Neuroscience and Biobehavioral Reviews 126 (2021) 252–264

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Anxiety, depression, trauma-related, and sleep disorders among healthcare workers during the COVID-19 pandemic: A systematic review and meta-analysis

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ARTICLE INFO

Keywords:
COVID-19
Depression
Anxiety
Stress disorders, traumatic, acute
Sleep wake disorders
Psychological trauma
Healthcare workers
Meta-analysis
Systematic review

ABSTRACT

Healthcare workers have been facing the COVID-19 pandemic, with numerous critical patients and deaths, and high workloads. Quality of care is related to the mental status of healthcare workers. This PRISMA systematic review and meta-analysis, on Pubmed/Psycinfo up to October 8, 2020, estimates the prevalence of mental health problems among healthcare workers during this pandemic. The systematic review included 70 studies (101 017 participants) and only high-quality studies were included in the meta-analysis. The following pooled prevalences were estimated: 300 % of anxiety (95 %CI, 24.2–37.05); 311 % of depression (95 %CI, 25.7–36.8); 565 % of acute stress (95 %CI - 30.6–80.5); 20,2% of post-traumatic stress (95 %CI, 9.9–33.0); 44.0 % of sleep disorders (95 %CI, 24.6–64.5). The following factors were found to be sources of heterogeneity in subgroups and meta-regressions analysis: proportion of female, nurses, and location. Targeted prevention and support strategies are needed now, and early in case of future health crises.

1. Introduction

In 2020, healthcare workers (HCWs) have been facing a dramatic pandemic due to a new, poorly known, and deadly disease: Coronavirus 2019 disease (COVID-19) (WHO, 2020). HCWs have been working in critical care conditions, including unprepared doctors and nurses who had to work in urgently opened critical care departments (Zangrillo et al., 2020). Doctors and nurses have been facing extreme work pressure, fast adaptations to intense critical care situations, unseen amounts of severe critical patients, numerous deaths of patients, and risks of infection (WHO, 2020; Guessoum et al., 2020; Spoorthy et al., 2020). Quality of care is known to be related to the mental status of HCWs (Tawfik et al., 2019; Pereira-Lima et al., 2019). Therefore, focusing on the mental health of HCWs during the COVID-19 pandemic is necessary for their wellbeing and for healthcare quality. Finally, these mental health problems contribute to the high turnover rate of HCWs, which affects the costs of medical institutions through training costs and decreased productivity (Kim et al., 2018).

COVID-19 was first reported in Wuhan in December 2019. COVID-19 quickly spread to the rest of China and then to the rest of the world, leading the World Health Organization (WHO) to declare the situation as a pandemic on March 11, 2020 (Huang et al., 2020). To date, more than 70.4 million cases and 1.6 million deaths due to COVID-19 have been reported (WHO, 2020). This sudden thread is an unprecedented worldwide burden on mortality and morbidity, which healthcare workers are directly exposed to.

Abbreviations: HCW, Healthcare worker.

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https://doi.org/10.1016/j.neubiorev.2021.03.024
Received 21 December 2020; Received in revised form 8 March 2021; Accepted 19 March 2021
Available online 24 March 2021
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Studies from previous epidemics, such as SARS, Ebola or MERS, have shown that the sudden onset of an unknown disease with a high mortality rate would affect the mental health of HCWs (Liu et al., 2012; Lung et al., 2009; Maunder et al., 2003; Wu et al., 2009). The lack of personal protective equipment, the reorganization of units and services with the integration of new teams, the fear of being infected or infecting family members or patients, the need to make difficult ethical choices about prioritizing care, feeling of helplessness, and the loss of social support due to lockdown could have a psychological impact on healthcare workers (Sun et al., 2020; Thomaier et al., 2020; Khusid et al., 2020). Moreover, some HCWs have been working in somehow dehumanized conditions, wearing protective personal equipment, and dramatically limiting family visits to all patients, including terminally ill ones (Guessoum et al., 2020; Mallet et al., 2020b).

Some studies have sought to assess the mental health of caregivers at earlier stages of the pandemic (Shaukat et al., 2020; Pappa et al., 2020; Carmassi et al., 2020). However, the pandemic is evolving fastly, and numerous studies have been published in the last months. There is a need to gather these data to get a worldwide overview on the mental health of healthcare workers during the COVID-19 pandemic. In addition, early reviews could not capture easily post-traumatic stress disorders, which need a one-month delay after exposure to traumatic events (American Psychiatric Association, 2013). We chose to study four indicators (anxiety, depression, trauma-related, and sleep disorders) for several reasons: First, they are renowned and validated outcomes described in DSM-5 (American Psychiatric Association, 2013), for which there are validated scales usable in the general population (Kroenke et al., 2001; Spitzer et al., 2006; Bastien et al., 2001; Creamer, Bell et al. 2003); Second, many studies have been led on these outcomes among healthcare workers; Third, some specific interventions exist on these outcomes; Finally, these four outcomes are also well described when facing stress factors or psychological trauma in case of crisis (such as COVID-19 pandemic) (Shanafelt et al., 2020; HAS, 2020).

The aim of this systematic review and meta-analysis is to estimate the prevalence of anxiety, depression, trauma-related, and sleep disorders of healthcare workers during the COVID-19 pandemic.

2. Methods

This study was conducted in accordance with the PRISMA statement, whose checklist was strictly followed (Table S1, supplementary materials), and conceived according to consensus among researchers (Liberati et al., 2009). This study was not prospectively registered with any formal registry.

2.1. Search strategy, selection criteria, study selection, and data extraction

MM and SBG searched on two databases (Pubmed and Psycinfo) using no language restriction. The following words were chosen in regard to previous studies on COVID-19 and mental health: ("Physicians" OR "Nurses" OR "Nursing Assistants" OR "Caregivers") AND ("severe acute respiratory syndrome coronavirus 2" OR "COVID-19") AND ("Depression" OR "Anxiety" OR "Suicidal Ideation" OR "stress disorders, traumatic, acute" OR "Mental Health" OR "Mental Disorders" OR "Sleep Initiation and Maintenance Disorders" OR "Stress Disorders, Post-Traumatic"). MM and SBG systematically screened then selected the studies by reading titles, abstracts, and full-texts for eligible studies. Additionally, they cross-referenced our research with the last meta-analyses on similar topics (Serrano-Ripoll et al., 2020; Salari et al., 2020a, 2020b). The search process is shown in the flowchart (Fig. 1).

