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The prevalence and severity of insomnia symptoms during COVID-19: A global systematic review and individual participant data meta-analysis



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ABSTRACT

Introduction: There have been no previous meta-analytic studies that have looked at the prevalence of insomnia symptoms in different COVID-19 groups using a single assessment instrument to evaluate insomnia symptoms while maintaining data homogeneity. The current review's associated goal is to undertake an individual participant data (IPD) analysis to further investigate past meta-analyses, a method that has been shown to be more robust than standard meta-analyses.

Methods: Only studies that used the Insomnia Severity Index (ISI) to assess insomnia are used in this analysis. The IPDMA was performed and registered in PROSPERO in compliance with the PRISMA IPD Statement (CRD42021275817). From November 2019 to August 2021, researchers explored seventeen databases and six preprint services for relevant studies.

Results: The pooled estimate of insomnia symptoms (subthreshold and clinically significant) was 52.57%. An estimated 16.66% of the population suffered from clinically significant insomnia, of which 13.75% suffered from moderate insomnia, and 2.50% suffered from severe insomnia. The different populations' grouping had no statistically significant differences in the prevalence of insomnia symptoms. Insomnia symptoms did not appear to be associated with age or sex.

Conclusion: Our findings imply that the COVID-19 pandemic is linked to a significant rise in subthreshold insomnia symptoms, but not to moderate or severe insomnia. Educating people from all walks of life about the importance of sleep and the risk of acquiring insomnia symptoms during this or future pandemics should be a top concern.

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1. Introduction

Since its emergence, the COVID-19 pandemic has threatened human physical and mental health leading to serious consequences, including sleep disturbances. Sleep problems related to the COVID-19 were highly prevalent in various populations, including COVID-19 patients (hospitalized: 33.3%–84.7%; discharged: 29.5–40%), healthcare workers (18.4–84.7%), and the general community (17.65–81%) [1]; and worsened health outcome in these populations [2–4]. COVID-19 related sleep disturbances may include poor sleep quality, sleepiness, or insomnia [4,5]. A systematic review and meta-analysis by Cénat et al. found a pooled prevalence of COVID-19 related insomnia of 16.45% in the general population and 36.52% in healthcare workers [6] with another review reporting a pooled prevalence of 36% among nurses [7].

Insomnia, difficulty initiating or maintaining sleep, is associated with multiple negative outcomes, including increased risk of depression, alcohol dependence, hypertension, metabolic syndrome, and coronary heart disease [8]. In addition, insomnia also leads to loss of productivity [8], increased healthcare utilization [8], and reduced quality of life [9]. Thus, providing a more accurate estimate of insomnia during COVID-19 across various at-risk populations has implications for developing specific, customized screening and intervention strategies to protect against the factors leading to the development of insomnia.

While critical appraisal of extant literature has emerged, to date, scant attention has been geared towards the establishing prevalence of COVID-19 related insomnia across different populations [10,11]. Prior systematic reviews have mainly focused on specific populations such as healthcare workers [7,12–17], students [10,18], COVID-19 patients [11], or children and adolescents [19]; whereas more limited research has compared prevalence rates of sleep disturbances across population types [1,5].

Further, no previous meta-analytic studies have investigated the prevalence of insomnia symptoms in various COVID-19 populations using a single assessment instrument to evaluate insomnia symptoms while maximizing data homogeneity. One previous meta-analysis focused on sleep quality using the Pittsburgh Sleep Quality Index [20] also included studies using other sleep measures with different scopes, scoring methodologies, and cutoff criteria utilized; leading to high levels of heterogeneity and limiting international comparisons of prevalence rates. In the current study, we utilize only studies that employed the Insomnia Severity Index (ISI) [21] to assess insomnia. The ISI is a widely used screening tool that has proven suitable for both clinical practice and research, and to be accurate in assessing the risk of insomnia symptoms in both clinical and community settings in various countries around the globe [22].

The related aim of the present review is to further scrutinize previous meta-analyses by conducting an individual participant data (IPD) analysis, an approach widely documented to be more robust compared to standard meta-analyses [23]. The IPD meta-analysis (IPDMA) allows disentangling study- and subject-level sources of heterogeneity. To our knowledge, this is the first IPD meta-analysis involving a large number of studies from across the globe evaluating the prevalence of insomnia symptoms during the COVID-19 pandemic. For these reasons, this IPDMA aimed to review available data on insomnia symptoms evaluated in different populations assessed by the ISI, specifically estimating raw and weighted prevalence rates of insomnia symptoms by severity for different population groups during the pandemic taking into account the effects of a single moderator and simultaneous interactions between several moderators.

2. Materials and methods

The IPDMA was completed in accordance with the PRISMA IPD Statement [24] and registered in PROSPERO (CRD42021275817). To avoid duplication, a comprehensive review of Prospero and the COVID-19 evidence network to support decision-making (COVID-END) resources was performed before registering our protocol. In addition, to avoid the shortcomings of some previous IPDMAs, we established an a priori protocol with a prespecified data syntheses plan.

2.1. Identification of studies

Seventeen databases and six preprint servers were searched for relevant studies from November 2019 through August 2021. The following databases were searched for relevant publications: 1) American Psychological Association PsycINFO; 2) Cochrane Library; 3) CNKI; 4) Cumulative Index to Nursing and Allied Health Literature (CINAHL); 5) EBSCOhost; 6) EMBASE; 7) Google Scholar; 8) LILACS; 9) MEDLINE; 10) Pro-Quest Medical; 11) SciELO; 12) ScienceDirect; 13) Scopus; 14) VIP; 15) Wanfang; 16) Web of Science and 17) WHO Global research on coronavirus disease (COVID-19). The following preprint servers were included: 1) [arXiv.org](https://arxiv.org); 2) biorxiv.org; 3) medRxiv.org; 4) Preprints.org; 5) psyarxiv.com; and 6) SSRN.com.

Cross-matching keywords were selected using key terms, and PubMed MeSH headings were the search strategies used. The search was developed using the Boolean logic operators of (OR, AND, NOT). Search syntax was changed according to the advanced search characteristics of each database. Keywords included were: “COVID-19” OR “2019-nCoV” OR “2019 coronavirus” OR “COVID-19 pandemic” OR “Wuhan coronavirus” OR “2019 novel coronavirus” OR “SARS-CoV-2” AND “sleep” OR “sleep medicine” OR “sleep disturbances” OR “sleep disorders” OR “sleep problems” OR “sleep quality” OR “Insomnia Severity Index” OR “ISI” OR “insomnia” OR “circadian rhythm”. To increase the likelihood of finding relevant original studies, reference lists of included studies and previous systematic reviews and meta-analyses of published articles were manually searched. The final search results were converted into a Microsoft Excel spreadsheet 2019 to filter and eliminate duplicates. Citations were managed with EndNote X9.3.3 using the Research Information System files.

In the current IPDMA, the primary outcome was the prevalence and severity of insomnia symptoms during the COVID-19 pandemic measured by the ISI. Specific inclusion criteria for study selection included: (1) publication date between November 1, 2019, to August 31, 2021; (2) original research articles published in English, Chinese, Korean, Spanish, German, Portuguese, French, Italian, or Arabic languages; and (3) studies that reported numerical values (e.g., arithmetic mean with standard deviation or prevalence rate) for insomnia symptoms using the ISI. Exclusion criteria were applied to the retrieved articles to eliminate factors that may incur potential methodologic and quality issues: abstracts, case reports, infographics, letters, editorials, narrative reviews, opinions, systematic reviews, meta-analyses, and position statements. Fig. 1 shows the PRISMA2020 flow diagram for study selection.

2.2. Outcomes and assessment of insomnia symptoms

The primary outcome was the estimated prevalence and severity of insomnia symptoms during the COVID-19 pandemic measured by the ISI. The ISI is a 7-item self-report questionnaire

