

What We Have Learned from Two Decades of Epidemics and Pandemics: A Systematic Review and Meta-Analysis of the Psychological Burden of Frontline Healthcare Workers

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Keywords

Severe acute respiratory syndrome · Coronavirus disease 2019 · Epidemic · Pandemic · Healthcare providers

Abstract

In light of the current coronavirus disease 2019 (COVID-19) pandemic and potential future infectious disease outbreaks, a comprehensive understanding of the negative effects of epidemics and pandemics on healthcare workers' mental health could inform appropriate support interventions. Thus, we aimed to synthesize and quantify the psychological and psychosomatic symptoms among frontline medical staff. We searched four databases up to March 19, 2020 and additional literature, with daily search alerts set up until October 26, 2020. Studies reporting psychological and/or psychosomatic symptoms of healthcare workers caring for patients with severe acute respiratory syndrome, H1N1, Ebola, Middle East respiratory syndrome, or COVID-19 were eligible for inclusion. Two reviewers independently conducted the search, study selection, quality appraisal, data extraction, and synthesis and involved a third reviewer in case of dis-

agreement. We used random effects modeling to estimate the overall prevalence rates of psychological/psychosomatic symptoms and the I^2 statistic. We included 86 studies, reporting data from 75,991 participants. Frontline staff showed a wide range of symptoms, including concern about transmitting the virus to the family (60.39%, 95% CI 42.53–76.96), perceived stress (56.77%, 95% CI 34.21–77.95), concerns about own health (45.97%, 95% CI 31.08–61.23), sleeping difficulties (39.88%, 95% CI 27.70–52.72), burnout (31.81%, 95% CI 13.32–53.89), symptoms of depression (25.72%, 95% CI 18.34–33.86), symptoms of anxiety (25.36%, 95% CI 17.90–33.64), symptoms of posttraumatic stress disorder (24.51%, 95% CI 18.16–31.46), mental health issues (23.11%, 95% CI 15.98–31.10), and symptoms of somatization (14.68%, 95% CI 10.67–19.18). We found consistent evidence for the pervasive and profound impact of large-scale outbreaks on the mental health of frontline healthcare workers. As the COVID-19 crisis continues to unfold, guaranteeing easy access to support structures for the entire healthcare workforce is vitally important.

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Introduction

In the last 20 years, climate change, environmental destruction, frequent zoonotic spillover, overpopulation, and poverty have contributed to an increasing occurrence of emerging and re-emerging infectious diseases [1–3]. Notable outbreaks have included the 2003 severe acute respiratory syndrome (SARS) epidemic [4], the 2009 H1N1 pandemic [5], the Middle East respiratory syndrome (MERS) epidemic first reported in 2012 [6], the 2014–2016 West Africa Ebola epidemic [7], and the current coronavirus disease 2019 (COVID-19) pandemic [8].

For public health, ensuring high standards of care during and after these emergencies is a top priority linked to numerous logistic, organizational, and clinical challenges. Healthcare workers play a key role at all levels of caregiving, but these large-scale outbreaks have shown that the enormous psychological burden of working under such stressful circumstances can severely affect their well-being and, consequently, work performance [9–13]. Although the strategic and ethical value of preserving and enhancing healthcare workers' well-being and resilience has been recognized [14–16], pursuing this goal during a global pandemic is challenging. Healthcare workers at the frontlines of COVID-19 care experience high levels of stress [17], face difficult ethical decisions, such as how to allocate limited ventilators [18–20], and are prone to developing psychological and psychosomatic symptoms [21, 22]. The psychological trauma has even led some healthcare providers to suicide [23, 24].

The COVID-19 pandemic cannot be compared to disasters like hurricanes or wildfires since it is not “confined in time and space” [25]. Indeed, more than 8 months after the World Health Organization declared COVID-19 a pandemic on March 11, 2020 [8], countries across Europe, Russia, and the United States are seeing a dramatic resurgence in infections [26–28]. Since healthcare institutions will have to deal with COVID-19 and its psychological consequences for many months to come, a thorough understanding of the negative effects of epidemics and pandemics on healthcare workers' mental health is needed to mitigate the traumatic impact and to develop appropriate support interventions.

In recent months, a few rapid reviews [29–32] have already investigated some of these aspects, but a systematic review and meta-analysis of the literature addressing the role of previous epidemics and pandemics has not been conducted.

In this study, we aimed to comprehensively synthesize and quantify the psychological and psychosomatic symptoms of healthcare providers on the frontline of past epidemics/pandemics (i.e., Ebola, H1N1, SARS, MERS) and the current pandemic (i.e., COVID-19).

Methods

The protocol of this study is registered in the International Prospective Register of Systematic Reviews (PROSPERO), registration number CRD42020175135.

