Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Review article

Prevalence of depression, anxiety, and insomnia symptoms among patients with COVID-19: A meta-analysis of quality effects model

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ABSTRACT

Background: Evidence from previous virus epidemics has shown that infected patients are at risk for developing psychiatric and mental health disorders, such as depression, anxiety, and insomnia. Hence, to collect high-quality data on the impact of COVID-19 pandemic on the prevalence of depression, anxiety, and insomnia symptoms among patients infected with SARS-CoV-2 should be the immediate priority.

Methods: A comprehensive search of Medline, Embase, Web of Science, and PsycINFO databases was conducted from January 1, 2020 to December 26, 2020 for eligible studies reporting on the prevalence of depression, anxiety, and insomnia symptoms in patients with COVID-19. Studies meeting the following criteria were included in the analysis: (1) included patients with COVD-19; (2) recorded the prevalence of depression, anxiety, or insomnia symptom; (3) sample size ≥30; (4) with validated screening tools; and (5) passed through the international peer-review process. Data extraction and quality assessment was independently performed by two reviewers. The quality effects meta-analysis was conducted further to calculate the pooled prevalence.

Results: Twenty-two studies were included for analysis with a total of 4318 patients. The pooled prevalence of depression, anxiety and insomnia symptoms was 38% (95% CI = 25–51), 38% (95% CI = 24–52), and 48% (95% CI = 11–85), respectively. Neither subgroup analysis nor sensitivity analysis can explain the source of high heterogeneity. In addition, the prevalence estimates of depression, anxiety and insomnia symptoms varied based on different screening tools.

Conclusions: The present systematic review and meta-analysis suggest that depression, anxiety, and insomnia symptoms are prevalent in a considerable proportion of patients with COVID-19. Thus, early detection and properly intervention for mental illness in this population are of great significance. Additionally, the quality of included studies to date has been variable, and ongoing surveillance is essential.

1. Introduction

In late December 2019, coronavirus disease 2019 (COVID-19), a highly contagious respiratory syndrome, broke out in Wuhan, China, and subsequently the source of this disease was confirmed to be a novel coronavirus, which was termed the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The World Health Organisation declared COVID-19 a pandemic on 11 March 2020 [1,2]. According to a report on transmissibility of the virus, the basic reproductive rate of SARS-COV-2 may has exceeded that of SARS and MERS [3]. As of the end of December 2020, nearly 80 million confirmed cases and 1.7 million deaths in over 200 countries have been reported [4].

Evidence from previous SARS and MERS outbreaks suggests that viral infections and quarantine can rapidly culminate into insomnia, anxiety, and depressive episodes [5]. Because of the excessive work pressure of medical workers, much attention has been paid to the treatment of physiological fallouts caused by COVID-19, and psychological problems of COVID-19 patients have likely been underestimated or ignored. Yet, psychological health plays an important role in the rehabilitation process of COVID-19 patients. For instance, a study indicated that negative attitudes of patients with depression towards antiviral therapy may reduce the treatment adherence [6]. Similarly, the level of anxiety in patients who died of Covid-19 was found to be significantly higher than that of surviving patients in a study [7].

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Another study reported that COVID-19 inpatients with insomnia disorder are more likely to have higher fatigue severity than those without insomnia disorder [8]. In addition, similar to the SARS epidemic, psychiatric complications of infected patients can last for more than 2 years, and the medical costs of hospitalised patients with psychiatric comorbidities have increased greatly, which is causing heavy economic burden to the individual family and whole society [9,10].

Many observational studies have shown that patients with COVID-19 are susceptible to depression, anxiety, and insomnia [8,11]. A review article by Rogers et al. (2020) examined the psychiatric and neuropsychiatric presentations associated with SARS, MERS, and COVID-19; however, the prevalence of depression, anxiety, and insomnia could not be reported in the review because of the lack of relevant data [12]. A meta-analysis of data (published up to August 2020) conducted by Deng et al. (2020) showed that the prevalence of depression, anxiety, and sleep disturbances in COVID-19 patients are 45%, 47% and 34%, respectively [13]. Regrettably, the meta-analysis included many studies that have not been internationally peer reviewed. Additionally, with the accumulation of knowledge on COVID-19 and the improvement of therapeutic measures, we assume that the prevalence of these disorders will decrease. In the present study, we adopted a new data synthesis method, namely, the quality effects (QE) model [14], to evaluate the prevalence of depression, anxiety, and insomnia symptoms in patients with COVID-19.

2. Material and methods

The systematic review was conducted in accordance with the PRISMA statement [15]. Information was organised according to the meta-analyses of observational studies in epidemiology (MOOSE) checklist. Additionally, the review protocol was registered on the official website of PROSPERO (CRD 42020193037).

2.1. Search strategy

Three authors independently and systemically retrieved the articles published from 1 January 2020, to 26 December 2020, by systematically searching the PubMed, Embase, Web of Science, and PsycINFO databases for eligible studies on the prevalence of depression, anxiety, and insomnia in patients with COVID-19. To include as many studies as possible, 'snowball sampling' by searching reference lists and citation tracking was performed for each retrieved article, and no language restrictions were applied. Queries regarding the methodology or results of the studies under consideration were attempted to be resolved by contacting the corresponding authors for clarification. To retrieve the PubMed articles, we first searched the MeSH column to determine the theme words and entry terms and then combined the terms for further searches (see Supplementary Material 1).

2.2. Inclusion and exclusion criteria

Studies fulfilling the following criteria were included in the analysis: (1) included patients with COVD-19; (2) recorded the prevalence of depression, anxiety, or insomnia symptom; (3) sample size $\geq$30 [16]; (4) used validated screening tools; and (5) passed through the international peer-review process. Publications were excluded on the basis of the following: (1) publication type (e.g. reviews, editorials, and comments); (2) studied population (e.g. studies conducted in general population, health care workers, or COVID-19 patients with known psychiatric disorders); (3) study design (e.g. animal studies and single patient case studies); and (4) data insufficiency (e.g. studies with insufficient information on the prevalence rate). All primary observational studies, including longitudinal cohort, cross-sectional, or case-control studies, were included if detailed data on the prevalence of depression, anxiety, or insomnia symptom in confirmed cases of SARS-CoV-2 infection were available in those studies.

