






## Original Article

## The prevalence of depression, anxiety, and sleep disturbances in COVID-19 patients: a meta-analysis

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Evidence from previous coronavirus outbreaks has shown that infected patients are at risk for developing psychiatric and mental health disorders, such as depression, anxiety, and sleep disturbances. To construct a comprehensive picture of the mental health status in COVID-19 patients, we conducted a systematic review and random-effects meta-analysis to assess the prevalence of depression, anxiety, and sleep disturbances in this population. We searched MEDLINE, EMBASE, PubMed, Web of Science, CINAHL, Wanfang Data, Wangfang Med Online, CNKI, and CQVIP for relevant articles, and we included 31 studies ( $n = 5153$ ) in our analyses. We found that the pooled prevalence of depression was 45% (95% CI: 37–54%,  $I^2 = 96\%$ ), the pooled prevalence of anxiety was 47% (95% CI: 37–57%,  $I^2 = 97\%$ ), and the pooled prevalence of sleeping disturbances was 34% (95% CI: 19–50%,  $I^2 = 98\%$ ). We did not find any significant differences in the prevalence estimates between different genders; however, the depression and anxiety prevalence estimates varied based on different screening tools. More observational studies assessing the mental wellness of COVID-19 outpatients and COVID-19 patients from countries other than China are needed to further examine the psychological implications of COVID-19 infections.

**Keywords:** depression; anxiety; sleep disturbance; coronavirus; meta-analysis; pandemic

### Introduction

In December 2019, a series of acute, atypical respiratory diseases was identified in Wuhan, China. The source of the illnesses was attributed to a novel coronavirus, named the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), and the subsequent disease it causes was named the coronavirus disease 2019 (COVID-19).<sup>1–3</sup> SARS-CoV-2 shares considerable homology with previous coronaviruses capable of infecting humans, including SARS-CoV and MERS-CoV,<sup>4,5</sup> which were responsible for causing the SARS epidemic and MERS outbreak in 2003 and 2012, respectively. However, preliminary studies have shown that SARS-CoV-2 may exceed previous coronaviruses in terms of transmissibility; its mean basic reproduction

number ( $R_0$ ) was found to be 3.28 in a previous review,<sup>6</sup> as compared with 2.4 for SARS-CoV, or 0.9 for MERS-CoV.<sup>7</sup> As a result, COVID-19 has quickly evolved into a global pandemic as declared by the World Health Organization on March 11, 2020.<sup>8,9</sup> Since its discovery, there have been nearly 25 million confirmed cases and 800,000 deaths in over 200 countries.<sup>10</sup>

While much clinical attention and research focus has been given to treating the physiological fallout caused by the novel coronavirus, the psychological effects of the virus on infected patients should be considered as well. As evidenced by the previous SARS and MERS outbreaks, viral infections and the subsequent isolation and quarantine can quickly culminate into sleep disturbances, anxiety,

and depressive episodes.<sup>11</sup> Among MERS patients, for example, 70.8% exhibited psychiatric symptoms and 41.7% received a definitive psychiatric diagnosis and medication throughout their hospital stay.<sup>12</sup> The psychological impact of the COVID-19 pandemic, however, may exceed previous coronavirus outbreaks as a result of the rampant spread of misinformation enabled by social media,<sup>13,14</sup> as well as its colossal scale that overexerted healthcare workers and resulted in a shortage of critical supplies, such as ventilators.<sup>15</sup> In addition, previous studies have shown that hospitalization in intensive care units (ICUs) and the use of mechanical ventilation are both risk factors for developing acute psychiatric symptoms;<sup>16,17</sup> since COVID-19 patients have a greater mean duration of stay in the ICU compared with previous coronavirus outbreaks,<sup>18,19</sup> it is possible that COVID-19 patients who require intensive care could potentially become a high-risk group for developing psychiatric disorders.<sup>15,20</sup>

As healthcare workers are pressured to offer time-efficient care amidst supply and personnel shortages during the COVID-19 pandemic, the time that treatment teams spend with individual patients is severely limited.<sup>21</sup> As a result, psychiatric symptoms in patients diagnosed with COVID-19 are likely undervalued and undertreated as physicians prioritize physical illnesses. Yet, psychological health plays a crucial role in accelerating patient recovery. For instance, depressed inpatients have been shown to have poorer outcomes, increased length of hospital stay, and a greater likelihood of hospital readmission, as shown in a previous systematic review.<sup>22</sup> A recent small-scale observational study has also found that higher cortisol levels, which were positively correlated with anxiety severity, were potentially linked to greater mortality in COVID-19 patients.<sup>23</sup> In addition, hospitalized patients with psychiatric comorbidities may result in increased medical costs,<sup>24</sup> worsening the economic impact of the pandemic on healthcare networks, and financially disadvantaged individuals.<sup>25</sup> It is likely that these infection-related psychiatric symptoms will persist long after recovery; as demonstrated by the SARS epidemic, psychiatric complications in SARS-infected patients can last for more than 2 years after the outbreak.<sup>26</sup> These long-term psychiatric disorders may, therefore, pose as significant economic and social burdens to the postpandemic world.<sup>27</sup>

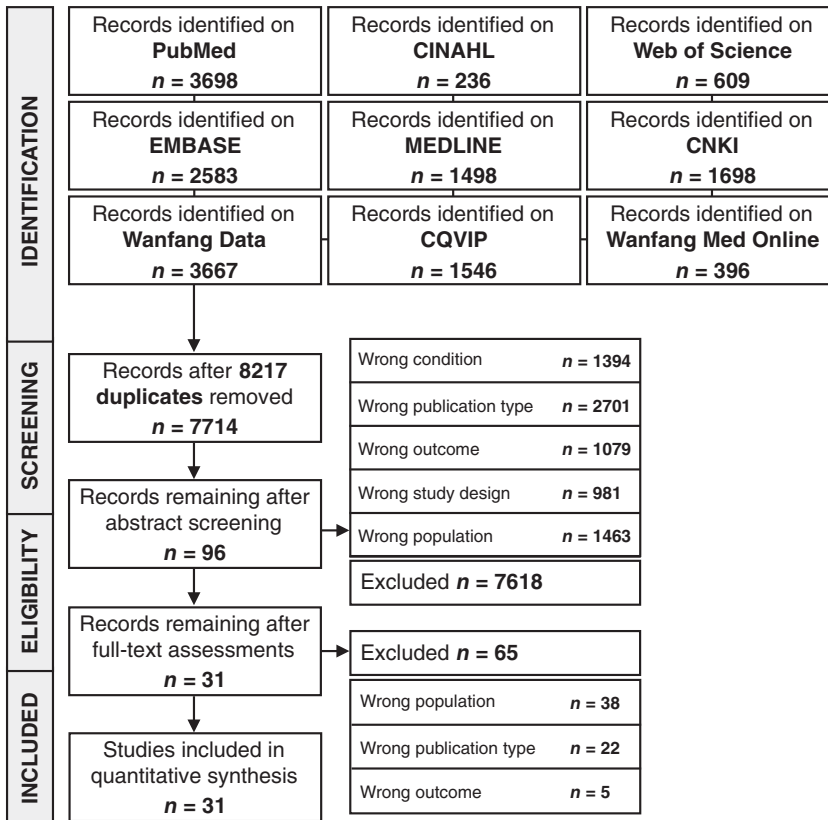
Despite the importance of managing psychiatric disorders in COVID-19 patients, current evidence regarding the prevalence of psychiatric disorders in infected patients is lacking and unclear. In an early review paper published by Rogers *et al.*,<sup>28</sup> summarizing psychiatric and neuropsychiatric presentations associated with SARS, MERS, and the COVID-19 outbreaks, it was found that delirium was common in patients with acute stages of COVID-19. However, the prevalence of other psychiatric disorders, such as depression, anxiety, and sleep disturbances, was not evaluated due to a lack of published data.<sup>28</sup> Recent case reports and observational studies have suggested that COVID-19 patients are likely susceptible to developing depression, anxiety, and sleep disturbances,<sup>29</sup> and these disorders should be adequately diagnosed and addressed by clinicians to improve prognosis, decrease the length of stay, and avoid long-term mental health issues. To construct a comprehensive picture on the impact of the pandemic on COVID-19 patients' mental health, as well as to raise awareness for the importance of psychiatric screening and treatment in COVID-19 patients, we conducted a systematic review and meta-analysis to assess the prevalence of depression, anxiety, and sleep disturbances in patients with COVID-19.

## Materials and methods

We conducted this systematic review and meta-analysis in accordance with the Cochrane Handbook for Systematic Reviews of Interventions<sup>30</sup> and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)<sup>31</sup> framework (see Table S1 for the PRISMA checklist, online only). This systematic review was prospectively registered on PROSPERO (CRD42020192093).