Search and Selection Process

We systematically searched the electronic databases PubMed, Web of Science Core Collection, MEDLINE, and PsycINFO up to March 19, 2020, without restriction to publication date or language. The search strategy read as follows: (swine flu OR A/H1N1 OR 2009 H1N1 OR H1N1 OR [H1N1]pdm09 virus OR viral hemorrhagic fever OR Ebola OR Ebola virus disease OR Ebola hemorrhagic fever OR EVD OR coronavirus infection OR coronavirus disease OR COVID-19 OR 2019 novel coronavirus OR 2019-nCoV OR severe acute respiratory syndrome coronavirus 2 OR SARS-CoV-2 OR SARS-CoV OR SARS coronavirus OR severe acute respiratory syndrome OR SARS OR MERS-CoV OR Middle East respiratory syndrome OR MERS) AND (healthcare worker OR healthcare provider OR health professional OR health personnel OR nurse OR physician OR clinician) AND (emotion OR professional burnout OR mental health OR psychological impact OR psychosocial effect OR experience OR psychological response OR psychological symptom OR feeling OR psychosomatic symptom OR emotional distress) (see online suppl. File 1; for all online suppl. material, see www.karger.com/doi/10.1159/000513733).

To identify additional literature, we searched reference lists of reviews, general discussion papers, commentaries, and editorials and screened grey literature by using specific databases (i.e., Open Grey database, Grey Literature Project; see online suppl. File 2). Moreover, to identify newly published, potentially eligible articles, we set up automatic, daily e-mail search alerts for the database PubMed from March 20, 2020 to October 26, 2020.

Studies were considered eligible for inclusion if (1) original findings were reported, (2) participants were healthcare workers exposed to/taking care of patients infected with or suspected to have SARS, H1N1, Ebola, MERS, or COVID-19 and/or working in high-risk settings, such as emergency departments, infectious disease departments, fever clinics, radiology units, or intensive care units, (3) the psychological impact of these epidemics/pandemics on healthcare workers was reported quantitatively, and (4) they were published in English, Italian, or German (languages spoken by the authors). No restrictions on setting (inpatient or outpatient care), healthcare profession, age, sex, or other sociodemographic characteristics were applied. Editorials, general discussion papers, commentaries, letters, book chapters, single case studies, case series, qualitative studies, and all types of reviews were excluded.

Two reviewers (I.M.B. and F.M.) independently screened the titles and abstracts of the retrieved records using Rayyan, a systematic review web application [33]. The two reviewers retrieved and independently evaluated the full texts of all potentially eligible studies. In case of disagreement, they discussed the appropriate-

ness of inclusion/exclusion and involved a third reviewer (M.R.) to further assess it.

We recorded the search and selection process following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement by Moher et al. [34].

Quality Appraisal

Two appraisers (I.M.B. and M.R.) independently assessed the methodological quality of the included studies applying the standardized 8-item Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-Sectional Studies [35] or the 11-item Joanna Briggs Institute Critical Appraisal Checklist for Cohort Studies [36] for cross-sectional and longitudinal studies, respectively. Any potential disagreement was resolved by discussion and/or by involving a third appraiser (F.M.).

Main Outcomes

The main outcomes were the prevalence rates, the mean scores (standard deviations), and/or the median scores of psychological and psychosomatic symptoms (e.g., emotional distress, anxiety, depression) of healthcare workers on the frontline of epidemics/pandemics (i.e., SARS, H1N1, Ebola, MERS, COVID-19) at baseline, and, if available, at follow-up.

If available, potential differences in psychological and psychosomatic symptoms between frontline and non-frontline healthcare workers/general public and/or odds ratios and the respective 95% CI were described.

Data Extraction and Synthesis

Two reviewers (I.M.B. and M.R.) independently collected the study characteristics (e.g., authors, year, country, setting and population, sample size) as well as the outcome measures (i.e., psychological and psychosomatic symptoms) and the results of the selected studies. Microsoft Excel was used for data extraction, storage, and synthesis. Discrepancies between the reviewers were discussed and, if necessary, a third reviewer (F.M.) was involved.

We applied the following general rules for data extraction and synthesis:

(1) If primary studies assessed two or more groups of participants with different levels of exposure to the respective virus: (a) We only reported the data that were separately available for these groups. Data on mixed populations were not taken into account. (b) We extracted only the outcome measures (psychological and psychosomatic symptoms) for which data on frontline healthcare workers were available. Outcomes measures that were only administered to subsamples with low/no risk of exposure were not taken into account.

(2) We only reported data on psychological and psychosomatic symptoms separately for different professions (e.g., nurses, doctors) if numbers for the entire group of frontline healthcare workers were not provided.

(3) If primary studies reported the distribution of severity of symptoms (e.g., mild, moderate, severe) among frontline healthcare workers, we extracted only the data on moderate and severe symptoms.