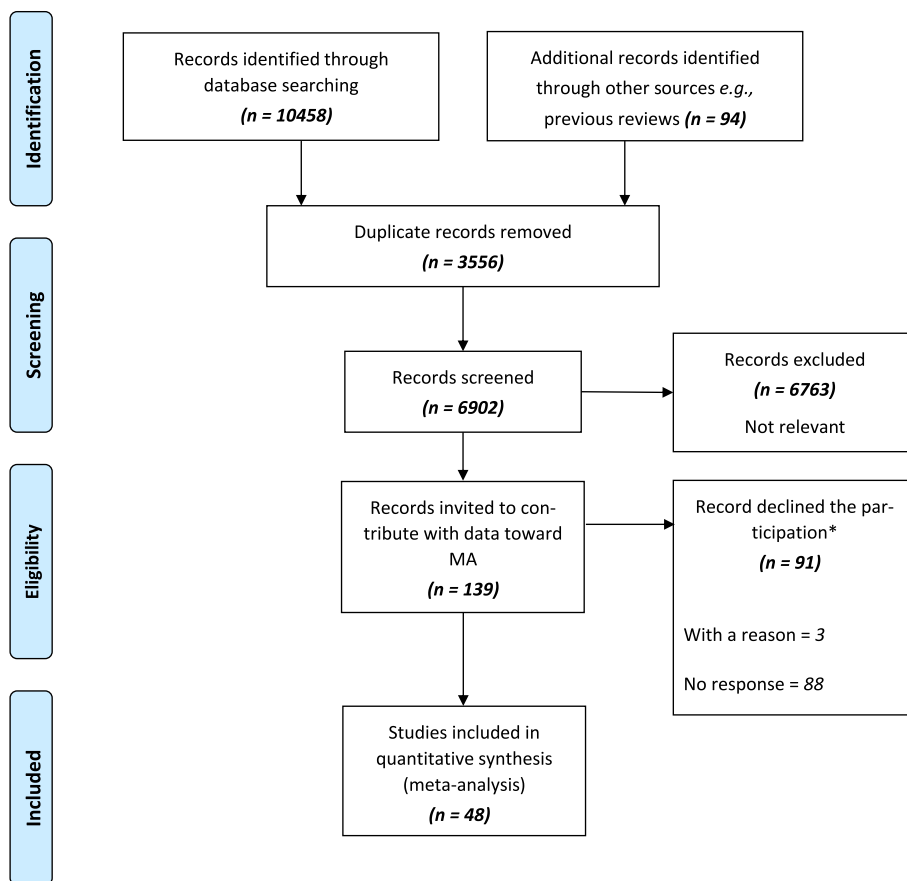


Fig. 1. Prisma flow diagram for study selection.

assessing the nature, severity, and impact of insomnia symptoms [21,25]. The usual recall period is the “last month,” and the dimensions evaluated were: severity of sleep onset, sleep maintenance, and early morning awakening problems, sleep dissatisfaction, interference of sleep difficulties with daytime functioning, noticeability of sleep problems by others, and distress caused by the sleep difficulties. A 5-point Likert scale is used to rate each item (e.g., 0 = no problem; 4 = very severe problem), yielding a total score ranging from 0 to 28. The total score is interpreted as follows (according to severity): absence of insomnia (0–7); sub-threshold insomnia (8–14); moderate insomnia (15–21); and severe insomnia (22–28) [21,25].

In presenting the results of this IPDMA, the term, “cumulative prevalence of insomnia symptoms”, refers to the combined three categories of subthreshold, moderate, and severe insomnia. On the other hand, the term, “cumulative prevalence of insomnia”, refers to only the combination of the moderate and severe insomnia categories.

2.3. Study screening and selection

Based on the inclusion criteria, two reviewers (depending on the language: HJ, AH, AFA, FFR, WC, HD, GNP) independently evaluated each entry, including titles and abstracts of all retrieved publications. In addition, the complete texts of possibly relevant papers were examined further using the above criteria. Finally, discussion/consultation with a blinded author (ASB) resolved any disagreements between the two reviewers.

2.4. Data extraction and obtaining individual participant data

Data extraction was limited to study information and complete citation. The corresponding author of each included study was contacted by the principal investigator seeking the relevant IPD in a standardized Microsoft Excel file. Instructions were provided about the data coding, which included four main variables for each individual participant (age in years, sex, ISI total score, and population grouping, e.g., general population). Developing data-sharing agreements to be signed by the participating research teams was also included in the logistical process. An independent Research Ethics Committee approved all studies and ensured they followed the ethical principles of the Helsinki Declaration (1996 and 2000), as well as applicable good clinical practice requirements in local guidelines.

Data collection agreements considered different regulations regarding data sharing across different countries to collect data from ongoing studies. For example, researchers in the United States were required to comply with the Health Insurance Portability and Accountability Act of 1996 (HIPAA), European researchers were required to satisfy the General Data Protection Regulation, and researchers in India were suggested to gain approval from the Indian Council of Medical Research for the sharing of research data. The corresponding author(s) (or their representative) of each participating study was invited to be an author in the project Covid-19 insoMnia Ipd meTa-analYsis(COMITY) collaboration. Invited authors were informed that they need to meet the authorship criteria of the international committee of medical journal editors to be listed as contributors. A secure data exchange protocol and

secure repository were established by the principal investigator specifically for this study. Anonymous, de-identified IPD were shared with the data analyst.

2.5. Quality assessment and risk of bias

We assessed the methodological quality and bias risk of the studies using the Newcastle-Ottawa Scale (NOS). As part of the NOS checklist, three aspects were analyzed (participant selection, comparability, and outcome and statistics). The checklist comes in three variations: for cross-sectional studies (seven items), for case-control studies (eight items), and cohort or longitudinal studies (eight items). Scores of 8–10 indicated good quality and low bias risk, 5–7 indicated moderate quality and moderate bias risk, and 0–4 indicated low quality and high bias risk [26]. The results of the quality assessment were presented visually in a traffic light plot, which provides the judgment for each study in each area of the NOS. In addition, the proportion of information within each judgment for each domain for all studies was also depicted using a summary plot (weighted).

2.6. Data analysis

For IPD meta-analysis, there are two competing statistical approaches: a two-stage or a one-stage approach [27]. In this IPD meta-analysis, we used a two-stage approach. First, we analyzed the IPD from each study separately to obtain aggregate (summary) data of interest (such as an effect estimate and its confidence interval), and then we combined these using a traditional random-effects meta-analysis model. Two-stage IPD meta-analyses are more robust, computationally intuitive, and easy to replicate [28,29].

In order to account for both within-study and between-study variations, a random effect model was used for the studies included [30]. DerSimonian and Laird estimates of effect size were used with the general inverse variance approach, the logit transformed proportions, and their standard errors [31]. We used logit transformation because a random intercept logistic regression model is used by default, i.e., argument method = “generalized linear mixed models = GLMM” [30]. The logit transform does not stabilize the variance, but prevents the pooled 95% CI from exceeding 0–1 [30]. The 95% confidence interval (95%CI) was calculated using the Cropper-Pearson interval [31,32]. A forest plot represents the findings of a meta-analysis as a point estimate with a 95% confidence interval. We also reported the 95% prediction interval (95%PI) which is defined as the range of effect sizes that a new study would fall into if it were randomly selected from the same population of studies already included in the meta-analysis [33].

To quantify the variability in sample size impact estimates across these studies, the I^2 statistic was applied [34]. The I^2 statistic shows how much variance between research is attributable to heterogeneity versus chance [35]. A heterogeneous population is classified as mild when the I^2 is less than 25%, moderate when the I^2 is 25–50%, severe when the I^2 is 50–75%, and extremely severe when the I^2 exceeds 75% [35]. We used a leave-one-out sensitivity analysis to demonstrate that no single study contributed to our findings jackknife approach was used [36].

To determine the degree of heterogeneity between the studies, Cochran's Q test [37], τ [38], and τ^2 [38] statistics were used. Cochran's Q, with weights based on the pooling method, is the sum of squared differences between individual study effects and the pooled effect across studies [37]. Q was distributed using the chi-square statistic with k (number of studies) minus 1° of freedom [37]. The τ^2 statistic measures variation in effect size parameters

across all studies in a population, and it represents the variance in real effect sizes; τ denotes this integer's square root [37]. As a means of further examining heterogeneity, the H statistic was defined as the ratio of a random-effects meta-analysis' estimated overall effect size to a fixed-effects meta-analysis' estimate of its effect size [34].

An analysis of publication bias was conducted using funnel plots [39]. A funnel plot is a basic scatter plot that shows the impact estimates of individual interventions versus some metric of study size or precision [39]. In a formal analysis of publication bias, Egger's regression was used [39], as well as rank correlation test by Begg and Mazumdar [40]. Begg and Mazumdar's rank correlation test is widely used in meta-analysis to check for publication bias in clinical and epidemiological studies [41]. It is based on using Kendall's tau as the measure of association to correlate the standardized treatment effect with the variance of the treatment effect [41]. If necessary Duval and Tweedie's trim and fill method were used to produce modified point estimates to account for funnel plot asymmetry due to possible publication bias [42]. This method can be used to estimate the number of studies missing from a meta-analysis since the most extreme results on one side of the funnel plot are suppressed. Adding data to the funnel plot makes it more symmetric [42]. A more valid assessment of the overall effect or outcome should not be the purpose of this approach; rather, it is to establish how sensitive the results are to one specific selection process [42].

A moderator analysis was performed to explain the dispersion of effect sizes or heterogeneity. We performed subgroup meta-analyses to see if the prevalence of insomnia symptoms varied across the populations studied. Analyses of subgroups based on categorical factors, such as the study population and country, were conducted. In addition to a meta-regression approach, we considered four covariates, including mean age and female sex proportion, as continuous variables of insomnia symptoms.

During the process of the IPDMA we have implemented two quality control procures to ensure the integrity of the data and associated results. First, we invited all participating/contributing authors to a live webinar to present results upon completion of the analyses. Second, we sought critical revisions from all participating/contributing authors prior to submission to ensure that data are accurate and precise.

