Sleep Duration and the Risk of Metabolic Syndrome in Adults: A Systematic Review and Meta-Analysis

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Objective: Epidemiological studies have reported inconsistent findings for the association between sleep duration and metabolic syndrome. We aimed to clarify the effects of short and long sleep durations on metabolic syndrome in adults by performing a meta-analysis.

Methods: Adopting random-effects models, this study analyzed the effects of short and long sleep durations based on data from prospective cohort studies and cross-sectional studies retrieved from four electronic databases from inception to May 2020.

Results: We collected data from 235,895 participants included in nine prospective cohort studies and 340,492 participants included in 27 cross-sectional studies. In cohort studies, short sleep duration was associated with an increased risk of metabolic syndrome (RR, 1.15; 95% CI, 1.05–1.25, \(I^2 = 63.1\%\), \(P < 0.001\)) compared with normal sleep duration. While long sleep duration was not associated with new-onset metabolic syndrome (RR, 1.02, 0.85–1.18, \(I^2 = 38.0\%\), \(P = 0.491\)). In cross-sectional studies, both short (OR, 1.06, 95% CI, 1.01–1.11, \(I^2 = 66.5\%\), \(P < 0.001\)) and long (OR, 1.11, 95% CI, 1.04–1.17, \(I^2 = 73.8\%\), \(P < 0.001\)) sleep durations were associated with a high prevalence of metabolic syndrome.

Conclusions: Only a short sleep duration was associated with an increased risk of metabolic syndrome. Future studies should address whether the association is casual and modifiable.

Keywords: sleep duration, metabolic syndrome, cohort study, meta-regression, meta-analysis

INTRODUCTION

Metabolic syndrome (MetS) is a cluster of disorders that occur together, including central obesity, hypertension, increased fasting glucose levels, higher triglyceride (TG) levels, or low high-density cholesterol (HDL) levels. The National Cholesterol Education Program's Adult Treatment Panel III (NECP ATP-III), the American Heart Association/National Heart Lung and Blood Institute (AHA-NHLBI), and other organizations have issued their own definitions for this syndrome. The prevalence of metabolic syndrome ranges from 20 to 45% in the population (1) and from 20 to 30% among different ethnicities in the United States (2) and is ~24% in Asia (3, 4). Metabolic syndrome is associated with adverse cardiovascular events, even after adjusting for diabetes and obesity (5, 6).
It not only imposes a strain on global health but also imposes a financial burden on patients and the health system due to the need for multiple medications (7). Therefore, the modifiable risk factors for metabolic syndrome must be identified (8).

Short and long sleep durations are known to increase the risk of serious health outcomes, including diabetes, cardiovascular disease, and mortality (9, 10), which have strong associations with metabolic syndrome (5, 6). Several meta-analyses have examined the association between sleep duration and metabolic syndrome (11–13) and reported mixed results. Nevertheless, in the primary results of the previous studies, ORs and HRs were pooled together, whereas they were not statistically interchangeable in our study. First, the OR provides a snapshot of the association at a certain time point, while HR takes into account both the number and timing of event occurrence (14). Studies assessing the association using a prospective cohort design have less substantial bias and might provide stronger support for causality (10, 15, 16). Second, the prevalence of metabolic syndrome is >20%. The RR is difficult to estimate from the OR (17).

By the time Ju conducted a meta-analysis in 2013, two cohort studies assessing the effects of short sleep duration, and only one cohort study examining the effects of a long sleep duration had been published (11). Moreover, many articles were published after the completion of the previous meta-analysis, necessitating an update of the overall association. Therefore, we conducted a systemic review and meta-analysis to (1) examine the association between short/long sleep duration and metabolic syndrome in adults compared with moderate sleep duration and (2) assess prospective cohort studies and cross-sectional studies separately.

**MATERIALS AND METHODS**

We performed this study according to Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Table 1).

Two independent researchers (JNH and HZJ) separately assessed the eligibility, extracted data, and assessed the quality of the included studies. Any disagreement in screening the articles was resolved through discussion between these two investigators, with adjudication by a third researcher (QF) if disagreements persisted.

**Search Strategy**

A systematic search strategy was employed to identify all articles published from database inception to May 2020. Articles were identified through searches of Medline, Embase, CINAHL, and PsycINFO. The search terms for each database are shown in Supplementary Appendix 1. This strategy combined terms characterizing metabolic syndrome as the outcome variable and sleep duration as the exposure variable. The considered articles were not limited to English-language articles. We also screened conference proceedings, journals, and reference lists of included studies and previous systemic reviews.

**Selection Criteria**

We used the following PICOS criteria (population, intervention, control, comparison, outcome, study) to define the selection criteria.

- **P**: For prospective cohort studies, the study population was adults without metabolic syndrome at baseline. For cross-sectional studies, the population was adults.
- **I**: Individuals with short or long sleep duration.
- **C**: Individuals with moderate sleep duration.
- **O**: Metabolic syndrome.
- **S**: Prospective cohort studies or cross-sectional studies.

If multiple articles reported associations based on the same cohort, only the article with the largest sample size was included. The inclusion of studies was conducted in two stages: (1) screening of the title and abstract and (2) screening of the full text (Figure 1).