2.3. Data extraction and quality assessment

Data extraction and quality assessment were independently performed by the first two authors. The data extraction sheet comprised the following information: (1) first author, (2) publication date, (3) country of origin, (4) study design, (5) sample size, (6) questionnaire response rate, (7) demographics (e.g. gender and mean/median age), (8) screening tools and cut-off values, and (9) subgroup data. Inspired by the methodology of previous reviews [13,17], the quality of included studies was assessed using the modified form of the Newcastle-Ottawa scale (MNOS) based on 5 aspects: (1) representativeness of the sample (inclusion of all subjects or the use of random sampling); (2) sample size (justified using methods such as power analysis); (3) comparability between respondents and non-respondents; (4) validated screening tools for depression, anxiety, or insomnia; and (5) adequacy of descriptive statistics. In addition, regarding the cohort studies, we extracted the prevalence data from baseline. The total quality score ranged between 0 and 5. High and low quality scores were defined as scores of $\geq$3 and $<$ 3, respectively. Potential disagreements on data extraction and quality assessment were discussed with an independent third author.

2.4. Data synthesis and analysis

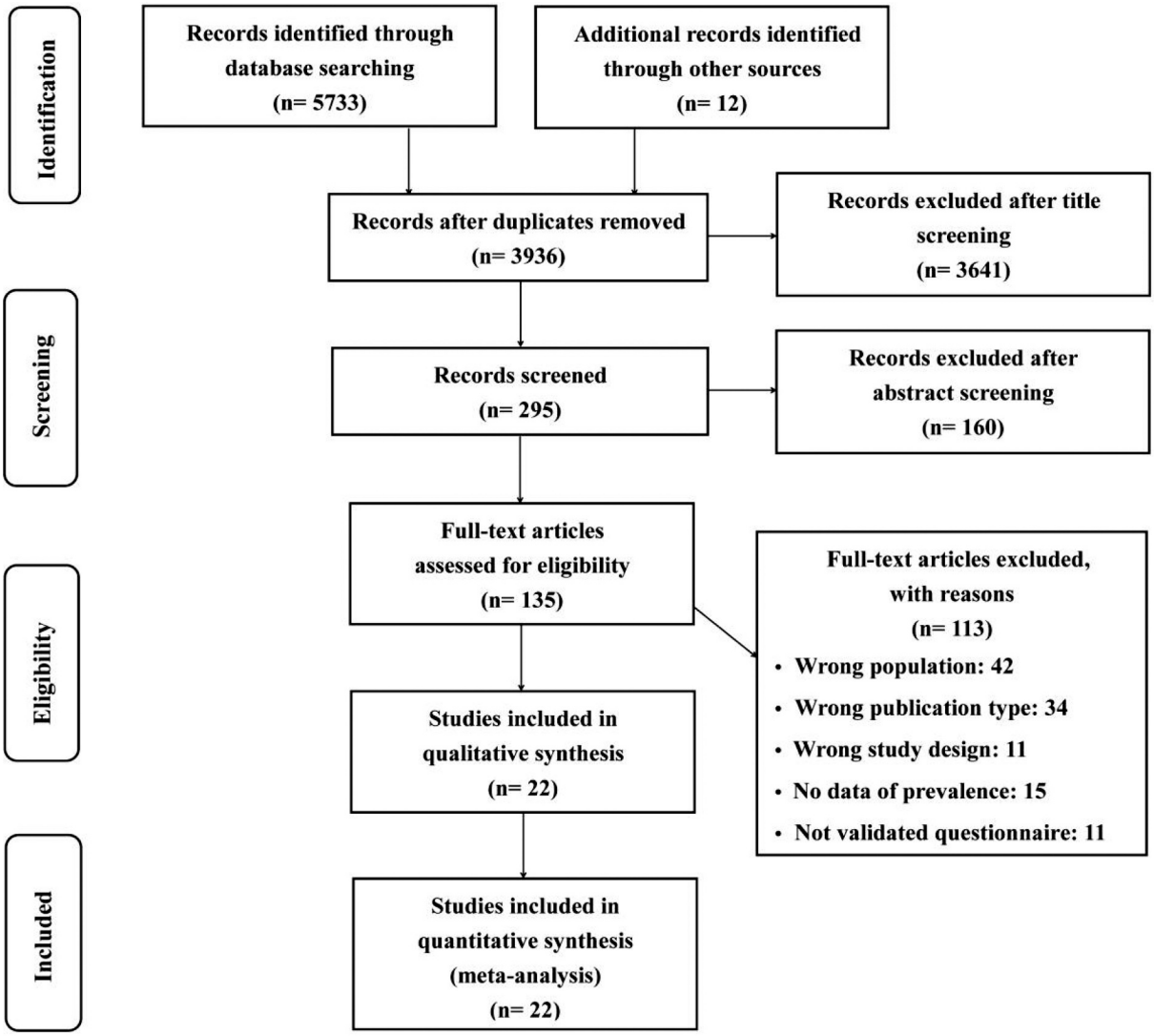
All statistical analyses were conducted using MetaXL (www.epigear.com), an add-in for meta-analysis in Microsoft Excel. The pooled prevalence was synthesised using the QE model according to the quality score derived for each study. In MetaXL, the quality score of each study was converted into Q index (Qi), quality ranks between 0 and 1, by dividing each score by the score of the highest scoring study in the group. Thus, we assigned higher weights to studies of better quality, and substantial heterogeneity was defined as $I^2 > 75\%$. Because the studies with prevalence close to 0 or 1 affected the variance, leading to an inappropriately heavy weight in the meta-analysis, the double arcsine method was used to convert the proportion, and the inverse conversion was performed to facilitate the explanation [18].

The funnel plot and Luis Furuya-Kanamori (LFK) index are used to estimate the publication bias when the number of included studies is greater than or equal to 10. LFK indices $<$1, between 1 and 2, and $>$2 were considered to represent no, minor, and major asymmetry, respectively [19]. Subgroup analyses were performed using differences in screening tools, gender, country, study design, severity, and disease stage to identify the moderating effects on the prevalence of depression, anxiety, and insomnia symptoms. Additionally, sensitivity analysis was performed by subtracting each study and calculating the aggregated prevalence rate of the remaining studies to further identify the source of heterogeneity. Our main results were prevalence (p), confidence intervals (CI), and prevalence percentage ($p \times 100\%$).