All data analyses and visualizations were performed using R for statistical computing version 4.1.0 [43]. The packages ‘meta’ [44] and ‘metafor’ [45] were used to perform all meta-analytics. Quality assessment plots were produced using risk-of-bias visualization ‘robvis’ [46].

3. Results

A total of 48 studies from 25 countries during COVID-19 involved 133,006 participants (See Fig. 1), with a mean ISI of 8.70 ± 2.00 . Using the raw data of the 133,006 participants 76650 (57.62%) reported no clinically significant insomnia ($ISI < 8$); 39662 (29.81%) reported subthreshold insomnia ($ISI > 7$ and < 15); and 59077 (12.57%) reported moderate to severe insomnia ($ISI > 14$). The characteristics of the participants are shown in Table 1.

The 25 individual countries contributing IPD included Argentina (K = 2, N = 1643); Bahrain (K = 1, 549); Bangladesh (K = 1, N = 294); Canada (K = 1, N = 303); Chile (K = 1, N = 125); China (K = 9, 82162); Ecuador (K = 1, N = 1060); Egypt (K = 2, N = 897); Finland (K = 1, N = 1744); Germany (K = 1, N = 484); India (K = 6, N = 3135); Indonesia (K = 1, N = 101); Italy (K = 4, N = 17665); Korea (K = 1, N = 221); Libya (K = 1, N = 10296); Morocco (K = 1, N = 549); Nepal (K = 1, N = 475); Nigeria (K = 1, N = 884); Oman (K = 1, N = 1136); Paraguay (K = 1, N = 126); Saudi Arabia (K = 2,

Table 1
Key features, methodologies, and citations of studies that were included in this review about insomnia symptoms during COVID-19.

ID	Authors, year (Ref.)	Country	Sample size and Population	Sample Characteristics	Quality score/NOS
1	Agberotimi et al., 2020 [69]	Nigeria	n = 884; Population = Multiple.	Age = 28.72 years; Female % = 45.48%.	6
2	Al Ammari et al., 2020 [70]	Saudi Arabia	n = 720; Population = Healthcare workers.	Age = NR years; Female % = 64.17%.	8
3	Alamrawy et al., 2021 [71]	Egypt	n = 447; Population = Multiple.	Age = 20.73 years; Female % = 70.25%.	8
4	AlAteeq et al., 2021 [47]	Saudi Arabia	n = 1313; Population = Healthcare workers.	Age = 34.76 years; Female % = 55.83%.	7
5	Ali et al., 2021 [72]	Bangladesh	n = 294; Population = Special population.	Age = 28.86 years; Female % = 43.54%.	6
6	Alshekaili et al., 2020 [73]	Oman	n = 1136; Population = Special population.	Age = 36.35 years; Female % = 79.18%.	7
7	Atac et al., 2020 [74]	Turkey	n = 149; Population = Healthcare workers.	Age = 35.7 years; Female % = 71.54%.	6
8	Atas et al., 2021 [75]	Turkey	n = 106; Population = Special population.	Age = 44.15 years; Female % = 40.57%.	6
9	Bacaro et al., 2020 [65]	Italy	n = 2652; Population = General population.	Age = 38.47 years; Female % = 76.28%.	8
10	Bajaj et al., 2020 [76]	India	n = 391; Population = General population.	Age = 37.71 years; Female % = 53.45%.	8
11	Chatterjee et al., 2021 [49]	India	n = 140; Population = Special population.	Age = 37.67 years; Female % = 100%.	7
12	Elhadi et al., 2021 [77]	Libya	n = 10296; Population = General population.	Age = 28.89 years; Female % = 77.61%.	7
13	Erizo et al., 2021 [78]	Ecuador	n = 1060; Population = Healthcare workers.	Age = NR years; Female % = 68.68%.	6
14	Essangri et al., 2021 [79]	Morocco	n = 549; Population = University students.	Age = 21.93 years; Female % = 73.95%.	8
15	Fekih-Romdhane et al., 2020 [80]	Tunisia	n = 210; Population = Healthcare workers.	Age = 28.6 years; Female % = 70.48%.	8
16	Giardino et al., 2020 [81]	Argentina	n = 1059; Population = Healthcare workers.	Age = 41.7 years; Female % = 72.9%.	8
17	Gu et al., 2020 [82]	China	n = 983; Population = Multiple.	Age = 39.35 years; Female % = 71.62%.	8
18	Gualano et al., 2020 [83]	Italy	n = 624; Population = Multiple.	Age = 43.4 years; Female % = 72.44%.	8
19	Gupta et al., 2020 [50]	India	n = 903; Population = Multiple.	Age = 38.27 years; Female % = 40.75%.	7
20	Hendrickson et al., 2020 [84]	United States	n = 694; Population = Multiple.	Age = 41.48 years; Female % = 20.41%.	6
21	Jahrami et al., 2021 [85]	Bahrain	n = 549; Population = General population.	Age = 27.33 years; Female % = 53.92%.	8
22	Jain et al., 2020 [86]	India	n = 512; Population = Special population.	Age = NR years; Female % = 44.34%.	8
23	Khanal et al., 2020 [87]	Nepal	n = 475; Population = Healthcare workers.	Age = 28.2 years; Female % = 52.63%.	8
24	Khoury et al., 2021 [88]	Canada	n = 303; Population = General population.	Age = 32.09 years; Female % = 100%.	7
25	Kim et al., 2021 [89]	Korea	n = 221; Population = Special population.	Age = 50.12 years; Female % = 76.02%.	6
26	König et al., 2021 [90]	Germany	n = 484; Population = Healthcare workers.	Age = NR years; Female % = 80.87%.	7
27	Lahiri et al., 2021 [91]	India	n = 1081; Population = General population.	Age = 33.15 years; Female % = 41.72%.	8
28	Laukkala et al., 2021 [92]	Finland	n = 1744; Population = Healthcare workers.	Age = 47.06 years; Female % = 87.33%.	9
29	Marelli et al., 2021 [93]	Italy	n = 400; Population = General population.	Age = 26.14 years; Female % = 24.25%.	7
30	Marroquin et al., 2020 [94]	United States	n = 435; Population = General population.	Age = 39.21 years; Female % = 46.44%.	7
31	Mongkhon et al., 2021 [95]	Thailand	n = 4004; Population = Multiple.	Age = 29.07 years; Female % = 69.26%.	9
32	Que et al., 2020 [96]	China	n = 2285; Population = Healthcare workers.	Age = 31.06 years; Female % = 69.06%.	9
33	Sagherian et al., 2020 [51]	United States	n = 587; Population = Healthcare workers.	Age = 37.62 years; Female % = 68.04%.	8
34	Sahin et al., 2020 [97]	Turkey	n = 939; Population = Special population.	Age = 34.22 years; Female % = 66.03%.	8
35	Salfi et al., 2021 [98]	Italy	n = 13989; Population = Multiple.	Age = 33.84 years; Female % = 77.68%.	9
36	Samaniego et al., 2020 [99]	Paraguay	n = 126; Population = Healthcare workers.	Age = 31.86 years; Female % = 84.3%.	6
37	Scotta et al., 2020 [100]	Argentina	n = 584; Population = University students.	Age = 22.5 years; Female % = 81.58%.	8
38	Sekartaji et al., 2021 [101]	Indonesia	n = 101; Population = University students.	Age = 22.86 years; Female % = 57.41%.	6
39	Sharma et al., 2020 [102]	India	n = 108; Population = Healthcare workers.	Age = NR years; Female % = 69.44%.	6
40	Shi et al., 2020 [103]	China	n = 56679; Population = Multiple.	Age = 35.97 years; Female % = 47.9%.	9
41	Song et al., 2020 [104]	China	n = 709; Population = General population.	Age = 35.35 years; Female % = 74.19%.	8
42	Sun et al., 2020 [105]	China	n = 6906; Population = General population.	Age = 33.89 years; Female % = 83.17%.	8
43	Urzua et al., 2020 [106]	Chile	n = 125; Population = Healthcare workers.	Age = 30.23 years; Female % = 72.17%.	6
44	Xu et al., 2021 [107]	China	n = 11254; Population = University students.	Age = 19.99 years; Female % = 63.98%.	9
45	Youssef et al., 2020 [108]	Egypt	n = 450; Population = Special population.	Age = 37.22 years; Female % = 45.76%.	7
46	Yu et al., 2020 [109]	China	n = 1138; Population = General population.	Age = NR years; Female % = 65.61%.	9
47	Zhang et al., 2020 [110]	China	n = 2182; Population = Multiple.	Age = NR years; Female % = 64.21%.	9
48	Zhuo et al., 2020 [111]	China	n = 26; Population = Special population.	Age = 41.92 years; Female % = 46.15%.	5

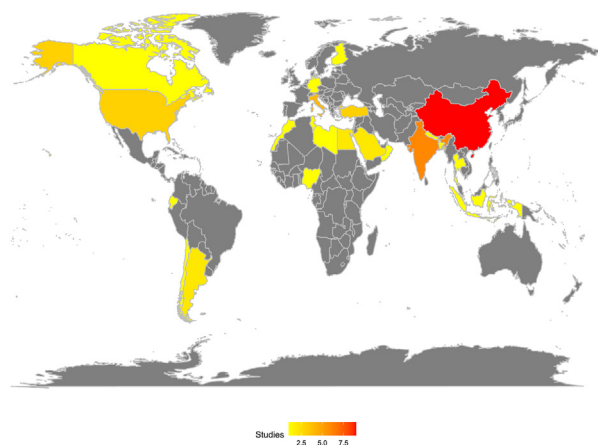


Fig. 2. The geographic distribution and the number of studies per country.