**Data Extraction**

The following information was extracted from each eligible study: author name and publication year, study type, study location (country and continent), sample size, participant characteristics (age range, mean age, and sex composition), exposure and outcome measurements (sleep measurement, metabolic syndrome measurement/diagnostic criteria for metabolic syndrome, and definition of long or short sleep duration), and main results.

Since the definition of sleep duration varies among studies (18), the three categories of sleep duration (short, long, and moderate) were extracted in one of two ways. For some papers, the author had already divided the sleep duration into three categories based on cultures and ethnicities. For others in which sleep duration was divided into more than three groups, short or long sleep duration was defined as the shortest or longest range reported in the article (10). The midpoint of the categories was defined as the moderate sleep duration range. Regarding the main results, the adjusted estimates that reflected the most comprehensive control were extracted. Sleep measurement is the method used to assess sleep duration, such as questionnaires, interviews (self-reported), and polysomnography (objective).

Data were extracted by two investigators (JNH and HZJ) independently. Any disagreement in screening the articles was resolved by discussion between the two investigators. Consultation with a third investigator (QF) was performed if necessary.

**Exposure and Outcome Measures**

Regarding the measurement of sleep duration, two studies used objective measurements, while others used interviews or questionnaires.

The diagnostic criteria of metabolic syndrome varied between studies. Ten studies used the Third Report of the National Cholesterol Education Program’s Adult Treatment Panel III (NECP ATP-III), four studies used the modified NCEP ATP-III, 14 studies used the American Heart Association/National Heart Lung and Blood Institute (AHA-NHLBI), three studies used the...
# TABLE 1 | PRISMA 2009 checklist.

| Section/topic | # | Checklist Item                                                                                                                                 | Reported on page # |
|---------------|---|------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| Title         | 1 | Identify the report as a systematic review, meta-analysis, or both.                                                                                | 1                 |
| Abstract      | 2 | Provide a structured summary including the following information as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2                 |
| Introduction  | 3 | Describe the rationale for the review in the context of what is already known.                                                                  | 3                 |
| Methods       | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 3-4               |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | NA               |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS and length of follow-up) and report characteristics (e.g., years considered, language, and publication status) used as criteria for eligibility, giving the rationale. | 4                 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact study authors to identify additional studies) in the search and date last searched. | 4                 |
| Search        | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.                       | 4, Supplementary Appendix 1 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 3-4               |
| Data collection process | 10 | Describe the method of data extraction from reports (e.g., piloted forms, independently, or in duplicate) and any processes for obtaining and confirming data from investigators. | 4-5               |
| Data items    | 11 | List and define all variables for which data were sought (e.g., PICOS and funding sources) and any assumptions and simplifications made.                | 4-5               |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this procedure was performed at the study or outcome level), and how this information is to be used in any data synthesis. | 5                 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio and difference in means).                                                               | 5                 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if conducted, including measures of consistency (e.g., P²) for each meta-analysis. | 5                 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias and selective reporting within studies). | 5                 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression analysis), if conducted, indicating which were pre-specified. | 5-6               |
| Results       | 17 | Provide the numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusion at each stage, ideally with a flow diagram. | 6, Figure 1       |
| Study selection characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, and follow-up period) and provide the citations. | 6, Tables 2, 3   |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).                     | 6, Tables 2, 3   |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally in a forest plot. | Tables 2, 3, Figures 2-5 |
| Synthesis of results | 21 | Present the results of each meta-analysis conducted, including confidence intervals and measures of consistency. | 6-7               |
| Risk of bias across studies | 22 | Present the results of any assessment of risk of bias across studies (see item 15).                                                             | 7                 |
| Additional analysis | 23 | Present the results of additional analyses, if performed (e.g., sensitivity or subgroup analyses, meta-regression analysis [see item 16]). | 7-8, Tables 4, 5  |

(Continued)
TABLE 1 | Continued

| Section/topic     | #  | Checklist item                                                                 | Reported on page # |
|-------------------|----|--------------------------------------------------------------------------------|-------------------|
| **Discussion**    |    | Summarize the main findings including the strength of evidence for each main      | 8                 |
|                   |    | outcome; consider their relevance to key groups (e.g., healthcare providers,       |                   |
|                   |    | users, and policy makers).                                                       |                   |
| **Limitations**   |    | Discuss limitations at study and outcome levels (e.g., risk of bias), and at the | 9-10              |
|                   |    | review level (e.g., incomplete retrieval of identified research and reporting bias).|                   |
| **Conclusions**   |    | Provide a general interpretation of the results in the context of other evidence, | 10                |
|                   |    | and implications for future research.                                            |                   |
| **Funding**       |    | Describe sources of funding for the systematic review and other support (e.g.,   | 10                |
|                   |    | supply of data); role of funders in the systematic review.                       |                   |

Moher et al. (76).

FIGURE 1 | Flowchart for the included studies.
International Diabetes Federation (IDF) (12), and five studies used other criteria.