### Search strategy

We searched the following databases from 2019 to August 18, 2020, for relevant studies: (1) MEDLINE, (2) EMBASE, (3) PubMed, (4) Web of Science, and (5) Cumulative Index of Nursing and Allied Health Literature (CINAHL). We also searched the following Chinese databases using a Chinese search strategy: (1) Wanfang Data, (2) Wanfang Med Online, (3) China National Knowledge Infrastructure (CNKI), and (4) Chongqing VIP Information (CQVIP). Nonpeer-reviewed articles indexed on PubMed, such as the articles from the health



**Figure 1.** PRISMA flowchart for the identification and selection of observational trials. CINAHL, Cumulative Index to Nursing and Allied Health Literature; CNKI, Chinese National Knowledge Infrastructure; CQVIP, Chongqing VIP Information.

sciences preprint server medRxiv, were included for article screening and selection as well. The search strategy used for the database searches can be found in Tables S2 and S3 (online only). In addition to the database searches, we hand-searched the reference sections of previous reviews identified from the database search for relevant studies.

**Inclusion criteria**

Studies satisfying the following criteria were included in our systematic review: (1) included patients with COVID-19, and (2) reported the prevalence of depression, anxiety, or sleep disturbances. We included all primary observational studies, including longitudinal cohort, cross-sectional, or case–control studies with a sample size of  $\geq 10$  participants. Studies that specifically defined COVID-19 patients with known mental disorders as their target population were excluded. We did not place limitations on the publication’s

language or its country of origin, nor did we limit the age or gender of the included patients.

**Study selection**

Duplicate entries from the database search were removed using EndNote X9. Eight reviewers (J.D., F.Z., W.H., Z.S., C.Y.W., O.C., E.H., and Q.K.Z.) screened the deduplicated entries independently and in duplicate using Rayyan<sup>32</sup> based on the aforementioned inclusion criteria. Entries deemed relevant by two reviewers were then entered into an in duplicate full-text screening process. We resolved disagreements by recruiting a third author for arbitration.

Figure 1 shows the PRISMA flow diagram<sup>33</sup> of our study identification and selection process. Studies were excluded due to wrong conditions (e.g., studies that assessed mental illness in patients with non-COVID diseases), wrong publication type (e.g., review, editorials, and letters to the editor without

usable data), wrong outcome (studies that did not report any of our outcomes of interest), wrong study design (e.g., animal studies and single patient case studies), and wrong population (e.g., studies focusing on the general population or other populations at-risk for developing mental illness, such as university students, and studies that included COVID-19 patients with known psychiatric disorders).

### Data extraction

Data extraction was completed by eight reviewers (J.D., F.Z., W.H., Z.S., C.Y.W., O.C., E.H., and Q.K.Z.) independently and in duplicate. We used a standardized data extraction form developed *a priori*. The data extraction form included the following items: (1) author names, (2) study title, (3) publication date, (4) digital object identifier, (5) country of origin, (6) study design, (7) sample size, (8) questionnaire response rate, (9) patient demographics (i.e., gender and mean/median age), (10) screening tools and cutoff values used to identify psychiatric disorders, (11) outcome measures, and (12) relevant subgroup data. For cohort studies, we extracted the outcome data from baseline. Disagreements were resolved by recruiting a third author to review the data. We made attempts to contact the principal investigators from studies with unclear or missing information to obtain relevant unpublished data.

### Outcomes and measures

The main outcomes in this systematic review were the prevalence of depression, anxiety, and sleep disturbances, as assessed using clinical interviews or self- and clinician-rated screening tools/questionnaires. Patients exhibiting depressive or anxious symptoms, such as hyperventilation, irritability, or fatigue, but were not assessed using interviews and/or questionnaires were not included in the analysis. Sleep disturbances were defined as sleep initiation or maintenance disorders, excessive somnolence, disorders of sleep-wake schedule, poor sleep quality, and/or other sleep impairments<sup>34</sup> as evaluated using interviews or questionnaires.

To comply with quarantine requirements and social distancing guidelines, a majority of patients were assessed using self-rated electronic questionnaires, including Zung Self-Rating Depression Scale (SDS),<sup>35</sup> Zung Self-Rating Anxiety Scale (SAS),<sup>36</sup> General Anxiety Disorder 7-item scale (GAD-7),<sup>37</sup> Patient Health Questionnaire depression module-

9 (PHQ-9),<sup>38</sup> the Hospital Anxiety and Depression Scale (HADS),<sup>39</sup> Symptom Checklist-90 (SCL-90),<sup>40</sup> Pittsburgh Sleep Quality Index (PSQI),<sup>41</sup> and Insomnia Severity Index (ISI).<sup>42</sup>

**Zung SDS.** The SDS is a 20-question self-reporting survey aimed to assess patients' level of depression. The questions are answered using a 4-point Likert scale.<sup>35</sup> In our included studies, the raw total scores were multiplied by 1.25 to yield an index score. A majority of studies chose an index score  $\geq 50$  as the cutoff for diagnosing depression; however, two studies<sup>43,44</sup> used a cutoff of  $\geq 53$  as prior studies had suggested that this cutoff may be more appropriate for the Chinese population.<sup>45,46</sup> The SDS was only administered to Chinese patients in our included studies; its Chinese translation had been validated previously.<sup>47,48</sup>

**Zung SAS.** The SAS is a 20-question self-reporting survey aimed at assessing patients' anxiety levels. The questions are designed to quantify four manifestations of anxiety, including cognitive, autonomic, motor, and central nervous symptoms. It is scored on a 4-point Likert scale.<sup>36</sup> Similar to the SDS, the raw scores for the SAS were multiplied by 1.25 to yield an index score. Only an index score cutoff of  $\geq 50$  was used for diagnosing anxiety in our included studies. The SAS was administered, typically with the SDS, to Chinese patients and its Chinese translation had been validated previously.<sup>48-50</sup>

**GAD-7.** The GAD-7 is a self-rated screening tool for the rapid detection of possible anxiety disorders. It consists of seven questions and is rated on a 4-point Likert scale.<sup>37</sup> A cutoff value of  $\geq 5$  was used for diagnosing anxiety in our included studies. It was administered to patients from China, Iran, and Ecuador in Chinese, Persian/Farsi, and Spanish, respectively. It had been validated in these languages.<sup>51-55</sup>

**PHQ-9.** The PHQ-9 is a self-rated module for diagnosing depression. It consists of nine questions relating to the patients' mental health, with each item rated on a 4-point Likert scale.<sup>38</sup> A cutoff value of  $\geq 5$  was used for diagnosing depression in our included studies. It was administered, typically with the GAD-7, to patients from China, Iran, and Ecuador in Chinese, Persian/Farsi, and

Spanish respectively. It had been validated in these languages.<sup>53,56–60</sup>

**HADS.** The HADS is a self-reported screening tool used to measure patients' psychological levels of anxiety and depression. The scale consists of 14 items across two subscales: HADS-D for depression, and HADS-A for anxiety. It employs a 4-point Likert scale yielding a total score of 0–21 in each subscale.<sup>39</sup> In our included studies, a cutoff of  $\geq 8$  in each subscale was used for diagnosing anxiety or depression. It was only administered to Chinese patients and its Chinese translation had been previously validated.<sup>61,62</sup>

**SCL-90.** The SCL-90 is a self-reporting diagnostic tool for the assessment of a wide range of psychopathological distress. The survey contains 90 items, measuring nine principal dimensions in psychopathology, including somatization, obsessive-compulsive behaviors, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoia, and psychoticism.<sup>40</sup> Only data relating to the depression and anxiety dimensions were included in the analysis. A cutoff score of  $\geq 2$  in these two dimensions was used for diagnosing anxiety or depression. The SCL-90 was only administered to Chinese patients in our included studies and its Chinese translation had been previously validated.<sup>63–65</sup>

**PSQI.** The PSQI is a self-reporting questionnaire for the assessment of sleep quality. It consists of 19 items on a 4-point Likert scale, and is designed to measure sleep disturbances and sleep habits over a 1-month period.<sup>41</sup> In our included studies, a PSQI score between 16 and 21 was considered as an indication for sleep disturbance. It was administered to Chinese patients and had been previously validated in Chinese.<sup>66–68</sup>

**ISI.** The ISI is a self-reporting psychometric questionnaire designed to assess the severity of insomnia in adults. It consists of seven items rated on a 5-point Likert scale.<sup>42</sup> A cutoff of  $\geq 8$  was used for diagnosing insomnia/sleep disturbance in our included studies. It was administered to Chinese patients and had been previously validated in Chinese.<sup>69</sup>

**Custom questionnaires and clinical interviews.** Custom screening tools were used by four Chinese studies<sup>70–73</sup> for evaluating depression, anxiety, and/or sleep disturbances. Two studies<sup>74,75</sup>

used interviews for evaluating depression, anxiety, and sleep disturbances. The interview results were reviewed and confirmed by expert neurologists; however, the exact diagnostic criteria and interview questions were not disclosed in these studies.