N = 2033); Thailand (K = 1, N = 4004); Tunisia (K = 1, N = 210); Turkey (K = 3, N = 1194); United States (K = 3, N = 1716). The geographic distribution and the number of studies per country is summarized in Fig. 2.

The majority of the studies were mid-sample size with a median sample size of 605 participants (range 26–56679). The mean age of participants was 33.84 ± 7.14 years [95%CI 31.66; 36.03], and females accounted for a total of 65% of participants. Many of the studies involved healthcare workers (K = 14, 29%), the general adult population (K = 11, 23%) or multiple populations (K = 10, 21%). Others included special populations such as pregnant women, or people with medical or psychiatric comorbidity (K = 9, 19%), and university students (K = 4, 8%).

In the meta-analysis, the mean NOS quality score was 7.43 ± 1.10, with a range of 5.0–9.0. Fig. S1 describes the quality assessment process (traffic light plot) for each study included in the IPDMA. Overall, 85.5% of the studies were high quality (low risk of bias) and the remaining 14.6% were of moderate quality. Fig. S2 shows that most risk bias was associated with selection in terms of sample size and representativeness. Table 1 summarizes the

characteristics of all included studies.

3.1. Cumulative prevalence of insomnia symptoms (subthreshold, moderate and severe)

Using all available studies, a random-effects meta-analysis evaluated the prevalence of insomnia symptoms in all populations (K = 48, N = 133,006) generated a pooled cumulative prevalence of insomnia symptoms using a random-effects model = 52.57% [47.44; 57.65%]; 95% PI [20.40; 82.66%]; $\tau^2 = 0.5143$ [0.2758; 0.8359]; $\tau = 0.7171$ [0.5252; 0.9143]; $I^2 = 99.6%$; H = 16.09 [15.50; 16.70]; Q = 12168.85 (df = 47), $p < 0.001$ See Fig. 3. A (leave-one-out) sensitivity analysis found that no study had a greater than 1% impact on the global prevalence estimate. Visual inspection of funnel plots indicated no clear publication bias, with Egger's regression $p = 0.4$, confirming the absence of publication bias. Meta-regression analysis revealed that neither age nor sex moderated the cumulative prevalence of insomnia symptoms

during the COVID-19 pandemic $p = 0.6$ and $p = 0.5$, respectively. Detailed results are presented in Table 2 (see Table 3 and Table 4).

3.2. Cumulative prevalence of insomnia (moderate and severe)

Cumulative prevalence of insomnia symptoms (moderate and severe) using a random-effects model = 16.66% [13.57; 20.29%]; 95% PI [3.49; 52.51%]; $\tau^2 = 0.7069$ [0.3054; 0.8761]; $\tau = 0.8407$ [0.5527; 0.9360]; $I^2 = 99.4%$ [99.4%; 99.5%]; H = 13.46 [12.90; 14.04]; Q = 8511.02 (df = 47), $p < 0.001$ See Fig. 4. A (leave-one-out) sensitivity analysis found that no study had a greater than 1% impact on the global prevalence estimate. Visual inspection to funnel plots indicated no clear publication bias, Egger's regression $p = 0.3$, confirmed the absence of publication bias. Meta-regression analysis revealed that neither age nor sex moderates the cumulative prevalence of insomnia symptoms (moderate and severe) during the COVID-19 pandemic $p = 0.8$ and $p = 0.5$, respectively. Detailed results are presented in Table 2.

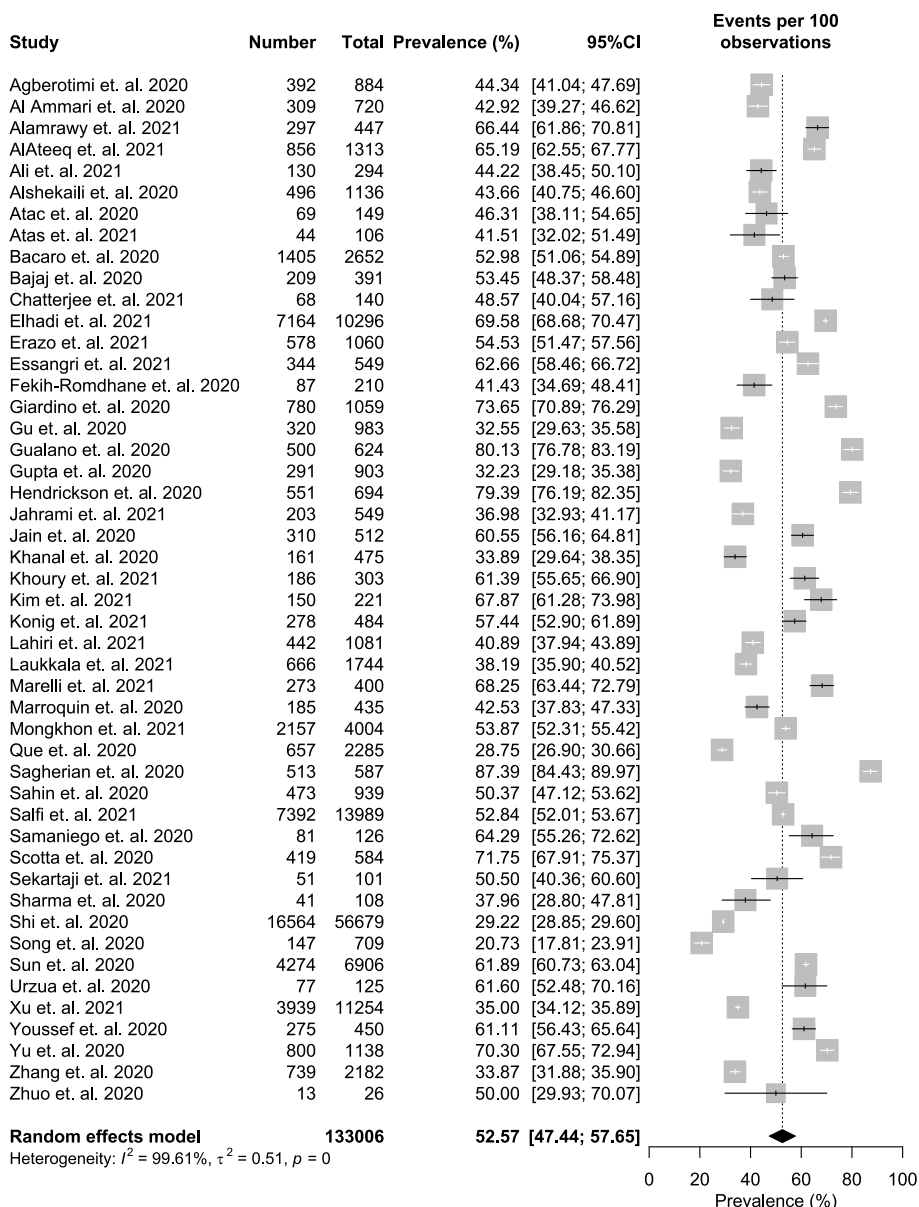


Fig. 3. Cumulative prevalence of insomnia symptoms (subthreshold, moderate and severe).

Table 2
Insomnia symptoms during COVID-19 by severity: a meta-analysis, a moderator analysis, and assessment of heterogeneity.

Component	K	N	Random-effects meta-analysis		Heterogeneity				Moderators		Publication Bias
			Pooled results [95%CI]	Forest Plot	I ²	H	τ ²	Q	Age	Sex (% Female)	
Cumulative prevalence of insomnia symptoms (subthreshold, moderate and severe)	48	133006	52.57 [47.44; 57.65]	Fig. 3	99.6%	16.09	0.5143	12168.85	0.6	0.5	Egger's 0.4 = ; Rank = 0.6.
Cumulative prevalence of insomnia (moderate and severe)	48	133006	16.66 [13.57; 20.29]	Fig. 4	99.4%	13.46	0.7069	8511.02	0.8	0.5	Egger's = 0.3; Rank = 0.3.
Prevalence of subthreshold insomnia symptoms	48	133006	33.42 [30.89; 36.04]	Fig. 5	98.7%	8.62	0.1547	3490.18	0.5	0.6	Egger's = 0.4; Rank = 0.2.
Prevalence of moderate insomnia symptoms	48	133006	13.75 [11.18; 16.79]	Fig. 6	99.3%	12.21	0.6695	7001.48	0.8	0.6	Egger's = 0.4; Rank = 0.2.
Prevalence of severe insomnia symptoms	48	133006	2.50 [1.93; 3.25]	Fig. 7	97.5%	6.32	0.7803	1876.19	0.9	0.4	Egger's = 0.9; Rank = 0.1.

