



Prevalence of posttraumatic stress disorder after infectious disease pandemics in the twenty-first century, including COVID-19: a meta-analysis and systematic review

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Abstract

Pandemics have become more frequent and more complex during the twenty-first century. Posttraumatic stress disorder (PTSD) following pandemics is a significant public health concern. We sought to provide a reliable estimate of the worldwide prevalence of PTSD after large-scale pandemics as well as associated risk factors, by a systematic review and meta-analysis. We systematically searched the MedLine, Embase, PsycINFO, Web of Science, CNKI, WanFang, medRxiv, and bioRxiv databases to identify studies that were published from the inception up to August 23, 2020, and reported the prevalence of PTSD after pandemics including sudden acute respiratory syndrome (SARS), H1N1, Poliomyelitis, Ebola, Zika, Nipah, Middle Eastern respiratory syndrome coronavirus (MERS-CoV), H5N1, and coronavirus disease 2019 (COVID-19). A total of 88 studies were included in the analysis, with 77 having prevalence information and 70 having risk factors information. The overall pooled prevalence of post-pandemic PTSD across all populations was 22.6% (95% confidence interval (CI): 19.9–25.4%, I^2 : 99.7%). Healthcare workers had the highest prevalence of PTSD (26.9%; 95% CI: 20.3–33.6%), followed by infected cases (23.8%: 16.6–31.0%), and the general public (19.3%: 15.3–23.2%). However, the heterogeneity of study findings indicates that results should be interpreted cautiously. Risk factors including individual, family, and societal factors, pandemic-related factors, and specific factors in healthcare workers and patients for post-pandemic PTSD were summarized and discussed in this systematic review. Long-term monitoring and early interventions should be implemented to improve post-pandemic mental health and long-term recovery.

Introduction

The explosive spread of the coronavirus disease 2019 (COVID-19) outbreak around the world within a very short period of time once again brought public attention to infectious disease pandemics. Since 2000, with rapid changes and increases in urbanization and global travel, infectious disease pandemics have become more frequent and more complex, notable examples of which are Ebola, severe acute respiratory syndrome (SARS), Middle East respiratory syndrome coronavirus (MERS-CoV), Nipah, influenza A subtype H5N1, and Zika [1]. The SARS pandemic of 2003 was the first global public health emergency in the twenty-first century, which was followed shortly by the H5N1 outbreak of 2005–2006. Since then, the World Health Organization has declared another five Public Health Emergencies of International Concern: H1N1 influenza

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virus pandemic (2009), resurgence of wild poliovirus (2014), West Africa Ebola virus outbreak (2014), Zika virus outbreak (2018), and COVID-19 (2020) [2, 3]. Large-scale pandemics can significantly increase global morbidity and mortality and result in severe economic, social, and political disruption [4]. Moreover, a major infectious disease pandemic may have widespread and pervasive detrimental effects on individuals' mental health [5, 6]. For example, a sudden disease outbreak that is associated with high infectivity and rapid transmission results in fear, distress, and anxiety in the public [7–9]. Long-term stress and anxiety that are caused by a pandemic may further induce symptoms of depression [10, 11]. This ongoing exposure to danger, illness, death, disaster situations, stigma, and discrimination during a pandemic can induce an acute stress response and even cause posttraumatic stress reactions [5, 12–14].

Posttraumatic stress disorder (PTSD) is a common, serious, and complex mental disorder that occurs following exposure to traumatic events. It is characterized by intrusion and reexperiencing the trauma through flashback-like dissociative reactions, efforts to avoid trauma-related thoughts, feelings, places, or people, persistent negative cognition and mood, and hyperarousal, such as anxiety, sleep difficulties, and irritability [15]. Failed recovery from PTSD can have long-term harmful effects on an individual's social function, family life, and personal health [16].

Numerous studies have investigated the prevalence of PTSD after pandemics. However, controversy exists with regard to the prevalence and pattern of PTSD (e.g., PTSD with acute onset or delayed onset) after such infectious disease outbreaks. The prevalence of PTSD that has been reported in epidemiological studies has varied widely, depending on the particular outbreak, target population, and methods that are used to assess the disorder. Such prevalence estimates range from 2.3 to 55.1% [17, 18]. For example, a study in 2006 evaluated post-SARS PTSD among SARS survivors and found that the rate of PTSD 3 and 12 months after the patients' discharge was 46.2% and 38.8%, respectively [19]. Jalloh et al. [20] assessed the mental health impact of the 2014–2016 Ebola epidemics on the general population in affected countries and found that 76.4% of the general public showed any symptom of PTSD, 27% met the level of clinical concern for PTSD, and 16% met the level of a probable diagnosis of PTSD. A recent survey on posttraumatic stress symptoms during the COVID-19 pandemic among residents in the hardest-hit areas in China indicated a prevalence of 7% [21]. Although epidemiological data on PTSD are growing, the global prevalence of PTSD and its drivers in individuals after pandemics remain largely unknown.

With the spread of COVID-19 pandemic, the global estimate of burden of PTSD following pandemic is vital for

the development of intervention and management strategy. However, to the best of our knowledge, no systematic review or meta-analysis has reported the pooled prevalence of PTSD after infectious disease pandemics and potential risk factors. Such information would help guide public health responses, medical resource allocation, and health policy planning in anticipation of and during such worldwide public health emergencies. The present systematic review sought to provide a reliable estimate of the worldwide prevalence of infectious disease pandemic-related PTSD and investigate the effects of demographic characteristics, clinical stage, and other factors on such prevalence.

Methods

Search strategy and selection criteria

We performed a systematic review and meta-analysis according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [22]. We systematically searched the MedLine, Embase, PsycINFO, Web of Science, CNKI, WanFang, medRxiv, and bioRxiv databases to identify studies that were published from the inception up to August 23, 2020, that reported the prevalence of PTSD after infectious disease pandemics, including SARS, H1N1, poliomyelitis, Ebola, Zika, Nipah, MERS-CoV, H5N1, and COVID-19, as well as risk factors contributing to PTSD. The search terms that were used to search the titles and abstracts are listed in the Appendix. We also scanned reference lists and review articles for additional studies that might meet the inclusion criteria.

Two authors, YMG and L. Liu, independently assessed the articles for their eligibility for inclusion. Studies were included if they were longitudinal or cross-sectional studies regarding infectious disease pandemics, including SARS, H1N1, poliomyelitis, Ebola, Zika, Nipah, MERS-CoV, H5N1, and COVID-19 and met any of following criteria: (1) peer-reviewed articles without language restriction that reported the prevalence of PTSD after these pandemics using a wide range of PTSD measurement tools, including international diagnostic criteria, actual medical records, and standard questionnaires or instruments; (2) peer-reviewed articles that analyzed the influential factors for high-risk of post-pandemic PTSD. The following types of articles were excluded: case reports, reviews, and dissertations. If the same sample was used in more than one publication, only the data set with the most comprehensive information was included to avoid data duplication in the meta-analysis. The process of identifying eligible studies and reasons for exclusion are presented in Fig. 1.