3. Results

3.1. Characteristics of included studies

Of the 5733 potentially eligible papers identified through the initial literature search, 22 studies (14 conducted in China and 8 outside China) met the study criteria and were included for analysis [2,6,8,11,20–37] (Fig. 1). Of the included studies, 19 (86%) were cross-sectional studies and the remaining 3 (14%) were single-arm cohort studies (Kim et al., 2020; Yang et al., 2020; Zhang et al., 2020a). The median number of participants with valid responses was 104 (range 30–770), with a total of 4318 patients included in the analysis. Moreover, the median questionnaire response rate was 99% (range 66–100%), with a median male representation of 50% (range 35.1–73.3%). Details of included studies are presented in Table 1.



NOTE: 1281 in PubMed, 871 in Embase, 2992 in Web of Science, and 589 in PsycINFO
(1) Wrong population (e.g. studies conducted in general population, health care workers, or COVID-19 patients with known psychiatric disorders); (2) Wrong publication type (e.g. reviews, editorials, and comments); and (3) Wrong study design (e.g. animal studies and single patient case studies)

Fig. 1. Flow chart of study selection process.
NOTE: 1281 in PubMed, 871 in Embase, 2992 in Web of Science, and 589 in PsycINFO. (1) Wrong population (e.g. studies conducted in general population, health care workers, or COVID-19 patients with known psychiatric disorders); (2) Wrong publication type (e.g. reviews, editorials, and comments); and (3) Wrong study design (e.g. animal studies and single patient case studies)

3.2. Evaluation of the quality of the studies

Table 2 displays the MNOS score of the included studies, and the median was 2 (range 1–5). Fourteen studies (64%) had a high risk of bias (quality score < 3) [2,6,11,20,23,24,26,28–31,33,34,36], and 8 studies (36%) had a low risk of bias (quality score ≥ 3) [8,21,22,25,27,32,35,37]. Although a majority of included studies involved the use of appropriate statistical methods and validated screening tools with clear cut-offs and had considerable response rates, only a few studies had justified the choice of sample size or used random sampling. In addition, the Qi was calculated according to the MNOS score of each study.

3.3. The pooled prevalence of depression symptom

Of the 22 studies, depression symptom had been evaluated in 20 studies [2,6,11,20–27,29–37], with a pooled prevalence of 38% (95% CI = 25–51; I^2 = 98), as shown in Fig. 2. In sensitivity analysis, the exclusion of none of the studies was found to affect the pooled prevalence by more than 3% or the I^2 value by more than 2%. An LFK index of

Table 1
Characteristics of included studies.

Study	Country	Study Design	Response Rate (%)	Sample Size (n)	Male (%)	Age (mean ± SD)	Assessment scales and cutoff value		
							Depression	Anxiety	Insomnia
Dai et al.	China	CS	–	307	56.7	*a*	SDS ≥ 53	SAS ≥ 50	PSQI ≥6
Gu et al.	China	CS	90.0	461	35.1	*b*	PHQ-9 ≥ 10	GAD-7 ≥ 5	ISI ≥ 8
Guo et al.	China	CS	100	103	57.0	42.5 ± 12.5	PHQ-9 ≥ 5	GAD-7 ≥ 5	–
Hu et al.	China	CS	100	85	49.5	48.8 ± 14.3	PHQ-9 ≥ 5	GAD-7 ≥ 5	ISI ≥ 8
Kim et al.	South Korea	SAC	66.0	33	–	45.0 ± 18.3	HADS-D ≥ 8	HADS-A ≥ 8	ISI ≥ 8
Li et al. (a)	China	CS	99.0	296	58.4	39.7 ± 10.1	SCL-90 ≥ 2	SCL-90 ≥ 2	–
Li et al. (b)	China	CS	–	99	54.5	*c*	HADS-D ≥ 8	HADS-A ≥ 8	–
Ma et al.	China	CS	98.2	770	48.0	50.4 ± 13.1	PHQ-9 ≥ 5	–	–
Nie et al.	China	CS	100	78	42.3	58.4 ± 13.0	SDS ≥ 50	SAS ≥ 50	–
Pandey et al.	India	CS	–	118	61.9	*d*	–	HAMA-14 ≥ 14	–
Paz et al.	Ecuador	CS	–	306	49.0	38.3 ± 10.9	PHQ-9 ≥ 5	GAD-7 ≥ 5	–
Samrah et al.	Jordan	CS	72.5	66	40.9	35.8 ± 16.2	PHQ-9 ≥ 5	–	–
Sensoy et al.	Turkey	CS	–	31	48.0	46.0 ± 19.0	BDI ≥ 17	BAI ≥ 10	–
Tomasoni et al.	Italy	CS	95.2	105	73.3	*e*	HADS-D ≥ 8	HADS-A ≥ 8	–
Wang et al.	China	CS	99.0	484	49.8	52.5 ± 14.3	–	–	ISI ≥ 8
Wu et al.	China	CS	–	370	54.9	50.5 ± 13.1	PHQ-9 ≥ 5	GAD-7 ≥ 5	–
Yang et al.	China	SAC	–	35	60.0	57.0 ± 13.4	PHQ-9 ≥ 5	GAD-7 ≥ 5	PSQI ≥11
Zandifar et al.	Iran	CS	100	106	51.9	55.0 ± 16.9	DASS-21	DASS-21	–
Zarghami et al.	Iran	CS	74.5	82	39.0	*f*	PHQ-9 > 5	GAD-7 > 5	–
Zhang et al. (a)	China	SAC	100	30	50.0	42.5 ± 13.3	PHQ-9 ≥ 5	GAD-7 ≥ 5	ISI ≥ 8
Zhang et al. (b)	China	CS	–	57	50.9	46.9 ± 15.4	PHQ-9 ≥ 5	GAD-7 ≥ 5	–
Zhang et al. (c)	China	CS	98.9	296	58.4	*g*	HADS-D ≥ 8	HADS-A ≥ 8	–

[a]The age of all included patients was divided into three grades: ≤ 44, $n = 156$; 45–59, $n = 119$; ≥ 60, $n = 32$.
[b]The age of all included patients was divided into four grades: 18–30, $n = 26$; 31–40, $n = 78$; 41–50, $n = 121$; > 50, $n = 236$, with a range of 18–65.
[c]The median age was 51.4, with a range of 30–73.
[d]The median age was 39.0, with a range of 18–90.
[e]The median age was 55.0, with a range of 43–65.
[f]The mean age of inpatients was 40.3 ± 14.4, and the mean age of outpatients was 43.6 ± 15.8.
[g]The age of all included patients was divided into four grades: 18–20, $n = 8$; 21–40, $n = 157$; 41–60, $n = 120$; > 60, $n = 11$.
CS, cross-sectional; SAC, single-arm cohort; GAD-7, General Anxiety Disorder 7-Item Scale; HADS-D, Hospital Anxiety and Depression Scale (Depression Subscale); HADS-A, Hospital Anxiety and Depression Scale (Anxiety Subscale); ISI, Insomnia Severity Index; SD, standard deviation; HAMA-14, Hamilton Anxiety Scale-14; SCL-90, Symptom Checklist-90; SDS, Self-Rating Depression Scale; SAS, Self-Rating Anxiety Scale; PHQ-9, Patient Health Questionnaire Depression Module-9; BDI, The Beck Depression Inventory; BAI, the Beck Anxiety Inventory; DASS-21, The Depression, Anxiety and Stress Scales-21; PSQI, Pittsburgh Sleep Quality Index.
"-"indicate that the study author did not provide any relevant information.