The inclusion criteria were: (1) study evaluating prevalence rates of mental health symptoms of HCWs in practice during the COVID-19 pandemic, (2) using validated scales, (3) published until October 8th, 2020 in peer-reviewed scientific journals.

The exclusion criteria were : (1) Letter to the editor not providing

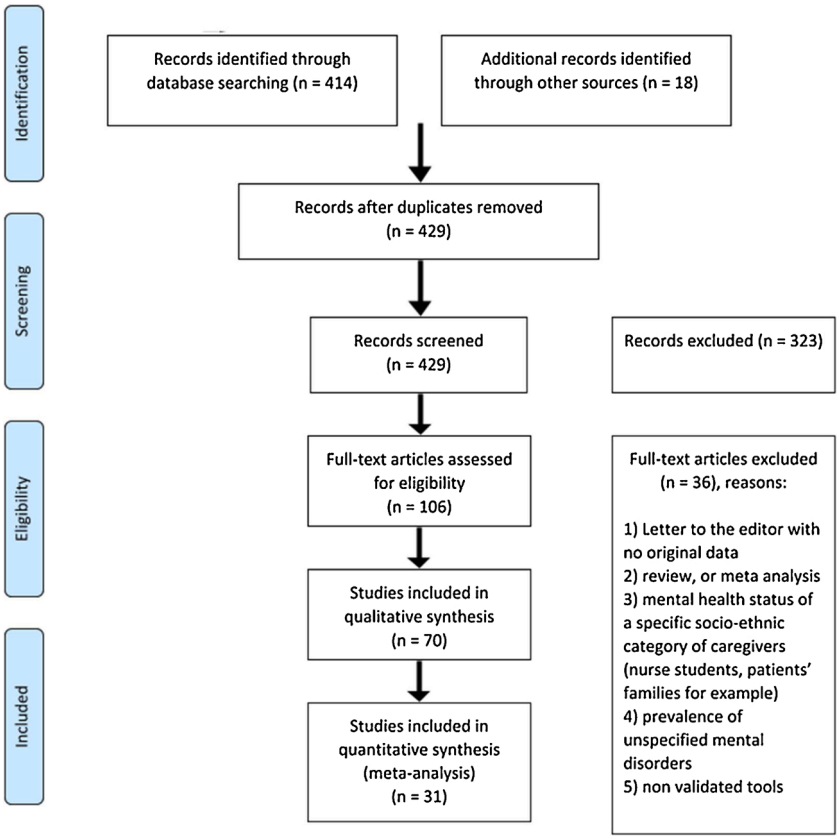


Fig. 1. Flowchart diagram.

original results, (2) duplicated publications, (3) studies evaluating impact of the quarantine, (4) mental health status of a particular socio-ethnic category of caregivers (nurse students for example), (5) case reports, qualitative studies, literature reviews, and meta-analyses, (6) full-text non-available, (7) prevalence of unspecified mental disorders. When unclear, inclusion or exclusion was discussed within the group of researchers.

For the meta-analysis, the outcome measure was the prevalence of four well defined mental health outcomes: depression, anxiety, trauma-related disorders (Acute Stress and Post-traumatic Stress), and sleep disorders in HCWs during the COVID-19 pandemic.

MM and SBG extracted data on the following variables independently: authors, year, region, time, study design, target population, study setting, sample size, participation rate, healthcare worker type, gender proportion, assessment methods, and cut-off used. If any of this information was not reported, the necessary calculations (e.g. from percentage to number of HCWs) were done, where possible. When similar scales were used across studies, we selected common cut-offs as much as possible, admitting different cut-offs if no other option. In case of disagreement, the issue was discussed within the group of researchers.

2.2. Quality assessment of the reviewed studies

The risk of bias was evaluated through quality assessment of the studies, using the following criteria, extracted from the Agency for Healthcare Research and Quality (AHRQ), the NIH's quality assessment tool for Observational Cohort and Cross-Sectional Studies, and the Crombie's items in order to be applicable for our review question (Crombie, 1996; NIH, 2020; Zeng et al., 2015): (a) clearly specified and defined population, (b) participation rate $\geq$ 50 %, (c) time period used for identifying subjects is indicated, (d) sample size $>$ 600, and consistency in the number of subjects reported throughout the study, (e) outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants. Each item answered "yes" scored 1.

2.3. Data analysis

For the meta-analysis's main outcomes, we extracted data from studies with a score $\geq$ 4/5.

A proportion meta-analysis was performed to assess the overall pooled prevalence of each outcome. Heterogeneity was assessed by using the Cochran Q test, P values below 0.10 were considered indicative of heterogeneity (Higgins et al., 2019). I2 values were calculated to estimate variation among studies attributable to heterogeneity, with I2 $\geq$ 75 % representing high heterogeneity (Higgins and Thompson, 2002). Since a high heterogeneity across studies was expected, a random-effect model (DerSimonian-Laird) was considered, as opposed to the fixed effects model to adjust for the observed variability (Ades et al., 2005). This heterogeneity was further explored through subgroup analyses and metaregressions (to test the influence of sample size, study location, proportion of nurses, of females, and scale). Definitions of frontline HCWs were too different from a study to another to enable subgroup analyses. A Freeman-Tukey transformation was used to calculate the weighted summary proportion under the random-effects model, as previously described (Miller, 1978). Meta-analysis results were displayed with forest plots in which the measure of effect for each study is represented by a square, triangle or circle, and the area of each square is proportional to study weight. In addition, we calculated the prediction interval. Sensitivity analyses were performed to assess the potential impact on the results (leave-one-out method).

We evaluated the potential publication bias by funnel plots supplemented by the Egger regression asymmetry test (p value$<$0.10). All statistical tests were two-sided. Significant level α was set at 0.05. Statistical analysis was performed using MedCalc© (Version 19.1, Ostend, Belgium) and OpenMetaAnalyst software. We used the JAMOVI software package for R to perform the Forest and Funnel Plots.

3. Results

3.1. Search results

414 articles were analyzed over database research. After de-duplication and complete screening of the papers, plus cross-referencing with other systematic-reviews, 70 articles were included in the present systematic review (flowchart, Fig. 1).

3.2. Characteristics of the studies

The 70 cross-sectional studies included 101,017 participants. They are presented in Table 1. Most of the studies were conducted in China (30), India (6), Turkey (5), and the USA (4). The other studies were conducted in 19 countries of Asia and Europe. 43 studies included both physicians and nurses, 12 included nurses only, and 15 included physicians only.