### Quality assessment

We assessed the quality of our included studies using a modified version of the Newcastle–Ottawa Quality Assessment Scale adapted for cross-sectional studies,<sup>76</sup> which is similar in format to the scale used in previous meta-analyses.<sup>77</sup> Because we expected a majority of our included studies to be single-arm observational studies, we removed irrelevant sections of the Newcastle–Ottawa Scale (NOS), such as comparability and assessment of the outcome. The modified scale evaluated the quality of our included studies based on five domains: (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) nonrespondents (response rate is  $\geq 80\%$ ); (4) valid measurement tool (appropriate screening tools used to evaluate depression, anxiety, or sleep disturbances); and (5) appropriate statistical analysis (appropriate and clearly described statistical tests). The total quality score ranged between 0 and 5; studies scoring  $\geq 3$  points were regarded to have a low risk of bias, while studies with  $< 3$  points were regarded to have a high risk of bias.

### Statistical analysis

We conducted all statistical analyses using R 4.0.2 (<https://www.r-project.org/>), and random-effects meta-analyses were performed using the *meta* 4.12 library (<https://cran.r-project.org/web/packages/meta/>).<sup>78</sup> To avoid variance instability when the prevalence trends toward 0% or 100% and to prevent confidence intervals (CIs) from extending beyond 0% and 100%, we transformed the extracted prevalence values using the Freeman–Tukey double arcsine method for prevalence pooling.<sup>79</sup> We then converted the results back to prevalence values with 95% CIs for ease of interpretation.

The Cochran's *Q*-test, with a significance level of  $P < 0.10$ , was used to assess the presence of heterogeneity, as recommended by the Cochrane Handbook. We further quantified heterogeneity using  $I^2$  statistics.<sup>30,80</sup> An  $I^2$  value  $\geq 75\%$  was considered to indicate serious heterogeneity as recommended by the Cochrane Handbook.<sup>30</sup>

### Subgroup analyses

We performed subgroup analyses by different screening tools and cutoff values, gender, country, study design, the severity of depression, anxiety, and sleep disturbances, as well as the patients' hospitalization status. We also performed subgroup analyses to study differences in pooled prevalence from peer- and nonpeer-reviewed (preprint) articles, and between articles using validated versus unvalidated screening tools.

### Meta-regression

We performed meta-regression analyses<sup>81</sup> to examine correlations between the pooled prevalence and study-level covariates. We chose the mean age and percentage male representation as our covariates of interest.

### Sensitivity analyses

We performed sensitivity analyses by subtracting each study and calculating the pooled prevalence and  $I^2$  of the remaining studies, in order to identify studies that may severely affect the pooled prevalence or heterogeneity.

### Publication bias

We examined the presence of small study effects as an indication for publication bias using funnel plots and Egger's regression tests.<sup>82–84</sup>

## Results

### Study characteristics

We included 31 studies<sup>43,44,70–75,85–107</sup> with 5153 patients in our analysis, including two preprint articles<sup>43,93</sup> (see Fig. 1). Table 1 shows the characteristics of the included studies. Twenty-seven (87%) studies<sup>43,44,70–73,85–94,96–105,107</sup> were conducted in China, and the remaining four studies were, respectively, conducted in Italy,<sup>75</sup> Ecuador,<sup>95</sup> Turkey,<sup>74</sup> and Iran.<sup>106</sup> Twenty-eight (90%) studies were cross-sectional studies,<sup>43,44,70–75,85–88,90,92–101,103–107</sup> and three (10%) studies were single-arm cohort studies.<sup>89,91,102</sup> The median number of participants with valid responses across the included studies was 97 (range 15–770), with a median male representation of 49% (range 25–62%). The median questionnaire response rate was 100% (range 52–100%).

### Quality of included studies

Figure 2 shows the NOS of the included studies. The median NOS was 3 (range 2–4). Twelve (39%) studies<sup>43,44,72,73,75,85,92,93,95,96,105,106</sup> had a high

risk of bias (quality score <3), and 19 (61%) studies<sup>70,71,74,86,88–91,94,97–104,107,108</sup> had a low risk of bias (quality score  $\geq 3$ ). While a majority of the studies employed appropriate statistical methods, used validated screening tools, and had low nonrespondent rates, very few studies justified their choice of sample size or used random sampling.

### The pooled prevalence of depression

The pooled prevalence of depression of 23 studies ( $n = 4028$ )<sup>43,44,70,71,73,75,85,87–89,92–96,98–101,104–107</sup> was 45% (95% CI: 37–54%). There was significant serious between-study heterogeneity ( $I^2 = 96%$ ,  $P_Q < 0.01$ ).

**Meta-regression and publication bias.** There were no significant correlations between the pooled depression prevalence and percentage male representation ( $P = 0.31$ ) or mean age ( $P = 0.95$ ) as shown by the meta-regression analyses. There was no evidence of publication bias according to visual inspection of the funnel plot (see Fig. S1, online only) and Egger's regression test ( $P = 0.22$ ).

**Sensitivity analysis.** In the sensitivity analysis, no study affected the pooled prevalence by over 2%, or affected the  $I^2$  value by over 1%, when excluded (see Fig. S2, online only).

**Study design and preprints.** There was one single-arm cohort study<sup>89</sup> that reported depression prevalence. The remaining studies were cross-sectional studies. The single-arm cohort study reported a prevalence of 74% (95% CI: 62–83%), which is significantly higher compared with the pooled prevalence of cross-sectional studies (44%, 95% CI: 36–53%,  $I^2 = 96%$ ). There was a significant subgroup difference between the pooled prevalence from cross-sectional versus cohort studies ( $P < 0.01$ ); however, omitting the cohort study did not result in any substantial changes in the pooled prevalence compared with the original analysis (see Fig. S3, online only).

Two preprint articles,<sup>43,93</sup> which were not peer-reviewed, were included in the study. They yielded a pooled prevalence of 22% (95% CI: 16–28%,  $I^2 = 0%$ ), which was significantly lower ( $P < 0.01$ ) compared with the pooled prevalence of the peer-reviewed articles (48%, 95% CI: 39–56%,  $I^2 = 97%$ ). Omitting the preprint articles did not result in any substantial changes in the pooled

**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	Sleep disturbances
Cao <i>et al.</i> <sup>85</sup>	China	CS	–	148	47	50.2 ± 15.6	SDS ≥ 50	SAS ≥ 50	Custom questionnaire
Cheng <i>et al.</i> <sup>86</sup>	China	CS	100	76	41	35.9 ± 10.6	–	SAS ≥ 50	–
Cheng <i>et al.</i> <sup>70</sup>	China	CS	98.3	59	41	–	Custom questionnaire	Custom questionnaire	–
Guo <i>et al.</i> <sup>108</sup>	China	CS	100	103	57	42.5 ± 12.5	PHQ-9 ≥ 5	GAD-7 ≥ 5	–
He <i>et al.</i> <sup>88</sup>	China	CS	100	214	46	<sup>a</sup>	PHQ-9 ≥ 5	–	PSQI 16–21
Hu <i>et al.</i> <sup>98</sup>	China	CS	100	85	51	48.8 ± 14.3	PHQ-9 ≥ 5	GAD-7 ≥ 5	ISI ≥ 8
Huang <i>et al.</i> <sup>71</sup>	China	CS	92.4	86	52	<sup>b</sup>	Custom questionnaire	–	Custom questionnaire
Karadaş <i>et al.</i> <sup>74</sup>	Turkey	CS	100	239	56	46.5 ± 15.4	–	–	Interview
Kong <i>et al.</i> <sup>93</sup>	China	CS	–	144	49	49.9 ± 13.7	HADS-D ≥ 8	HADS-A ≥ 8	–
Kuang <i>et al.</i> <sup>89</sup>	China	SAC	100	68	47	35.2 ± 9.7	SDS ≥ 50	SAS ≥ 50	–
Li <i>et al.</i> <sup>90</sup>	China	CS	100	118	55	39.8 ± 12.4	–	SAS ≥ 50	–
Li <i>et al.</i> <sup>103</sup>	China	CS	100	46	61	<sup>c</sup>	–	HADS-A ≥ 8	–
Liguori <i>et al.</i> <sup>75</sup>	Italy	CS	100	103	57	55.0 ± 14.6	Interview	Interview	Interview
Liu <i>et al.</i> <sup>107</sup>	China	CS	100	15	53	47.0 ± 8.4	PHQ-9 ≥ 5	GAD-7 ≥ 5	ISI ≥ 8
Liu and Yu <sup>72</sup>	China	CS	89.8	97	–	57.6 ± 9.2	–	Custom questionnaire	–
Ma <i>et al.</i> <sup>100</sup>	China	CS	98.2	770	48	50.4 ± 13.1	PHQ-9 ≥ 5	–	–
Mi and Yu <sup>91</sup>	China	SAC	100	20	50	39.0 ± 13.2	–	SAS ≥ 50	–
Nie <i>et al.</i> <sup>94</sup>	China	CS	91.8	78	42	<sup>d</sup>	SDS ≥ 50	SAS ≥ 50	–
Paz <i>et al.</i> <sup>95</sup>	Ecuador	CS	–	306	49	38.3 ± 10.9	PHQ-9 ≥ 5	GAD-7 ≥ 5	–
Qi <i>et al.</i> <sup>43</sup>	China	CS	52.4	41	42	40.1 ± 10.1	SDS ≥ 53	SAS ≥ 50	–
Qin <i>et al.</i> <sup>105</sup>	China	CS	–	112	53	<sup>e</sup>	SCL-90 ≥ 2	SCL-90 ≥ 2	–
Wang <i>et al.</i> <sup>92</sup>	China	CS	–	376	25	36.1 ± 9.7	SDS ≥ 50	SAS ≥ 50	PSQI 16–21
Wang <i>et al.</i> <sup>97</sup>	China	CS	99.0	484	50	52.5 ± 14.3	–	–	ISI ≥ 8
Wang <i>et al.</i> <sup>104</sup>	China	CS	99.2	652	53	51.5 ± 13.9	SCL-90 ≥ 2	SCL-90 ≥ 2	–
Xue <i>et al.</i> <sup>73</sup>	China	CS	95.3	41	46	<sup>f</sup>	Custom questionnaire	Custom questionnaire	–