Abbreviations: CI, Confidence interval. K = denotes the number of studies. N = denotes the number of participants. NA = Not applicable. NI = Not indicated. NS = Not Significant.
Methodological details: I² statistic describes the percentage of variation across studies due to heterogeneity rather than chance. In a random-effects meta-analysis, the extent of variation among the effects observed in different studies (between-study variance) is referred to as τ-squared. Cochran's Q, which is calculated as the weighted sum of squared differences between individual study effects and the pooled effect across studies, with the weights being those used in the pooling method. Meta-regression was performed using Method of Moments Estimator for Random Effect Multivariate Meta-Analysis. Publication bias was not observed in the Funnel plot. Adjusted results were calculated using trill-and-fill.

Table 3
Insomnia symptoms during COVID-19 by population: a meta-analysis, a moderator analysis, and assessment of heterogeneity.

Population	K	N	Random-effects meta-analysis		Heterogeneity			
			Pooled results [95%CI]		I ²	τ	τ ²	Q
General population	11	24860						
- Subthreshold insomnia symptoms			34.05 [30.12; 38.21]		97.3%	0.2941	0.0865	366.05
- Moderate insomnia symptoms			13.24 [9.78; 17.68]		98.7%	0.5653	0.3196	790.11
- Severe insomnia symptoms			2.85 [1.91; 4.22]		96.7%	0.6261	0.3920	301.02
Healthcare workers	14	10445						
- Subthreshold insomnia symptoms			32.61 [28.68; 36.81]		94.3%	0.3330	0.1109	229.46
- Moderate insomnia symptoms			14.91 [10.30; 21.10]		98.1%	0.7890	0.6225	682.67
- Severe insomnia symptoms			2.32 [1.52; 3.52]		90.1%	0.7225	0.5220	131.87
Multiple	10	81389						
- Subthreshold insomnia symptoms			33.73 [27.35; 40.76]		99.5%	0.4819	0.2322	1965.38
- Moderate insomnia symptoms			12.01 [7.94; 17.74]		99.5%	0.7335	0.5380	1908.85
- Severe insomnia symptoms			2.00 [1.34; 2.98]		96.7%	0.6263	0.3923	272.14
Special population	9	3824						
- Subthreshold insomnia symptoms			33.75 [30.73; 36.92]		69.7%	0.1638	0.0268	26.36
- Moderate insomnia symptoms			14.85 [11.73; 18.62]		86.3%	0.3587	0.1287	58.26
- Severe insomnia symptoms			3.23 [2.06; 5.03]		79.8%	0.5884	0.3462	39.59
University students	4	12488						
- Subthreshold insomnia symptoms			33.40 [25.53; 42.31]		95.9%	0.3700	0.1369	73.49
- Moderate insomnia symptoms			15.12 [5.58; 34.95]		99.3%	1.1143	1.2417	449.57
- Severe insomnia symptoms			3.26 [0.97; 10.36]		97.8%	1.2295	1.5116	137.25

Abbreviations: CI, Confidence interval. K = denotes the number of studies. N = denotes the number of participants. NA = Not applicable. NI = Not indicated. NS = Not Significant.
Methodological details: I² statistic describes the percentage of variation across studies due to heterogeneity rather than chance. In a random-effects meta-analysis, the extent of variation among the effects observed in different studies (between-study variance) is referred to as τ-squared.
Cochran's Q, which is calculated as the weighted sum of squared differences between individual study effects and the pooled effect across studies, with the weights being those used in the pooling method.
Meta-regression was performed using Method of Moments Estimator for Random Effect Multivariate Meta-Analysis.
Publication bias was not observed in the Funnel plot.
Adjusted results were calculated using trill-and-fill.

3.3. Prevalence of subthreshold insomnia symptoms

Prevalence of subthreshold insomnia symptoms using a random-effects model = 33.42% [30.89; 36.04%]; 95% PI [18.39; 52.78%]; τ² = 0.1547 [0.0879; 0.2671]; τ = 0.3933 [0.2965; 0.5169]; I² = 98.7% [98.5%; 98.8%]; H = 8.62 [8.14; 9.12]; Q = 3490.18 (df = 47), p < 0.001 See Fig. 5. A (leave-one-out) sensitivity analysis found that no study had a greater than 1% impact on the global prevalence estimate. Visual inspection to funnel plots indicated no clear publication bias, Egger's regression p = 0.4, confirmed the absence publication bias. Meta-regression analysis revealed that

neither age nor sex moderated the prevalence of subthreshold insomnia symptoms during the COVID-19 pandemic p = 0.5 and p = 0.6, respectively. Detailed results are presented in Table 2.

Subgroup analysis of the prevalence of subthreshold insomnia symptoms by population grouping revealed that no statistically difference was observed between groups p = 0.99. Rates of subthreshold insomnia symptoms were as follow: healthcare workers 32.61% [28.68; 36.81%]; multiple populations 33.73% [27.35; 40.76%]; general population 34.05% [30.12; 38.21%]; special population 33.75% [30.73; 36.92%]; university students 33.40% [25.53; 42.31%]. Subgroup analysis of the prevalence of subthreshold

Table 4
Insomnia symptoms during COVID-19 by country: a meta-analysis, a moderator analysis, and assessment of heterogeneity.

Population	K	N	Random-effects meta-analysis		Heterogeneity			
			Pooled results [95%CI]	I ²	τ	τ ²	Q	
China	9	82162	- Subthreshold insomnia symptoms	27.27 [22.30; 32.88]	99.4%	0.3928	0.1543	1278.05
- Moderate insomnia symptoms			7.52 [4.97; 11.23]	99.4%	0.6548	0.4287	1242.59	
- Severe insomnia symptoms			2.04 [0.87; 4.73]	99.4%	1.2692	1.6110	1367.59	
India		3135	- Subthreshold insomnia symptoms	28.91 [24.90; 33.28]	82.6%	0.2227	0.0496	28.66
- Moderate insomnia symptoms			12.53 [8.44; 18.20]	93.3%	0.5177	0.2680	74.18	
- Severe insomnia symptoms			2.85 [1.52; 5.28]	86.2%	0.7221	0.5214	36.30	
Italy	4	17665	- Subthreshold insomnia symptoms	46.82 [38.24; 55.61]	98.4%	0.3531	0.1247	182.34
- Moderate insomnia symptoms			14.29 [12.98; 15.71]	65.3%	0.0858	0.0074	8.65	
- Severe insomnia symptoms			1.80 [1.27; 2.56]	76.3%	0.2801	0.0785	12.67	
United States	3	1716	- Subthreshold insomnia symptoms	38.31 [28.54; 49.13]	94.9%	0.3797	0.1442	39.27
- Moderate insomnia symptoms			25.55 [14.95; 40.10]	97.2%	0.5811	0.3377	71.24	
- Severe insomnia symptoms			4.27 [2.69; 6.71]	73.8%	0.3575	0.1278	7.64	
Turkey	3	1194	- Subthreshold insomnia symptoms	35.11 [32.45; 37.86]	0.0%	0	0	0.96
- Moderate insomnia symptoms			10.96 [7.38; 15.97]	62.5%	0.2978	0.0887	5.34	
- Severe insomnia symptoms			2.12 [1.43; 3.12]	0.0%	0	0	0.52	

Abbreviations: CI, Confidence interval. K = denotes the number of studies. N = denotes the number of participants. NA = Not applicable. NI = Not indicated. NS = Not Significant.

Methodological details: I² statistic describes the percentage of variation across studies due to heterogeneity rather than chance. In a random-effects meta-analysis, the extent of variation among the effects observed in different studies (between-study variance) is referred to as τ-squared. Cochran's Q, which is calculated as the weighted sum of squared differences between individual study effects and the pooled effect across studies, with the weights being those used in the pooling method. Meta-regression was performed using Method of Moments Estimator for Random Effect Multivariate Meta-Analysis. Publication bias was not observed in the Funnel plot. Adjusted results were calculated using trim-and-fill.

insomnia symptoms by country revealed that a statistically significant difference existed between countries $p < 0.001$. Specifically rates of subthreshold insomnia symptoms were: China 27.27% [22.30; 32.88%], India 28.91% [24.90; 33.28%], Italy 46.82% [38.24; 55.61%], Turkey 35.11% [32.45; 37.86%], and United States 38.31% [28.54; 49.13%].