A meta-analysis (Table S2, supplementary materials) was performed on the whole sample (heterogeneous quality), then focused on high-quality studies (score $\geq$ 4/5): 22 for anxiety, 25 for depression, 9 for ASD and PTSD, and 10 for sleep disorders. The results of the risk of bias assessment are provided in Table S2. There was no publication bias when focusing on studies assessed $\geq$ 4/5 (funnel plot and Egger's test p-value $>$ 0.1). For each pooled prevalence presented in this research, there was no significant change in the degree of heterogeneity even if an attempt was done to exclude the expected outliers or according quality criteria $\geq$ 4/5.

3.3. Anxiety

The pooled prevalence of anxiety was 30,0 % (95 % CI, 24,2 - 37,0), in a total of 51 942 participants, with substantial heterogeneity (I2 = 99,55 %, p $<$ 0.001) (Fig. 2A). No factor explained high heterogeneity (criteria $\geq$ 4/5, female or nurse proportion, location, scale, sample size) (supplementary materials).

3.4. Depression and depressive symptoms

The pooled prevalence of depression and depressive symptoms was 31,1 % (95 % CI, 25,7 - 36,8), in a total of 68 030 participants, with substantial heterogeneity (I2 = 99,55 %, p $<$ .001). (Fig. 2B). No factor explained high heterogeneity in subgroup analyses and metaregressions (criteria $\geq$ 4/5, female or nurse proportion, location, scale, sample size) (supplementary materials).

3.5. Post-Traumatic Stress and Acute Stress

The pooled prevalence of psychotraumatic disorders was 31,4 % (95 % CI - 17,5 - 47.3), out of 25 412 participants, with substantial heterogeneity (I2 = 99,79 %, p $<$ .001). No factor explained high heterogeneity (criteria $\geq$ 4/5, female or nurse proportion, location, scale, sample size) (supplementary materials). Sensitivity analysis identified Sahin et al. (Şahin et al., 2020) as a possible outlier.

Focusing on acute stress, the pooled prevalence was 56,5% (95 % CI, 29.9–82.3), among 3 studies (quality score $\geq$ 4/5), in a total of 2 845 participants, with substantial heterogeneity (I2 = 99,56 %, p $<$ .001). The estimated pooled prevalence of post-traumatic stress in 6 studies was 21.5 % (95 %CI, 11.2–31.8), I2 = 99.62 %.

3.6. Sleep disorders

The pooled prevalence of sleep disorders was 44,0 % (95 % CI, 24,568−64,497), out of 12 428 participants, with substantial heterogeneity (I2 = 99,81 %, p $<$ .001) (Fig. 2D). These studies used 3 different

Table 1
Systematic review.

Reference	Country & date (months of year 2020)	Total of participants No	response rate	Assessment tools	Cut off	Healthcare workers (%)			Gender	Anxiety No (%)	Depression No (%)	PTSD No (%)	ASD No (%)	Burn Out No (%)	Sleep disorders No (%)	Distress No (%)	Appraised quality of the study
						Physicians	Nurses	Others	Female %, No								
Abdulah et al., 2020	Iraqi Kurdistan April	268	67%	AIS	6	100 %			29.9 %, 80						183 (68.3)		4
AlAteeq et al., 2020	Saudi Arabia March	502	N-A	PHQ-9 GAD-7	5 5	22,10 %	26,30 %	51,60 %	319%, 160	258 (51,4)	277 (55,2)						3
Almater et al., 2020	Saudi Arabia March April	107	30,60 %	PHQ-9 GAD-7 ISI PSS-10	5 5 8 14	100,00 %			43,9%, 47	50 (46,7)	54 (50,5)				48 (44,9)	77 (72)	3
An et al., 2020	China March	1103	N-A	PHQ-9	5		100%		90,8 %, 1002		481 (43,6)						4
Apisarnthanarak et al., 2020	Thailand March	160	N-A	GAD-7	5	32 %	38 %	30 %	59 %, 94	68 (42,5)							3
Arafa et al., 2020	Egypt, Saudi Arabia April	426	N-A	DASS-21 - depression - anxiety - stress	10 8 15	48,40 %	24,20 %		49,8 %, 212	251 (58,9)	294 (69)					238 (55,9)	3
Azoulay et al., 2020	France, April-May	1058	67,00 %	HADS - depression - anxiety	7 7	29,10 %	68,30 %	2,60 %	71 %, 751	533 (50,4)	322 (30,4)						5
Badahdah et al., 2020	Oman April	509	N-A	GAD-7	10	38 %	62 %		80 %, 407	132 (26)							3
Caliskan et al., 2020	Turkey March	290	N-A	HADS - depression - anxiety	7 10	100 %			38.26 %, 111	103 (35.52)	180 (62.07)						3
Chatterjee et al., 2020	India March-April	152	N-A	DASS-21	N-A	100 %			21.7 %, 33	60 (39.5)	53 (34.9)					50 (32.9)	2
Chew et al., 2020	Singapore & India February-April	906	90,60 %	DASS-21 - depression - anxiety - stress IES-R	10 8 15 24	29,60 %	39,20 %	31,20 %	64,3 %, 583	142 (15,7)	96 (10,6)	67 (7,4)				47 (5,2)	5
Cai et al., 2020	China January February	709	N-A	PHQ-9 GAD-7 ISI IES-R	5 5 8 34		100 %		96,5 %, 684	333 (46,9)	374 (52,8)	184 (26)			66 (9,3)		4
Civantos et al. 2020	USA April	349	8,00 %	Mini-Z Burnout Assesment GAD-7 IES PHQ-2	3 10 26 2	100 %			39 %, 136	167 (47,9)	37 (10,6)	96 (27,5)		76 (21,8)			3
Corbett et al., 2020	Ireland April-May	240	40 %	GAD-7 PHQ-9	N-A N-A	15 %	36.25 %	48.75 %	88.83 %, 175	50 (21.0)	49 (20.3)						2
De Sio et al., 2020	Italie April	695	32,40 %	GHQ-12	4	100 %			45,5 %, 316							619 (89,1)	4
Di Tella et al., 2020	Italie March April	145	N-A	STAI-Y BDI-II PCL-5	41 13 33	50 %	50 %		72 %, 104	103 (71)	106 (31)	38 (26,2)					3
Dosil et al., 2020	Spain April	421	N-A	DASS-21 AIS	N-A 6	N-A	N-A	N-A	80.285 %, 338	156 (37)	115 (27,4)				122 (28,9)	197 (46,7)	1
Elbay et al. 2020	Turkey March	442	N-A	DASS	N-A	100 %			57 %, 252	228 (51,6)	286 (64,7)					182 (41,2)	2
Elkholy et al., 2020	Egypt April may	502	N-A	PHQ GAD-7 ISI PSS	5 5 8 9	60 %	40,00 %		50 %, 251	384 (76,4)	388 (77,2)				340 (67,7)	406 (80,8)	3
Gupta et al., 2020	India March-April	1124	79,44 %	HADS	8	66,60 %	12 %		36,1 %, 406	419 (37,2)	353 (31,4)						5
Han et al., 2020	China February	21199	96,21 %	SAS SDS	50 53		100 %		99 %, 20987	4573 (20,6)	6371 (28,7)						5
Hong et al., 2020	Chine February	4692	N-A	PHQ-9 GAD-7	10 10		100 %		96,9 %, 4547	380 (8,1)	441 (9,4)						4