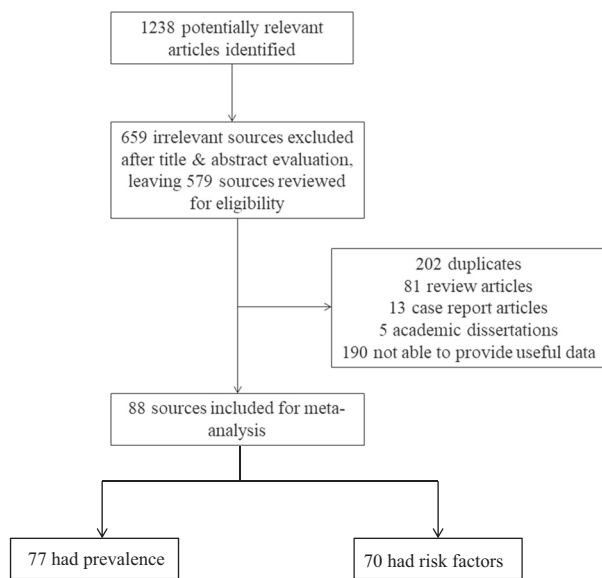


Fig. 1 Flow chart of study selection. Among 88 eligible studies included in the meta-analysis, 77 included prevalence information and 70 included risk factor information.

The following information was extracted from each study according to a prespecified protocol: (1) first author, (2) publication year, (3) region of research, (4) type of infectious outbreak, (5) time of survey relative to the end of pandemic, (6) PTSD assessment instrument, (7) study population, (8) sample size, (9) PTSD prevalence (Table 1), and (10) risk factors for PTSD. Only baseline data within 12 months after pandemics from longitudinal studies were included when calculating overall prevalence. These data were independently extracted from eligible papers by five of the authors (YMG, SST, L. Liu, YJW, AYZ, and XXL) and subsequently double-checked by two other authors (YMG and YJW). Quality assessments of eligible studies were conducted independently by two of the authors (YMG and YJW) using the 11-item Agency for Healthcare Research and Quality (AHRQ) for cross-sectional studies [23] and 9-star Newcastle-Ottawa Scale (NOS) for cohort studies [24]. Studies with eight or more stars on the AHRQ and NOS were determined to be high quality. All discrepancies were resolved by group discussion and consensus.

Data analysis

All of the analyses were calculated using the statistical packages for meta-analysis in Stata 12 software. Given the potential clinical and methodological heterogeneities, a random effects model was used to allow for a more conservative approach to calculate pooled prevalence estimates. Pooled prevalence estimates are expressed as mean estimates and 95% confidence intervals (CIs). We used an I^2 statistic estimate of $\geq 50\%$ as an indicator of large

statistical heterogeneity. To explore potential sources of heterogeneity, subgroups and meta-regression analyses were conducted when possible using the following variables: population type (patients/infected survivors, health-care workers, and general public), time of the survey relative to the start of the pandemic (within 6 months vs. over 6 months), gender (male and female), diagnostic methods (clinical diagnosis and scales), income level of countries (high-income vs. low- and middle-income countries based on the World Bank standard) [25], type of infectious disease (SARS, H1N1, Poliomyelitis, Ebola, Zika, Nipah, MERS-CoV, H5N1, and COVID-19), quarantine experience, and frontline work experience. Visual examinations of funnel plots, Begg's test, and Egger's test were used to assess the possibility of publication bias and small-study effects. Sensitivity analyses were conducted to identify the influence of individual studies on the pooled estimates by excluding each of the studies from the pooled estimate.

Results

A total of 1238 papers were initially retrieved (Fig. 1). After screening, 659 were excluded based on the title and abstract, 202 were excluded because they were duplicate studies, 81 were excluded because they were reviews and systematic reviews, and 18 were excluded because they were case reports and academic dissertations. After screening, 278 articles remained to be reviewed of the full-text for eligibility. Of these articles, 190 were excluded because they did not focus on the post-pandemic prevalence or risk factors of PTSD, leaving a total of 88 eligible studies included in the meta-analysis. Among these, 77 included prevalence information [18–21, 26–98] and 70 included risk factor information [8, 20, 21, 26, 29–32, 34–39, 42, 43, 47, 49–51, 53–58, 60–62, 64–67, 69–79, 81, 83–88, 90, 91, 92, 93–108].

Post-pandemic PTSD prevalence

Of the 77 studies that included prevalence data, three major populations were analyzed and described, including 28 studies (24,815 participants) of healthcare workers, 14 studies (2161 participants) of infected patients, and 38 studies (176,855 participants) of the general public. Twenty-three studies (29.9%) focused on SARS, 47 (61.0%) on COVID-19, 3 (3.9%) on Ebola, 2 (2.6%) on MERS, 1 (1.3%) on H1N1, and 1 on multiple diseases including SARS, H5N1, and H1N1. Seventy studies (90.9%) used questionnaires to identify PTSD, and 7 studies (9.1%) made a PTSD diagnosis by professional mental health workers. As not all eligible studies reported gender information, quarantine

Table 1 Summary of longitudinal and cross-sectional studies included in meta-analysis.

Study	Year of publication	Region	Infectious outbreak	Time of survey after traumatic events (mo)	PTSD measurement	Population (patients/healthcare workers/general public)	Total sample size	PTSD prevalence	Score of literature quality
Arpacioglu et al. [99]	2020	Turkey	COVID-19	During	STSS	HCW	563	/	7 ^a
Austin et al. [100]	2020	Spain	COVID-19	During	PCL-C	General public	10541	/	7 ^a
Bai et al. [26]	2004	China	SARS	During	Author designed questionnaire	HCW	338	5%	6 ^a
Berthelot et al. [27]	2020	Canada	COVID-19	During	PCL-5	General public	496	1.19%	8 ^a
Chan et al. [122]	2004	Singapore	SARS	2	IES	HCW	661	19.2%	7 ^a
Chen et al. [29]	2005	China	SARS	During	IES	HCW	128	11%	7 ^a
Chew et al. [30]	2020	Singapore India	COVID-19	During	IES-R	HCW	906	7.4%	6 ^a
Chong et al. [8]	2004	Taiwan China	SARS	During	IES	HCW	1257	/	9 ^a
Fekih-Romdhane et al. [31]	2020	Tunisia	COVID-19	During	IES-R	General public	603	33.0%	7 ^a
Feng et al. [90]	2020	China	COVID-19	During	PCL-C	General public	53427	4.75%	10 ^a
Forté et al. [32]	2020	Italy	COVID-19	During	IES-R	General public	2291	27.72%	8 ^a
Gao et al. [19]	2006	China	SARS	3 and 12	PTSD-SS; CCMD-III	Patients	67	3 mo: 46.2% 12 mo: 38.8%	8 ^a
Garcia-Fernandez et al. [101]	2020	Spain	COVID-19	During	ASDI	General public	2710	/	8 ^a
Giusti et al. [33]	2020	Italy	COVID-19	During	IES-R	HCW	330	36.7%	8 ^a
Gonzalez Ramirez et al. [34]	2020	Mexico	COVID-19	During	IES-R	General public	3932	27.7%	8 ^a
Gonzalez-Sanguino et al. [35]	2020	Spain	COVID-19	During	PCL-C-2	General public	3480	15.8%	7 ^a
Guo et al. [37]	2020	China	COVID-19	During	PCL-5	Patients; general public	P:103 G:103	P: 1% G: 1.9%	7 ^a
Guo et al. [36]	2020	China	COVID-19	During	PCL-5	General public	2441	20.4%	8 ^a
Hawryluck et al. [38]	2004	Canada	SARS	3	IES-R	General public	129	28.9%	6 ^a
Ho et al. [102]	2005	China, Hong Kong	SARS	During	CIES-R	HCW	SI: 82 S2: 97	/	8 ^a
Hong et al. [39]	2009	China	SARS	2, 7, 10, 20, and 46	CCMD-III; IES	Patients	70	Total: 44.1% 2 mo: 40.0% 7 mo: 41.0% 10 mo: 38.6% 20 mo: 39.7% 46 mo: 42.1%	7 ^a
Huang et al. [40]	2020	China	Covid-19	During	PTSD-SS	HCW	230	27.39%	7 ^a
Hugo et al. [41]	2015	Sierra Leone	Ebola	1	TSQ	Patients	74	21%	6 ^a
Jalloh et al. [20]	2018	Sierra Leone	Ebola	12	IES-6	General public	3564	16%	9 ^a
Jiang et al. [103]	2020	China	Covid-19	During	PCL-5	General public	6,049	/	8 ^a
Joseph [42]	2020	Saudi Arabia	COVID-19	During	IES-6	General public	584	65.5%	9 ^a
Karatzias et al. [43]	2020	Ireland	Covid-19	During	ITQ	General public	1041	17.7%	8 ^a
Keita et al. [44]	2017	Guinea	Ebola	During	ICD-10 or DSM-IV	Patients	68	4.46%	6 ^a
Kwek et al. [45]	2006	Singapore	SARS	3 mo post discharge	IES	Patients	63	41.7%	9 ^a
Lam et al. [46]	2009	Hong Kong, China	SARS	41.4	CIES-R; SCID	Patients	233	23.2%	9 ^a
Lau et al. [47]	2005	Hong Kong, China	SARS	During	IES	General public	818	15.7%	7 ^a
Lee et al. [98]	2006	China	SARS	2-3	CIES-R	General public	146	8.9%	10 ^a