*Continued*

**Table 1. Continued**

Study	Country	Study design	Response rate (%)	Sample size ( <i>n</i> )	Male (%)	Age (mean ± SD)	Assessment scales and cutoff value		
							Depression	Anxiety	Sleep disturbances
Zarghami <i>et al.</i> <sup>106</sup>	Iran	CS	74.5	82	39	§	PHQ-9 ≥ 5	GAD-7 ≥ 5	–
Zhang <i>et al.</i> <sup>44</sup>	China	CS	–	86	45	72.6 ± 12.1	SDS ≥ 53	SAS ≥ 50	–
Zhang <i>et al.</i> <sup>101</sup>	China	CS	98.9	296	58	–	HADS-D ≥ 8	HADS-A ≥ 8	–
Zhang <i>et al.</i> <sup>96</sup>	China	CS	–	57	51	46.9 ± 15.4	PHQ-9 ≥ 5	GAD-7 ≥ 5	–
Zhao <i>et al.</i> <sup>99</sup>	China	CS	100	106	43	35.9 ± 11.9	PHQ-9 ≥ 5	GAD-7 ≥ 5	–
Zhu <i>et al.</i> <sup>102</sup>	China	SAC	100	45	62	59.8 ± 15.4	–	–	PSQI 16–21

<sup>a</sup>The author indicated that all included patients were over 18 years old.

<sup>b</sup>The author indicated that the age range of the included patients was 17–78.

<sup>c</sup>The author indicated that the mean age was 60.9; however, no standard deviation was reported.

<sup>d</sup>The author indicated that the mean age was 58.4; however, no standard deviation was reported.

<sup>e</sup>The author reported that the median age was 40, with a range of 19–80.

<sup>f</sup>The author reported a range of 18–82.

<sup>g</sup>The author reported that the mean age of inpatients was 40.34 ± 14.39, and the mean age of outpatients was 43.62 ± 15.81.

CS, cross-sectional; 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; SCL-90, Symptom Checklist-90; SDS, Self-Rating Depression Scale; SAS, Self-Rating Anxiety Scale; PHQ-9, Patient Health Questionnaire Depression Module-9; PSQI, Pittsburgh Sleep Quality Index; SAC, single-arm cohort.

Note: Cells containing “–” indicate that the study author did not provide any relevant information for that column.

prevalence compared with the original analysis (see Fig. S4, online only).

**Depression screening tools.** For depression assessment methods (see Fig. 3), nine studies<sup>88,95,96,98–100,106–108</sup> used the criteria of PHQ-9 ≥ 5 with a pooled prevalence of 52% (95% CI: 45–59%,  $I^2 = 83\%$ ) and four studies<sup>85,89,92,94</sup> used SDS ≥ 50 with a pooled prevalence of 53% (95% CI: 42–65%,  $I^2 = 86\%$ ). Other criteria included HADS-D ≥ 8,<sup>93,101</sup> SDS ≥ 53,<sup>43,44</sup> and SCL-90 (depression subscale) ≥ 2,<sup>104,105</sup> which were used by two studies each and yielded a pooled prevalence of 20% (95% CI: 16–23%,  $I^2 = 0\%$ ), 53% (95% CI: 6–97%,  $I^2 = 97\%$ ), and 19% (95% CI: 17–22%,  $I^2 = 0\%$ ), respectively. The remaining studies used unvalidated custom questionnaires or interviews. There were significant subgroup differences between different screening tool subgroups ( $P < 0.01$ ).

Nineteen studies,<sup>43,44,85,87–89,92–96,98–101,104–107</sup> using validated screening tools, yielded a pooled depression prevalence of 45% (95% CI: 36–54%,

$I^2 = 96\%$ ). Four studies,<sup>70,71,73,75</sup> using unvalidated screening tools, reported a pooled prevalence of 47% (95% CI: 15–80%,  $I^2 = 97\%$ ). There were no significant subgroup differences between the two prevalence estimates ( $P = 0.92$ , see Fig. S5, online only).

#### The pooled prevalence of anxiety

Anxiety was assessed in 25 studies ( $n = 3315$ ),<sup>43,44,70,72,73,75,85–87,89–96,98,99,101,103–107</sup> with a pooled prevalence of 47% (95% CI: 37–57%). There was significant serious between-study heterogeneity ( $I^2 = 97\%$ ,  $P_Q < 0.01$ ).

**Meta-regression and publication bias.** There were no significant correlations between pooled anxiety prevalence and percentage male representation ( $P = 0.68$ ) or mean age ( $P = 0.44$ ) as shown by the meta-regression analyses. There was no evidence of publication bias (Egger’s test,  $P = 0.06$ , see Fig. S6, online only).