(4) We only reported odds ratios or prevalence ratios if the strength of the association between exposure to the respective virus and psychological/psychosomatic outcome was described. Odds ratios or prevalence ratios measuring the association be-

tween other potential risk factors (e.g., sex, age) and psychological/psychosomatic outcomes were not extracted.

(5) If data on subscores of questionnaires were presented in the primary studies, we reported only the differences in the specific subscores between frontline and non-frontline groups, without mentioning means (standard deviations) and/or median scores.

Meta-Analyses

To account for potential heterogeneity across studies, we applied random effects modeling for all meta-analyses using Stata 16 [37, 38]. To calculate the overall prevalence of psychological and psychosomatic symptoms among frontline healthcare workers (95% CI), we pooled the individual prevalence rates of at least three primary studies at baseline using the “metaprop” command in Stata [38]. To do this, we grouped the variables of interest, extracted from the primary studies, which corresponded in terms of content and wording (see online suppl. File 3).

We investigated statistical heterogeneity by visually assessing forest plots and calculating I^2 statistics (0–40%: not important; 30–60%: moderate heterogeneity; 50–90%: substantial heterogeneity; 75–100%: considerable heterogeneity) [39].

Formal Narrative Synthesis

Additionally, we performed a formal narrative synthesis of the findings extracted from the primary studies, following, where applicable, the Synthesis without Meta-Analysis guidelines [40] to enhance transparency. We provide (1) a structured tabulation of study characteristics and statistically significant and nonsignificant results of the primary studies grouped by the type of epidemic/pandemic (i.e., SARS, H1N1, Ebola, MERS, COVID-19), (2) a structured tabulation of statistically significant differences in psychological and psychosomatic symptoms between frontline and non-frontline healthcare workers/general public, and (3) a synthesis of long-term mental outcomes in frontline healthcare workers as reported by the included longitudinal studies, presented as narrative text.

Results

Selection and Inclusion of Studies

We retrieved 1,640 records from the electronic databases (after removal of duplicates) and 355 from the additional searches. After screening of title and/or abstract, we assessed 417 full texts for eligibility, of which 331 were excluded for a variety of reasons (e.g., mismatch with inclusion criteria, mixed population, wrong focus), and 86 [41–126] were included that met all inclusion criteria (see online suppl. Files 4 and 5).

Quality Appraisal

All 79 cross-sectional studies [41, 42, 44–50, 52–54, 56–63, 65–74, 77–122, 124–126] met four or more quality criteria, with 38 studies meeting all eight [41, 44, 48, 50, 54, 57, 59, 60, 63, 65–67, 74, 78–80, 83, 87–89, 91, 93, 96, 99–102, 104, 105, 107–109, 113, 119–121, 124, 126].

Most of the studies clearly defined criteria for inclusion in the sample, described study subjects and setting in detail, measured the exposure in a valid, reliable way, and used objective standard criteria for measurement of condition and appropriate statistical analysis. However, several studies had shortcomings regarding the identification of confounding factors [45, 47, 62, 112, 116, 122], strategies to deal with confounders [42, 45, 47, 53, 62, 63, 90, 92, 111, 112, 116, 117, 122], and the measurement of outcomes in a valid and reliable way [42, 45, 46, 62, 73, 90, 106].

The seven studies [43, 51, 55, 64, 75, 76, 123] with a longitudinal design showed satisfactory quality, meeting seven or more criteria. However, no study met all eleven criteria. In most of the studies, the two groups were similar and recruited from the same population, exposures were measured similarly, exposures and outcomes were assessed in a valid and reliable way, and appropriate statistical analysis was used. However, all articles lacked clarity regarding whether or not participants were free of psychological and psychosomatic symptoms at the start of the study or at the moment of exposure. Some studies also showed shortcomings in dealing with incomplete follow-up [51, 64] and confounding factors [43, 64]. Appraisers' judgments of each study are presented in detail in online supplementary Files 6 and 7, respectively.

Characteristics of Primary Studies

The 86 included primary studies, published between 2004 and 2020 and all written in English, reported sample sizes ranging from 18 [58] to 10,178 [87], reaching a total number of 75,991 participants (referring to sample sizes at baseline). Online supplementary Files 8–12 give a detailed overview of the study characteristics, the outcome measures, and the main findings of the primary studies (statistically significant findings highlighted in bold).

Seventeen articles focused on the 2003 SARS epidemic [41–57], 61 on the current COVID-19 pandemic [66–126], four on the MERS epidemic of 2015 and 2016 [62–65], and two each on the 2014–2016 West Africa Ebola epidemic [60, 61] and on the 2009 H1N1 pandemic [58, 59].