Table 1 (continued)

Study	Year of publication	Region	Infectious outbreak	Time of survey after traumatic events (mo)	PTSD measurement	Population (patients/healthcare workers/general public)	Total sample size	PTSD prevalence	Score of literature quality
Lee et al. [104]	2007	China, Hong Kong	SARS	12	IES-R	Patients	2003:79 2004:96	/	9 ^a
Um et al. [48]	2017	South Korea	MERS	During	IES-R-K	HCW	64	4.7%	6 ^a
Lee et al. [105]	2018	South Korea	MERS	During	IES-R	HCW	359	/	8 ^a
Leng F. [91]	2020	China	COVID-19	During	IES-R	HCW	72	73.61%	8 ^a
Leng et al. [49]	2020	China	COVID-19	During	PCL-C	HCW	90	5.60%	8 ^a
Li et al. [92]	2020	China	COVID-19	During	PCL-C	HCW	205	50.73%	9 ^a
Li Q. [50]	2020	China	COVID-19	1	IES-R	General public	1109	67.09%	8 ^a
Li et al. [51]	2020	China	COVID-19	During	IES-R	General public	1442	11.1%	8 ^a
Liang et al. [52]	2020	China	COVID-19	During	PCL-C	General public	584	14.4%	7 ^a
Lin et al. [53]	2007	Taiwan	SARS	1–2	DTS-C	HCW	92	19.3%	6 ^a
Lin et al. [54]	2020	China	COVID-19	During	ASDS	General public	5461	15.8%	7 ^a
Liu et al. [55]	2020	USA	COVID-19	During	PCL-C	General public	898	31.8%	9 ^a
Liu et al. [21]	2020	China	COVID-19	During	PCL-5	General public	285	7%	8 ^a
Liu et al. [56]	2020	China	COVID-19	During	PCL-5	Patients	675	12.44%	7 ^a
Luceno-Moreno et al. [57]	2020	Spain	COVID-19	During	IES-R	HCW	1422	56.6%	8 ^a
Mak et al. [58]	2010	China	SARS	30	SCID	Patients	90	25.6%	5 ^b
Mazza et al. [59]	2020	Italy	COVID-19	During	IES-R PCL-5	Patients	402	28%	8 ^a
McAlonan et al. [106]	2007	Hong Kong, China	SARS	12	IES-R	HCW	184	/	7 ^a
Nie et al. [60]	2020	China	COVID-19	During	IES-R	HCW	263	73.8%	9 ^a
Park et al. [61]	2016	South Korea	MERS	12	IES-R-K	Patients	63	42.9%	7 ^a
Plomecka et al. [107]	2020	Multiple countries	COVID-19	During	IES	General public	12817	/	10 ^a
Qi et al. [62]	2020	China	COVID-19	During	PCL-C	Patients	41	12.2%	8 ^a
Reynolds et al. [64]	2008	Canada	SARS	2–3	IES-R	General public	1057	14.6%	8 ^a
Ren et al. [63]	2020	China	COVID-19	During	ASDS; PCL-5	General public	1172	7%	5 ^a
Rossi et al. [65]	2020	Italy	COVID-19	During	GPS-PTSS	HCW	1379	49.38%	9 ^a
Rossi et al. [66]	2020	Italy	COVID-19	During	GPS-PTSS	General public	18147	37.14%	8 ^a
Seyahi et al. [67]	2020	Turkey	COVID-19	During	IES-R	General public	535 917	46.4% 29.1%	7 ^a
Shahrour et al. [68]	2020	Jordan	COVID-19	During	SASRQ	HCW	448	64%	8 ^a
Shi et al. [69]	2020	China	COVID-19	During	ASDS	General public	56679	24.4%	9 ^a
Shi et al. [70]	2005	China	SARS	8–9	PCL-C	Patients; HCW; general public	162	P: 50% H: 3.9% G: 6.7%	8 ^a
Si et al. [71]	2020	China	COVID-19	During	IES-6	HCW	863	40.2%	9 ^a
Sim et al. [72]	2010	Singapore	SARS	During	IES-R	General public	415	25.8%	9 ^a
Sim et al. [73]	2004	Singapore	SARS	During	IES-R	HCW	277	9.4%	6 ^a
Sprang et al. [75]	2013	America Mexico and avian Canada	H1N1, SARS, and avian influenza	Not clear	Parents: PCL-C; Children: parent-report version of PTSD-R1	General public	796	Quarantined parents:28%; non- quarantined parents:5.8%; quarantined children:30%; non-quarantined children:1.1%	7 ^a
Song et al. [74]	2020	China	COVID-19	During	PCL-5	HCW	14825	9.1%	7 ^a
Styra et al. [108]	2008	Canada	SARS	During	IES-R	HCW	248	/	8 ^a

Table 1 (continued)

Study	Year of publication	Region	Infectious outbreak	Time of survey after traumatic events (mo)	PTSD measurement	Population (patients/healthcare workers/general public)	Total sample size	PTSD prevalence	Score of literature quality
Su et al. [81]	2007	China	SARS	1	DTS-C	HCW	102	28.4%	5 ^b
Sun et al. [76]	2020	China	COVID-19	During	PCL-C	General public; HCW	1722 320	G: 5.2% H: 4.4%	8 ^a
Sun et al. [77]	2020	China	COVID-19	During	IES	General public	1912	17.67%	8 ^a
Tan et al. [78]	2020	China	COVID-19	During	IES-R	General public	673	10.8%	8 ^a
Tang et al. [79]	2020	China	COVID-19	During	PCL-C	General public	2485	2.7%	8 ^a
Tham et al. [80]	2004	Singapore	SARS	6	IES	HCW	96	17.7%	9 ^a
Tian et al. [18]	2020	China	COVID-19	During	PTSD-SS	General public	87	2.3%	6 ^a
Wang et al. [83]	2020	China	COVID-19	During	PCL-C	HCW	202	16.83%	10 ^a
Wang et al. [82]	2020	China	COVID-19	During	SASRQ	HCW	332	38.3%	9 ^a
Wei et al. [93]	2020	China	COVID-19	During	IES-R	General public	266	60.2%	8 ^a
Wu et al. [84]	2005	China	SARS	1 and 3	IES-R	Patients	131	1 mo: 4%; 3 mo: 5%	6 ^a
Wu et al. [85]	2009	China	SARS	36	IES-R	HCW	549	10%	6 ^a
Xu et al. [94]	2020	China	COVID-19	During	PCL-C	General public	2514	11.2%	7 ^a
Xu et al. [86]	2011	China	H1N1	During	PCL-C	General public	1082	2%	7 ^a
Yan et al. [87]	2004	China	SARS	3	CID2.1	Patients	286	9.79%	7 ^a
Yang et al. [95]	2007	China	SARS	12	CCMD-III	HCW	112	8.92%	6 ^a
Yin et al. [88]	2020	China	COVID-19	During	PCL-5	HCW	371	3.8%	9 ^a
Zhang et al. [96]	2006	China	SARS	Not clear	IES-R	Patients; HCW; general public	296	P: 55.10% H: 25.80% G: 31.18%	6 ^a
Zhang et al. [97]	2020	China	COVID-19	During	PCL-C	General public	4255	10.6%	6 ^a
Zhao et al. [89]	2020	China	COVID-19	During	PCL-5	General public	515	5.6%	7 ^a