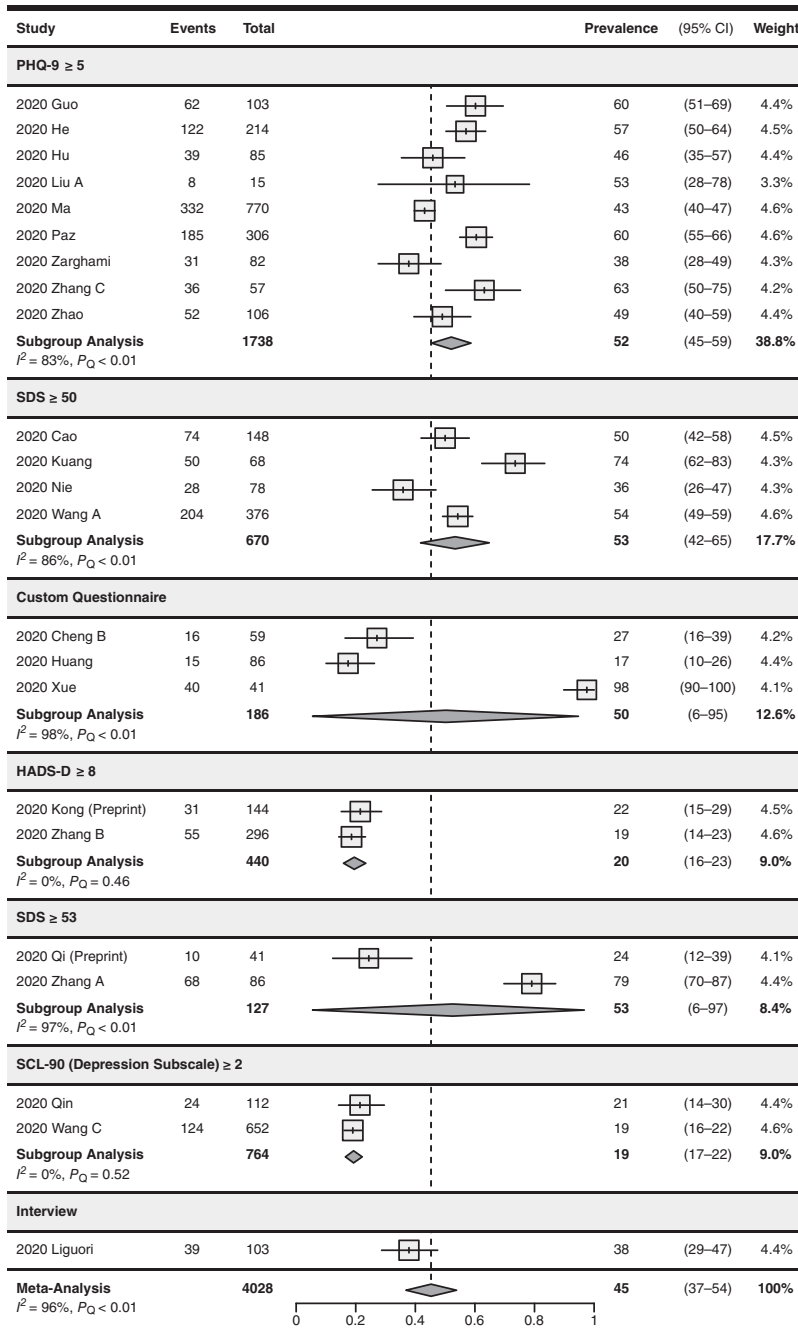


Study	Representativeness	Sample Size	Non Respondents	Valid Measurement Tool	Valid Statistical Methods	Overall Score
2020 Cao						2
2020 Cheng A						3
2020 Cheng B						4
2020 Guo						3
2020 He						4
2020 Hu						3
2020 Huang						3
2020 Karadaş						3
2020 Kong (Preprint)						2
2020 Kuang						3
2020 Li A						3
2020 Li B						3
2020 Liguori						2
2020 Liu A						3
2020 Liu B						2
2020 Ma						3
2020 Mi						3
2020 Nie						3
2020 Paz						2
2020 Qi (Preprint)						2
2020 Qin						2
2020 Wang A						2
2020 Wang B						3
2020 Wang C						3
2020 Xue						2
2020 Zarghami						2
2020 Zhang A						2
2020 Zhang B						4
2020 Zhang C						2
2020 Zhao						3
2020 Zhu						3

**Figure 2.** Quality ratings of included studies using the modified Newcastle–Ottawa Scale.

**Sensitivity analysis.** The maximum effect of removing a study on the pooled prevalence was 3% according to the sensitivity analysis. The maximum effect on the  $I^2$  value was 1% (see Fig. S7, online only).

**Study design and preprints.** There were two cohort studies<sup>89,91</sup> that reported anxiety prevalence. The remaining studies were cross-sectional studies. The single-arm cohort studies yielded a pooled prevalence of 89% (95% CI: 48–100%,  $I^2 = 93%$ ),



**Figure 3.** Forest plot for the pooling of depression prevalence. Studies were separated into subgroups based on the screening tool and cutoff values used for evaluating depression. The prevalence values are in percentages. Prevalence was not pooled for the interview subgroup as only one study was included. The differences between subgroups were statistically significant ( $P < 0.01$ ). CI, confidence interval; PHQ-9, Patient Health Questionnaire Depression Module-9; HADS-D, Hospital Anxiety and Depression Scale (Depression Subscale); SCL-90, Symptom Checklist-90; SDS, Self-Rating Depression Scale.

which is significantly higher ( $P < 0.05$ ) compared with the pooled prevalence of cross-sectional studies (43%, 95% CI: 33–53%,  $I^2 = 97\%$ ). Omitting the cohort studies did not result in any substantial changes in the pooled prevalence compared with the original analysis (see Fig. S8, online only).

Two preprint articles,<sup>43,93</sup> which were not peer-reviewed, were included in the study. They yielded a pooled prevalence of 25% (95% CI: 8–46%,  $I^2 = 85\%$ ), which was significantly lower ( $P < 0.05$ ), compared with the pooled prevalence of the peer-reviewed articles (49%, 95% CI: 38–60%,  $I^2 = 97\%$ ). Omitting the preprint articles did not result in any substantial changes in the pooled prevalence compared with the original analysis (see Fig. S9, online only).

**Anxiety screening tools.** For anxiety assessment methods (see Fig. 4), nine studies<sup>43,44,85,86,89–92,94</sup> used the criteria of SAS  $\geq 50$  with a pooled prevalence of 54% (95% CI: 32–75%,  $I^2 = 98\%$ ), seven studies<sup>95,96,98,99,106–108</sup> used GAD-7  $\geq 5$  with a pooled prevalence of 47% (95% CI: 37–58%,  $I^2 = 86\%$ ), three studies<sup>93,101,103</sup> used HADS-A  $\geq 8$  with a pooled prevalence of 34% (95% CI: 19–51%,  $I^2 = 91\%$ ), and two studies<sup>104,105</sup> used SCL-90 (anxiety subscale)  $\geq 2$  with a pooled prevalence of 18% (95% CI: 15–21%,  $I^2 = 0\%$ ). The remaining studies used unvalidated custom questionnaires or interviews. There were significant subgroup differences between different screening tool subgroups ( $P < 0.01$ ).

Twenty-one studies<sup>43,44,85–87,89–96,98,99,101,103–107</sup> used validated screening tools and yielded a pooled anxiety prevalence of 45% (95% CI: 34–56%,  $I^2 = 97\%$ ). Four studies<sup>70,72,73,75</sup> using unvalidated screening tools reported a pooled prevalence of 59% (95% CI: 36–80%,  $I^2 = 93\%$ ). There were no significant subgroup differences between the two prevalence estimates ( $P = 0.28$ , see Fig. S10, online only).

#### **Pooled prevalence of sleep disturbances**

Sleep disturbances were reported in 10 studies ( $n = 1795$ ),<sup>71,74,75,85,88,92,97,98,102,107</sup> with a pooled prevalence of 34% (95% CI: 19–50%). There was significant serious between-study heterogeneity ( $I^2 = 98\%$ ,  $P_Q < 0.01$ ).

**Meta-regression and publication bias.** There were no significant correlations between the pooled

prevalence of sleep disturbances and percentage male representation ( $P = 0.11$ ) or mean age ( $P = 0.16$ ) as shown by the meta-regression analyses. There was no evidence of publication bias (Egger's test,  $P = 0.45$ , see Fig. S11, online only).

**Sensitivity analysis.** According to the sensitivity analyses, the maximum effect of removing a study on the pooled prevalence was 5%, with a maximum effect of 1% on the  $I^2$  value (see Fig. S12, online only).

**Study design and preprints.** There was one single-arm cohort study<sup>102</sup> that reported sleep disturbances with a prevalence of 2% (95% CI: 0–9%). This is significantly lower ( $P < 0.01$ ) compared with the pooled prevalence of the remaining studies (39%, 95% CI: 23–55%,  $I^2 = 98\%$ ), which were all cross-sectional studies (see Fig. S13, online only). No preprint article reported sleep disturbances as one of their outcomes.

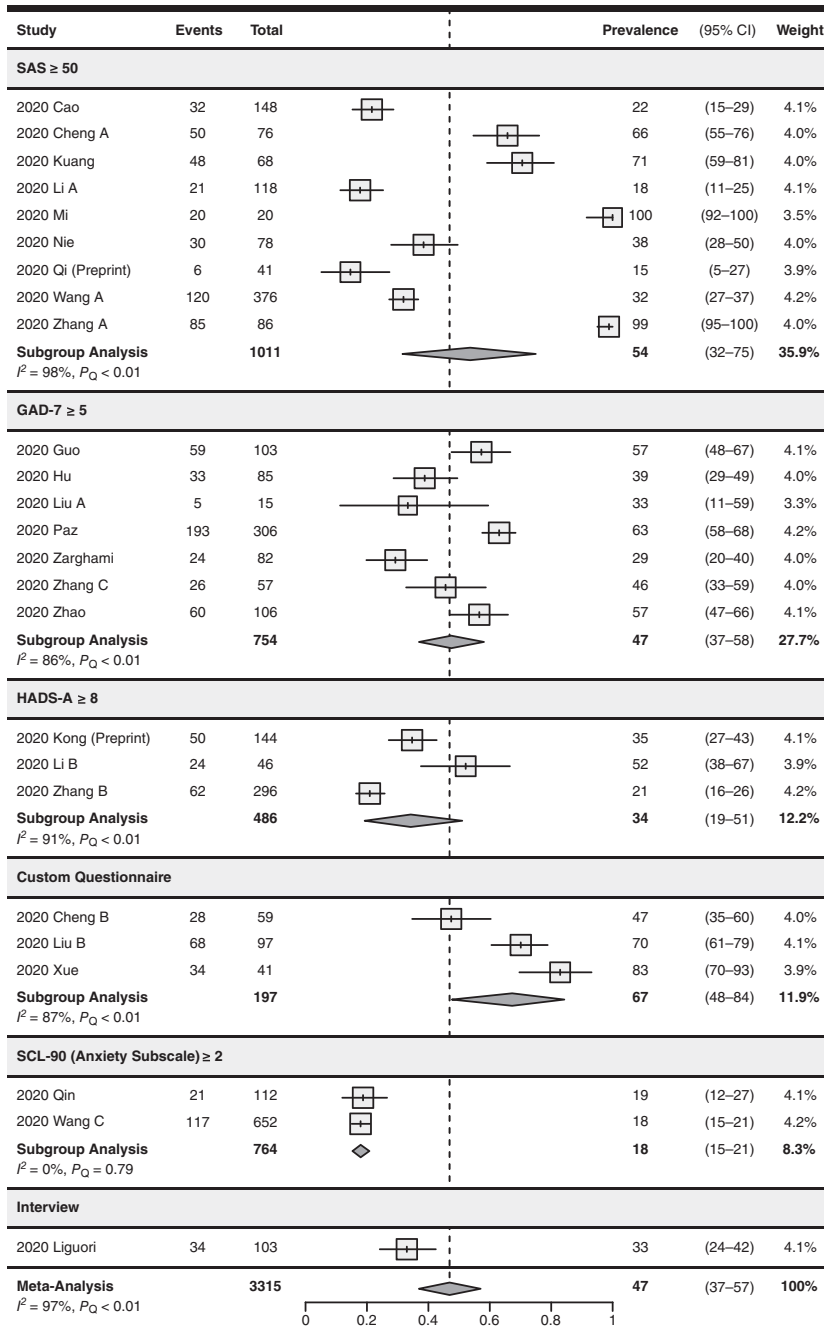
**Sleep disturbances screening tools.** The most common criteria for assessing sleep disturbances were PSQI 16–21<sup>88,92,102</sup> and ISI  $\geq 8$ ,<sup>97,98,107</sup> which are used by three studies each, yielding a pooled prevalence of 19% (95% CI: 0–68%,  $I^2 = 99\%$ ) and 43% (95% CI: 31–56%,  $I^2 = 73\%$ ), respectively. The remaining studies used unvalidated custom questionnaires or interviews for assessing sleep disturbances. There were no significant subgroup differences between different screening tool subgroups ( $P = 0.21$ , see Fig. 5).