1.53 and the corresponding funnel diagram illustrated minor publication bias (see Supplementary Materials 2 and 3).

Regarding screening tools, 11 studies had used the Patient Health Questionnaire Depression Module-9 (PHQ-9) with a pooled prevalence of 47% (95% CI = 30–63; $I^2 = 98$) [2,6,21–23,29,30,33–36]. Notably, Gu et al. (2020) applied a significantly high cut-off score of 10 (compared with the score of 5 used in other 10 studies). Four studies had used the Hospital Anxiety and Depression Scale (depression subscale) (HADS-D) with a pooled prevalence of 22% (95% CI = 2–46; $I^2 = 94$) [24,26,32,37], and 2 studies had used the Self-Rating Depression Scale (SDS) with a pooled prevalence of 21% (95% CI = 1–46; $I^2 = 94$) [20,27]. The remaining studies had used various other screening tools, such as the Beck Depression Inventory (BDI) [31], the Symptom Checklist-90 (SCL-90) [25], and the Depression, Anxiety and Stress Scales-21 (DASS-21) [11].

3.4. The pooled prevalence of anxiety symptom

Anxiety symptom had been assessed in 19 studies [2,11,20–29,31–37]. The pooled prevalence was 38% (95% CI = 24–52; $I^2 = 98$), as presented in Fig. 3. In sensitivity analysis, exclusion of none of the other studies, except for the exclusion of studies by Zhang et al. (2020c) or Zarghami et al. (2020), was found to affect the prevalence by more than 3%; the recalculated pooled prevalence was 41% (95% CI = 26–58; $I^2 = 98$) after exclusion of studies by Zhang et al. (2020c) and Zarghami et al. (2020). An LFK index of 2.25 and the corresponding funnel diagram illustrated major publication bias (see Supplementary Materials 4 and 5). The funnel plot indicates that the studies by Yang et al. (2020), Zandifar et al. (2020), and Zhang et al. (2020a) are far from the centre line; without these studies, the recalculated pooled prevalence was 31% (95% CI = 23–40; $I^2 = 98$). In addition, the whole funnel plot and the LFK value (LFK = 1.34) indicated a minor publication bias (see Supplementary Materials 6 and 7).

For anxiety assessment, 9 studies had used the General Anxiety Disorder 7-Item Scale (GAD-7) with similar cut-offs (GAD-7 ≥ 5) [2,21–23,29,33–36], and the pooled prevalence was 47% (95% CI = 27–67; $I^2 = 98$). Four studies had used the Hospital Anxiety and Depression Scale (anxiety subscale) (HADS-A) with a pooled prevalence of 24% (95% CI = 13–37; $I^2 = 82$) [24,26,32,37] and 2 studies had used the Self-Rating Anxiety Scale (SAS) with a pooled prevalence of 25% (95% CI = 7–47; $I^2 = 92$) [20,27]. Each of the 4 remaining studies had used a different questionnaire, namely the Hamilton Anxiety Scale-14 (HAMA-14) [28], SCL-90 [25], the Beck Anxiety Inventory (BAI) [31], and DASS-21 [11].

3.5. The pooled prevalence of insomnia symptom

Of the 22 retrieved studies, insomnia symptom had been estimated in 7 studies (Fig. 4) [8,20,21,23,24,33,35], and the pooled prevalence was 48% (95% CI = 11–85; $I^2 = 99$). In sensitivity analysis, exclusion of none of the studies was found to affect the I^2 value by more than 1%. However, the effect on the pooled prevalence exceeded 3% when the studies by Dai et al. (2020), Gu et al. (2020), or Zhang et al. (2020) were excluded; without these studies, the recalculated pooled prevalence was found to be 45% (95% CI = 15–79; $I^2 = 93$).

For the assessment of insomnia, 5 studies had used the Insomnia Severity Index (ISI) with similar cut-offs (ISI ≥ 8) [8,21,23–35], and the pooled prevalence was 37% (95% CI = 5–73; $I^2 = 99$). The remaining 2 studies had used the Pittsburgh Sleep Quality Index (PSQI) with a pooled prevalence of 85% (95% CI = 81–89; $I^2 = 0$) [20,33], although Yang

Table 2
Quality ratings of included studies using the modified Newcastle-Ottawa scale.

Studies	Modified Newcastle-Ottawa quality assessment scale					Score	Qi
	A	B	C	D	E		
Dai et al.	–	–	–	*	*	2	0.4
Gu et al.	–	–	*	*	*	3	0.6
Guo et al.	*	–	*	*	*	4	0.8
Hu et al.	–	–	*	*	–	2	0.4
Kim et al.	–	–	–	*	*	2	0.4
Li et al. (a)	*	*	*	*	*	5	1.0
Li et al. (b)	–	–	–	*	*	2	0.4
Ma et al.	–	–	–	*	*	2	0.4
Nie et al.	–	–	*	*	*	3	0.6
Pandey et al.	–	–	–	*	*	2	0.4
Paz et al.	–	–	–	*	*	2	0.4
Samrah et al.	–	–	–	*	*	2	0.4
Sensoy et al.	–	–	–	*	*	2	0.4
Tomasoni et al.	–	–	*	*	*	3	0.6
Wang et al.	–	–	*	*	*	3	0.6
Wu et al.	–	–	–	*	*	2	0.4
Yang et al.	–	–	–	*	*	2	0.4
Zandifar et al.	–	–	*	–	–	1	0.2
Zarghami et al.	–	–	–	*	*	2	0.4
Zhang et al. (a)	*	–	*	*	*	4	0.8
Zhang et al. (b)	–	–	–	*	*	2	0.4
Zhang et al. (c)	*	*	*	*	*	5	1.0

A: representativeness of the sample (inclusion of all subjects or the use of random sampling);
B: sample size (justified using methods such as power analysis);
C: comparability between respondents and non-respondents (response rate ≥ 80%);
D: validate measurement tools with clear cut-offs;
E: adequate statistics and no need for further calculations.

et al. (2020) adopted a higher cut-off score.

