Review article

The prevalence of post-traumatic stress disorder related symptoms in Coronavirus outbreaks: A systematic-review and meta-analysis

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ABSTRACT

Background: : Infectious disease outbreaks affect physical and mental health of humans worldwide. Studies showed that the prevalence of post-traumatic stress disorder (PTSD) symptoms increased in these conditions. This systematic-review and meta-analysis aimed to assess the prevalence of PTSD related symptoms in coronavirus outbreaks.

Methods: : Systematic search of literature was conducted in Scopus, Embase, PubMed, and Web of Science. Google Scholar and Grey literature including conference proceedings were also checked. Published articles from November 1, 2012 until May 18, 2020 were searched. Subgroup analysis, meta-regression and sensitivity analysis were also conducted to assess heterogeneity.

Results: : We found 38 articles with 19,428 individuals met the eligibility criteria. Of these papers, 35 studies were included in meta-analysis. The prevalence of PTSD symptoms was estimated to be about 18% (95%CI: 15% to 20%). These symptoms were more frequent in cohort studies (29%) compared to cross-sectional (15%) and case-control (11%) studies. Prevalence rates of PTSD symptoms in MERS (36%) outbreaks were higher than SARS (18%) and COVID-19 (9%) outbreaks. Meta-regression showed that the geographical location of study was the source of heterogeneity (R^2: 19.8%, P-value: 0.003). Meta-analysis reported that about three in every ten survivors of coronavirus infection, about two in every ten healthcare workers, and about one in every ten individuals of general population experienced PTSD symptoms in outbreaks.

Limitations: : PTSD cannot be objectively assessed and this can lead to information bias of included studies.

Conclusion: : PTSD symptoms are shown to be common in coronavirus outbreaks. Mental care should be, therefore, considered in the present COVID-19 pandemic.

1. Introduction

The Coronaviridae family consists of different viruses that have affected many individuals in the past century. The epidemic outbreak of severe acute respiratory syndrome coronavirus (SARS-CoV) occurred in 26 countries during 2002 to 2003 and led to over 770 deaths with mortality rate ranging from 7% to 17% in most affected areas (WHO, 2003) and up to 50% among elderly population (McIntosh & Perlman,

2015). The Middle East respiratory syndrome (MERS) was first reported on the Arabian Peninsula in September 2012. The most prevalent country was, however, Republic of Korea in 2015 (CDC, 2014). The Worldwide mortality rate due to MERS was reported to be 34% (over 850 deaths) (CDC, 2014). The novel coronavirus known as SARS-CoV-2 that cause Coronavirus disease 2019 (COVID-19) was thought to originate in Wuhan, China in December 2019 and declared as a pandemic outbreak by World Health Organization (WHO) on March, 11th, 2020;

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with an estimated 4% to 11% mortality rate (N. Chen et al., 2020; D. Wang et al., 2020).

Infectious disease outbreaks have not only affected the physical health but also mental health of those infected and even those not infected. Post-traumatic stress disorder (PTSD) and post-traumatic stress disorder related symptoms are prevalent and disabling conditions occur as a consequence of traumatic events. Based on diagnostic and statistical manual of mental disorders fifth edition (DSM-V), PTSD can be diagnosed according to eight criteria (A-H) and consists of symptoms including re-experiencing the traumatic event, intrusive behaviors, avoidance of the stimuli related to the traumatic event, and worsening of cognition and mood after the traumatic event. These symptoms should not be attributable to other disorders (APA, 2013) .

Different studies showed that PTSD and PTSD related symptoms could be common among individuals with medical illnesses. The highest prevalence of PTSD was reported in people admitted to intensive care units and treated for a potentially life threatening disease; mostly due to HIV infection (Tedstone & Tarrier, 2003). Infectious disease outbreaks can be considered as traumatic events and increase the risk of future PTSD symptoms among different populations; especially affected patients/ survivors (A1 criteria: "directly experiencing the traumatic event (s)") and healthcare workers (A4 criteria: "experiencing repeated or extreme exposure to aversive details of the traumatic event(s)") (APA, 2013). Some observational studies reported the prevalence of PTSD symptoms among individuals during and after outbreaks of SARS, MERS, and COVID-19. This was in the range of 3% among general population to over 40% among the survivors of coronavirus (Liang et al., 2020; Tang et al., 2020).

The aim of this study is to determine the global prevalence of trauma- and stress-related symptoms consistent with PTSD during and after the three most recent coronavirus outbreaks (specifically SARS-CoV, MERS, and SARS-CoV-2), in a variety of population groups including general population, patients/ survivors, and healthcare workers using the systematic review and meta-analysis protocol. The study goal is to ascertain the risk of development of PTSD related symptoms in high risk populations given the importance of mental care during the ongoing COVID-19 pandemic.