Six studies<sup>88,92,97,98,102,107</sup> used validated screening tools and yielded a pooled prevalence of 29% (95% CI: 10–52%,  $I^2 = 98\%$ ). Four studies<sup>71,74,75,85</sup> used unvalidated screening tools and reported a pooled prevalence of 42% (95% CI: 18–68%,  $I^2 = 97\%$ ). There were no significant subgroup differences between the two prevalence estimates ( $P = 0.45$ , see Fig. S14, online only).

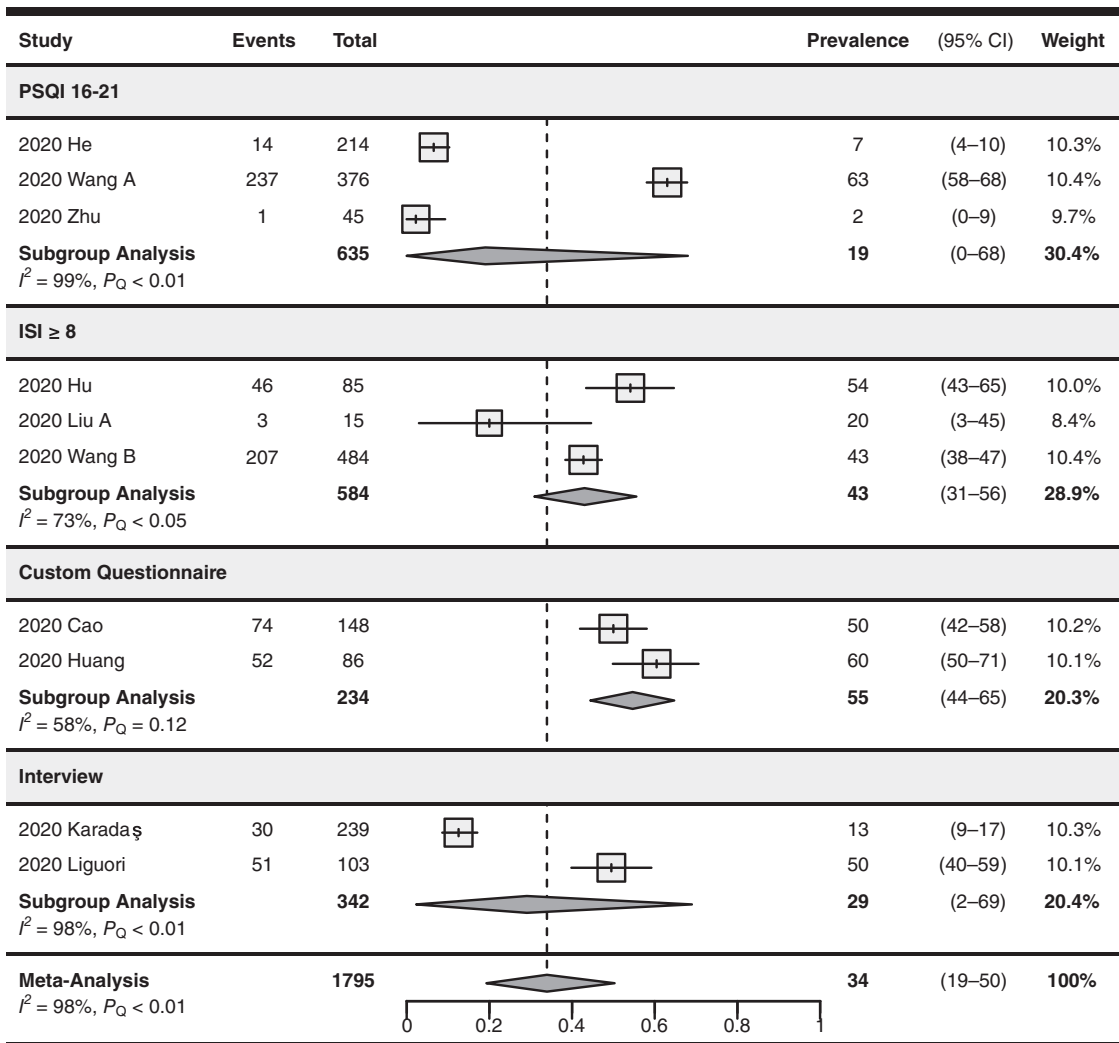
#### **Subgroup analyses**

Results of the subgroup analysis of the prevalence of depression, anxiety, and sleep disturbances by gender, severity, country, and hospitalization status are summarized in Table 2.

**Gender subgroups.** Subgroup data by gender were reported by nine studies<sup>70,73,75,94,98,100,101,106,108</sup> for depression prevalence, with a pooled prevalence of 39% for male and 50% for female patients (see Fig.



**Figure 4.** Forest plot for the pooling of anxiety prevalence. Studies were separated into subgroups based on the screening tool and cutoff values used for evaluating anxiety. The prevalence values are in percentages. Prevalence was not pooled for the interview subgroup as only one study was included. The differences between subgroups were statistically significant ( $P < 0.01$ ). CI, confidence interval; GAD-7, General Anxiety Disorder-7; HADS-A, Hospital Anxiety and Depression Scale (Anxiety Subscale); SAS, Self-Rating Anxiety Scale; SCL-90, Symptom Checklist-90.



**Figure 5.** Forest plot for the pooling of sleep disturbance prevalence. Studies were separated into subgroups based on the screening tool and cutoff values used for evaluating sleep disturbances. The prevalence values are in percentages. The differences between subgroups were not statistically significant (*P* = 0.21). CI, confidence interval; ISI, Insomnia Severity Index; PSQI, Pittsburgh Sleep Quality Index.

S15, online only). Eight studies<sup>70,73,75,94,98,101,106,108</sup> reported subgroup data for anxiety prevalence, with a pooled prevalence of 35% for males and 49% for females (see Fig. S16, online only). Three studies<sup>75,97,98</sup> reported subgroup data for sleep disturbance, with a pooled prevalence of 43% for males and 52% for females (see Fig. S17, online only). There were no statistically significant between-group differences in any of the gender subgroups (*P* = 0.24, 0.15, and 0.32 for depression, anxiety, and sleep disturbances, respectively).