3.6. The pooled prevalence of comorbid symptoms of depression and anxiety

Comorbid symptoms of depression and anxiety had been assessed in 8 studies [2,11,24,29,32,33,35,36], and the pooled prevalence was 29% (95% CI = 0–69; $I^2 = 99$). Of the 8 studies, 4 studies were conducted in China with a pooled prevalence of 29% (95% CI = 0–1; $I^2 = 99$). The prevalence of comorbid symptoms of depression and anxiety in South Korea, Ecuador, Italy and Iran were 12%, 16%, 10%, and 97%, respectively, as reported by one study in each country (see Supplementary Material 8).

3.7. Subgroup analysis

A subgroup analysis of the prevalence of depression, anxiety, and insomnia symptoms by gender, country, study design, severity, disease stage and MNOS score was further performed. Table 3 summarises the results of the subgroup analysis.

Regarding depression, gender data were available in 11 studies, with a pooled prevalence of 32% for male and 46% for female (see Supplementary Material 9). The a pooled prevalence reported in 13 studies conducted in China was 39% and that reported in 2 studies conducted in Iran was 65%. The prevalence rates of depression in South Korea, Ecuador, Jordan, Turkey, and Italy were 39%, 23%, 44%, 32%, and 11%, respectively, as reported by one study in each subgroup (see Supplementary Material 10). In terms of study design, 17 cross-sectional studies reported a prevalence of 34%, and the remaining 3 single-arm cohort studies reported a prevalence of 88% (see Supplementary Material 11). In terms of severity, 10 studies had calculated the prevalence, with a pooled prevalence of 29% for mild depression, 17% for moderate depression, and 10% for severe depression (see Supplementary Material 12). In terms of the disease stage, 17 studies had reported the depression prevalence of 42% in patients who were experiencing SARS-CoV-2 infection, and the remaining 3 studies conducted in patients who were at the recovery stage reported a depression prevalence of 14% (see Supplementary Material 13). In terms of the MNOS score, 7 high-quality studies (defined as scores of ≥3) had reported a prevalence of 38%, and the remaining 13 low-quality studies (defined as scores of <3) reported a prevalence of 34% (see Supplementary Material 14).

Regarding anxiety, gender data were available in 11 studies, with a pooled prevalence of 30% for male and 44% for female (see Supplementary Material 15). Twelve studies conducted in China reported a pooled prevalence of 39%, and 2 studies conducted in Iran reported a pooled prevalence of 64%. The prevalence rates of anxiety in South Korea, India, Ecuador, Turkey, and Italy were 18%, 21%, 24%, 55%, and 29%, respectively, as reported by one study in each subgroup (see Supplementary Material 16). In terms of study design, 16 cross-sectional studies reported a prevalence of 34%, and the remaining 3 single-arm cohort studies reported a prevalence of 84% (see Supplementary Material 17). In terms of severity, the prevalence could be calculated in 8 studies with a pooled prevalence of 30% for mild anxiety, 18% for moderate anxiety, and 15% for severe anxiety (see Supplementary Material 18). In terms of the disease stage, the prevalence in patients who were experiencing SARS-CoV-2 infection was 40%, as reported by 16 studies, and the remaining 3 studies conducted in patients who were at the recovery stage reported a prevalence of 22% (see Supplementary Material 19). In terms of the MNOS score, 8 high-quality studies (defined as scores of ≥3) had reported a prevalence of 38%, and the remaining 11 low-quality studies (defined as scores of <3) reported a prevalence of 29% (see Supplementary Material 20).

Regarding insomnia, gender data were available in 4 studies, with pooled prevalence of 34% for male and 40% for female (see Supplementary Material 21). A pooled prevalence of 49% was reported in 6 studies conducted in China, whereas 1 study conducted in South Korea reported a pooled prevalence of 30% (see Supplementary Material 22). In terms of study design, 4 cross-sectional studies reported a prevalence of 37%, and the remaining 3 single-arm cohort studies reported a prevalence of 86% (see Supplementary Material 23). In terms of severity, the prevalence could be calculated in 3 studies, with pooled prevalence of 53% for mild anxiety, 8% for moderate anxiety, and 3% for severe anxiety (see Supplementary Material 24). In terms of the MNOS score, 3 high-quality studies (defined as scores of ≥3) had reported a prevalence of 36%, and the remaining 4 low-quality studies (defined as scores of <3) reported a prevalence of 77% (see Supplementary Material 25).

4. Discussion

The outbreak of COVID-19 is profoundly affecting all aspects, including mental health and physical health, of individuals in the society. Hence, to collect high-quality data on the impact of COVID-19 pandemic on the mental health of vulnerable groups such as patients infected with SARS-CoV-2 should be the immediate priority [38]. The present systematic review and meta-analysis provided an up-to-date estimate of the prevalence of depression, anxiety, and insomnia symptoms among COVID-19 patients by combining the data of 22 observational studies using the QE model. Our results indicated that the overall prevalence of depression, anxiety, and insomnia symptoms among patients with COVID-19 is 38%, 38%, and 48%, respectively. In addition, the pooled prevalence of comorbid symptoms of depression and anxiety is 29%.

These prevalence estimates of depression, anxiety, and insomnia symptoms among patients with COVID-19 is higher than that of general population during the COVID-19 pandemic to a certain extent, particularly insomnia, which are estimated to be 33.7%, 31.9%, and 20.1%, respectively [39,40]. Furthermore, compared with the patients seen in general practice, this meta-analysis also reported an increased prevalence of comorbid symptoms of depression and anxiety (25% vs. 29%)