3.4. Prevalence of moderate insomnia symptoms

Prevalence of moderate insomnia symptoms using a random-effects model = 13.75% [11.18; 16.79%]; 95% PI [2.93; 45.71%]; $\tau^2 = 0.6695$ [0.2891; 0.8332]; $\tau = 0.8182$ [0.5377; 0.9128]; $I^2 = 99.3%$ [99.3%; 99.4%]; $H = 12.21$ [11.67; 12.77]; $Q = 7001.48$ ($df = 47$), $p < 0.001$. See Fig. 6 A (leave-one-out) sensitivity analysis found that no study had a greater than 0.5% impact on the global prevalence estimate. Visual inspection to funnel plots indicated no clear publication bias, Egger's regression $p = 0.4$, confirmed the absence of publication bias. Meta-regression analysis revealed that neither age nor sex moderates the prevalence of moderate insomnia symptoms during the COVID-19 pandemic $p = 0.8$ and $p = 0.6$, respectively. Detailed results are presented in Table 2.

Subgroup analysis of the prevalence of moderate insomnia symptoms by population grouping revealed that no statistically significant difference was observed between groups $p = 0.89$. Rates of subthreshold insomnia symptoms were as follow: healthcare workers 14.91% [10.30; 21.10%]; multiple populations 12.01% [07.94; 17.74%]; general population 13.24% [09.78; 17.68%]; special population 14.85% [11.73; 18.62%]; university students 15.12% [05.58; 34.95%]. Subgroup analysis of the prevalence of moderate insomnia symptoms by country revealed that a statistically significant difference existed between countries $p < 0.001$. Specifically rates of moderate insomnia symptoms were: China 07.52% [04.97; 11.23%], India 12.53% [08.44; 18.20%], Italy 14.29% [12.98; 15.71%], Turkey 10.96% [07.38; 15.97%] and United States 25.55% [14.95; 40.10%].

3.5. Prevalence of severe insomnia symptoms

Prevalence of severe insomnia symptoms using a random-effects model = 2.50% [1.93; 3.25%]; 95% PI [0.42; 13.44%]; $\tau^2 = 0.7803$ [0.3593; 1.0806]; $\tau = 0.8834$ [0.5994; 1.0395]; $I^2 = 97.5%$ [97.1%; 97.8%]; $H = 6.32$ [5.89; 6.78]; $Q = 1876.19$ ($df = 47$), $p < 0.001$. See Fig. 7 A (leave-one-out) sensitivity analysis found that no study had a greater than 0.25% impact on the global prevalence estimate. Visual inspection to funnel plots indicated no clear publication bias, Egger's regression $p = 0.9$, confirmed the absence of publication bias. Meta-regression analysis revealed that neither age nor sex moderates the prevalence of severe insomnia symptoms during the COVID-19 pandemic $p = 0.9$ and $p = 0.4$, respectively. Detailed results are presented in Table 2.

Subgroup analysis of the prevalence of severe insomnia symptoms by population grouping revealed that no statistically significant difference was observed between groups $p = 0.53$. Rates of subthreshold insomnia symptoms were as follow: healthcare workers 02.32% [01.52; 03.52%]; multiple populations 02.00% [01.34; 02.98%]; general population 02.85% [01.91; 04.22%]; special population 03.23% [02.06; 05.03%]; university students 03.26% [0.97; 10.36%]. Subgroup analysis of the prevalence of severe insomnia symptoms by country revealed that a statistically significant difference existed between countries $p < 0.001$. Specifically rates of severe insomnia symptoms were: China 02.04% [00.87; 04.73%], India 02.85% [01.52; 05.28%], Italy 01.80% [01.27; 02.56%], Turkey 02.12% [01.43; 03.12%] and United States 04.27% [02.69; 06.71%].

4. Discussion

The current systematic review and IPDMA of 48 studies from 25 countries with a total of 133,006 participants assessed for insomnia symptoms revealed that during the COVID-19 pandemic, the pooled estimated prevalence of cumulative prevalence of insomnia

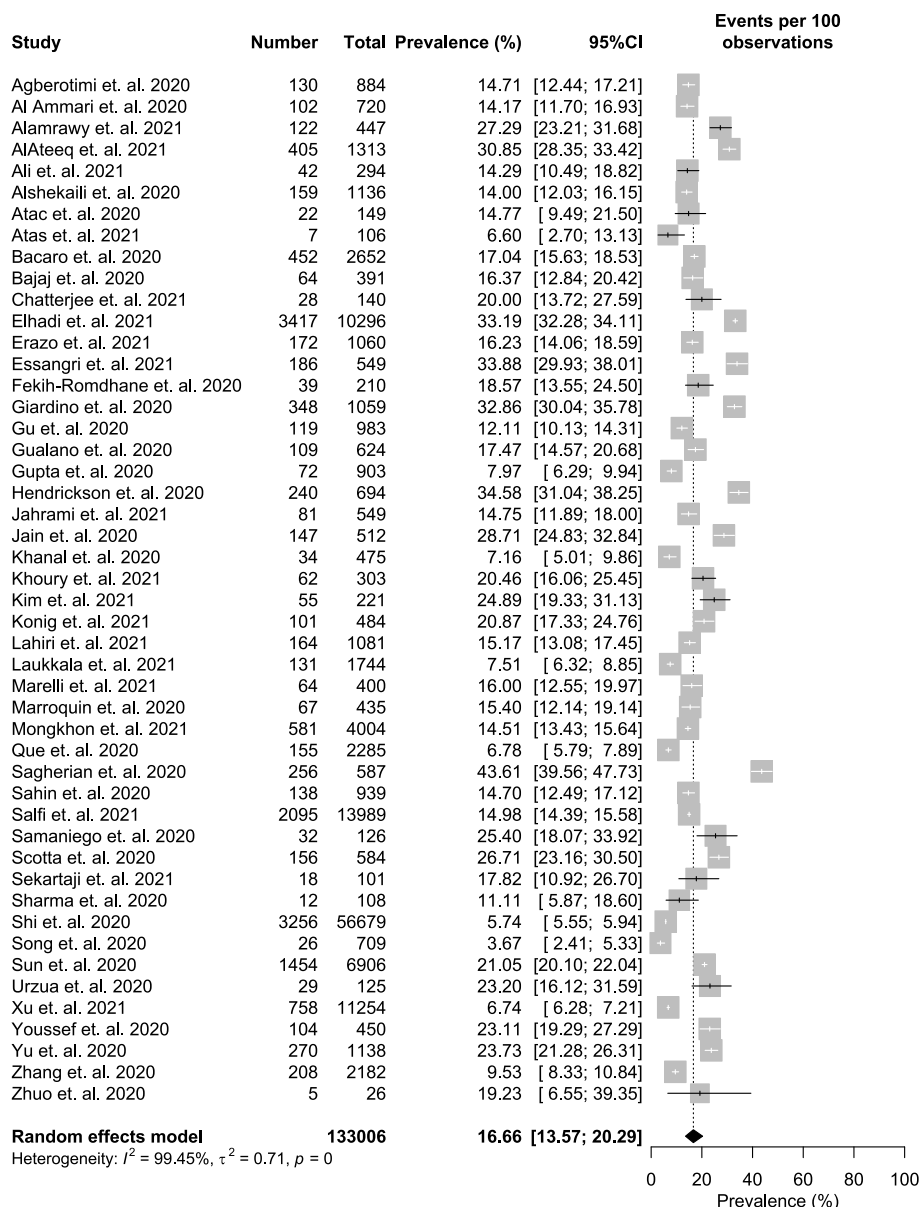


Fig. 4. Cumulative prevalence of insomnia (moderate and severe).

symptoms (including subthreshold insomnia symptoms and moderate and severe insomnia) was 52.57%. The novel contribution of IPD meta-analysis was to standardize and improve the quality of the data analysis. Furthermore, providing an analysis of insomnia using ISI by subgroups according to symptoms severity was never reported before during the COVID-19 pandemic. The prevalence of clinically significant insomnia was 16.66% when modeled together or 13.75% moderate insomnia and 2.50% severe insomnia when modeled separately. No statistically significant differences were detected in the prevalence of insomnia symptoms or insomnia among different population groupings. However, a statistically significant difference was observed between countries for all severities of insomnia symptoms. Neither age nor sex appeared to be moderators of the prevalence of cumulative prevalence of subthreshold insomnia symptoms or of clinically significant insomnia.

Several studies have confirmed the concomitant increase in sleep disturbances in the general population caused by COVID-19 [3,4,7,47–51]. The pooled prevalence rate of insomnia symptoms

during COVID-19 (40–50%) observed in the current study is consistent with two previous meta-analyses [5,48]. In addition, one of these meta-analyses reported that age and sex did not affect estimates of sleep disturbance prevalence [5]. Similar findings were reported in previous reviews [5,48,52]. A previous systematic review and meta-analysis conducted by our group reported a subgroup meta-analysis of aggregate ISI data and obtained an overall prevalence of insomnia symptoms of 30.98% [26.77; 35.54%] [53].

Insomnia is the most frequently occurring sleep disorder in the adult population [54], with a pre-COVID-19 prevalence of 5.0–20.0% using formal diagnostic procedures [55]. The findings of the current review showed that the post-COVID-19 prevalence of moderate to severe insomnia is similar to rates of pre-COVID-19 insomnia. This suggests that although the pandemic COVID-19 has been associated with increased rates of cumulative prevalence of subthreshold insomnia and insomnia, individuals meeting diagnostic criteria for insomnia remained the same, while prevalence of subthreshold insomnia increased [56].