The included SARS studies were performed in Taiwan ($n = 5$) [43, 46, 47, 49, 55], Hong Kong ($n = 5$) [42, 44, 51, 53, 56], Singapore ($n = 2$) [41, 52], China ($n = 2$) [48, 57], and Canada ($n = 3$) [45, 50, 54], countries that represented SARS hotspots. The primary studies on H1N1 were published in New Zealand [58] and Japan [59], the studies on Ebola in Germany [60] and Liberia [61], and the articles on MERS covered the outbreaks in South Korea [63–

65] and Saudi Arabia [62]. The majority of the studies on COVID-19 were published in China ($n = 32$) [67, 73–76, 84–86, 88, 91–93, 95–97, 99, 101, 102, 107, 110, 113, 114, 116–119, 121–126] and Italy ($n = 6$) [71, 72, 78, 79, 83, 103]. Other studies were conducted in the United States [68, 89, 106], Iran [100, 105, 112], Turkey [80, 104, 111], Germany [90, 120], Pakistan [66, 87], Poland [115], India [108], Egypt [81], Brazil [77], France [70], Spain [94], Saudi Arabia [98], and Singapore [109]. Two studies recruited participants from different countries [69, 82]. Several articles (e.g., Honey and Wang [58], Elshami et al. [82], An et al. [67]) resulted from international collaboration.

Most of the 86 studies applying a cross-sectional study design assessed the psychological impact at a single point in time. Namely, 29 studies performed data collection in earlier phases of the outbreak in the respective country [64–66, 77, 79–81, 84–89, 91, 96, 98, 100, 103, 105, 106, 108, 109, 111–115, 120, 126], nine during the outbreak [69, 73, 82, 95, 97, 101, 110, 118, 125], 32 in later phases [41, 42, 44–46, 50, 53, 54, 56, 59–61, 67, 68, 70–72, 74, 78, 83, 90, 92–94, 102, 104, 107, 117, 119, 121, 122, 124], and eight after the end of the outbreak [47–49, 52, 57, 58, 63, 99]. Another seven studies focusing on SARS [43, 51, 55], MERS [64], and COVID-19 [75, 76, 123] also included follow-up data.

More than two-thirds of the studies ($n = 60$) [41–45, 47, 48, 50, 51, 53–55, 57, 59, 60, 62–68, 71, 72, 74, 75, 78–80, 83, 87–93, 99–105, 107–109, 111–117, 119–122, 124, 126] compared psychological and psychosomatic symptoms between frontline staff and other groups of participants (e.g., non-frontline healthcare providers, general public).

Prevalence of Psychological and Psychosomatic Symptoms

Meta-Analyses. We computed the overall prevalence rates for ten symptoms experienced by healthcare providers working at the frontline of epidemics/pandemics, namely concern about transmitting the virus to the family (60.39%, 95% CI 42.53–76.96), perceived stress (56.77%, 95% CI 34.21–77.95), concerns about own health (45.97%, 95% CI 31.08–61.23), sleeping difficulties/insomnia (39.88%, 95% CI 27.70–52.72), burnout (31.81%, 95% CI 13.32–53.89), symptoms of depression (25.72%, 95% CI 18.34–33.86), symptoms of anxiety (25.36%, 95% CI 17.90–33.64), symptoms of posttraumatic stress disorder (PTSD) (24.51%, 95% CI 18.16–31.46), mental health issues (23.11%, 95% CI 15.98–31.10), and symptoms of somatization (14.68%, 95% CI