**Country subgroups.** Twenty Chinese studies<sup>43,44,70,71,73,85,88,89,92–94,96,98–101,104,105,107,108</sup> reported a pooled depression prevalence of 45% from China. The depression prevalence for Italy,<sup>75</sup> Ecuador,<sup>95</sup> and Iran<sup>106</sup> was 38%, 60%, and 38%, respectively, as reported by one study in each subgroup (see Fig. S18, online only). Twenty-two studies<sup>43,44,70,72,73,85,86,89–94,96,98,99,101,103–105,107,108</sup> reported a pooled anxiety prevalence of 48% from China. The anxiety prevalence for Italy,<sup>75</sup> Ecuador,<sup>95</sup> and Iran<sup>106</sup> was 33%, 63%, and

**Table 2.** Subgroup analysis of depression, anxiety, and sleep disturbance prevalence

		Depression	Anxiety	Sleep disturbances
Gender	Male	39%, 95% CI: 26–53% $I^2 = 92%$	35%, 95% CI: 21–49% $I^2 = 88%$	43%, 95% CI: 30–57% $I^2 = 77%$
	Female	50%, 95% CI: 38–62% $I^2 = 89%$	49%, 95% CI: 37–62% $I^2 = 84%$	52%, 95% CI: 41–64% $I^2 = 66%$
Country	China	45%, 95% CI: 36–55% $I^2 = 97%$	48%, 95% CI: 37–59% $I^2 = 97%$	35%, 95% CI: 19–54% $I^2 = 98%$
	Iran	38%, 95% CI: 28–49% <sup>a</sup>	29%, 95% CI: 20–40% <sup>a</sup>	–
	Turkey	–	–	13%, 95% CI: 9–17% <sup>a</sup>
	Italy	38%, 95% CI: 29–47% <sup>a</sup>	33%, 95% CI: 24–42% <sup>a</sup>	50%, 95% CI: 40–59% <sup>a</sup>
	Ecuador	60%, 95% CI: 55–66% <sup>a</sup>	63%, 95% CI: 58–68% <sup>a</sup>	–
Hospitalization	Inpatients	48%, 95% CI: 35–61% $I^2 = 97%$	42%, 95% CI: 31–54% $I^2 = 95%$	29%, 95% CI: 13–48% $I^2 = 98%$
	Outpatients	35%, 95% CI: 22–48% <sup>a</sup>	33%, 95% CI: 21–46% <sup>a</sup>	–
Severity	Mild	33%, 95% CI: 26–39% $I^2 = 86%$	29%, 95% CI: 23–36% $I^2 = 82%$	20%, 95% CI: 2–49% $I^2 = 80%$
	Moderate	14%, 95% CI: 11–16% $I^2 = 36%$	12%, 95% CI: 6–21% $I^2 = 94%$	16%, 95% CI: 9–25% $I^2 = 0%$
	Severe	7%, 95% CI: 4–10% $I^2 = 83%$	6%, 95% CI: 3–10% $I^2 = 87%$	2%, 95% CI: 0–7% $I^2 = 0%$

<sup>a</sup>Only one study was included in this subgroup.  
CI, confidence interval.

29%, respectively, as reported by one study in each subgroup (see Fig. S19, online only). Eight studies<sup>71,85,88,92,97,98,102,107</sup> reported a pooled prevalence of sleep disturbances of 35% from China. The prevalence of sleep disturbances for Turkey<sup>74</sup> and Italy<sup>75</sup> was 13% and 50%, respectively, as reported by one study in each subgroup (see Fig. S20, online only). There were significant between-group differences for subgroup analysis by country for prevalence of depression, anxiety, and sleep disturbances ( $P < 0.01$  for all three outcomes).

**Inpatient and outpatient subgroups.** Only one study<sup>106</sup> reported depression and anxiety prevalence for outpatients, which was 35% and 33%, respectively. These figures are lower compared with the pooled prevalence for inpatients, which was 48% (reported by 12 studies,<sup>73,75,88,92,94,98,99,104–108</sup> see Fig. S21, online only) and 42% (reported by 13 studies,<sup>72,73,75,92,94,98,103–108</sup> see Fig. S22, online only) for depression and anxiety, respectively; however, these differences between inpatients and outpatients were not significant ( $P = 0.16$  and  $0.28$  for depression and anxiety prevalence, respectively).

There were no outpatient data reported for prevalence of sleep disturbances. The pooled prevalence of sleep disturbances was 29% for inpatients, as reported by eight studies (see Fig. S23, online only).<sup>74,75,88,92,97,98,102,107</sup>

#### Severity subgroups.

Eleven studies<sup>44,85,89,94–96,98–100,107,108</sup> reported the prevalence of mild, moderate, and severe depression. Additionally, one study<sup>92</sup> only reported the prevalence of severe depression. The pooled prevalence of mild, moderate, and severe depression was 33%, 14%, and 7%, respectively (see Fig. S24 for the criteria used for determining depression severity, online only). Thirteen studies<sup>44,72,85,86,89,90,94–96,98,99,107,108</sup> reported the prevalence of mild, moderate, and severe anxiety, with one study<sup>92</sup> only reporting the prevalence of severe anxiety. The pooled prevalence of mild, moderate, and severe anxiety was 29%, 12%, and 6%, respectively (see Fig. S25 for the criteria used for determining anxiety severity, online only). Two studies<sup>98,107</sup> reported the pooled prevalence of mild, moderate, and severe sleep disturbances as 20%, 16%, and 2%, respectively (see Fig. S26 for the

criteria used for determining the severity of sleep disturbances, online only).

## Discussion

This systematic review and meta-analysis aimed to provide an up-to-date estimate of the prevalence of depression, anxiety, and sleep disturbances among COVID-19 patients by combining the data of 31 observational studies with a total of 5153 patients. Our results showed that the overall prevalence of depression, anxiety, and sleep disturbances among COVID-19 patients is 45%, 47%, and 34%, respectively.

These data on the prevalence of depression in COVID-19 patients can be examined in comparison to that of pre-pandemic depression prevalence in hospital inpatients and outpatients, which are estimated to be 5–34%<sup>109</sup> and 27.0%,<sup>110</sup> respectively. In this meta-analysis, we found the prevalence of depression for COVID-19 inpatients to be 48%, which is a substantial increase compared with pre-pandemic depression levels. Additionally, the prevalence of depression for outpatients, estimated to be 35% based on one study, is also higher compared with the pre-pandemic prevalence. Furthermore, these prevalence estimates of depression, anxiety, and sleep disturbances display a substantial increase to that of the general population during the COVID-19 pandemic, which are estimated to be 33.7%, 31.9%,<sup>111</sup> and 20.1%,<sup>112</sup> respectively.

### *Effect of screening tools on prevalence*

We found that the screening tools used for assessing depression and anxiety had a significant effect on the resultant prevalence values. Regarding depression prevalence, both PHQ-9 (with a cutoff of  $\geq 5$ ) and Zung SDS (with a cutoff of  $\geq 50$  or  $\geq 53$ ) yielded similar prevalence values at 52–53%. However, this prevalence estimate is substantially higher than the prevalence yielded by HADS-D at a cutoff of  $\geq 8$  and SCL-90 (depression subscale) at a cutoff of  $\geq 2$ , which estimated the prevalence at 19–20%. This matches previous findings that determined that the difference in depression prevalence between assessments using PHQ-9  $\geq 5$  and HADS-D  $\geq 8$  was around 30%.<sup>113</sup> Similarly, GAD-7 (with a cutoff of  $\geq 5$ ) and Zung SAS (with a cutoff of  $\geq 50$ ) yielded higher anxiety prevalence values compared with HADS-A (with a cutoff value of  $\geq 8$ ) and SCL-90 (anxiety subscale) with a cutoff value of  $\geq 2$ . One

likely explanation for these observations may be due to the use of low cutoff values for PHQ-9, GAD-7, SAS, and SDS. Whereas previous studies had shown that the cutoffs used for HADS ( $\geq 8$ ) were optimal,<sup>114</sup> using a cutoff value of 8–11 for PHQ-9<sup>45</sup> and GAD-7,<sup>115</sup> as well as 60 for SDS,<sup>116</sup> may increase the validity of these scales. The increased cutoff values will likely result in decreased prevalence of mental illness as assessed using these scales, potentially increasing agreement with HADS. For example, by using a cutoff value of  $\geq 10$  for the PHQ-9, its agreement with HADS-D  $\geq 8$  was significantly improved compared with a cutoff of  $\geq 5$ .<sup>113</sup> For future studies, higher cutoffs should be considered to increase the validity of PHQ-9, GAD-7, SDS, and SAS, as well as to increase agreement with HADS.

However, it must also be noted that there were substantial differences in the sample size of different screening tool subgroups. Subgroups with higher prevalence, such as PHQ-9 and SAS, included more studies and patients compared with subgroups with lower prevalence estimates, such as HADS and SCL-90. Thus, it is unclear whether the significant subgroup differences we observed were valid. In addition, there was significant, serious between-study heterogeneity in the PHQ-9, GAD-7, SAS, SDS, and HADS-A subgroups. This suggests that the results from individual studies in these subgroups are inconsistent; therefore, the validity of the subgroup prevalence estimates was uncertain. These factors should be considered when interpreting the results of the subgroup analyses by screening tools, as the addition of future studies may improve between-study consistency, increase the validity of subgroup estimates, and reduce the observed subgroup differences.<sup>117</sup>

While there were no significant differences between the prevalence values yielded by different sleep disturbance assessment tools, the results of the subgroup analysis must be interpreted with caution due to differences in the design of PSQI and ISI questionnaires, as well as the cutoff values of PSQI. For assessing sleep disturbances, PSQI is preferred over ISI as it provides an overview of sleep quality by assessing multiple categories of sleep disturbances. By contrast, ISI is limited to insomnia and does not include items relevant to other sleep disturbances.<sup>118</sup> Additionally, PSQI had been shown to have an optimal cutoff of 6;<sup>119,120</sup> the 16–21 cutoff used by the included studies was typically

used to detect severe forms of sleep impairment<sup>121</sup> and may have resulted in an underestimation of the prevalence of sleep disturbances.