(*continued on next page*)

Table 1 (*continued*)

Reference	Country & date (months of year 2020)	Total of participants No	response rate	Assessment tools	Cut off	Healthcare workers (%)			Gender	Anxiety No (%)	Depression No (%)	PTSD No (%)	ASD No (%)	Burn Out No (%)	Sleep disorders No (%)	Distress No (%)	Appraised quality of the study
						Physicians	Nurses	Others	Female %, No								
Hu et al., 2020	China February	2014	99,60 %	SAS SDS	50 50		100 %		87,1 %, 1754	834 (41,4)	876 (43,5)						5
Huang et al., 2020	China February	364	N-A	SAS	50		32,70 %	67,30 %	59 %, 214	85(23,4)							3
Imran et al., 2020	Pakistan April May	178	N-A	PHQ-9 GAD-7 SASRQ	8 7 N-A	100 %			56 %, 100	40 (22,6)	47 (26,4)		8 (4,4)				ESA : 3 Depression : 4 Anxiety : 4
Jahrami et al., 2020	Bahrain April	257	91.78%	PSQI PSS	5 14	31.1%	46.3 %	22.6 %	70.0 %, 180						193 (75.2)	216 (84)	4
Juan et al., 2020	Chine February	456	91,20 %	PHQ-9 GAD-7 IES-R	5 5 24	42,80 %	57,20 %		70,6 %, 322	144 (31,6)	135 (29,6)		197 (43,2)				Depression : 4 Anxiety : 4 ASD : 3
Kannampallil et al., 2020	USA April	393	29,00 %	DASS-21 - depression - anxiety - stress PFI	10 8 15 1,33	100,00 %			55 %, 216	73 (18,6)	107 (27,2)			160 (40,7)		97 (24,7)	3
Khanal et al., 2020	Nepal April-May	475	N-A	HADS - depression - anxiety ISI	8 8 8	33,90 %	35,20 %		526%, 250	112 (23,6)	114 (24)				127 (26,7)		3
Khanna et al., 2020	India April	2355	N-A	PHQ-9	5	100 %			43.44 %, 1023		768 (32,6)						4
Koksal et al., 2020	Turkey April	702	N-A	HADS - depression - anxiety	- 7 - 10		48,30 %	51,70 %	70,1 %, 492	404 (57,5)	259 (36,9)						4
Labrague and Santos, 2020	Philippine N-A	325	93,00 %	COVID-19 anxiety scale	9		100 %		74,8 %, 243	123 (37,8)							3
Lai et al., 2020	Chine January February	1257	68,70 %	PHQ-9 GAD-7 ISI IES-R	10 7 15 26	39,20 %	60,80 %		76,7 %, 964	561 (44,6)	634 (50,4)		440 (35)		427 (34)		5
Li et al., 2020	Chine January-February	176	N-A	HAMA	7		100 %		77,3 %, 136	136 (77,3)							2
Liu et al., 2020	China February	512	14,70 %	SAS	50	N-A	N-A	N-A	84,7 %, 433	64 (12,5)							3
Lu et al., 2020	China February	2299	94.88 %	HAMA HAMD	7 7	88,82 % (physicians + nurses)		11.18 %	77.64 %, 1785	569 (24.75)	268 (11.66)						3
Mahendran et al., 2020	China April	120	96,00 %	GAD-7	N-A	30 %	50 %	20 %	73 %, 88	64 (53,3)							3
Ng et al., 2020	Singapore April	421	92,00 %	GAD-7 MBI - EE - DP	10 27 10	57 % (physicians + nurses)		43 %	73,9 %, 311	59 (14)				183 (43,5)			3
Ni et al., 2020	China February	214	N-A	GAD-2 PHQ-2	3 3	37,80 %	50,5	11,6	68,8 %, 147	47 (22.0)	41 (19.2)						3
Nie et al., 2020	China February	263	30 à 40 %	IES-R GHQ-12	20 4		100 %		76,7 %, 202				194 (73,8)			66 (25,1)	2
Ning et al., 2020	China February	612	N-A	SAS SDS	50 53	51,80 %	48,20 %		72,9 %, 446	100 (16,3)	153 (25)						4
Podder et al., 2020	Inde April	373	N-A	PSS-10	14	100 %			44,5 %, 171							320 (85,9)	3
Pouralizadeh et al., 2020	Iran April	441	N-A	GAD-7 PHQ-9	10 10		100 %		95,2 %, 420	171 (38,7)	165 (37,5)						3
Prasad et al., 2020	USA April	347	N-A	Mini-Z GAD-7 IES PHQ-2	3 5 26 3		71,50 %	28,50 %	908%, 315	241 (69,5)	79 (22,8)		208 (60)	104 (30)		327 (94,2)	ASD : 2 Depression : 3 Anxiety : 3

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Table 1 (*continued*)