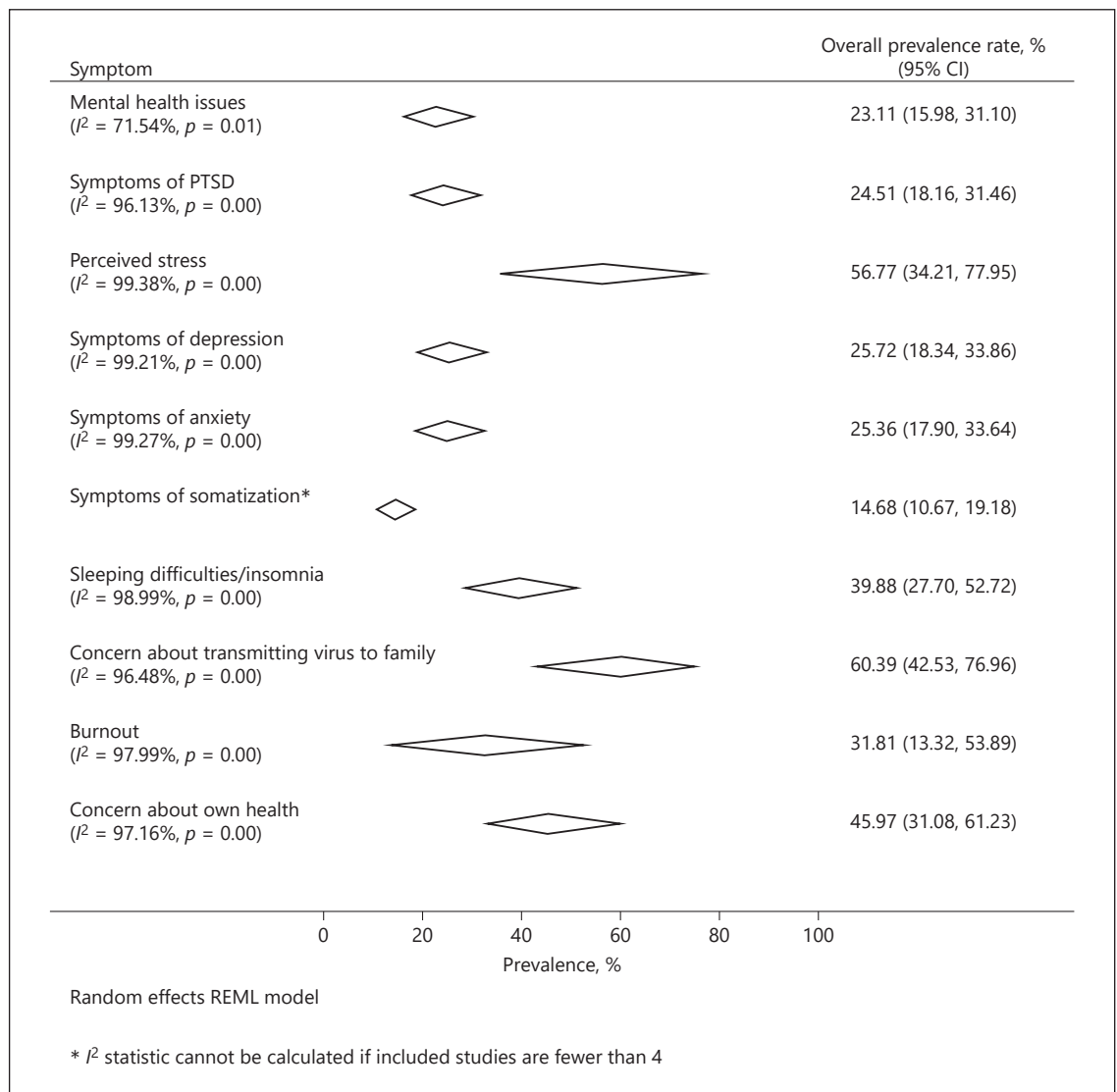


Fig. 1. Overall prevalence rates of the psychological and psychosomatic symptoms among frontline healthcare staff. PTSD, posttraumatic stress disorder.

10.67–19.18) (Fig. 1). I^2 estimates ranged from 71.54 to 99.38%, indicating substantial to considerable heterogeneity across studies [39]. A table subdividing the studies included in the meta-analysis by epidemic/pandemic as well as all individual forest plots can be found in online supplementary Files 13 and 14, respectively.

Additional Psychological Symptoms (Unpooled Prevalence Rates). Due to insufficient data from the primary studies and/or too heterogeneous variables of interest, we were not able to pool all the extracted prevalence rates. Namely, prevalence rates of suicidal ideation (12.0% [74];

13.0% [124]), fatigue (70.3% [51]; 71.0% [44]), fear of social contact (41.7% [51]; 46.0% [44]), and worry related to uncertainty about the future course of the outbreak among frontline healthcare workers (45% [117]; 92.3% [46]) were each reported twice. Lastly, for other psychological conditions and symptoms, such as allostatic load (15.8% [99]), low quality of life (44.44% [108]), poor subjective well-being (71.42% [78]), sadness (49.6% [70]), obsessive-compulsive symptoms (7.3% [88]), and feeling of isolation (4.3% [65]), prevalence rates were only recorded once.

Comparison between Frontline and Non-Frontline Healthcare Workers/the General Public

As mentioned above, 61 primary studies compared different groups and/or subgroups, i.e., healthcare staff working in high-risk settings (i.e., contact with/caring for patients diagnosed with the disease, contact with/caring for patients under investigation) and staff working in low-risk settings or in nonclinical areas (i.e., not providing direct care/working in other clinical departments, working in nonclinical areas). Few studies used additional subgroups, such as nonmedical workers or the general public [92, 99, 112, 124]. A structured synthesis of statistically significant group differences in psychological and psychosomatic symptoms is provided in online supplementary File 15.

A variety of psychological (e.g., depression, anxiety, PTSD) and psychosomatic symptoms (e.g., insomnia, bodily pain) were compared between groups. Whereas all studies on SARS, H1N1, Ebola, and MERS demonstrated worse mental health and lower psychological well-being among frontline healthcare providers versus non-frontline groups, the findings of the recent COVID-19 studies are less consistent. Indeed, three studies [92, 109, 117] found higher scores of trauma as well as higher prevalence of burnout and anxiety among non-frontline groups versus frontline groups. However, as it can be seen in online supplementary Files 8–12, not all group comparisons revealed significant differences between frontline and non-frontline staff.