ASDI Acute Stress Disorder Inventory, *ASDS* Acute Stress Disorder Scale, *CCMD-III* the Third Edition of Chinese Classification and Diagnostic Criteria of Mental Disorders, *CID2.1* the Composite International Diagnostic Interview 2.1, *CIES-R* the Chinese Version of Impact of Event Scale-Revised, *DSM-IV* the Fourth Edition of Diagnostic and Statistical Manual of Mental Disorders, *DTS-C* Chinese version of the Davidson Trauma Scale, *GPS-SPSS* the Global Psychotrauma Screen, posttraumatic stress symptoms subscale, *ICD-10* the International Statistical Classification of Diseases and Related Health Problems 10th Revision, *IES* Impact of Event Scale, *IES-R* Impact of Event Scale-Revised, *IES-R-K* IES-R-Korean Version, *IES-6* validated, shortened version of the full IES-R, *ITQ* the International Trauma Questionnaire, *PCL-C* PTSD Checklist-Civilian Version, *PCL-C-2* PCL-C-Reduced Version, *PCL-5* PTSD Checklist for DSM-5, *PTSD-R* Posttraumatic Stress Disorder Reaction Index, *PTSD-SS* PTSD self-rating scale, *SASRQ* Stanford Acute Stress Reaction Questionnaire, *SCID* the Structured Clinical Interview for the DSM-IV, *STSS* Secondary Traumatic Stress Scale, *TSQ* Trauma Screening Questionnaire.

^aAHRQ: Agency for Healthcare Research and Quality.

^bNOS: Newcastle-Ottawa Scale.

exposure, or frontline experiences, we only identified 11 studies (14.3%) in gender subgroup analysis, 13 (16.9%) in quarantine subgroup analysis, and 14 (18.2%) in frontline healthcare workers subgroup analysis. In the quality assessment of the 88 eligible articles, 49 (55.7%) scored 8–10 points, 37 (42.0%) scored 6–7 points, and 2 (2.3%) scored 5 points. The main problems with study quality were generally associated with the following: no indication of whether evaluators of subjective components of the study were masked to other aspects of the status of the participants and lack of information about any patient exclusions.

Almost all of the eligible studies evaluated the prevalence of PTSD within 12 months after the infectious outbreak, with the exception of four studies which included the prevalence at 30, 36, 41.4, 46 months, respectively [39, 46, 58, 85]. The estimated prevalence of PTSD after the pandemics was 22.6% (95% CI: 19.9–25.4%, I^2 : 99.7%). We conducted subgroup analyses based on the different populations and found that the prevalence of post-pandemic PTSD in healthcare workers, infected patients, and the general public was 26.9% (95% CI: 20.3%–33.6%), 23.8% (95% CI: 16.6%–31.0%), and 19.3% (95% CI: 15.3%–23.2%), respectively (Fig. 2). Further subgroup analyses were conducted and stratified by different population type, assuming there was a sufficient number of eligible studies for each clinical feature.

Subgroup analyses were performed with regard to the time of PTSD assessment after the infectious outbreak, gender, quarantine experience, diagnostic method, type of infectious outbreak, and frontline experience (Fig. 3). We did not find significant difference between the pooled prevalence of PTSD more than 6 months after infectious outbreak (21.1%; 95% CI: 15.7–26.6%) and that of within 6 months after infectious outbreak (22.5%; 95% CI: 19.6–25.4%). However, there were different time patterns in prevalence observed among the three populations, though no statistical difference was observed ($p = 0.947$). The PTSD prevalence in infected patients more than 6 months after the pandemic (28.8%; 95% CI: 14.7–42.8%) was higher than that within 6 months after the pandemic (18.6%; 95% CI: 12.0–25.2%). However, among healthcare workers and the general public, the PTSD prevalence more than 6 months after the pandemic (10%, 95% CI: 5.7%–14.4%; 12.4%, 3.6%–21.3%, respectively) was lower than within 6 months after the pandemic (28.6%, 95% CI: 21.4%–35.8%; 19.4%, 15.2%–23.5%, respectively).

The pooled prevalence of PTSD in males and females after infectious disease outbreak was 26.2% (95% CI: 9.3%–43%) and 27.2% (95% CI: 15.4%–39.1%), respectively ($p = 0.916$). Individuals with quarantine exposure during the pandemic had higher prevalence of PTSD (combined: 15.2%, 95% CI: 10.2–20.3%; healthcare workers: 17.0%, 95% CI: 5.5–28.5%; general public:

16.6%, 95% CI: 10.7–22.5%) than the individuals without quarantine experience (combined: 4.7%, 95% CI: 3.0–6.4%; healthcare workers: 4.0%, 95% CI: 1.8–6.2%; general public: 5.7%, 95% CI: 3.1–8.3%), though the differences were not significant ($p = 0.162$). Among healthcare workers, the pooled post-pandemic prevalence of PTSD in frontline was 30.8% (95% CI: 16.2–45.4%), which was higher than in non-frontline workers (8.2%, 95% CI: 0.6–15.9%) ($p = 0.051$).

When dividing eligible studies in terms of diagnostic methods, there was no difference of pooled post-pandemic prevalence of PTSD between studies diagnosed by a professional's clinical standard (21.5%, 95% CI: 12.3–30.8%) and studies using self-reported scales or questionnaire (22.6%, 95% CI: 19.8–25.4%) ($p = 0.935$). The subgroup PTSD prevalence was 23.8% (95% CI: 13.2–34.4%) in patients and 8.9% (95% CI: 1.5–16.4%) in healthcare workers by clinical diagnosis, and 24.1% (95% CI: 15.0–33.2%) and 26.9% (95% CI: 20.5–33.4%) by questionnaire. All the studies with general public participants were assessed by scales with the estimated PTSD prevalence of 19.1% (95% CI: 15.2–23.0%). The estimated post-pandemic prevalence of PTSD overall in high-income regions and combined low- and middle-income regions was 24.6% (95% CI: 18.2%–31.1%) and 21.2% (95% CI: 18.3%–24.1%), respectively. The combined prevalence of PTSD during the COVID-19, SARS, and other epidemics (Ebola, MERS, and H1N1) was 24.6% (95% CI: 21.1%–28.1%), 19.9% (95% CI: 16.3%–23.4%), and 13.7% (95% CI: 5.5%–21.9%), respectively. There was no difference between subgroups among different income levels ($p = 0.492$) and pandemic types ($p = 0.999$).