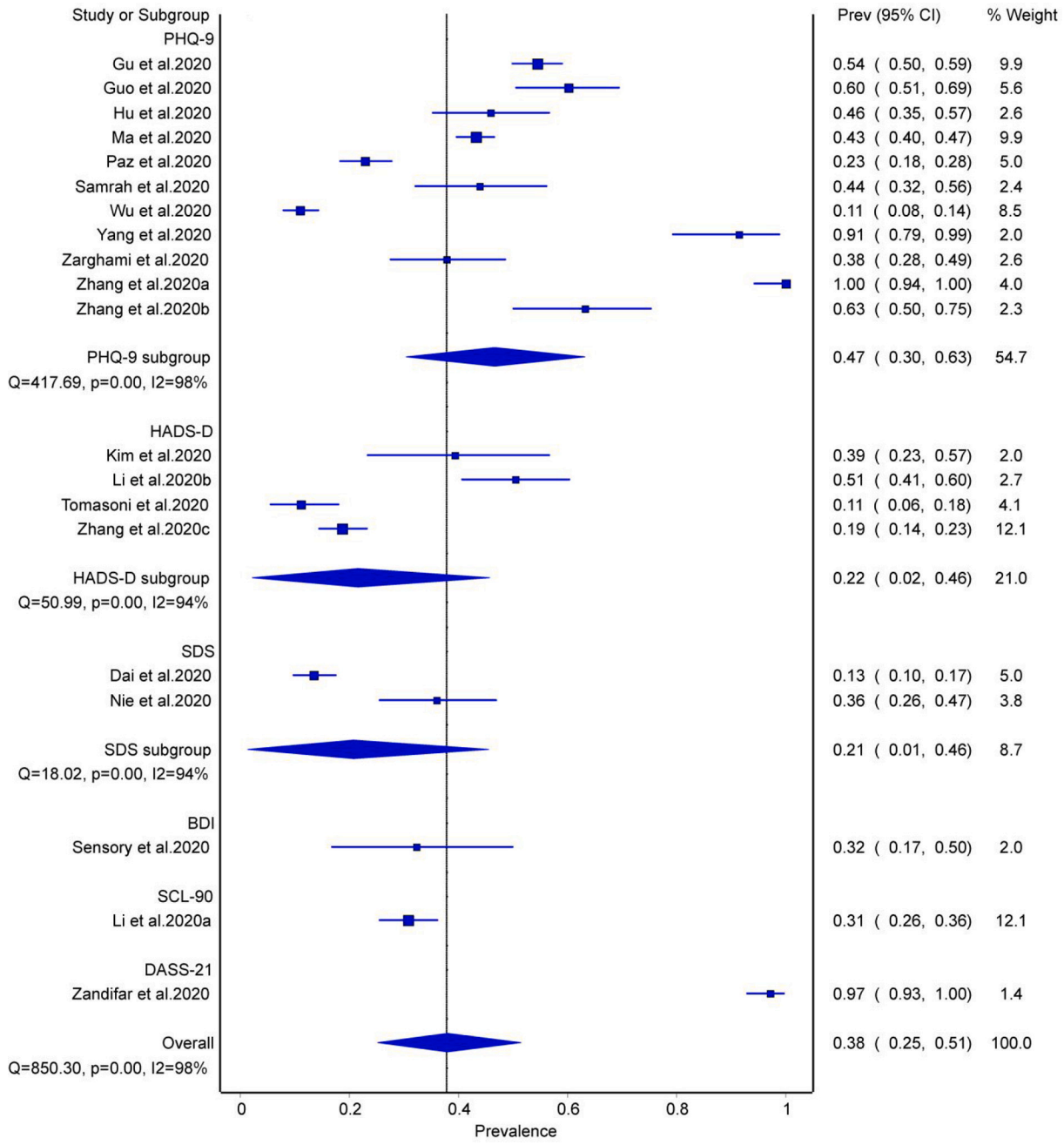


Fig. 2. Pooled prevalence of depression symptom by screening scales.

[41]. A meta-analysis evaluated the prevalence of depression, anxiety, and sleep disturbances among COVID-19 patients by using the random effects (RE) model [13]; however, the heterogeneity between the included studies was extremely high ($I^2 > 95\%$) in the meta-analysis. A large number of simulation studies have confirmed that the QE model can maintain the correct coverage probability of the confidence interval without considering the heterogeneity level, and the observed variance of the QE model is lower than that of the RE model [14]. Compared with the results of Deng et al. (2020), this meta-analysis using the QE model revealed a decreased prevalence of depression and anxiety symptoms among COVID-19 patients (45% vs. 38%; 47% vs. 38%) and an increased prevalence of insomnia symptom (34% vs. 48%).

4.1. *Influence of screening tools on prevalence*

Figs. 2, 3, and 4 indicate that different screening tools have a significant impact on the prevalence of depression, anxiety, and insomnia symptoms. For the assessment of depression, PHQ-9 (with a cut-off of ≥5) and HADS-D (with a cut-off of ≥8) were the most frequently used tools, and the pooled prevalence with these assessment tools was 47% and 22%, respectively. The finding is consistent with a previous finding suggesting that the difference in the prevalence of depression between assessment scales of PHQ-9 ≥ 5 and HADS-D ≥ 8 is approximately 30% [42]. Similarly, for assessing the prevalence of anxiety, GAD-7 (with a cut-off value of ≥5) and HADS-A (with a cut-off of ≥8) were the most frequently used tools, and the pooled prevalence with these assessment tools was 47% and 24%, respectively. One possible explanation for this difference may be the use of low cut-off values for PHQ-9 and GAD-7. Studies have indicated that the cut-off values of 10 for PHQ-9 or GAD-7 are optimal and could increase the assessment validity, and the increased cut-off values may indicate decreased prevalence of depression and anxiety, potentially increasing