Quality Appraisal
The quality of all studies was evaluated using the Newcastle-Ottawa Quality Assessment Scale (NOS) (19). The total score ranged from 0 to 9 points. For the outcome category and comparability category, all the studies had a similar quality. The difference between studies lies in the study design category (Supplementary Table 1).

Data Analysis
We conducted all the analyses described below separately for cohort studies and cross-sectional studies and for study-specific short and long sleep durations.

In the analysis of cohort studies, hazard ratios (HRs) were regarded as risk ratios (RRs). For studies that provided only odds ratios (ORs), we calculated RRs using the ORs and control event rates (CERs) in individuals with moderate sleep durations. Using random-effect models, we estimated the pooled RR and 95% CI. For cross-sectional studies, we calculated the pooled OR and 95% CI using random-effect models.

Heterogeneity between the studies was assessed using Cochran Q statistics ($P < 0.1$ indicates statistically significant heterogeneity) and $I^2$ statistics ($I^2 > 50\%$ indicates statistically significant heterogeneity) (20). We used a funnel plot, Egger's regression test, and the Begg and Mazumdar test to examine publication bias (21, 22). The “trim and fill” method was used to adjust the funnel plot and recalculate the results (23, 24). The sensitivity analysis was performed by sequentially excluding each study to test the robustness of the pooled estimates.

A subgroup analysis was conducted to explore the potential heterogeneity among cross-sectional studies after stratification according to sex, geographic region, the methods used to measure sleep duration, the definitions of short or long sleep duration and metabolic syndrome, study population, sample size, and study quality. We used the $z$ test to compare the pooled estimates of each subgroup (25). Univariate and multivariate meta-regression analyses were conducted to study the effect of possible influential confounders, including the mean age, proportion of males, definition of sleep duration, sample size, and study quality. For cohort studies, subgroup and meta-regression analyses were not performed due to the small number of datasets included in the meta-analysis.

All statistical analyses were performed using Stata 15.1 (Stata Corp, College Station, TX) and the “metafor” package in R-3.4.3 (24). R was used to perform the subgroup analysis and “trim and fill” analysis.

RESULTS

Search Results
The initial electronic search yielded 1,140 articles, among which 789 were reviewed based on the title and abstract. A total of 127 full-text articles were retrieved, and 36 studies were included in the final analysis (Figure 1).

Characteristics of Study Samples
We identified nine prospective cohort studies that examined the association between sleep duration and the incident risk of metabolic syndrome in 235,895 participants. The sample size ranged from 293 to 162,121. The mean follow-up duration ranged from 2 to 8 years (Table 2).

Another 27 studies were cross-sectional studies, including 340,492 individuals. The sample size ranged from 263 to 88,678 (Table 3).

Tables 2, 3 present the characteristics of all 36 studies. The individuals were all adults. The mean (SD) age of the individuals ranged from 31 (8.7) to 67.6 (7.3) years. The studies were conducted on five continents, 60% of which were performed in Asia. The definitions of short and long sleep durations varied between studies. Approximately 75% of studies defined a “short sleep duration” as < 6 or < 7 h, and ~80% of studies defined a “long sleep duration” as > 8 or > 9 h.

Primary Analysis

Sleep Duration and the Risk of New-Onset Metabolic Syndrome
Compared with a moderate sleep duration, short sleep duration was associated with a statistically significant increase in new-onset metabolic syndrome, with an RR of 1.15 (95% CI = 1.05–1.25, $P < 0.001$, $I^2 = 63.6\%$, N of datasets = 11; Figure 2).

Compared with moderate sleep duration, the association between long sleep duration and the risk of metabolic syndrome was not statistically significant, with an RR of 1.02 (95% CI = 0.85–1.18, $P = 0.491$, $I^2 = 38.0\%$, N = 9; Figure 3), using a random-effect model. The RR was reduced to 0.94 (95% CI = 0.89–0.99, $P = 0.050$, $I^2 = 38.0\%$, N = 9; data not shown) using a fixed-effect model.

Among the seven studies that examined the effect of long sleep duration, six did not observe a significant association. Only Li X. found that a long sleep duration increased the risk of metabolic syndrome among men (adjusted HR = 1.96, 95% CI = 1.35–2.85).

Sleep Duration and the Prevalence of Metabolic Syndrome
Compared with individuals with moderate sleep duration, people with a short or long sleep duration had a higher prevalence of metabolic syndrome. The pooled OR of metabolic syndrome in individuals with a short sleep duration compared to individuals with a moderate sleep duration was 1.06 (95% CI = 1.01–1.11, $P < 0.001$, $I^2 = 66.5\%$, N = 32; Figure 4). The pooled OR of metabolic syndrome in individuals with a long sleep duration compared to individuals with a moderate sleep duration was 1.11 (95% CI = 1.04–1.17, $P < 0.001$, $I^2 = 73.8\%$, N = 31; Figure 5).