Begg's and Egger's tests indicated no apparent publication bias (Fig. 4). A sensitivity analysis that excluded each study individually provided similar estimates of PTSD prevalence, suggesting that no single study included in the meta-analysis was likely to have an inordinate impact on the reported prevalence estimates.

Risk factors for post-pandemic PTSD

Seventy eligible studies reported risk factors for PTSD. However, because of the considerable heterogeneity and limited number of studies for each risk factor, only a systematic review but not a meta-analysis was conducted. We categorized predisposing factors for higher risk of post-pandemic PTSD into three groups: personal, family, or societal factors; infectious-related factors; and factors specific to subgroups. In terms of personal, family, or societal factors, individuals who are female [21, 31, 32, 34, 35, 39, 51, 57, 58, 65–67, 75, 76, 83, 86, 88, 90, 94, 97, 99, 100, 103, 104, 107], younger [32, 43, 66, 69, 73–75, 87, 101, 103], with low annual income

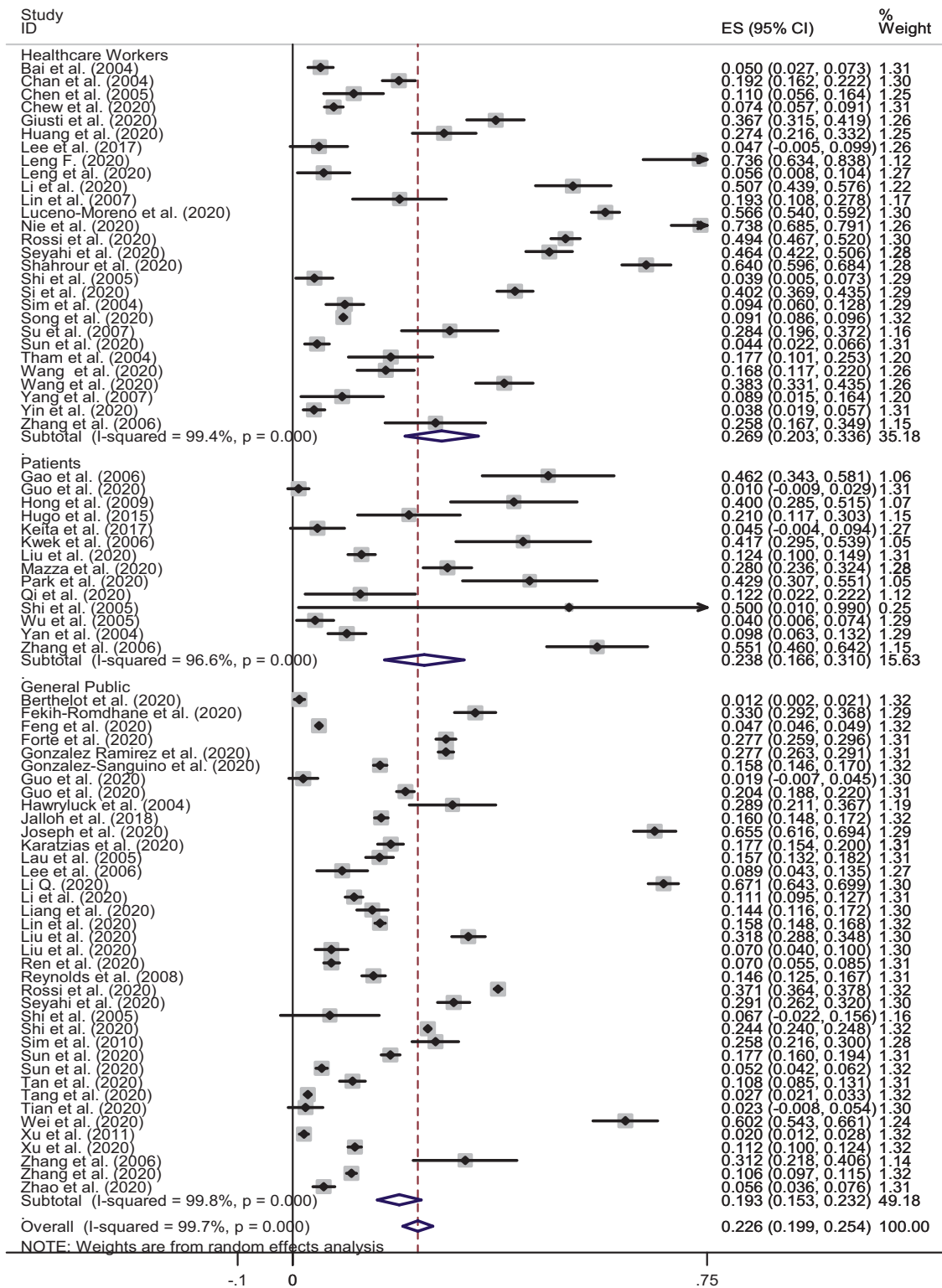


Fig. 2 Combined prevalence of post-pandemic PTSD. The estimated prevalence of PTSD after the pandemics was 22.6%. ES: estimated prevalence; CI: confidence interval; Subtotal: estimated prevalence of each subgroup.

[38, 69] and low level of education [67, 90, 97, 103] had higher risk of suffering from post-pandemic PTSD. Those who lived in a city [43] and previous or current tobacco users

[67, 71] were also at greater risk. Poor psychological status including higher levels of anxiety and depression [43, 51, 91, 99], poor sleep quality [21, 76, 79], high stress