Reference	Country & date (months of year 2020)	Total of participants No	response rate	Assessment tools	Cut off	Healthcare workers (%)			Gender	Anxiety No (%)	Depression No (%)	PTSD No (%)	ASD No (%)	Burn Out No (%)	Sleep disorders No (%)	Distress No (%)	Appraised quality of the study
						Physicians	Nurses	Others	Female %, No								Stress : 3 Burn Out : 3
Que et al., 2020	Chine February	2285	N-A	GAD7 PHQ-9 ISI	10 10 15	78%	9%	13 %	69 %, 1577	1052 (46,04)	1014 (44,37)				657 (28,75)		4
Ruiz-Fernández et al., 2020	Spain March April	506	N-A	ProQoL/Burn Out	19	21,30 %	78,70 %		76,7%, 388					425 (84)			3
Sahin et al., 2020	Turkey April May	931	N-A	PHQ-9 GAD-7 ISI IES-R	10 5 10 24	61,80 %	27,10 %		66 %, 614	559 (60)	722 (77,6)		711 (76,4)		469 (50,4)		4
Sandesh et al., 2020	Pakistan May	112	N-A	DASS-21	N-A	N-A	N-A	N-A	42,9 %, 48	96 (85,7)	81 (72,3)					101 (90,1)	1
Sanghavi et al., 2020	Portugal April	29	78,00 %	BDI-II	14	100 %			62 %, 18		8 (28)						4
Shah et al., 2020	UK N-A	207	N-A	PHQ-2 GAD-2	3 3	100 %			81,1 %, 168	51 (24,6)	33 (15,9)						2
Shechter et al., 2020	USA April	657	13,70 %	PC-PTSD PHQ-2 GAD-2	3 3 3	52,40 %	47,60 %		70 %, 460	217 (33)	315 (48)		374 (57)				4
Si et al., 2020	China February-March	863	76,00 %	IES-6 DASS-21	10 N-A	43,70 %	24,40 %		70,7 %, 610	120 (13,9)	117 (13,6)	347 (40,2)				74 (8,6)	PTSD : 5 DASS : 4
Skoda et al., 2020	Germany March	2224	N-A	GAD-7	10	22,10 %	67,90 %	10 %	76 %, 1690	211 (9,5)							4
Song et al., 2020	China February-March	14825	N-A	CES-D PCL-5	16 33	41,10 %	58,90 %		64,3 %, 9532		3736 (25,2)	1349 (9,1)					4
Stojanov et al., 2020	Serbia N-A	201	63.0%	GAD-7 SDS	10 60	49%	61 %		65.67 %, 132	76 (37.6)	32 (15.78)						3
Suryavanshi et al., 2020	India May	197	24,00 %	PHQ-9 GAD-7	5 5	63 %	24 %	13 %	51 %, 99	99 (50)	93 (47)						3
Tu et al., 2020	Chine February	100	100,00 %	PSQI GAD-7 PHQ-9	7 4 4		100 %		100 %, 100	46 (46)	40 (40)				60 (60)		3
Uyaroğlu et al., 2020	Turkey April	113	N-A	GAD-7	5	100 %			46,9 %, 53	56 (49,6)							3
Vafaei et al., 2020	Iran March	599	N-A	PHQ-9	5	54,10 %	45,9 % (+ midwives)		100 %, 599		407 (67,9)						3
Wang et al., 2020	Chine February-March	202	96,00 %	PCL-C	38		100 %		88 %, 178			34 (16,83)					4
Huang et al., 2020	China February	1045	80,10 %	HADS -depression -anxiety ISI	11 11 15	14,30 %	74 %	11,70 %	85,8 %, 897	209 (20)	142 (13,6)				109 (10,4)		5
Xiong et al., 2020	China February	223	61,80 %	GAD-7 PHQ-9	5 5		100 %		97,3 %, 217	91 (40,8)	59 (26,4)						4
Yang et al., 2020	China February	449	N-A	SAS	N-A	63,50 %	36,50 %		N-A	131 (29,18)							1
Yin et al., 2020	China February	371		PCL-5	33	18,10 %	71,20 %	10,20 %	61,5 %, 228			14 (3,8)					3
Zhan et al., 2020	Chine March	2667	N-A	GAD-7 PHQ-9 CPSS	N-A N-A N-A		100 %		96,96 %, 2586	1062 (39,82)	1458 (54,65)					1654 (62)	3
	China March	2182	N-A			31,20 %					231 (10,6)				740 (33,9)		4

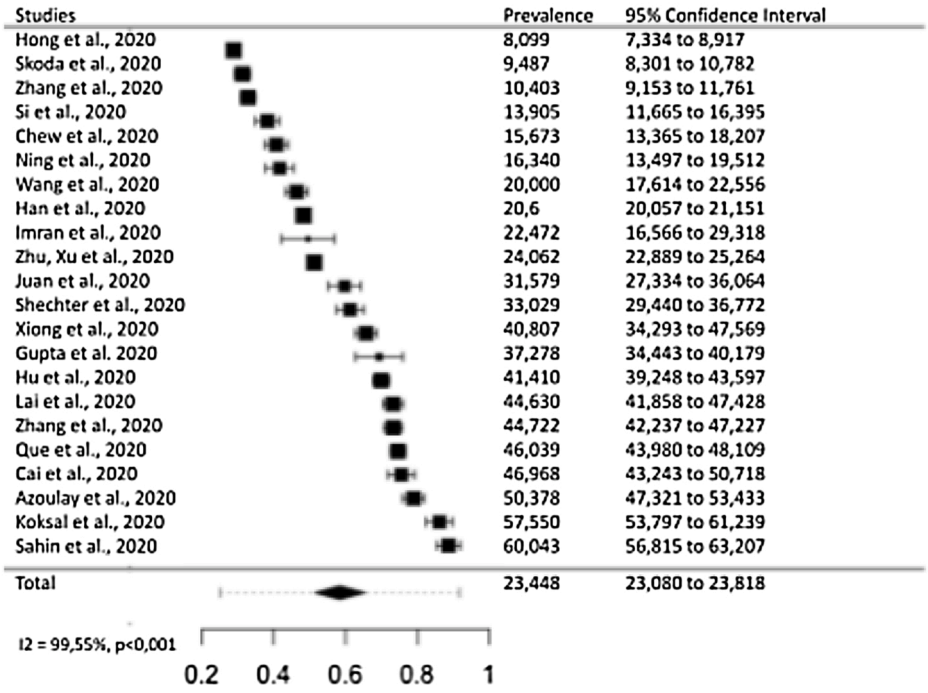
(*continued on next page*)

Table 1 (*continued*)