Possible Publication Bias in the Primary Analysis
The results of the Begg and Mazumdar and Egger tests are shown in Supplementary Table 2. No significant publication bias was observed. The “trim and fill” test indicated that the primary results remained significant after the data from the missing studies were filled (Supplementary Table 3). A visual inspection
### TABLE 2 | Characteristics of cohort studies.

| References | Study type (follow-up year) | Country, Continent | Sample size | Mean age ± SD, range | % Male | Study population | Sleep measurement | Metabolic syndrome measurement | Sleep (h) | Main findings reported in original articles: Adjusted HR/RR/OR (95% CI) |
|------------|-----------------------------|--------------------|-------------|----------------------|--------|----------------|-------------------|--------------------------|-----------|---------------------------------------------------------------------|
| Choi et al. (41) (male) | Cohort (2-4) | Korea, Asia | 2,093 | 40–55 | 0 | Community | Interview | NECP ATP-III | <6 | aHR 1.80 (1.06–3.05) |
| Choi et al. (41) (female) | Cohort (2-4) | Korea, Asia | 2,133 | 40–55 | 100 | Community | Interview | NECP ATP-III | <6 | aHR 0.62 (0.24–1.64) |
| Otsuka et al. (28) | Cohort (3.7) | Japan, Asia | 2,090 | 44.6 35-63 | 47.2 | Community | Questionnaire | Japanese Criteria | ≤5 | aHR 1.66 (0.71–3.88) |
| Chaput et al. (42) | Cohort (6) | Canada, North America | 293 | 39.2 ± 14.3 18–65 | NA | Community | Questionnaire | AHA-NHLBI | ≤6 | aHR 1.82 (1.16–4.79) |
| Kim et al. (43) (male) | Cohort (2.6) | Korea, Asia | 2,579 | 54.1 ± 8.3 ≥20 | 34.5 | Company or office | Interview | AHA-NHLBI | <6 | aOR 1.41 (1.06–1.88) |
| Li et al. (44) (male) | Cohort (4.4) | China, Asia | 4,774 for all | 30–65 | 100 | Community | Questionnaire | AHA-NHLBI | ≤6 | aHR 1.87 (1.51–2.30) |
| Li et al. (44) (female) | Cohort (4.4) | China, Asia | 4,774 for all | 30–65 | 0 | Community | Questionnaire | AHA-NHLBI | ≤6 | aHR 1.96 (1.35–2.85) |
| Song et al., (45) | Cohort (2) | China, Asia | 11,661 | 47.0 ± 12.0 18–98 | 82.1 | Hospital | Questionnaire | AHA-NHLBI | ≤5.5 | aHR 1.22 (1.00–1.49) |
| Deng et al. (46) | Cohort (8) | Taiwan, Asia | 162,121 | 20–80 | 47.4 | Community | Questionnaire | AHA-NHLBI | <6 | aHR 1.09 (1.05–1.13) |
| Itani et al. (47) (male) | Cohort (7) | Japan, Asia | 39,182 | 42.4 ± 9.8 ≥20 | 100 | Company or office | Questionnaire | Japanese Criteria | ≤5 | aHR 1.08 (1.03–1.14) |
| Yingnan et al. (48) | Cohort (3) | China, Asia | 8,969 | 56.7 ± 7.7 35–75 | 35 | Community | Questionnaire | Chinese Criteria | ≤6 | aOR 1.25 (0.75–2.08) |

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| References   | Study type       | Country/Area, Continent       | Sample size | Mean age ± SD, range | % Male | Study population  | Sleep measurement | Metabolic syndrome measurement | Sleep (h) | Main findings reported in original articles: Adjusted HR/RR/OR (95% CI) |
|--------------|------------------|-------------------------------|-------------|----------------------|--------|-------------------|-------------------|--------------------------|------------|---------------------------------------------------------------------|
| Santos et al. (49) | Cross-sectional | Portugal, Europe              | 832         | 18–92                | 100    | Community Interview | NECP ATP-III      | ≤6                      | aOR 1.40 (0.76-2.60) |
| Santos et al. (49) | Cross-sectional | Portugal, Europe              | 1,332       | 18–92                | 0      | Community Interview | NECP ATP-III      | ≤6                      | aOR 1.50 (0.50-2.60) |
| Choi et al. (50)  | Cross-sectional | Korea, Asia                   | 4,222       | 44.1 ± 0.4 ≥20       | 43.2   | Community Questionnaire | Modified NECP ATP-III | ≤6                      | aOR 0.92 (0.55-1.50) |
| Hall et al. (51)  | Cross-sectional | USA, North America            | 1,214       | 44.4 ± 6.830-54      | 46.6   | Community Interview | AHA-NHLBI         | ≤6                      | aOR 1.76 (1.13-2.74) |
| Aroar et al. (52) | Cross-sectional | China, Asia                   | 29,333      | 61.6 ± 7.1 >50       | 65.1   | Community Interview | Modified NECP ATP-III | ≤6                      | aOR 0.97 (0.88-1.06) |
| Kobayashi et al. (53) | Cross-sectional | Japan, Asia                   | 44,452      | 44.8 ± 12.8          | 49.4   | Hospital Questionnaire | Japanese criteria 2008 | ≤6                      | aOR 1.40 (1.21-1.60) |
| Okubo et al. (60) | Cross-sectional | Japan, Asia                   | 1,481       | 57.5 ± 14.0          | 37.1   | Community Questionnaire | Japanese criteria 2005 | ≤6                      | aOR 1.24 (0.98-1.57) |
| Saleh and Janssen (61) | Cross-sectional | USA, North America            | 1,371       | 57.9 ± 13.6 ≥20      | 56.0   | Community Questionnaire | AHA-NHLBI         | ≤6                      | aOR 0.79 (0.62-1.33) |
| Yu et al. (62)   | Cross-sectional | China, Asia                   | 1,618       | 54.4 ± 10.8 ≥35      | 100    | Community Questionnaire | Modified NECP ATP-III | ≤7                      | aOR 0.91 (0.62-1.33) |
| Yu et al. (62)   | Cross-sectional | China, Asia                   | 4,488       | 53.4 ± 10.3 ≥35      | 0      | Community Questionnaire | Modified NECP ATP-III | ≤7                      | aOR 0.95 (0.62-1.39) |