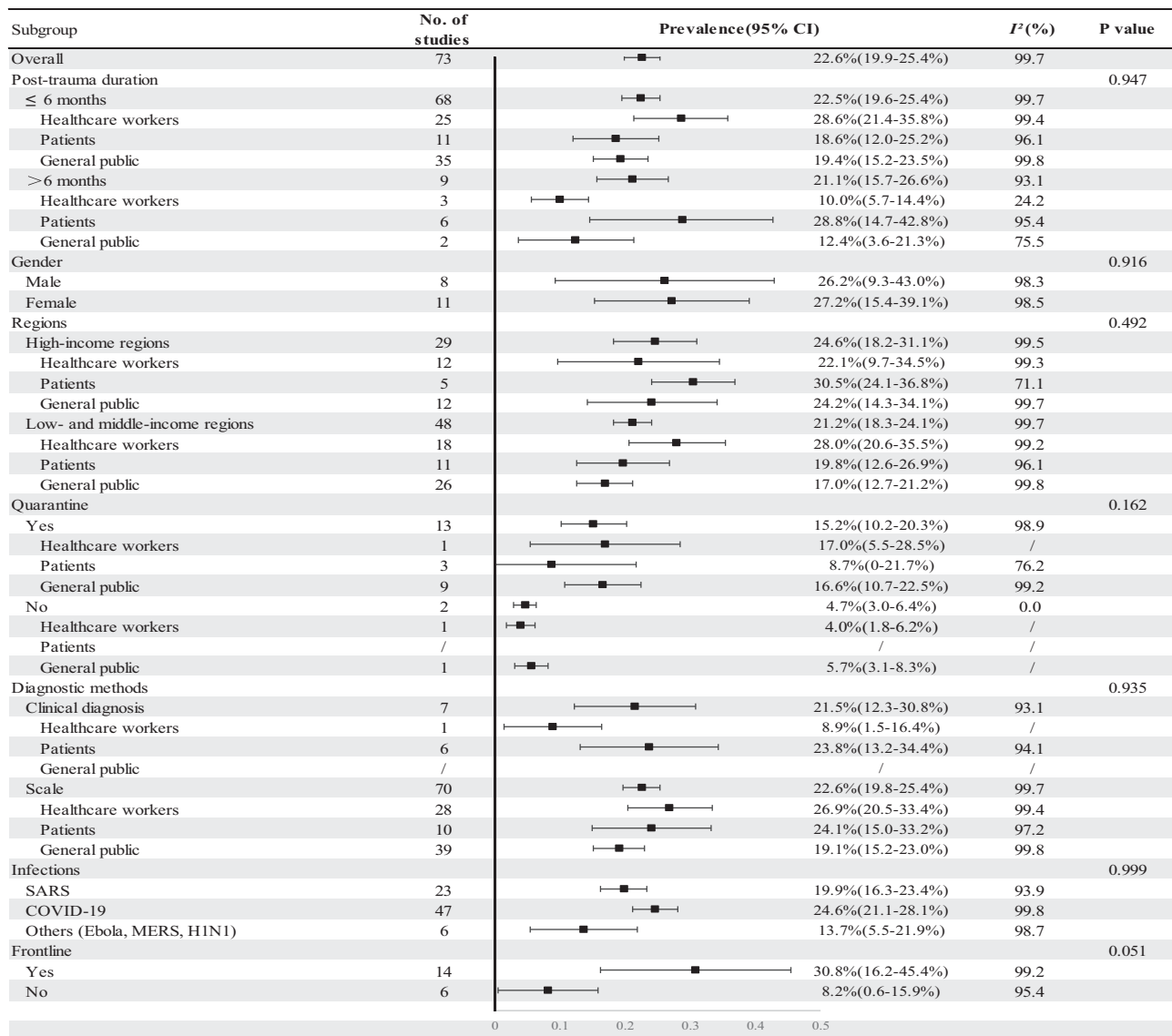


Fig. 3 Subgroup analysis of post-pandemic PTSD prevalence across variables. Estimated prevalence of each subgroups of Post-trauma duration, Gender, Regions, Quarantine experience, Diagnostic methods, Infections disease and Frontline work experience are provided. P value less than 0.05 refers to statistical difference in subgroups. CI: confidence interval.

levels [8, 49, 51], low levels of distress tolerance [55], neurotic and psychopathic personality [70, 78], and any other psychiatric disorder or history [31, 35, 50, 58, 61, 67, 69, 73, 84, 107] all were associated with higher risk of PTSD. In addition to these aspects of an individual's psychological status, personal physical comorbidities [30, 39, 58, 67, 71] and PTSD symptoms among their family members were also associated with more risk [75]. Encountering traumatic events [51, 99, 107] before the outbreak also put an individual at higher risk of developing post-pandemic PTSD, especially when individuals utilized inappropriate coping strategies when dealing with the adverse events [36, 60, 62, 70-73, 83, 96]. Family and societal factors included low family/social support level [8, 47, 55, 74, 94, 97, 107], having or living with

children [43, 56, 67, 94, 103], and limited living space [34, 103].

Some pandemic-related factors were associated with increased risk of developing PTSD. Quarantine or the experience of social isolation due to pandemic [26, 34, 38, 64, 66, 69, 75] was a major risk factor for post-pandemic PTSD, along with poor social life [47, 108], economic loss [34, 77, 93, 101], and impact on livelihood [34, 36, 66, 78]. In addition, having high risk or perception of high risk of contracting infection was also associated with greater risk of post-pandemic PTSD. This included being suspected or confirmed to be infected [35, 37, 69, 86], knowing relatives/friends/acquaintances infected/hospitalized/died due to the infection [20, 32, 35, 38, 39, 42, 66, 69, 71, 76, 85-87, 103], having family/friends with more exposure to the

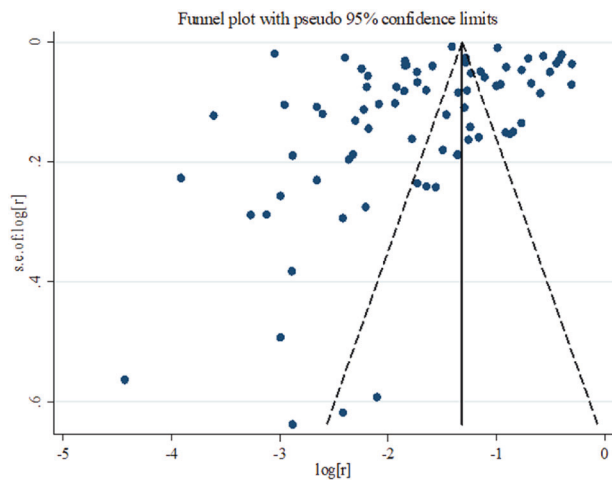


Fig. 4 Begg's funnel plot. Begg's funnel plot indicated no apparent publication bias and Begg's and Egger's tests confirmed that (p value of both Begg's and Egger's tests are greater than 0.05). r : estimated prevalence.

infection [103], perceiving there was a high risk/threat of contracting infection [20, 34, 42, 43, 54, 57, 60, 69, 76–79, 85, 86, 98, 103, 106, 108], and exposure to excessive negative information about the infection [42, 67]. Negative psychological responses to the infection, including feeling anxious/depressed [61, 99, 108], stressful [47, 53, 66, 70], extremely fearful and helpless [47, 55, 71, 79, 86], and any other negative feelings [81], during the pandemic were all risk factors for post-pandemic PTSD. Other pandemic-related factors that increased PTSD risk included individuals having uncertainty of the possibility of contracting infection [32] and those who felt stigmatized because of the pandemic [77].

Some risk factors were specific to healthcare workers and some to patients. Among healthcare workers, nurses [29, 71, 74], frontline workers [8, 53, 65, 95, 105, 108], those working in high-risk community [57], technicians [8], general practitioners [65], nonlocal aid workers supporting the highest-hit areas [92], were all groups at higher risk of developing post-pandemic PTSD. Healthcare workers who had less working experience [8, 49, 74, 91, 108], low job satisfaction [83], and longer work shifts [74, 92] were at more risk. Feeling fearful of potential harm, death, and life out of control due to the pandemic [102], having a colleague infected/hospitalized/in quarantine/deceased [65, 91], and having concerns that a person the healthcare worker lived with may be infected [57] were also associated with healthcare workers being at higher risk. As for infected patients, some clinical factors including higher disease severity [56], low level of SaO₂ during hospitalization [84], feelings of discrimination [56, 61], and death of family members from infection [56] were major risk factors for PTSD development. Box 1 summarizes the

categorized risk factors determined by our systematic review.

Discussion

To our knowledge, this is the first systematic review and meta-analysis that specifically focused on the pooled estimate of prevalence of PTSD after large-scale infectious disease outbreaks, including COVID-19 pandemic, as well as risk factors contributing to higher post-pandemic PTSD. A number of meta-analyses and systematic reviews of PTSD have been conducted after natural disasters, such as floods, earthquakes [109, 110], and other significant traumatic events, such as the World Trade Center disaster in 2001 [111]. The combined prevalence of PTSD after infectious disease pandemics that was found in the present study (23%) was even higher than the estimated pooled prevalence after other disasters, such as major traumatic events (~20%) [112] and floods (~16%) [110]. Our results indicate that PTSD is common in individuals who experience infectious diseases outbreaks, which may persist over a relatively long period of time. Confirmed cases of infection, frontline healthcare workers, and quarantined individuals tend to be vulnerable populations who have a higher potential of developing post-pandemic PTSD. We reviewed and categorized the numerous potential risk factors for post-pandemic PTSD and these findings indicate that early screening and timely evidence-based interventions and social support should be applied to potentially mitigate post-pandemic PTSD and related psychological problems during COVID-19 and future pandemics.