Trends in the Psychological Distress of Frontline Healthcare Workers over Time

As noted above, seven studies also conducted follow-ups. While five studies [43, 55, 64, 75, 76] revealed a general trend towards improvement of frontline healthcare workers' emotional well-being at follow-up, two studies [51, 123] showed a worsening of psychological symptoms in this population.

Notably, Lee et al. [64], examining hospital workers involved in MERS-related tasks, observed lower but still elevated subjective distress levels at the second time point. Similarly, Chen et al. [43], assessing healthcare workers belonging to a SARS task force, found a significant improvement in their general health status ($p < 0.05$). Likewise, Su et al. [55], investigating nurses working in SARS units (i.e., general SARS unit, SARS intensive care unit) found an improvement of depressive and PTSD symptoms over time ($p < 0.001$) as well as anxiety, but noted that the sleep quality of those working in the regular SARS units was still impaired at the end of the study ($p < 0.05$).

Chen et al. [43] and Cai et al. [75], assessing healthcare providers at the COVID-19 frontline, found a significant decrease in mental health issues ($p < 0.05$) and a significantly lower risk for depression, anxiety, and PTSD symptoms ($p < 0.01$) at follow-up.

In contrast, McAlonan et al. [51] reported an increase in the stress levels of the SARS frontline group 1 year later ($p < 0.05$), and Zhao et al. [123] documented a worsening of sleep quality among COVID-19 frontline workers at 1-month follow-up ($p < 0.001$).

Discussion

This appears to be the first systematic review and meta-analysis to comprehensively synthesize and quantify the wide range of psychological and psychosomatic symptoms among healthcare workers delivering care in different global infectious disease outbreaks. The focus on past epidemics as well as the current global pandemic allowed us to draw a broad picture of the psychological trauma experienced by frontline medical workers in different countries.

Our results suggest that a substantial number of frontline healthcare workers suffer greatly from a variety of psychological and psychosomatic problems ranging from sleep disturbance, somatization symptoms, anxiety, and perceived stress to depression, PTSD, and burnout. These symptoms are commonly triggered by stressful, traumatic events and can have far-reaching consequences for healthcare providers' physical and psychological well-being, relationships to others, and performance at work [127–129].

Further, in the studies that assessed psychological reactions to uncertainty or perceived risk of infection (i.e., worry about own health, concern about spreading the virus to the family, fear of social contact, worry related to uncertainty regarding the future course of the outbreak), a great proportion of healthcare workers expressed concerns and worries. This corroborates the idea from previous research [130] that a core element underlying the onset of global psychological distress could be the perceived lack of control of one's own professional and personal life. However, considering the large number of frontline healthcare workers who were infected with SARS [131], H1N1 [132], MERS [133], Ebola [134], and COVID-19 [135], the fears of infection were well-founded.

Given the risk of infection and the numerous other stressors faced by frontline workers, it is surprising that three of the included studies on COVID-19 [92, 109, 117]

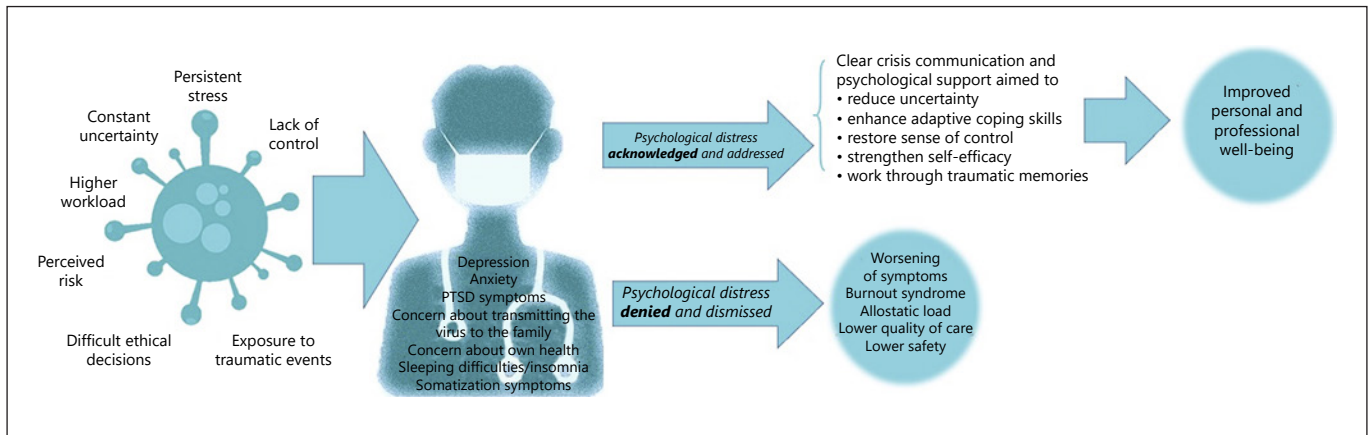


Fig. 2. Acknowledging and addressing healthcare workers’ psychological distress during the current pandemic. PTSD, posttraumatic stress disorder.