(Continued)
### TABLE 3 | Continued

| References       | Study type | Country/Area, Continent | Sample size | Mean age ± SD, range | % Male | Study population | Sleep measurement | Metabolic syndrome measurement | Sleep (h) | Main findings reported in original articles: Adjusted HR/RR/OR (95% CI) |
|------------------|------------|-------------------------|-------------|----------------------|-------|------------------|-------------------|-----------------------------|-----------|---------------------------------------------------------------|
| Canuto et al.    | Cross-sectional | Brazil, South America | 902         | 31.0 ± 8.7, 20-60    | 34.1  | Company or office | Questionnaire    | AHA-NHLBI             | <5        | aOR 1.70 (1.09-2.24)                                          |
| Chang et al.     | Cross-sectional | Taiwan, Asia           | 796         | 37.1 ± 7.6          | 100   | Company or office | Standard questionnaire | AHA-NHLBI             | <5        | aOR 1.04 (0.51-2.13)                                          |
| Wu et al.   (male) | Cross-sectional | China, Asia            | 11,380      | 63.6 ± 7.7          | 100   | Company or office | Questionnaire    | IDF                 | <7        | aOR 1.04 (0.93-1.17)                                          |
| Wu et al.     (female) | Cross-sectional | China, Asia            | 13,804      | 63.6 ± 7.7          | 0     | Company or office | Questionnaire    | IDF                 | <7        | aOR 1.01 (0.94-1.10)                                          |
| Lin et al.      | Cross-sectional | Taiwan, Asia           | 4,197       | NA                  | 46.0  | Community        | Questionnaire    | IDF                 | <7        | aOR 1.01 (0.97-1.10)                                          |
| Wu et al.    | Cross-sectional | China, Asia            | 11,380      | 63.6 ± 7.7          | 100   | Company or office | Questionnaire    | IDF                 | <7        | aOR 1.54 (1.05-2.47)                                          |
| Xiao et al.     | Cross-sectional | China, Asia            | 13,505      | 18-74               | 100   | Community        | Questionnaire    | IDF                 | <7        | aOR 0.75 (0.59-0.85)                                          |
| Suliga et al.   | Cross-sectional | Polish, Europe         | 3,056       | 37-66               | 100   | Community        | Questionnaire    | NECP ATP-III       | <7        | aOR 0.83 (0.68-1.02)                                          |
| Suliga et al.   | Cross-sectional | Polish, Europe         | 7,311       | 37-66               | 0     | Community        | Questionnaire    | NECP ATP-III       | <7        | aOR 1.20 (0.95-1.52)                                          |
| Cole et al.     | Cross-sectional | China, Africa          | 263         | 46.0 ± 11.6         | 41.0  | Community        | Objective        | AHA-NHLBI           | <7        | aOR 1.09 (0.94-1.26)                                          |
| Xiao et al.     | Cross-sectional | China, Asia            | 13,505      | 18-74               | 100   | Community        | Questionnaire    | IDF                 | <7        | aOR 0.96 (0.39-1.38)                                          |
| Cole et al.     | Cross-sectional | China, Africa          | 263         | 46.0 ± 11.6         | 41.0  | Community        | Questionnaire    | IDF                 | <7        | aOR 1.98 (0.92-2.26)                                          |
| Kaira et al.    | Cross-sectional | Netherlands            | 1,679       | 60.8 ± 6.4          | 47.4  | Community        | Standard questionnaire | NECP ATP-III | <7        | aOR 0.98 (0.91-1.07)                                          |
| Kim et al.      | Cross-sectional | Korea, Asia            | 44,930      | 40-69               | 100   | Community        | Interview        | NECP ATP-III       | <6        | aOR 1.00 (0.94-1.07)                                          |
| Kim et al.      | Cross-sectional | Korea, Asia            | 88,678      | 40-69               | 0     | Community        | Interview        | NECP ATP-III       | <6        | aOR 1.05 (0.96-1.16)                                          |
| Ostadrahimi et al. | Cross-sectional | Iran, Asia             | 14,916      | 35-70               | 50.0  | Community        | Standard questionnaire | NECP ATP-III | <6        | aOR 0.98 (0.7-1.3)                                           |
| Titova et al.   | Cross-sectional | Sweden, Europe         | 19,691      | 60.4 ± 8.5          | 44.0  | Community        | Interview        | AHA-NHLBI           | <6        | aOR 0.85 (0.69-1.02)                                          |
| Qian et al.     | Cross-sectional | China, Asia            | 4,579       | 67.6 ± 6.3          | 48.0  | Community        | Questionnaire    | NECP ATP-III       | <7        | aOR 1.12 (1.05-1.19)                                          |

References: (63), (64), (65), (66), (67), (68), (69), (70), (71), (72), (73), (74), (75)
of the funnel plots also did not reveal apparent publication bias (Supplementary Figure 2).