According to the Diagnostic and Statistical Manual of Mental Disorders, PTSD has a variable course. Acute stress disorder can be present in the initial month after a traumatic event, after which only a proportion of these people will subsequently develop PTSD [113]. In addition, a small proportion of people can develop delayed PTSD with the onset of the disorder occurring at least 6 months after the traumatic event [114]. Recent work shows that many cases of delayed-onset PTSD actually reflect worsening of symptoms over time as a result of stressors that occur after the traumatic event [115]. We performed a subgroup analysis using 6 months as the dividing time point. We observed that the pooled prevalence of PTSD within 6 months and after 6 months was both stable at a high level (about 20%), though there was an increasing trend of the post-pandemic prevalence of PTSD among patients (≤ 6 months: 19%; > 6 months: 29%). One study included in our meta-analysis even reported that the prevalence of PTSD among SARS survivors over 46 months was high at about 40% [39]. The reasons for this high and essentially stable prevalence over 4 years might involve the following:

Box 1 Factors that increase risk of post-pandemic PTSD

Personal, family, or societal factors	Infectious-related factors	Factors specific to subgroups
<p>Personal factors</p> <p>Demographic characteristics</p> <p>Age^a</p> <p>Older [39, 90, 94, 98, 99]</p> <p>Younger [32, 43, 66, 69, 73–75, 87, 101, 103]</p> <p>Gender</p> <p>Male [8, 43, 69, 74]</p> <p>Female [21, 31, 32, 34, 35, 39, 51, 57, 58, 65–67, 75, 76, 83, 86, 88, 90, 94, 97, 99, 100, 103, 104, 107]</p> <p>Low annual income [38, 69]</p> <p>Occupation</p> <p>Business units [90, 93]</p> <p>Healthcare Workers [64, 84, 90, 104]</p> <p>Education</p> <p>Lower level [67, 90, 97, 103]</p> <p>Being a graduating/final year student [79, 97]</p> <p>Living in a city [43]</p> <p>Smoker [67, 71]</p> <p>Physiological and psychological comorbidity or history</p> <p>Comorbidity: anxiety [43, 51, 91, 99], depression [43, 51, 91, 99], poor sleep quality [21, 76, 79], higher stress level [8, 49, 51], having physical comorbidity [30, 39, 58, 67, 71]</p> <p>History: psychiatric or neurological disorder history [31, 35, 50, 58, 61, 67, 69, 73, 84, 107], neurotic and psychopathic personality [70, 78], low distress tolerance [55], trauma or adverse experience history [99, 107] experiences [51]</p> <p>Family member having higher PTSD score [75]</p> <p>Inappropriate coping strategy</p> <p>High internet addiction [51] or anxiolytic substances use [101]</p> <p>Negative or passive coping strategy [36, 60, 62, 70–73, 83, 96]</p> <p>Family and societal factors</p> <p>Low family/friends support [8, 47, 55, 74, 94, 97, 107]</p> <p>Have/live with children [43, 56, 67, 94, 103]</p> <p>Limited living space [34, 103]</p> <p>Marital status</p> <p>Married [39, 73, 90, 94]</p> <p>Unmarried [34, 69, 78, 87]</p>	<p>Decreased support status</p> <p>Quarantine [26, 34, 38, 64, 66, 69, 75]</p> <p>Economic loss [34, 77, 93, 101]</p> <p>Poorer social life [47, 108]</p> <p>Impact on livelihood (change in routine, less activity, work life) [34, 36, 66, 78]</p> <p>Perceived high risk of infection</p> <p>Being infected or having infection-associated symptoms [35, 37, 69, 86]</p> <p>Knowing or exposing to someone infected or hospitalized [20, 32, 35, 38, 39, 42, 66, 69, 71, 76, 85–87, 103]</p> <p>Perception of having high risk/threat of contracting infection [20, 34, 42, 43, 54, 57, 60, 69, 76–79, 85, 86, 98, 103, 106, 108]</p> <p>Perception of poor hygiene in the workplace [78]</p> <p>Negative information exposure [42, 67]</p> <p>Psychological response toward infection</p> <p>Having anxious or depressive affect [61, 99, 108]</p> <p>Having uncertainty of the possibility of contracting infection [32]</p> <p>Perceived negative feeling toward the infection [81]</p> <p>Elevated stress level [47, 53, 66, 70]</p> <p>Feel horrified, apprehensive and helpless/loneliness because of infection [47, 55, 71, 79, 86]</p> <p>Regarding oneself as having been the target of discrimination, stigma [77]</p>	<p>Factors specific to HCW</p> <p>Work in high-risk units/communities</p> <p>Nurses [29, 71, 74]</p> <p>Frontline [8, 53, 65, 95, 105, 108]</p> <p>Working in a hospital or high-risk community [57]</p> <p>Technician (inadequate protection) [8]</p> <p>General practitioner [65]</p> <p>Nonlocal aid worker [92]</p> <p>Work experience</p> <p>Fewer working experience [8, 49, 74, 91, 108] (with one exception [60])</p> <p>Lower degree of job satisfaction [83]</p> <p>Longer work shifts [74, 92]</p> <p>Psychological response</p> <p>Insecurity (fear of potential harm, death, and life out of control) followed by instability (work-environment changes and assignment to high-risk units) and infection [102]</p> <p>Having colleagues infected/hospitalized/in quarantine/deceased [65, 91]</p> <p>Concerning that a person he/she lives with may be infected [57]</p> <p>Factors specific to patients</p> <p>Higher disease severity [56]</p> <p>Lowest level of SaO₂ during hospitalization [84]</p> <p>Feeling discriminated [56, 61]</p> <p>Death of family members from infection [56]</p>

^aThe role of age in occurrence of post-infectious PTSD is not clear, though lots of studies reported that younger individuals are more at risk. In terms of the range of age, the results are mixed. Typically, individuals < 30 are classified as the younger, while individuals more than 60 are the older ones.

(1) PTSD is an enduring and pervasive mental disorder for many patients [116], and (2) the median recovery time may extend for years, especially in those who experience trauma directly. Long-term and sustained PTSD emphasizes the need for attention and continuous follow-up and studies of suitable interventions and the mechanisms by which this occurs. We could not perform the subgroup analysis over a time period longer than 1 year because of the limited number of studies that had sufficiently long assessment periods. More longitudinal studies with longer follow-up times are clearly needed.

Previous studies suggested that the female gender may be a significant risk factor for developing PTSD [58, 86, 117]. Moreover, PTSD persists for a longer period of time in females than in males [39]. However, in the present meta-analysis, there was no significant difference of the post-pandemic prevalence of PTSD between females (27%) and males (26%). This might be partially accounted for by a higher family burden of the males and being more

concerned about family members, which may compromise their mental health status [74]. Furthermore, more frequent risky behaviors during epidemics (e.g., going to crowded places or less likely to wear masks) and the resulting higher infective rate [118, 119] might also contribute to the similar prevalence of PTSD between females and males. These findings have important implications for the clinical practice and policymakers that both genders are equally susceptible to PTSD within the context of infectious diseases.