Reference	Country & date (months of year 2020)	Total of participants No	response rate	Assessment tools	Cut off	Healthcare workers (%)			Gender	Anxiety No (%)	Depression No (%)	PTSD No (%)	ASD No (%)	Burn Out No (%)	Sleep disorders No (%)	Distress No (%)	Appraised quality of the study
						Physicians	Nurses	Others	Female %, No								
Zhang et al., 2020a, 2020b				ISI PHQ-2 GAD-2 SCL-90-R - Psychosomatic - OCS - Phobic anxiety	8 3 3 2 2 2		11,30 %	57,50 %	64,2 %, 1401	227 (10,4)							
Zhang et al., 2020a, 2020b	China January February	1563	N-A	ISI PHQ-9 GAD-7 IES-R	8 5 5 26	29 %	63 %	8 %	82,7 %, 1293	699 (44,7)	792 (50,7)		585 (37,4)		564 (36,1)		ASD : 3 Depression : 4 Anxiety : 4 Sleep disorder : 4
Zhou et al., 2020	China February	1931	N-A	PSQI	7	16,40 %	83,60 %		85,4 %, 1843						355 (18,4)		4
Zhu et al., 2020	China February	165	N-A	SAS SDS	50 50	47,90 %	52,10 %		83 %, 137	33 (20)	73 (44,2)						3
Zhu, Xu et al., 2020	China February	5062	77,10 %	PHQ-9 GAD-7 IES-R	10 8 33	19,80 %	67,50 %	12,70 %	85 %, 4304	1218 (24,1)	681(13,5)	1509 (29,8)					5

Abreviations : No : number; PTSD : Post Traumatic Stress Disorder ; ASD : Acute Stress Syndrom ; N-A : non applicable ; AIS : Athens Insomnia Scale; SCL-90-R : Symptom Check List-90-revised; GHQ : General Health Questionnaire; ProQOl : Professional Quality of Life Scale; SAS : Statistical Anxiety Scale ; SDS : Statistical Depression Scale ; DASS : Depression Anxiety Stress Scale ; PHQ : Patient Health Questionnaire ; GAD : General Anxiety Disorder ; ISI : Insomnia Severity Index ; IES : Impact of Event Revised; IES-R : Impact of Event Scale Revised ; PCL-C : PTSD Checklist-Civilian ; CES-D : Center for Epidemiologic Studies Depressions Scale ; PCL : PTSD Checklist ; HADS : Hospital Anxiety and Depression Scale ; PC-PTSD : 4-item Primary Care PTSD screen ; BDI : Beck Depression Inventory ; MBI : Maslach Burnout Inventory ; EE : emotional exhaustion; DP : depersonalization; PSQI : Pittsburgh Sleep Quality Index ; PSS : Perceived Stress Scale ; STAI Y1 : State-Trait Anxiety Inventory-Form Y1 ; BDI-II : Beck Depression Inventory ; SASRQ : Stanford Acute Stress Reaction Questionnaire ; HADS : Hospital Anxiety and Depression Scale ; CPSS : Chines Perceived Stress Scale ; HAMA : Hamilton Anxiety Rating Scale; HAMD : Hamilton Depression Rating Scale.

2A. Anxiety



2B. Depression and depressive symptoms

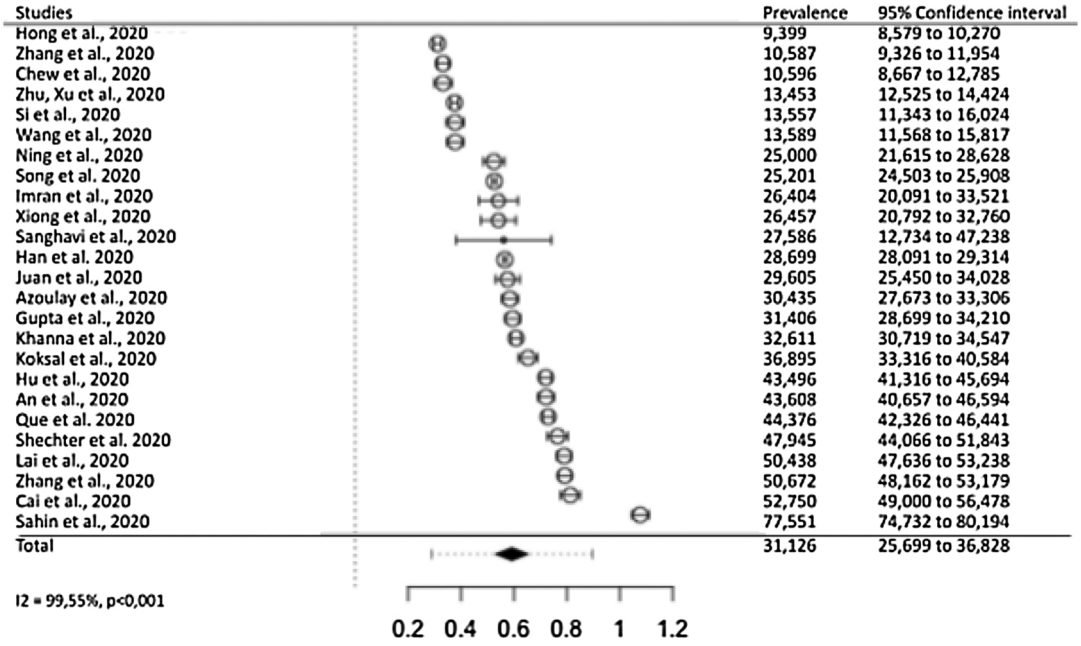


Fig. 2. A. Forest plots of the prevalence of symptoms of anxiety in healthcare workers during the COVID-19 pandemic.
The figure shows the results of the meta-analysis of the studies using random-effect models after Freeman-Tukey double arcsine transformation. Error bars represent the 95% confidence intervals.
B. Forest plots of the prevalence of symptoms of depression in healthcare workers during the COVID-19 pandemic.
The figure shows the results of the meta-analysis of the studies using random-effect models after Freeman-Tukey double arcsine transformation. Error bars represent the 95% confidence intervals
C. Forest plots of the prevalence of trauma-related symptoms in healthcare workers during the COVID-19 pandemic.
The figure shows the results of the meta-analysis of the studies using random-effect models after Freeman-Tukey double arcsine transformation. Error bars represent the 95% confidence intervals
D. Forest plots of the prevalence of symptoms of sleep disorders in healthcare workers during the COVID-19 pandemic.
The figure shows the results of the meta-analysis of the studies using random-effect models after Freeman-Tukey double arcsine transformation. Error bars represent the 95% confidence intervals.