Subgroup Analysis of Cross-Sectional Studies

The results from the subgroup analysis of the cross-sectional studies were shown in Table 4. No significant difference was observed for subgroups stratified by gender or continent. For other subgroups, we identified statistically significant effects of the subgroup ($P < 0.05$ for heterogeneity between groups). For individuals with short sleep duration, the specific subgroups were the study population, sleep measurement, measures of metabolic syndrome, and sample size. For individuals with long sleep duration, the specific subgroups were sleep measurement, definition of long sleep duration, measures of metabolic syndrome, sample size, and study quality. However, there was still unexplained heterogeneity ($I^2 > 50\%$) within some subgroups. In conclusion, the subgroup couldn’t fully explain the overall heterogeneity.

There was no significant difference between women and men with either short ($P = 0.121$) or long ($P = 0.272$) sleep durations. Sixty percent of studies were conducted in Asia. For a short sleep duration, the association was more evident for South America (OR = 1.70, 95% CI 1.19–2.44, $P = 0.016$, $N = 1$) than for Asia (OR = 1.08, 95% CI 1.01–1.17, $N = 19$). No detectable difference was identified between studies conducted in Asia and studies on other continents. For individuals with short sleep duration, hospital-based participants (OR = 1.36, 95% CI 1.21–1.53, $N = 5$) had a higher pooled OR than the community-based participants (OR = 1.03, 95% CI 0.98–1.08, $N = 21$). A significant difference was not observed between groups stratified by the methods used to measure the sleep duration (interview, standard questionnaire, and objective measurement in comparison with questionnaire). For a long sleep duration, studies using the Modified NECP ATP-III criteria (OR = 1.22, 95% CI 1.15–1.28, $N = 6$) had a higher overall OR value than studies using the NECP ATP-III criteria (OR = 1.07, 95% CI 0.98–1.15, $N = 12$). For a long sleep duration, the OR was lower in the studies with larger sample sizes. For both short and long sleep durations, the OR was lower in the studies of high quality.

Sensitivity Analysis

None of the sensitivity analyses substantially altered the effects of both long and short sleep durations on metabolic syndrome (Supplementary Figure 1).
A multivariable meta-regression analysis (Table 5) was conducted on cross-sectional studies to examine the potential effects of different factors on the natural logarithm of the OR of short or long sleep duration with the prevalence of MetS. For individuals with short sleep duration, a shorter definition of the duration was associated with a higher OR ($P = 0.011$ for the multivariable test and $P = 0.099$ for the univariable test). Higher study quality was associated with a lower OR ($P = 0.010$ for the univariable test and $P = 0.033$ for the multivariable test). The effect of the mean age was significant. However, the clinical effect ($\text{coef} = -0.01$) was limited. For individuals with long sleep duration, none of the study factors was significant.

DISCUSSION

To our knowledge, this meta-analysis is the most comprehensive study that has explored the relationship between sleep duration and metabolic syndrome. Currently, an increasing number of studies have linked both short and long sleep durations to adverse health outcomes (10, 26, 27). By combining the data from nine cohort studies, the present study showed that short sleep duration, instead of a long sleep duration, increased the risk of developing metabolic syndrome. In cross-sectional studies, both short and long sleep durations were associated with a higher prevalence of metabolic syndrome.

Our findings contribute important new information to previous reviews because of the separation of cohort studies and cross-sectional studies, our updated literature search, and the use of subgroup analysis. Three meta-analyses reported the association between sleep duration and metabolic syndrome. Ju 2013 and Iftikhar 2015 reported that only short sleep duration was associated with metabolic syndrome (11, 12), while Xi 2014 identified associations of both short and long sleep durations to metabolic syndrome (13). Notably, Ju 2013 pooled two cohort studies to examine the effect of short sleep duration on metabolic syndrome and only included one cohort study assessing the effect of long sleep duration on metabolic syndrome. One of the two cohort studies by Otsuka 2011 (28) was of low quality because of its comparability.