reported higher levels of traumatization, symptoms of PTSD, burnout, and anxiety for non-frontline than for frontline groups. Possible explanations for this unexpected finding may be the greater availability of psychological support for frontline staff, more up-to-date information on the outbreak, policies and infection control measures, and use of personal protective equipment in this group [92, 109, 117]. However, caution is due here because the comparison group in one of the three studies [92], which included also the general public, was poorly defined. It is possible that the participants in the comparison group differed from the specialized and highly educated medical staff with regard to educational and socioeconomic background. The fact that lower educational level and socioeconomic status are associated with worse physical and mental health [136, 137] might be another explanation for why these participants fared worse psychologically than those on the frontlines. Moreover, it is important to bear in mind that the general public may have faced a greater risk of becoming unemployed during the pandemic than the hospital staff [99], thus possibly adding to the psychological distress.

Unfortunately, it seems inevitable that emerging and re-emerging infectious diseases will be a recurring threat to healthcare systems in the future [1]. To maintain high standards of care, it is essential to prepare healthcare staff for future similar events, as also suggested by one of the included publications [109]. Tan et al. [109] reported a much lower prevalence of PTSD among healthcare workers during the COVID-19 pandemic than Chan and Huak [41] and Phua et al. [52], who examined healthcare worker in the same city (Singapore) during the SARS outbreak

in 2003. According to Tan et al. [109], this observed difference could be explained in part by better mental preparedness among healthcare staff and the adoption of rigid infection control measures after SARS. However, considering the heterogeneity among these studies, this finding must be interpreted with caution. For instance, while the two SARS studies [41, 52] collected data in later phases of the SARS outbreak in Singapore, Tan et al. [109] recorded the data in earlier phases of the COVID-19 outbreak in Singapore.

Lastly, we sought to explore whether the psychological distress following an epidemic/pandemic tends to improve or worsen over time. Although five of the seven follow-up studies seemed to suggest an overall improvement, only one [75] mentioned that psychological support interventions were available to the staff. The other studies did not report whether and what kind of psychological support was offered. Thus, no firm conclusion can be drawn from the findings of this small subsample, and future studies should examine this aspect further. In any case, previous research has found that high levels of stress, feeling of lack of control, anxiety, depression, insomnia – all symptoms with a high overall prevalence rate in our sample – can represent, if not properly acknowledged and managed, precursors to allostatic overload as well as burnout syndrome [18, 138–141].

Recommendations for Healthcare Organizations during the COVID-19 Pandemic

To prevent an increase in psychological and psychosomatic symptoms and burnout among the healthcare workforce on the frontlines of COVID-19, we urge health-

care organizations to acknowledge and address healthcare providers' psychological distress (Fig. 2). Clear, transparent crisis communication by leadership and supervisors offering accurate, updated information [63, 80, 117, 142, 143] and provision of psychological support, which gives healthcare workers the chance to work through traumatic memories, may help to reduce uncertainty, restore a sense of control, and strengthen self-efficacy. This may ultimately lead to improved personal and professional well-being and positive functioning, and thus also to better quality of care and patient safety [129, 144, 145].

Psychological support should be made available not only to healthcare workers directly caring for patients with COVID-19, but also to those who are exposed to the virus in other ways (e.g., laboratory, environmental services, laundry service) as well as to medical staff working in other departments. We recommend that healthcare institutions implement or expand already existing peer support programs to ensure easy and timely access to psychological first aid and emotional support and, if necessary, referral to mental health professionals.

As emphasized by Theorell [18] and Greenberg et al. [146], healthcare organizations should also actively monitor healthcare workers in the aftermath of the initial crisis to identify those struggling with the long-term effects of the traumatic experience and in need of psychological help. This is especially important given that after disasters, communities and individuals usually go through different phases in moods [142, 147]. With many countries facing again drastic surges in COVID-19 infections, hospitalizations, and deaths and with the future course of the pandemic being uncertain, the current "disillusionment phase" can be described as particularly lengthy and discouraging for healthcare workers. Enhancing healthcare providers' psychological resilience by acknowledging the experienced distress and by fostering adaptive coping skills [18, 129, 148] can not only help them to face acute critical situations in the care for COVID-19 patients, such as difficult ethical decisions, adverse events, and breaking bad news to patients [149], but also to better deal with the persistent stress in the coming months, which, in turn, may lower the risk of high allostatic load and burnout [18, 140, 141].