Several studies used custom questionnaires or interviews to assess the prevalence of mental illnesses. While these unvalidated tools produced similar prevalence estimates compared with validated tools, these studies did not publish their questionnaire or interview items nor report the reliability and validity of their screening tools. Future investigations should adopt validated scales with optimal cutoff values or structured interviews to both increase the validity of their studies and the transparency of their methodology.

### *Interpretation of subgroup analyses*

Given that a majority of the included studies were rapidly conducted and disseminated during the early phases of the pandemic, the patient population were often limited to those who were easily accessible by the investigators via convenience sampling. As a result, we found that a majority of the patient population were limited to Chinese and hospitalized patients. Our subgroup results for outpatients and patients originating from Italy, Ecuador, Iran, and Turkey were based on single studies. Therefore, the subgroup analyses by country and hospitalization status were not useful for detecting subgroup differences. This calls for further investigations into the mental status of outpatients and patients from non-Chinese countries in order to provide a more complete picture of the mental impact of COVID-19.

Our subgroup analyses by gender showed that there was no significant difference between the prevalence of depression, anxiety, and sleep disturbances in male and female patients, and there was no significant reduction in heterogeneity in both gender subgroups compared with the original analysis. In regards to the severity of depression, anxiety, and sleep disturbances, most patients only presented with mild symptoms, with a low proportion of patients suffering from severe symptoms of mental illness. Regardless, the prevalence of moderate and severe mental illness symptoms in COVID-19 patients may be higher compared with other patient groups and the general population. For example, a previous large-scale observational study found the prevalence of moderate and severe depression in cancer patients to be 11.3% and 3.7%,

respectively,<sup>122</sup> as compared with 14% and 7% in COVID-19 patients. This indicates that a similar or greater proportion of COVID-19 patients may experience moderate or severe depression compared with patients with serious, chronic conditions such as cancer. The increase in the prevalence of moderate and severe symptoms is more evident when compared with the general population before the pandemic, which reported a prevalence of 5.1% and 1.5% for moderate and severe depression, respectively.<sup>122</sup> These findings indicate that the severity of mental illnesses may be increased as well in addition to the overall prevalence in COVID-19 patients compared with other populations.

### *Study strengths and limitations*

Since this meta-analysis was conducted using data from early stages of the pandemic, it has several shortcomings, which must be noted. First, we observed significant between-study heterogeneity that was not resolved by our proposed subgroup analyses, sensitivity analyses, and meta-regressions. Second, all but two of our included studies used self-rating scales for assessing the prevalence of mental illness. While this was likely due to local quarantine guidelines, self-rated scales generally have lower sensitivity and specificity compared with clinician/observer-rated scales<sup>123</sup> or structured clinical interviews (e.g., the Structured Clinical Interview for DSM-5).<sup>124</sup> Thus, our results should be considered with this limitation in mind and future studies should incorporate clinician-rated tools or interviews, perhaps with the assistance of telemedicine technologies.<sup>125,126</sup> Lastly, there was a lack of subgroup data, which diminished the usefulness of our subgroup analyses by hospitalization status and country.

However, this study also has several notable strengths. First, we did not detect signs of publication bias as shown by funnel plots and Egger's regression analysis. In addition, our results were not substantially affected by the omission of one included study, nor were they greatly affected by the removal of preprint articles or single-arm cohort studies. We also did not find significant differences between the pooled prevalence from validated versus unvalidated screening tools. Last of all, a majority of our studies had a low risk of bias with high response rates, validated screening tools, and appropriate statistical methods.



### *Clinical implications*

In our subgroup analyses, we found that many COVID-19 patients experience depression, anxiety, and/or sleep disturbances. The cause of these psychiatric disorders is likely multifactorial. One possible factor is a lack of contact with families and loved ones during quarantine or hospitalization.<sup>127</sup> Fear relating to the disease due to poor knowledge<sup>128</sup> or misinformation<sup>13</sup> regarding to COVID-19, feeling of self-blame,<sup>129</sup> and social stigma<sup>130,131</sup> may also facilitate the development of psychiatric disorders in COVID-19 patients. In severe cases, COVID-19 patients had demonstrated suicidal and self-destructive tendencies,<sup>132,133</sup> which highlights the importance of early detection and intervention for mental health problems in this population. Hospitals should implement remote mental health screening programs and psychiatric consultations using technologies, such as telemedicine and internet-based mental health interventions,<sup>134,135</sup> along with establishing a system allowing proper communication between hospitalized/quarantined patients and their families.<sup>127</sup> Improving health literacy<sup>136</sup> and curbing false information for both COVID-19 patients and the general public may also help to reduce social stigma surrounding COVID-19 patients and to improve patients' mental health.

Our study has also demonstrated the need for further investigations into the mental health status of COVID-19 patients. Specifically, future research should focus more on COVID-19 outpatients who were underrepresented in this meta-analysis because of the excessive use of convenience sampling in hospital settings. Additionally, patients from countries with a high number of cases, such as the United States, Brazil, and India,<sup>10</sup> should be assessed for mental disorders as well. There are currently no such studies originating from these countries as per our latest database search.

### **Conclusions**

The objective of this systematic review and meta-analysis was to assess the prevalence of depression, anxiety, and sleep disturbances in COVID-19 patients. Our findings suggest that 45% of COVID-19 patients experience depression, 47% of patients experience anxiety, and 34% of patients experience sleep disturbances. A majority of the included patients were inpatients and patients from China. We did not find any differences in prevalence

between patients of different gender; however, the prevalence of depression and anxiety varied depending on the use of different screening tools. Further investigations assessing the mental health of COVID-19 outpatients and patients from different geographical regions around the world are needed to gain a more complete picture of the psychological implications of COVID-19 infections.

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### **Author contributions**

J.D. conceptualized and designed the methodology of the study, performed database searches, supervised and performed article screening and data extraction, performed all statistical analyses, drafted the manuscript, and critically reviewed and revised the manuscript. F.Z., W.H., Z.S., C.Y.W., O.C., E.H., and Q.K.Z. performed article screening, data extraction, and critically reviewed and revised the manuscript. All authors have read and approved the final version of the manuscript to be submitted and published. J.D. accepts responsibility for the integrity of the data analyzed.

### **Supporting information**

Additional supporting information may be found in the online version of this article.

**Table S1.** PRISMA checklist.

**Table S2.** English search strategy (MEDLINE).

**Table S3.** Chinese search strategy (CNKI).

**Figure S1.** Funnel plot, depression prevalence.

**Figure S2.** Sensitivity analysis, depression prevalence.

**Figure S3.** Subgroup analysis by study design, depression prevalence.

**Figure S4.** Subgroup analysis by peer-review status, depression prevalence.

**Figure S5.** Subgroup analysis by validated tools, depression prevalence.

**Figure S6.** Funnel plot, anxiety prevalence.

**Figure S7.** Sensitivity analysis, anxiety prevalence.

**Figure S8.** Subgroup analysis by study design, anxiety prevalence.

**Figure S9.** Subgroup analysis by peer-review status, anxiety prevalence.

**Figure S10.** Subgroup analysis by validated tools, anxiety prevalence.

**Figure S11.** Funnel plot, prevalence of sleep disturbances.

**Figure S12.** Sensitivity analysis, prevalence of sleep disturbances.

**Figure S13.** Subgroup analysis by study design, prevalence of sleep disturbances.

**Figure S14.** Subgroup analysis by validated tools, prevalence of sleep disturbances.

**Figure S15.** Subgroup analysis by gender, depression prevalence.

**Figure S16.** Subgroup analysis by gender, anxiety prevalence.

**Figure S17.** Subgroup analysis by gender, prevalence of sleep disturbances.

**Figure S18.** Subgroup analysis by country, depression prevalence.

**Figure S19.** Subgroup analysis by country, anxiety prevalence.

**Figure S20.** Subgroup analysis by country, prevalence of sleep disturbances.

**Figure S21.** Subgroup analysis by hospitalization status, depression prevalence.

**Figure S22.** Subgroup analysis by hospitalization status, anxiety prevalence.

**Figure S23.** Subgroup analysis by hospitalization status, prevalence of sleep disturbances.

**Figure S24.** Subgroup analysis by severity, depression prevalence.

**Figure S25.** Subgroup analysis by severity, anxiety prevalence.

**Figure S26.** Subgroup analysis by severity, prevalence of sleep disturbances.

## Competing interests

The authors declare no competing interests.

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