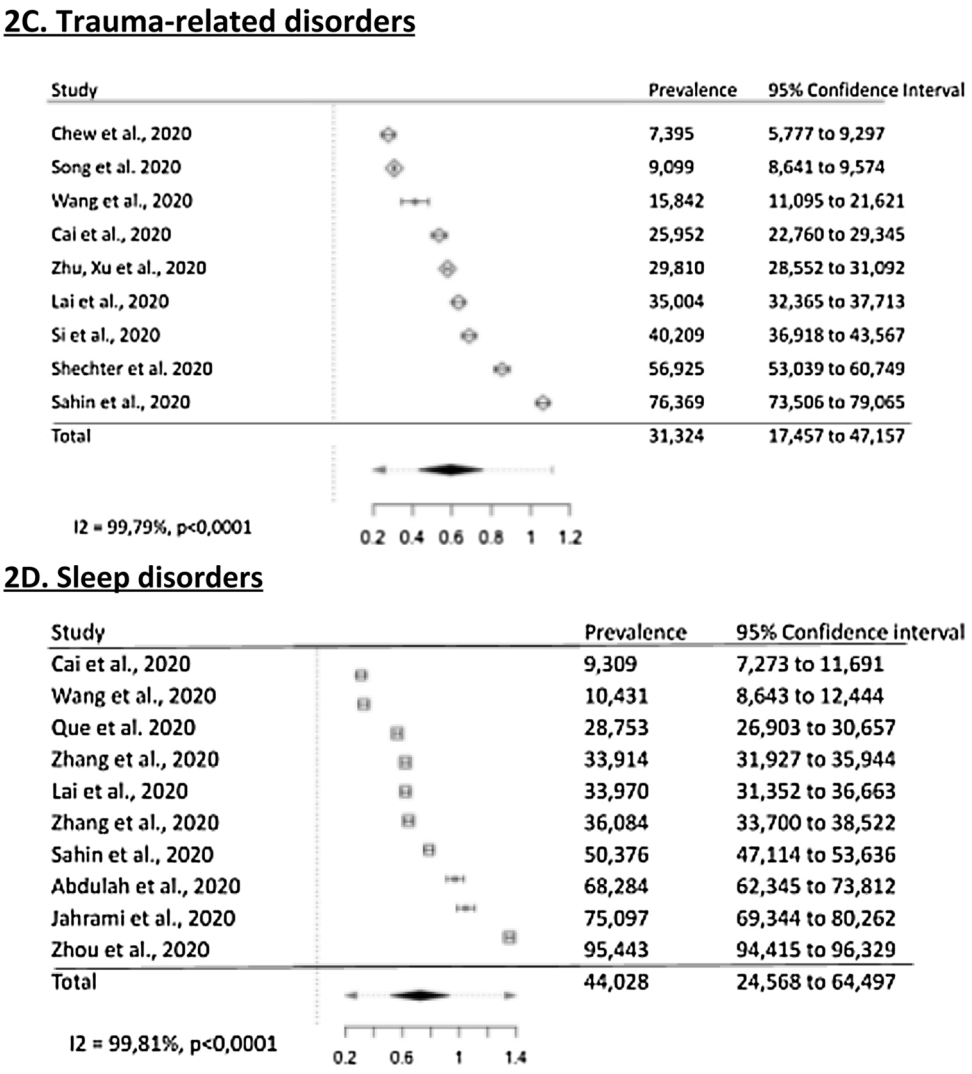


Fig. 2. (*continued*).

scales, mostly the Insomnia Severity Index (ISI), using different cut-offs, but the use of this scale was not identified as a moderator in the meta-regression. Subgroup analyses and metagressions identified two moderators: the female proportion ($p < 0.001$, associated with fewer sleep disorders), and the location (China studies being associated with lower prevalence). Nurse proportion, location, scale, and sample size did not explain high heterogeneity (supplementary materials).

3.7. Effect of time

For anxiety, depression, trauma, and sleep disorders, we calculated the time effect on the prevalence of each outcome, including all studies (quality $\geq$ 4/5) or only studies in China (to limit the effect of location). The results suggested increased sleep disorders throughout time (22,8% (95 % IC, 13,9–31,7) for january-february period versus 568% (95 % IC, 38,4–75,2) for march-may). No significant result was observed for other outcomes (supplementary materials). Overall, due to the scarcity of data, we could not conclude on any time effect on these outcomes among healthcare workers.

3.8. Assessment of psychiatric comorbidities

Three studies reported the ratio of comorbidity among these four psychiatric outcomes (anxiety, depression, trauma-related, and sleep disorders), using validated scales (within studies quality $\geq$ 4/5). Zhang et al. (Zhang et al., 2020a), find out that 26,2% had both insomnia (assessed with the ISI scale) and moderate to severe symptoms of acute stress (IES-R), 14,3 % had both insomnia and moderate to severe symptoms of depression (PHQ-9) and 10,8 % had both insomnia and moderate to severe symptoms of anxiety (GAD-7). Koksal et al. (Koksal et al., 2020), report that 34,0 % had both depression (HADS) and anxiety (HADS). Zhu, Xu et al. (Zhu, Xu et al. 2020), report that 20,3 % cumulated at least two outcomes: 7,5 % had both acute stress (IES-R) and anxiety (GAD-7), 1,5 % had both acute stress and depression (PSQ-9), 0, 9 % had both anxiety and depression and 10,4 % had acute stress, depression, and anxiety.

4. Discussion

4.1. Main findings

This systematic review and meta-analysis reports a high prevalence of anxiety, depression, trauma-related, and sleep disorders among caregivers in practice during the COVID-19 pandemic. Consequently, there is a major concern for the mental health of caregivers during the COVID-19 pandemic, as well as in potential future health crises.

During the MERS and SARS epidemics, a high rate of severe emotional distress and psychiatric symptoms among caregivers was also found, but studies were sporadic and do not allow any comparison to our results (Lee et al., 2018; Wu et al., 2009). Earlier reviews and

meta-analyses of HCWs' mental health during the COVID-19 pandemic reported high levels of anxiety (23.2 % (95 % CI, 17.8–29.1) (Pappa et al., 2020); 26 % (95 % CI, 18 %–34 %) (Luo et al., 2020) and depression (22.8 % (95 % CI, 15.1–31.5) (Pappa et al., 2020); 25 % (95 %CI, 19 %–32 %)(Krishnamoorthy et al., 2020)). These results, similar to ours, support the external validity of our study. Given the significant and steady increase in the number of publications since these papers, our review provides updated (versus researches until April in previous papers) and exhaustive data on this topic. The variation in prevalence estimation may be due to various factors including time-effect of the pandemic on the exhaustion of HCWs, and accumulation of adverse experiences.