We conducted a comprehensive subgroup analysis and meta-regression analysis of cross-sectional studies. Both our results and the results from previous studies showed no difference between sexes. The OR of studies conducted in Asia was not different from studies performed on other continents, except for South America. Ju 2013 reported a difference between Asia and Europe. We attributed their findings to the limited number of included studies. Hospitalized patients with a short sleep duration had a higher prevalence of metabolic syndrome. Not surprisingly,
hospital-based participants with worse health conditions more easily developed metabolic syndrome. Recently, an objective measurement of sleep duration has been considered more reliable than a subjective measurement. We did not observe a difference between the sleep duration recorded by questionnaire or objective measurement. Both a subgroup analysis and meta-regression analysis were used to examine the effects of the sample size and study quality on the pooled OR. Only a higher study quality was robustly associated with a lower OR for short sleep duration. In the multivariable meta-regression analysis, shorter sleep duration was linearly associated with a higher prevalence of metabolic syndrome. Longer sleep duration did not exhibit a linear association. This “J-shaped” association was quite different from the “U-shaped” association between sleep duration and health outcomes reported in many articles (29). However, this result should be interpreted cautiously, since “sleep duration” was a cut-off point defined by different studies examining different ethnicities in the meta-regression analysis. In one specific study, the author calculated the association among participants from the same ethnicity.

Several mechanisms linked sleep duration to metabolic syndrome. A short sleep duration might lead to the endocrine changes described below by affecting carbohydrate metabolism, the hypothalamo-pituitary-adrenal axis, and sympathetic activity. Decreased glucose tolerance and insulin sensitivity would increase glucose levels; increased levels of ghrelin,
decreased levels of leptin, and increased appetite correlate with higher waist circumferences; and increased cortisol concentrations are associated with higher blood pressure (30, 31). Individuals with a short sleep duration tend to present elevated levels of high-sensitivity C-reactive protein and IL-6, which correlate with cardiovascular events (32, 33). A long sleep duration is linked to sleep fragmentation, which would cause numerous health outcomes, including metabolic changes (34). Individuals with a long sleep duration also have less time for exercise, which might contribute to the association (35). Both short and long sleep durations display bidirectional associations with circadian rhythm, which is a risk factor for metabolic disorders (36, 37). Nonetheless, researchers have not yet clearly determined whether sleep duration is a causal risk factor for metabolic syndrome (38). Cohort studies are still unable to determine causality, although they have more power than cross-sectional studies. We must further examine the effect of changes in sleep duration (39) and perform a product Mendelian randomization study, a method using measured variation in genes, to prove a causal relationship.

The foremost strength of our study is that we pooled cohort studies and cross-sectional studies separately, which prevented misinterpretation of the results. By including nine cohort studies, we found that only a short sleep duration increased the incidence of metabolic syndrome. However, some limitations should be considered. First, most studies obtained the sleep duration using subjective measurements, such as interviews and questionnaires. Only two studies used objective measurements. We believe
### Table 4: Subgroup meta-analysis of cross-sectional studies.