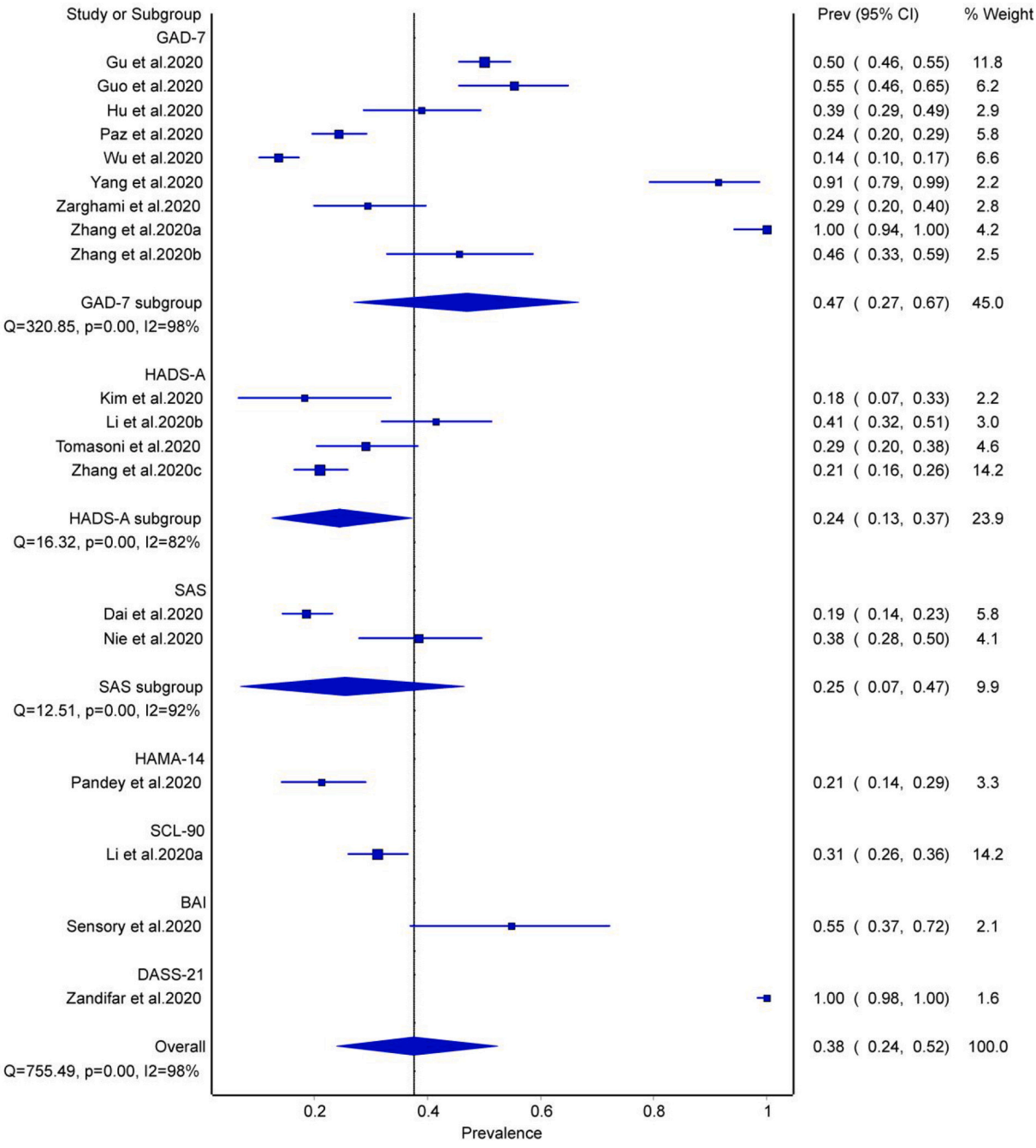


Fig. 3. Pooled prevalence of anxiety symptom by screening scales.

agreement with HADS [43,44]. For example, by using the cutoff value of PHQ-9 $\geq$ 10, the consistency with HADS-D $\geq$ 8 was significantly improved compared with the cutoff value $\geq$5 [45]. The pooled prevalence of insomnia symptom for 5 studies using the ISI scale was found to be significantly lower than that of 2 studies using the PSQI scale (37% vs. 85%). The ISI scale is mainly confined to insomnia assessment, whereas PSQI provides an overview of sleep quality by assessing multiple categories of sleep disturbances, and this difference may be related to the large difference in the prevalence rate observed between the two subgroups. Notably, the results of the subgroup analysis must be interpreted with caution due to differences in the design and cut-off values of PSQI and ISI questionnaires.

A large heterogeneity was observed between different subgroups according to screening scales, although the QE model could weaken the influence of heterogeneity among included studies on the pooled prevalence to some extent. Therefore, whether the subgroup prevalence estimates are accurate remains unclear. Heterogeneity observed between subgroups further suggests that the screening tools and cut-off values should be unified in future studies to obtain more convincing results.

4.2. *Interpretation of subgroup analyses*

Similar to the findings of Deng et al. (2020) [13], our subgroup analyses also implied a potential gender difference. The prevalence of depression, anxiety, and insomnia symptoms appeared to be higher in female, which possibly reflects the already established gender gap for depression and anxiety [45,46]. Considering that a majority of the included studies were conducted in China, the results of subgroup analyses by country may be invalid for detecting subgroup differences.

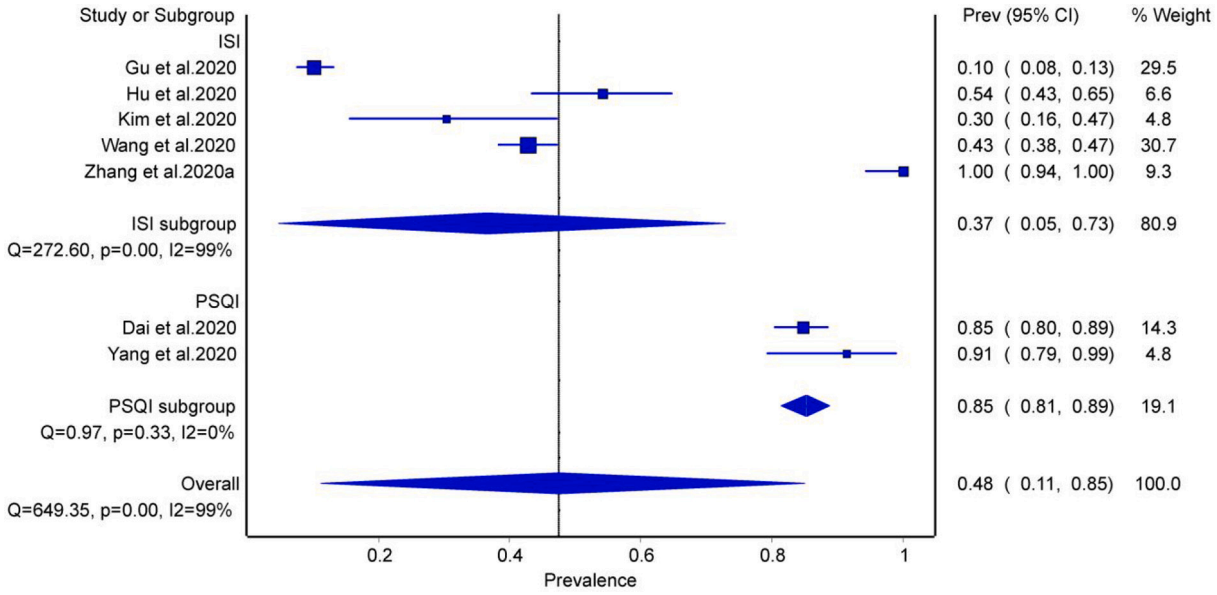


Fig. 4. Pooled prevalence of insomnia symptom by screening scales.