In the general population, some meta-analyses also found similar prevalences of anxiety (31.9 % (95 % CI, 27.5–36.7)), depression (33.7 % (95 % IC, 27.5–40.6)), post-traumatic stress symptoms (23.9 % (95 % CI, 14.01–33.76), and sleep problems (32.3 % (95 % CI, 25.3–40.2) (Cooke et al., 2020; Salari et al., 2020a; Jahrami et al., 2020)

Post-traumatic stress and acute stress among HCWs may be due to the high amounts of brutal and unexpectable deaths they are exposed to. Experiencing repeated or extreme exposure to aversive details of traumatic events are potentially traumatic (American Psychiatric Association, 2013). In the emergency context of the COVID-19 pandemic, healthcare workers are exposed to potentially traumatic or stress factors: unpredictability of daily caseloads, having to frequently manage patients and their families' expectations in unexpected situations, the making-decision burden, high daily fatality rates, and constant updates of hospital procedures (Carmassi et al., 2020; WJEM, 2020.; Fjeldheim et al., 2014). Lack of social support is also an important adverse factor for HCWs' mental health enhanced by quarantine, perceived stigmatization, and fear of contaminating relatives (Carmassi et al., 2020; Pappa et al., 2020; Serrano-Ripoll et al., 2020).

Sleep problems may be associated with other disorders, such as PTSD, depression, anxiety in a bidirectional relationship (Salari et al., 2020b; Sanghera et al., 2020; Geoffroy et al., 2020b). Two factors may contribute to sleep problems among HCWs: the high workload (including night work, which modifies circadian rhythms) and stress-induced sleep problems (Lucchini et al., 2020; Salari et al., 2020b).

4.2. Implications for public health

Mental health problems experienced by HCWs decrease productivity (Kim et al., 2018). Moreover, some studies have found a reduced quality of care when the psychological health of HCWs is impaired (Tawfik et al., 2019; Pereira-Lima et al., 2019), highlighting the potential impact of non-addressing this issue. The frequent occurrence of psychiatric symptoms and psychological suffering among HCWs during this pandemic should trigger measures to address the HCWs ongoing suffering, as they may have specific work-related stress factors. High work pressure and workload, uncertainty about a poorly known and deadly disease, dehumanized healthcare working conditions in protective personal equipment, shorter time for social interactions with patients, numerous deaths, and family visit bans, are examples of factors that may specifically contribute to the psychological suffering of HCWs (Guessoum et al., 2020; Mallet et al., 2020b).

In these unique situations, HCWs develop coping behaviors, such as physical exercise or talk therapy (Shechter et al., 2020). HCWs may experience positive feelings such as an increased sense of meaning (Shechter et al., 2020). However, healthcare managers need to take steps to protect the mental well-being of staff (Greenberg et al., 2020). Since the beginning of the pandemic, China set up online and telephone consultations without time restrictions (Zhang et al., 2020b) and information and prevention materials for caregivers (Bao et al., 2020), which was quickly followed by other countries (D'Agostino et al., 2020). In France, some university hospitals developed specific hotlines and programs for psychological support of HCWs during the pandemic (relaxation, empathetic support, soothing and low-impact physical activities, assistance of mental health professionals) (Lefèvre et al., 2020; Geoffroy et al., 2020a). In the UK, a team developed a digital learning and support package on psychological well-being (Blake et al., 2020). Such interventions need to be evaluated (Viswanathan et al., 2020).

4.3. Implications for research

This study presents several limitations. The reviewed studies have been conducted in real-world conditions, in the present context of global pandemic. In such a context of emergency, some studies had weak methods and could not be included in the final meta-analysis, in order to decrease clinical and methodological heterogeneity. The heterogeneity of methods in the different studies makes comparisons difficult (assessment scales, various thresholds). In addition, the study populations varied. For example, some studies included nurses exclusively; others included administrative staff and technicians. We tried to overcome these limitations by conducting subgroup analyses and meta-regressions and thus, examining potential sources of heterogeneity (female or nurse proportion, location, scale, sample size). Homogenizing future studies 'methods would allow better comparability across studies and countries. Moreover, most studies were cross-sectional. There is a need for longitudinal studies. Longitudinal studies are necessary to understand the time effect on these psychiatric outcomes. Indeed, there are limits in estimating the time effect by comparing different cross-sectional studies in different locations. Most studies were conducted with auto questionnaires, without clinical diagnostic confirmation. However, all the included studies have used validated screening tools. Third, the small number of studies included in some of the subgroups may have biased some of the subgroup analysis results (e.g acute stress). Fourth, most studies assessed large countries (US, China…). Consequently, although we performed metaregression according to large location, the results may not be generalizable to HCWs in other countries (and the location was identified as a moderator of the estimated prevalence of sleep disorders). Finally, no evidence of publication bias was found with the Egger test but the exclusion of grey literature and unpublished data may have introduced selection bias to this analysis.

Few studies reported the prevalence of comorbidity of these outcomes among healthcare workers, despite being clinically pertinent data. Reporting comorbidity of psychiatric outcomes would be indicated in all future studies. Indeed, quality of life is significantly impaired with increasing comorbidity (Watson et al., 2011).

As a supplementary concern regarding HCWs' health, focusing on substance abuse and suicidal ideations would be relevant. There are serious concerns regarding substance abuse in the general population during the COVID-19 pandemic (Mallet et al., 2020a).

4.4. Conclusion

This review and meta-analysis provides a relevant picture of the mental health status of HCWs across the world during the COVID-19 pandemic: they endure high levels of psychiatric symptoms, including anxiety, depression, acute stress, post-traumatic stress, and sleep disorders. For HCWs' wellbeing and the quality of care during the pandemic, targeted prevention and psychological support should be provided to this population during such situations.

Financial support

This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

Contributions

SBG designed the study. Two authors SBG and MM screened the titles and abstracts of the studies based on the inclusion and exclusion criteria.

They also collected the full texts, evaluated the eligibility of the studies for final inclusion, assessed the quality of the study. SBG drafted the manuscript. JM commented on the review, performed the meta-analysis and drafted the manuscript. CD suggested improvements, reviewed and drafted the manuscript. MRM supervised the whole research and drafted the manuscript. All authors analyzed/interpreted the data and approved the final version of the manuscript.

Availability of data and materials

The data analyzed during this study are included in this article.

Declaration of Competing Interest

All authors declare none.

Acknowledgments

Not applicable.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.neubiorev.2021.03.024.

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