Healthcare workers generally face enormous physical and mental pressures from a higher likelihood of burnout from overwork and being infected, the anxiety and distress that are associated with isolation, instinctive fear and frustration during work, and feeling stigmatized and rejected in their neighborhoods because of their hospital work [26, 30, 120]. Based on this analysis, healthcare workers had a higher trend of overall prevalence of PTSD and PTSD prevalence within 6 months after the pandemic (27% and 29%, respectively) compared with the general public (both 19%). Besides, the

pooled prevalence of post-pandemic PTSD was 31% among frontline healthcare workers and 8% among non-frontline healthcare workers. It suggested a much greater stress that is experienced by frontline healthcare workers and correspondingly greater need for proper preventive care and interventions for their mental health. Frontline nurses also deserve particular attention. Of 28 included investigations about post-pandemic PTSD prevalence among healthcare workers, 6 studies [29, 49, 60, 68, 81, 83] focused particularly on frontline nurses and found a high prevalence of PTSD, which indicates relative vulnerability of this group to develop post-pandemic PTSD. Uncomfortable working environments including the long-term use of personal protective equipment, intense and often overloaded work intensity of an extended duration because of severe pandemic conditions, a lack of understanding and specific drugs to fight the disease, and unavoidable psychological shock that is caused by the demise of infected patients all contribute to the high prevalence of PTSD among both frontline healthcare workers and frontline nurses. Another specific group of healthcare workers worth particular attention was those who worked on the frontline and who contacted the infection and became patients. Frontline healthcare workers are at very high risk of exposure to infection and are in very high potential risk to be infected. Once they become vectors of the virus and unaware of it, they will subsequently transmit it to their patients and colleagues through close contact. Therefore, frontline healthcare workers who became patients may not only feel fearful, stressful, lonely as other patients do, they may also be likely to feel guilty because they are unsure whether there are more victims because of them [8, 19, 28].

Quarantine is one of the major public health measures that is intended to prevent the further spread of an infectious disease, which has been shown to effectively contain a pandemic outbreak. However, the psychological impact of quarantine, including feelings of uncertainty, exhaustion, insomnia, and detachment from others, is wide ranging, long lasting, and substantial [121]. Moreover, evidence shows that the duration of quarantine is significantly associated with greater PTSD symptoms [38]. In the present meta-analysis, the pooled prevalence of post-pandemic PTSD among pandemic victims who had experience with quarantine during the outbreak (15%) was higher than that among victims without quarantine experience (5%), though there was no statistical difference. Furthermore, quarantine was also associated with other negative mental health outcomes such as anxiety, depression, and insomnia [66, 69]. To maximize the benefits of quarantine and minimize its negative impacts, policymakers are encouraged to keep the duration of quarantine as short as possible, give quarantined individuals as much necessary information as possible, provide adequate supplies, reduce boredom, improve communications, and ensure that quarantined people understand

the reasons for and implications of quarantine [121]. What is more, digital support including online health monitoring systems and online social platforms is particularly necessary during this period [122].

Previous studies have suggested that the annual income may be one of the important factors involved in mental disorders, and those with lower income levels were more likely to have depression, anxiety, insomnia, suicidal ideation, and suicide attempts [69, 123]. However, there was no significant difference of the post-pandemic PTSD prevalence between high-income regions (24.6%) and the low- to middle-income regions (21.2%) in our analysis. This might be partially accounted for by a lack of studies in low- to middle-income region studies (e.g., Ebola). Moreover, the majority of high-income region studies were drawn from SARS experiences in Taiwan and Hong Kong, which compromises the representativeness and generalizability of these data. These findings remind us that post-pandemic PTSD is a severe problem across all regions and populations. Hence, more investigations in different areas around the world using formal clinical diagnosis rather than self-rating questionnaires are encouraged to provide us with more accurate information as to post-pandemic PTSD prevalence and risk factors.

Most studies have suggested that age was another major demographic factor that contributes to higher risk of post-pandemic PTSD, although in our review, different studies had inconsistent conclusions regarding which age group was more likely to be PTSD victims. Through our review, those having children, married/widowed/divorced, working in business units, and encountering economic difficulties due to the infections are at high risk of developing PTSD [34, 39, 43, 56, 67, 73, 77, 90, 93, 94, 101, 103]. It suggests that the living conditions, responsibility, or source of stress at a given age are the “culprit” of individuals’ PTSD post-pandemic. Another risk factor worth our attention is perceived stigmatization or discrimination due to the pandemic [56, 61, 77]. Infected patients are not only the vectors of infection, but also often the victim of social stigma following the infection. Healthcare workers can also experience social stigmatization since they work directly with infected patients. As many studies have demonstrated a close relationship between stigmatization and psychiatric morbidities (e.g. [41, 46, 61]), there is a great need to enhance publicity and education of the harm of stigmatization to reduce the process of social stigmatization and its impact as well as to deploy psychological interventions for those perceiving stigmatization.

The significance of this study lies in the application of the present meta-analytic strategy, the inclusion of major large-scale twenty-first century pandemics, and the use of a relatively large sample to evaluate the combined post-pandemic prevalence of PTSD. Equally informative part was the use of subgroup analyses that identified several risk

factors for post-pandemic PTSD, including being infected survivors, the female gender, frontline medical and nursing staff, and having experience with quarantine during pandemic outbreaks. We also found that PTSD symptoms persisted over a relatively long period of time. These findings demonstrate that the burden of PTSD among infected survivors, frontline medical and nursing staff, and quarantined individuals is substantial and pervasive. Furthermore, 61% eligible studies in this meta-analysis focused on COVID-19, reflecting the great attention paid by all over the world toward this serious pandemic. This study sought to inform us about prevalence and risk factors that might be particularly salient for our understanding of the development of post-pandemic PTSD. Appropriate monitoring, timely interventions, social support, and long-term follow-up should be applied to mitigate post-pandemic PTSD and related psychological disturbances, particularly in high-risk populations. Our findings are also underscored by a large population study from the USA which found that having a psychiatric disorder in the preceding 12 months was a risk factor of contracting COVID-19 [124]. Our study indicated that as COVID-19 continues, addressing mental health may also be an important public health strategy for reducing transmission of the virus and promoting social and economic development [125].

This study has several potential limitations. First, the number of studies that performed longitudinal assessments was relatively small, and the time window of these studies was relatively short. Second, although we initially searched for all major large-scale pandemics since 2000, only 6 out of 77 eligible studies that focused on the prevalence of PTSD in pandemics (Ebola, MERS, and H1N1) other than SARS and COVID-19 were identified and analyzed. Third, we observed substantial heterogeneity in the estimates of PTSD prevalence across studies. The causes of this heterogeneity might be partly explained by geographical distribution, variability among different populations, measurement differences, and between-study differences in population characteristics, but the remaining unexplained heterogeneity was still substantial ($I^2 > 50\%$). However, given so many variables and responses to the trauma made by the public during each pandemic, clinical heterogeneity may not be surprising as the PTSD prevalence after a pandemic might not be a singular clinically meaningful entity. Finally, there were insufficient data to allow subgroup comparisons that could be stratified by other variables that are likely associated with PTSD, such as age and comorbidities.

Conclusions

In conclusion, the combined prevalence of PTSD in individuals after infectious disease pandemics exceeded

one-fifth, with the highest prevalence observed in healthcare workers, followed by infected patients and the general public. Our findings indicate that post-pandemic PTSD is a significant public health concern after infectious disease pandemics, including COVID-19. The PTSD should be paid attention to by policymakers all over the world because of the substantial burden in population regardless of the different sex, gender, geographical coverage, income levels, etc. Public health strategy involving mental health response is warranted, especially in the area of post-pandemic and even after long-term recovery period. Early detection and early interventions should be implemented comprehensively and extensively, especially for vulnerable populations, including infected survivors, frontline medical and nursing staff, and individuals with quarantine experience, to improve post-pandemic mental health and recovery in the long-term. More longitudinal studies with longer follow-up times after COVID-19 are needed.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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