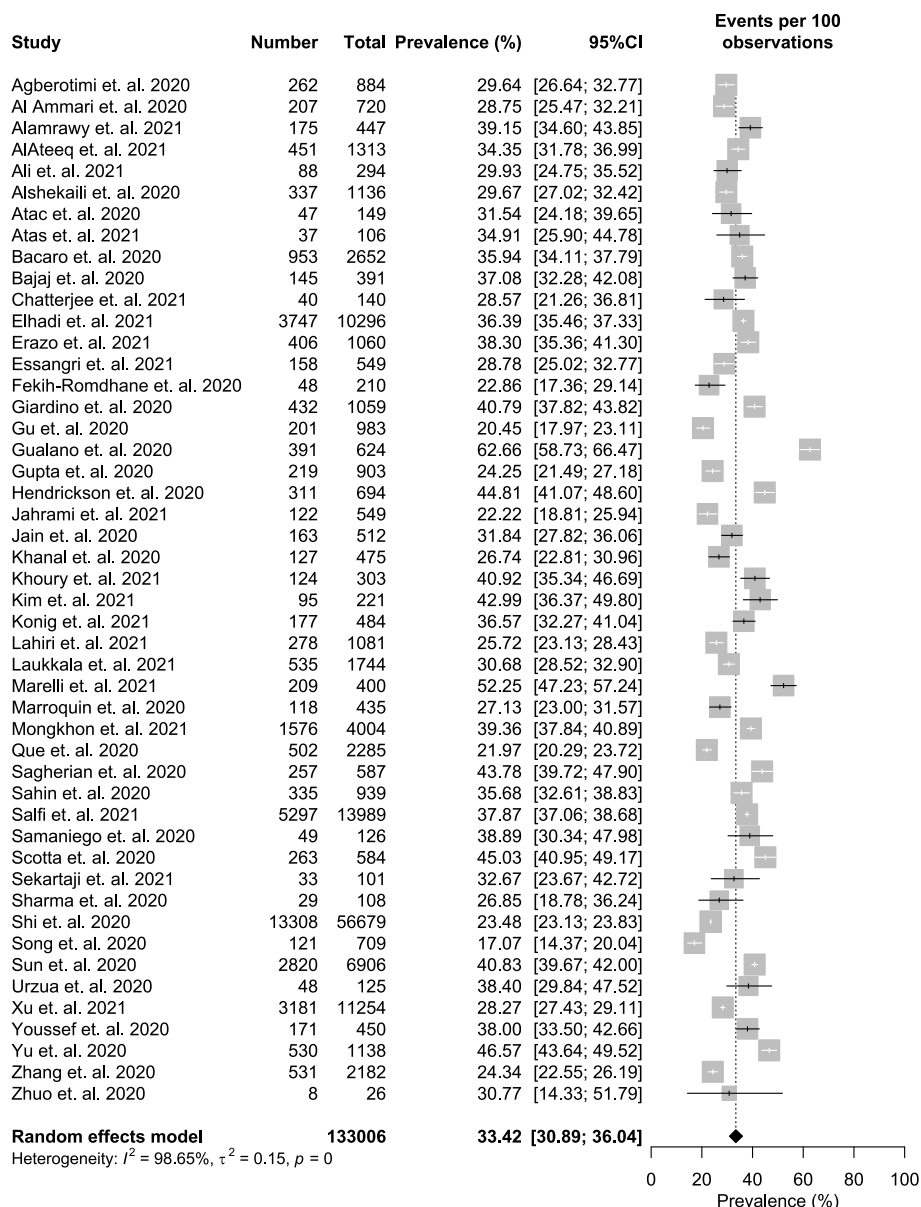


Fig. 5. Prevalence of subthreshold insomnia symptoms.

It has been proposed that the term “coronasomnia” or “COVID-somnia” encompasses a constellation of symptoms of sleep dysfunction, such as insomnia symptoms, interrupted sleep continuity, and changes in sleep-wake patterns during the COVID-19 pandemic [57].

Our findings indicate that there was a significant rise in the frequencies of subthreshold insomnia symptoms from before the COVID-19 pandemic while no comparable rise was seen in moderate to severe insomnia [56]. Educating diverse demographic groups about the significance of sleep and the risk of developing symptoms of insomnia during this or future pandemics should be a concern for the sleep medicine community, as should be developing measures to prevent the development of subthreshold insomnia so that the development of full-blown insomnia disorders can be prevented.

Several factors may contribute to insomnia symptoms caused by issues related to COVID-19. There were high levels of anxiety,

depression, post-traumatic stress disorder (PTSD), and stress in the general population across the globe during the COVID-19 pandemic [58]. Female gender, younger age group (< 35 years), history of psychiatric illnesses, unemployment, low educational status, and frequent exposure to social media/news regarding COVID-19 infection were reported as important risk factors [58]. The relationship between anxiety and depression and insomnia symptoms has long been recognized [59,60], and it has been found that mental distress has been more prevalent in the general population during the COVID-19 pandemic [61–63]. An analysis of 556 participants in a French study found that 19% of them met the diagnostic criteria for clinical insomnia and found that COVID-19-related worries and loneliness played a significant role in the development of their insomnia, as well as low education levels, virus infection, and preexisting mental health problems [64]. An Italian study of 1989 young to middle-aged adults found that approximately 19% had clinical insomnia during the pandemic, and insomnia symptom

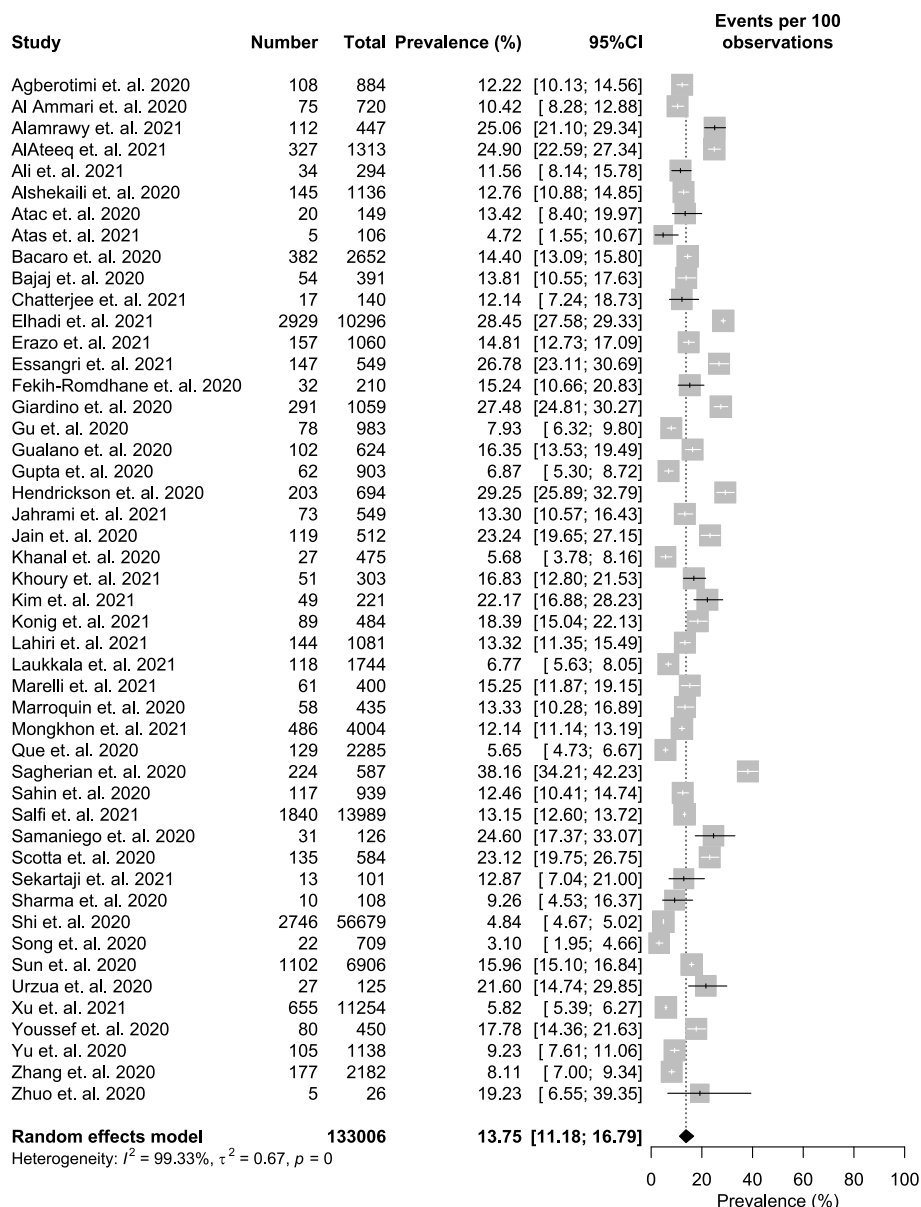


Fig. 6. Prevalence of moderate insomnia symptoms.

severity was associated with poor sleep hygiene behaviors, dysfunctional beliefs about sleep, self-reported stress, anxiety, and depression [65].