Aside from actions directly at the provider level, like mental health prevention and support, protecting healthcare workers' psychological and physical well-being also includes actions taken at the organizational and structural level [150]. As pointed out by Theorell [18], healthcare managers should ensure flexible work schedules,

which would allow healthcare providers to rest between tiring shifts and to maintain a healthy sleep hygiene, arrange for support systems for healthcare workers' families, and involve healthcare workers in decision processes to enhance their sense of self-efficacy and belonging.

Finally, to reduce human and financial losses [1] in potential future infectious disease outbreaks, healthcare institutions should plan ahead by creating infection control teams [42] and developing strategies to optimize the supply of personal protective equipment [151].

Limitations

This study should be interpreted in light of certain limitations. First, the observational design of the primary studies did not allow drawing causal conclusions between exposure and outcomes. Second, the majority of the included studies recruited participants on a voluntary basis, had a cross-sectional study design, and used self-report questionnaires. Therefore, it is possible that certain biases (e.g., self-selection bias, social desirability bias) might have influenced the results and in turn also the findings of our study. Moreover, in those studies that retrospectively assessed frontline healthcare workers' well-being, recall bias may have been introduced. Third, the included studies were heterogeneous in many regards, such as settings, populations, applied questionnaires, and cutoff scores, as shown by the high I^2 statistics and the wide CI around overall estimates of prevalence. The primary studies also differed in the timing of baseline data collection. While some studies administered the surveys in the beginning of the respective outbreak, others collected data in later phases. For instance, as noted by Cai et al. [73], articles assessing healthcare workers' mental health in the beginning of an outbreak may underestimate its negative emotional impact as psychological stress often increases over time. Similarly, exhaustion and depression may take longer to develop. On the contrary, it might also be possible that some healthcare providers feel more affected and anxious in the beginning of an epidemic/pandemic, when knowledge of the newly emerged disease is scarce and clinical work processes adapted to the new situation have not yet been optimized. Fourth, in several studies, the comparison groups including the general public and/or staff working in nonclinical areas were poorly defined with regard to socioeconomic and educational background as well as medical history. This might have confounded our findings to a certain degree. Fifth, considering the unprecedented surge in publications focusing on COVID-19 [152], we may have missed important papers published after we stopped screening the au-

omatic daily search alerts on PubMed on October 26, 2020. Finally, data extraction and formal narrative synthesis can be prone to subjective assessment and interpretation. Aiming to overcome this limitation, we followed, where applicable, the Synthesis without Meta-Analysis guidelines [40] and established a set of strict rules for extracting and synthesizing the data, which was then applied by two independent reviewers.

Directions for Future Research

Further research should be undertaken to prospectively assess frontline providers' mental health during different phases of the ongoing pandemic, such as, e.g., the current second waves of COVID-19 infections sweeping Europe as well as the long-term effects of this crisis.

The trajectory of healthcare workers' emotional well-being still needs to be defined. More data are needed to determine whether healthcare workers experience an improvement of symptoms at follow-up or further impairment, as suggested by the phases of disaster model [147]. Future longitudinal studies need to take into account whether participants received psychological support during or after the pandemic. Other potentially contributing factors, such as healthcare workers' history of mental disorders or the overall length of the outbreak, should also be considered.

Moreover, further investigation is needed of the differences and similarities between frontline and non-frontline groups, taking into account potential confounders such as educational, employment, and health status. Lastly, international collaboration should be strongly promoted in future work as a critical part of a global pandemic response in order to share expertise, good practice, and clinical guidelines as well as disseminate knowledge [153].

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Conclusions

Our systematic review and meta-analysis provides a comprehensive picture of the psychological burden on frontline health workers of epidemics and the current pandemic spanning two decades (i.e., SARS, H1N1, Ebola, MERS, and COVID-19). Including data from 75,991 participants, we found consistent evidence for the pervasive and profound impact of these infectious disease outbreaks on healthcare workers' mental health. As the current COVID-19 crisis continues to unfold, it will be vitally important to guarantee easy access for the entire healthcare workforce to psychological support structures so they can cope better with acute critical situations as well as prolonged periods of stress.

Conflict of Interest Statement

None of the authors have any conflicts of interest to declare.

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Author Contributions

All authors jointly designed the study. I.M. Busch, F. Moretti, and M. Rimondini were involved in the search and selection process, the quality assessment, the data extraction, and the formal narrative synthesis. M. Mazzi conducted the meta-analysis. I.M. Busch and M. Rimondini drafted the initial manuscript, which was then revised by F. Moretti, A.W. Wu, and M. Mazzi. All authors approved the final manuscript.

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