Regarding the study design, the pooled prevalence of depression, anxiety, and insomnia symptoms in single-arm cohort studies appears to be higher than that reported in cross-sectional studies. However, the sample size of single-arm cohort studies was generally small, and therefore, the research results should be interpreted with caution. Regarding the severity of depression, anxiety, and insomnia symptoms, most patients presented with only mild symptoms, and the proportion of COVID-19 patients with severe symptoms of mental illness was low. Similarly, with respect to the disease stage, the depression and anxiety symptoms in patients at the recovery stage improved obviously, and the finding concurs with that of Rogers et al. (2020) [12], which suggests that the prevalence of mental illness in patients with SARS or MERS is greatly reduced during the post-illness stage compared with the acute stage.

4.3. Implications for clinical practice

Under the COVID-19 pandemic scenario, many patients are experiencing depression, anxiety, or insomnia symptom, which may be related to several other factors. One of the most likely factors may be the lack of contact with family and loved ones during quarantine or hospitalisation [47], and the fact is consistent with the previous assertion that social isolation and loneliness are related to poor mental health outcomes [48]. Fear of disease deterioration due to poor knowledge, unemployment, feeling of self-blame, and perceived stigma may also facilitate the development of mental diseases in patients with COVID-19 [49,50]. COVID-19 patients with severe mental illness, such as anxiety and depression, have been reported to display an increased tendency of committing suicide [51]. Thus, early detection and properly intervention for mental illness in this population hold great significance.

Under the epidemic situation, wherein consultation in-person is restricted, online psychotherapy and consultation might improve patients' access to mental health care, particularly during the period of quarantine and isolation [52,53]. It does need to be highlighted that the effectiveness of online services in improving mental health services requires further evaluation [54]. In addition, improving health literacy and curbing the spread of false information on COVID-19 will also help reduce the perceived stigma of COVID-19 patients and improve their mental health [55].

4.4. Strengths and limitations

An important strength of our meta-analysis is that we adopted the QE model for the meta synthesis of included studies conducted in the past year that passed the international peer-review process. Compared with the RE model, it can eliminate the effect of high heterogeneity on the pooled prevalence of depression, anxiety, and insomnia symptoms to a certain extent. Furthermore, the prevalence data displayed in Tables and Figures allow further interpretations and provide insights that are of interest to researchers, practitioners, and policymakers.

The present systematic review has several shortcomings. First, 64% of the included studies were conducted in China, studies originating from countries with a high number of cases, such as the United States, and India, have not yet been retrieved currently, which limits the generalisation of our findings. Second, most studies included in our meta-analysis had used self-rating scales for assessing the symptoms of mental illness possibility due to local quarantine guidelines; the self-rated scale is usually less sensitive and specific than structured clinical interviews [56]. Lastly, although a majority of included studies had high response rates and involved validated measurement tools with clear cut-offs and appropriate statistical methods, the representativeness of sample was poor, and only a few studies had described the calculation processing of sample size.

5. Conclusion

The present systematic review and meta-analysis suggest that depression, anxiety, and insomnia symptoms are prevalent in a considerable proportion of patients with COVID-19. Thus, early detection and properly intervention for mental illness in this population are of great significance. Additionally, the quality of included studies to date has been variable, and ongoing surveillance is essential.

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Declaration of Competing Interest

None.

Table 3
Subgroup analysis of the prevalence of depression, anxiety, and insomnia symptoms.

		Depression	Anxiety	Insomnia
Gender	Male	32%, 95% CI = 17–47; I^2 = 96	30%, 95% CI = 18–43; I^2 = 93	34%, 95% CI = 4–70; I^2 = 97
	Female	46%, 95% CI = 32–60; I^2 = 95	44%, 95% CI = 29–58; I^2 = 93	40%, 95% CI = 1–84; I^2 = 98
Country	China	39%, 95% CI =25–54; I^2 = 98	39%, 95% CI = 24–54; I^2 = 97	49%, 95% CI = 10–88; I^2 = 99
	Iran	65%, 95% CI = 0–100; I^2 = 99	64%, 95% CI = 0–100; I^2 = 99	–
	South Korea	39%, 95% CI = 23-57[a]	18%, 95% CI = 7-33[a]	30%, 95% CI = 16-47[a]
	India	–	21%, 95% CI = 14-29[a]	–
	Ecuador	23%, 95% CI = 18-28[a]	24%, 95% CI = 20–29[a]	–
	Jordan	44%, 95% CI = 32-56[a]	–	–
	Turkey	32%, 95% CI = 17-50[a]	55%, 95% CI = 37-72[a]	–
	Italy	11%, 95% CI = 6-18[a]	29%, 95% CI = 20-38[a]	–
Study design	Cross-sectional	34%, 95% CI = 21–46; I^2 = 98	34%, 95% CI = 20–47; I^2 = 98	37%, 95% CI = 0–82; I^2 = 99
	Single-arm cohort	88%, 95% CI = 44–100; I^2 = 95	84%, 95% CI = 0–100; I^2 = 97	86%, 95% CI = 33–100; I^2 = 96
Severity	Mild	29%, 95% CI: 24–34; I^2 = 76	30%, 95% CI = 22–38; I^2 = 85	53%, 95% CI = 12–93; I^2 = 93
	Moderate	17%, 95% CI = 11–22; I^2 = 86	18%, 95% CI = 7–31; I^2 = 95	8%, 95% CI = 0–21; I^2 = 88%
	Severe	10%, 95% CI = 2–20; I^2 = 97	15%, 95% CI = 0–44; I^2 = 99	3%, 95% CI = 2–5; I^2 = 0
Disease stage	Undergoing	42%, 95% CI = 29–56; I^2 = 97	40%, 95% CI = 24–57; I^2 = 98	–
	Recovery	14%, 95% CI = 0–48; I^2 = 97	22%, 95% CI = 5–43; I^2 = 94	–
MNOS score	≥3	38%, 95% CI = 17–60; I^2 = 98	38%, 95% CI = 23–55; I^2 = 96	36%, 95% CI = 0–82; I^2 = 99
	<3	34%, 95% CI = 16–54; I^2 = 98	29%, 95% CI = 6–54; I^2 = 98	77%, 95% CI = 41–100; I^2 = 96

[a] Only one study was included in this subgroup.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychores.2021.110516.

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