In their study of 5461 Chinese participants, Lin and colleagues found that insomnia was more common among women and young people living in the ‘epicenter’ and experiencing a high level of threat from COVID-19 infection [66]. During the COVID-19 pandemic period, another large Chinese study of 12,000+ adolescents and young adults found that approximately 25% of them had insomnia symptoms with female sex, depression and anxiety, and living in the city were observed to be the greatest risk factors, while subjective and objective social support were protective [67]. Some researchers have attempted to study the effects of lockdown and quarantine periods, in particular, on both subthreshold insomnia symptoms and clinically significant insomnia symptoms among the general public, even though many of the studies pertaining to the general population include people in lockdown (as was the case in many countries during the pandemic).

An investigation by Papa et al. (2020) looked at the prevalence of subthreshold insomnia symptoms and clinically significant insomnia among healthcare providers dealing with COVID-19 patients; the study found that 39% of the healthcare providers had insomnia [17].

This systematic review and IPDMA has several strengths. The prevalence of insomnia symptoms has been estimated (by severity) in different populations using individual participants data providing a more accurate understanding of the effects of COVID-19 on insomnia symptoms. The NOS checklist was used to assess the methodological quality of each analyzed study. Subgroup analysis and meta-regression provided a robust approach in exploring heterogeneity in the findings. The present review’s findings are also generalizable since the synthesized sample size was large, and participants were recruited from 25 countries.

Nevertheless, this review also has limitations. The review focused only on ISI data and did not consider other insomnia symptom assessment measures, e.g., the Regensburg Insomnia

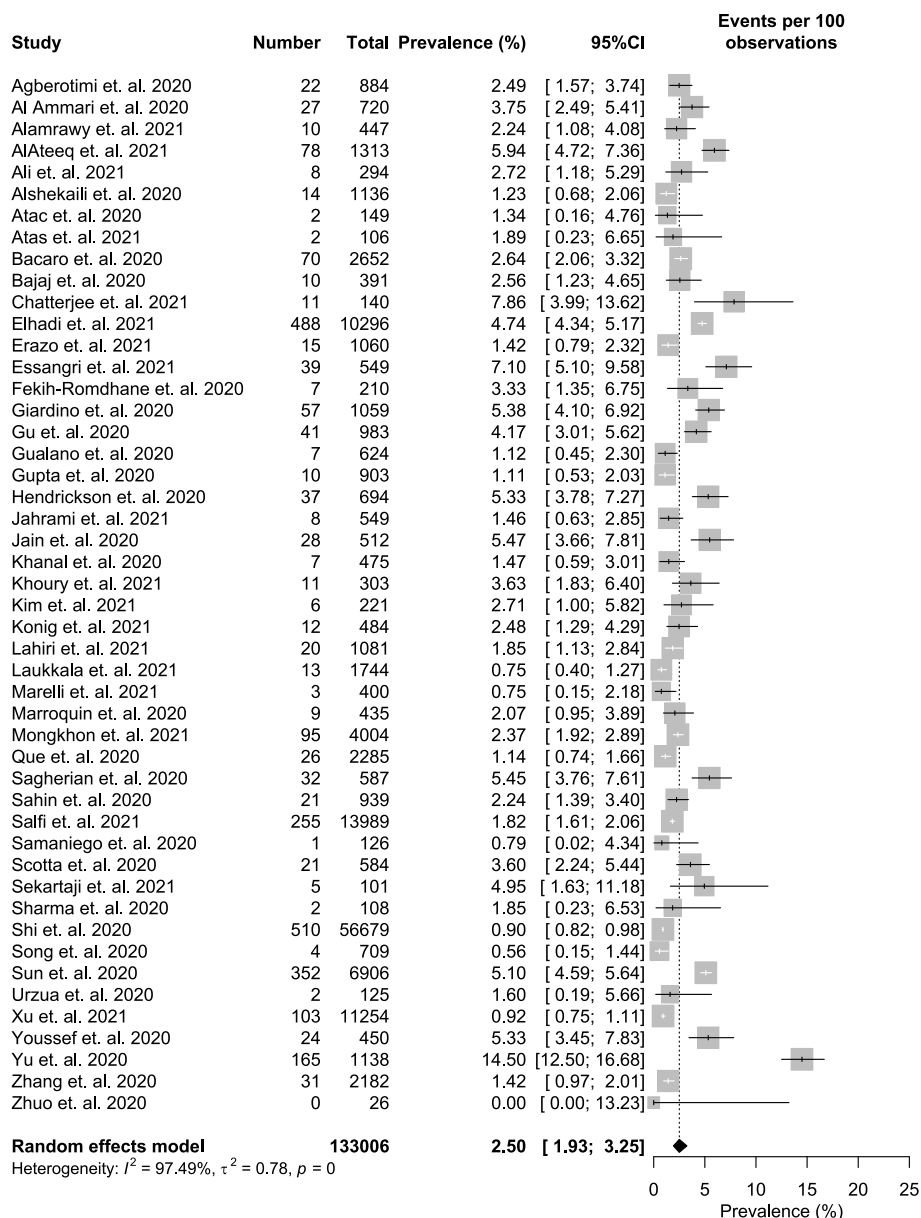


Fig. 7. Prevalence of severe insomnia symptoms.

Scale (RIS) or the Athens Insomnia Scale (AIS). There may be bias in this study's estimations of prevalence of insomnia, since other measures may capture insomnia severity differently. All of the studies reviewed here used the ISI self-report to assess insomnia as opposed to a formal interview and diagnostic process. Therefore, results in the present review might be influenced by the psychometric strength of each language translation. COVID-19 has dynamic effects on insomnia [48]; therefore, people may suffer from different levels of insomnia based on the severity of the COVID-19 outbreak in their area. The policies used to control the COVID-19 outbreak have also been different in different countries. Thus, the estimated results in this review do not necessarily reflect COVID-19's impact over a specific period. The bulk of the included studies were from Chinese and Italian populations, a limitation to generalizability. Additionally, most synthesized samples were young adults from the general population or healthcare workers groups. Thus, the results of this review are not generalizable to various ethnic and age groups (i.e., older people and children). The elderly

were identified as a high-risk group for insomnia during the COVID-19 pandemic; partially because COVID-19 infection is associated with increased vulnerability as a person ages [68]. Another limitation of this review was the response rate, whereby approximately 50% of authors agreed to participate and provided original datasets for secondary analyses. Finally, the generalization of the present review should be taken within the background of the observed high statistical heterogeneity. A high I^2 estimate is not necessarily synonymous with important heterogeneity [33]. In the same way, a low value of I^2 is not always an indicator of consistent and homogenous results [33]. For example, a meta-analysis of prevalence commonly yields high I^2 estimates, and authors of meta-analyses sometimes conclude their results are heterogeneous [33]. However, the I^2 statistic is not an absolute index for the amount of variability observed, and its estimation can be impacted by some factors such as the number of studies or the pooled result. Therefore, the high I^2 must be interpreted along with the prediction intervals shown in our review [33].

5. Conclusion

The pooled estimate of insomnia symptoms (subthreshold and clinically significant) was 52.57%. An estimated 16.66% of the population suffered from clinically significant insomnia, of which 13.75% suffered from moderate insomnia, and 2.50% suffered from severe insomnia. The different populations' grouping had no statistically significant differences in the prevalence of insomnia symptoms. Insomnia symptoms did not appear to be associated with age or sex. Our data suggests that the COVID-19 pandemic is associated specifically with a marked increase in the rates of subthreshold insomnia symptoms but not moderate or severe insomnia. Educating diverse demographic groups about the significance of sleep and the risk of developing symptoms of insomnia during this or future pandemics should be a concern for the sleep medicine community, as should be developing measures to prevent the development of subthreshold insomnia and from its progression to more severe forms of the disorder.

Author agreement

All authors were involved in writing the paper and have seen and approved the manuscript.

Ethical statement

This article does not contain any studies with human participants performed by any of the authors.

Informed consent

For this type of study (meta-analysis) formal consent is not required.

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(continued on next page)

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Contributors

HJ designed the study. MMR, FFR, GNP, ZS, AFA, AH, WC, HD coordinated data collection, data entry and data cleaning. HJ performed statistical analyses and MMR, FFR, GNP, ZS, AFA, AH, WC, HD, NB, SRP wrote the first draft. ASB, MVV provided intellectual contributions to strengthening the manuscript and edited original draft. All authors provided critical revisions of manuscript, involved in writing and approved the final version.

Declaration of competing interest

The authors do not have any conflicts of interest to disclose.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.sleep.2022.06.020>.

Appendix B

(continued)

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