| Subgroup | Short sleep duration | Long sleep duration | No. | OR (95% CI) | I² | P | No. | OR (95% CI) | I² | P |
|----------|----------------------|---------------------|-----|-------------|----|---|-----|-------------|----|---|
| **Sex**  |                      |                     |     |             |    |   |     |             |    |   |
| Male     | 7                    | 1.05 (0.98, 1.12)   | 46.0| Ref.        |    |   | 7   | 1.03 (0.99, 1.08) | 14.0| Ref. |
| Female   | 7                    | 0.99 (0.89, 1.09)   | 56.8| 0.121       |    |   | 7   | 1.09 (1.00, 1.18) | 67.9| 0.272 |
| **Continent** |                   |                     |     |             |    |   |     |             |    |   |
| Asia     | 19                   | 1.08 (1.01, 1.17)   | 75.8| Ref.        |    |   | 20  | 1.12 (1.05, 1.20) | 79.0| Ref. |
| Europe   | 6                    | 1.03 (0.98, 1.08)   | 20.8| 0.271       |    |   | 6   | 1.17 (1.01, 1.36) | 64.6| 0.583 |
| North America | 5                   | 1.31 (0.99, 1.74)   | 24.5| 0.205       |    |   | 4   | 1.22 (0.75, 2.00) | 15.0| 0.736 |
| South America | 1                   | 1.70 (1.19, 2.44)   | 0.0 | 0.016       |    |   | 1   | 1.08 (0.92, 4.26) | 0.0 | 0.147 |
| Africa   | 1                    | 0.96 (0.51, 1.81)   | 0.0 | 0.708       |    |   | 1   | 1.01 (0.51, 2.08) | 0.0 | 0.974 |
| **Study population** |                 |                     |     |             |    |   |     |             |    |   |
| Community | 21                  | 1.03 (0.98, 1.08)   | 57.7| Ref.        |    |   | 22  | 1.14 (1.07, 1.21) | 65.9| Ref. |
| Hospital | 5                    | 1.36 (1.21, 1.53)   | 45.7| <0.001      |    |   | 5   | 1.10 (0.77, 1.59) | 91.6| 0.885 |
| Company or office | 6                  | 1.15 (0.93, 1.41)   | 37.6| 0.334       |    |   | 4   | 1.09 (0.93, 1.28) | 0.0 | 0.644 |
| **Sleep measurement** |                |                     |     |             |    |   |     |             |    |   |
| Questionnaire | 16               | 1.08 (0.99, 1.18)   | 69.4| Ref.        |    |   | 15  | 1.11 (1.03, 1.20) | 87.6| Ref. |
| Interview | 8                    | 1.13 (1.04, 1.23)   | 76.3| 0.496       |    |   | 8   | 1.12 (1.01, 1.24) | 36.6| 0.893 |
| Standard questionnaire | 6              | 1.02 (0.92, 1.13)   | 0.0 | 0.363       |    |   | 6   | 1.13 (0.90, 1.40) | 81.1| 0.947 |
| Objective | 2                    | 0.92 (0.67, 1.28)   | 0.0 | 0.349       |    |   | 2   | 1.27 (0.63, 2.56) | 28.3| 0.733 |
| **Definition of sleep duration** |              |                     |     |             |    |   |     |             |    |   |
| < 5 h short or > 9 h long | 5               | 1.23 (0.98, 1.5)    | 29.2| Ref.        |    |   | 7   | 1.09 (0.92, 1.29) | 67.3| Ref. |
| < 6 h short or > 8 h long | 13              | 1.13 (1.02, 1.24)   | 82.4| 0.492       |    |   | 17  | 1.18 (1.09, 1.27) | 53.6| 0.405 |
| < 7 h short or > 7 h long | 2               | 1.04 (0.98, 1.11)   | 20.4| 0.164       |    |   | 6   | 1.01 (0.92, 1.11) | 93.0| 0.464 |
| < 8 h short | 2               | 0.98 (0.90, 1.06)   | 0.0 | 0.065       |    |   | 2   | 1.27 (0.63, 2.56) | 28.3| 0.733 |
| **MetS measurement** |                 |                     |     |             |    |   |     |             |    |   |
| NECP ATP-III | 12             | 1.06 (0.98, 1.16)   | 68.2| Ref.        |    |   | 10  | 1.07 (0.98, 1.15) | 73.8| Ref. |
| Modified NECP ATP-III | 6             | 1.00 (0.94, 1.07)   | 34.3| 0.308       |    |   | 6   | 1.22 (1.15, 1.28) | 35.8| 0.006 |
| AHA-NHLBI | 9                    | 1.20 (1.03, 1.39)   | 44.3| 0.186       |    |   | 9   | 1.23 (1.01, 1.50) | 27.3| 0.195 |
| IDF      | 3                    | 1.05 (0.88, 1.25)   | 21.0| 0.879       |    |   | 5   | 1.07 (1.01, 1.14) | 33.4| 0.945 |
| Others   | 2                    | 1.40 (1.22, 1.61)   | 14.1| <0.001      |    |   | 1   | 0.98 (0.81, 1.19) | 10.1| 0.426 |
| **Sample size** |                |                     |     |             |    |   |     |             |    |   |
| <5,000   | 23                   | 1.07 (0.99, 1.06)   | 49.7| Ref.        |    |   | 18  | 1.28 (1.12, 1.47) | 56.2| Ref. |
| 5,000–20,000 | 5              | 1.09 (0.96, 1.25)   | 57.4| 0.842       |    |   | 8   | 1.05 (0.95, 1.15) | 82.0| 0.018 |
| >20,000  | 4                    | 1.11 (1.00, 1.23)   | 51.3| 0.638       |    |   | 5   | 1.09 (1.01, 1.18) | 82.1| 0.044 |
| **Study quality** |                |                     |     |             |    |   |     |             |    |   |
| High     | 7                    | 1.03 (1.00, 1.06)   | 26.9| Ref.        |    |   | 7   | 1.03 (0.97, 1.09) | 60.5| Ref. |
| Low      | 25                   | 1.06 (1.03, 1.09)   | 63.4| 0.013       |    |   | 23  | 1.15 (1.06, 1.25) | 70.7| 0.030 |

P-value of the two-sample z test for estimates between subgroups. 
P-value for heterogeneity. 
For effects of short sleep duration, this category included those who defined < 5 h as short sleep duration. For effects of long sleep duration, this category included those who defined > 9 h as long sleep duration. The same meaning for the following terms.

that subjective measurements would still be more applicable and utilized in epidemiological studies, although they have less accuracy and validity. Second, the cut-off points of short and long sleep duration and definition of metabolic syndrome varied between countries and studies (27). This limitation prevented us from translating our results into practical advice for the public.
Third, we did not include other dimensions of sleep, such as sleep quality and sleep-disordered breathing. Sleep quality is a mechanism linking a short or long sleep duration with negative health outcomes (40). Fourth, we only included nine cohort studies, which prevented us from conducting further research, such as a subgroup analysis and meta-regression analysis.

CONCLUSIONS

A short sleep duration, rather than a long sleep duration, was associated with a significant increase in the incidence of metabolic syndrome. Both short and long sleep durations were cross-sectionally associated with a high prevalence of metabolic syndrome. A sufficient sleep duration should be recommended to prevent metabolic syndrome.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

HW and JH contributed to the conception and design of the study. JH and HJ organized the database and performed the statistical analyses. JH wrote the first draft of the manuscript. QF and HJ reviewed the manuscript. All authors approved the final version of the paper.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2021.635564/full#supplementary-material

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or ﬁnancial relationships that could be construed as a potential conﬂict of interest.