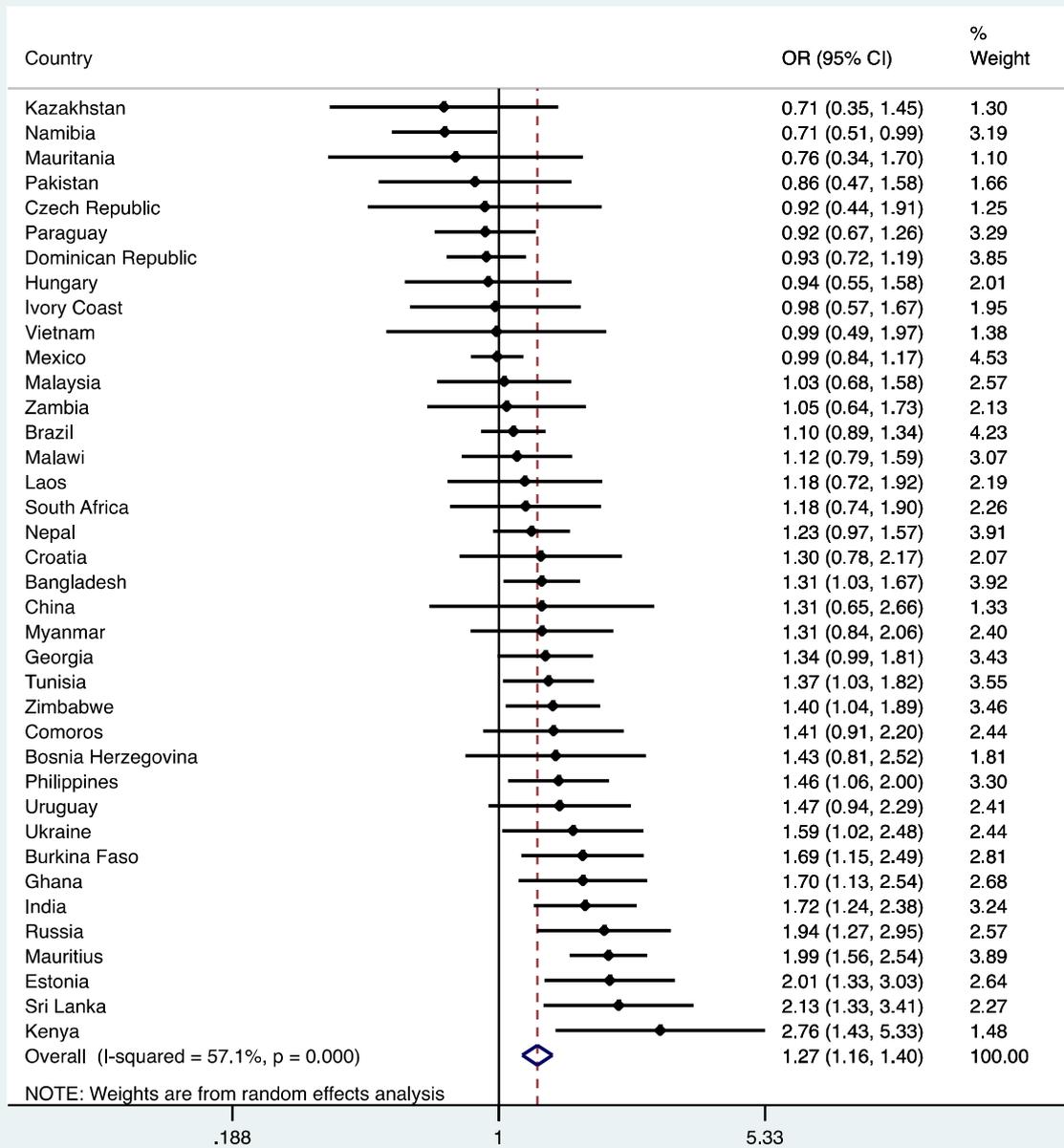


**Figure 1** Prevalence of sleep problems by physical activity status (overall and by country income level)

Estimates are based on weighted sample.

Bars denote 95% confidence intervals.

The total amount of moderate-to-vigorous physical activity over the last week was calculated and those scoring <150 minutes were considered to have low physical activity.



**Figure 2** Country-wise association between low physical activity (exposure) and sleep problems (outcome) assessed by multivariable logistic regression adjusted for age and sex

Abbreviation: OR Odds ratio; CI Confidence interval

Overall estimate was obtained by meta-analysis with random effects.

The total amount of moderate-to-vigorous physical activity over the last week was calculated and those scoring <150 minutes were considered to have low physical activity.

**eTable 1** Countries included in the study and their sample sizes

Low-income countries		Middle-income countries	
Country	N	Country	N
Bangladesh	5,942	Bosnia Herzegovina	1,031
Burkina Faso	4,948	Brazil	5,000
Comoros	1,836	China	3,994
Ghana	4,165	Croatia	993
India	10,687	Czech Republic	949
Ivory Coast	3,251	Dominican Republic	5,027
Kenya	4,640	Estonia	1,020
Laos	4,988	Georgia	2,950
Malawi	5,551	Hungary	1,419
Mauritania	3,902	Kazakhstan	4,499
Myanmar	6,045	Malaysia	6,145
Nepal	8,820	Mauritius	3,968
Pakistan	6,501	Mexico	38,746
Vietnam	4,174	Namibia	4,379
Zambia	4,165	Paraguay	5,288
Zimbabwe	4,290	Philippines	10,083
		Russia	4,427
		South Africa	2,629
		Sri Lanka	6,805
		Tunisia	5,202
		Ukraine	2,860
		Uruguay	2,996

**Highlights**

- The prevalence of sleep problems is higher among those with low physical activity.
- Sleep problems are associated with low physical activity from adulthood to old age.
- This association is found irrespective of mental and physical health problems.

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