2. Methods

We used preferred reporting items for systematic reviews and meta-analyses (PRISMA) to improve the present study (Supplement 1) (Moher, Liberati, Tetzlaff, & Altman, 2009). The authors (MaS and MoS) developed the study protocol and published previously (Salmanian, Salehi, & Hooshyari, 2020).

2.1. Search strategy

A systematic search of the literature was conducted in Scopus, Embase, PubMed, and Web of Science to identify studies assessing the prevalence of PTSD during and after coronavirus outbreaks. Published articles from November 1, 2012 until May 18, 2020 were searched. The search strategy was developed using the following MeSh terms: "(Post-traumatic stress OR Post traumatic stress OR PTSD OR PTSS) AND (Coronavirus OR COVID-19 OR COVID19 OR SARS-CoV-2 OR 2019-nCoV OR Wuhan coronavirus OR SARS2 OR severe acute respiratory syndrome coronavirus 2 OR MERS OR SARS OR Middle east respiratory syndrome OR severe acute respiratory syndrome OR SARS-COV OR MERS-COV)". To control publication bias, we searched Google Scholar to find additional articles. Grey literature including conference proceedings was also searched. The reference lists of relevant articles were checked. The last search was performed in May, 2020.

2.2. Eligibility criteria

Inclusion criteria were all observational studies reporting data on

prevalence of PTSD and PTSD related symptoms during and/or after coronavirus (SARS, MERS, and COVID-19) outbreaks or pandemics. Studies on general population, healthcare workers, affected patients with coronavirus, and/or survivors were included. PTSD diagnosis could be according to made either thought a structured clinical interview for DSM-IV or using various instruments; such as post-traumatic stress disorder checklist-civilian version (PCL-C), PCL-reduced version, impact of events scale (IES), IES-revised (IES-R), PTSD checklist for DSM-V (PCL-5), symptom check list 95 (KSCL 95), or Davidson trauma scale. The search was not restricted to any location or language. The exclusion criteria were 1) studies conducted on populations with specific ethnicity, socioeconomic status, and/or educational background; 2) duplicate records; and 3) case-reports and publications other than original articles (e.g. reviews). Three authors (MoS, MaS, MA) independently searched through databases and decided to include or exclude publications based on above-mentioned criteria. Any disagreement was resolved by discussion or it was consulted with other authors (MM and NR).

2.3. Data extraction and quality assessment

Two authors (MoS and MaS) independently assessed the methodological quality of included studies using modified strengthening the reporting of observational studies in epidemiology (STROBE) checklist (Vandenbroucke et al., 2014). We extracted study characteristics; including the first author name, publication year, continent and country where the study took place, study design (cross-sectional, case-control, longitudinal studies), setting (general population, healthcare worker, patient, survivor), type of pandemics or outbreaks (SARS, MERS, COVID-19), time of measurement, response rate, total sample size, gender, age, instruments measured PTSD, and outcomes measured. The overall inter observer agreement was about 90 percent. In case of any disagreement, third author (MA) reassessed the manuscript.

2.4. Statistical analysis

Data were reported as numbers and percentages with 95% confidence interval (95%CI). All analyses were conducted with STATA (Release 12. statistical software. College Station, Texas: STATA Corp LP). The graphical methods and random-effects models were used to aggregate prevalence estimates. Heterogeneity across the studies was assessed using the I^2 statistic. We used subgroup analysis to assess the possible source of heterogeneity. Subgroup analysis was performed based on the quality of study, the region of study, the study design, type of outbreaks, measurement tools, and time of measurement. Meta-regression and Sensitivity analysis were also conducted. The publication bias was assessed using graphical methods and statistical tests; including Egger's and Begg's tests, and Begg's funnel plot. P-values< 0.05 were considered statistically significant.

3. Results

3.1. Study characteristics

We identified 1303 records through database searching. Of these papers, 1112 were excluded based on the titles and abstracts; and 114 full-text articles were retrieved after removing duplicate records and finding additional papers through Google Scholar (Figure 1). Overall, 38 articles met the eligibility criteria that are reported in Table 1.

The eligible studies consisted of 19,428 individuals from 8 countries: Canada (n= 4) (Assar, Moallef, Gardner, & Patcai, 2010; Hawryluck et al., 2004; Lancee, Maunder, & Goldbloom, 2008; Reynolds et al., 2008), China (n= 11),(Guo et al., 2020; Hao et al., 2020; Hong et al., 2009; Huang & Zhao, 2020; Liang et al., 2020; Liu et al., 2020; Sun et al., 2020; Tang et al., 2020; C. Wang et al., 2020; P. Wu et al., 2009; Yin et al., 2020), Hong Kong (n= 5) (Lee et al., 2006)(Lau et al., 2006; Mak
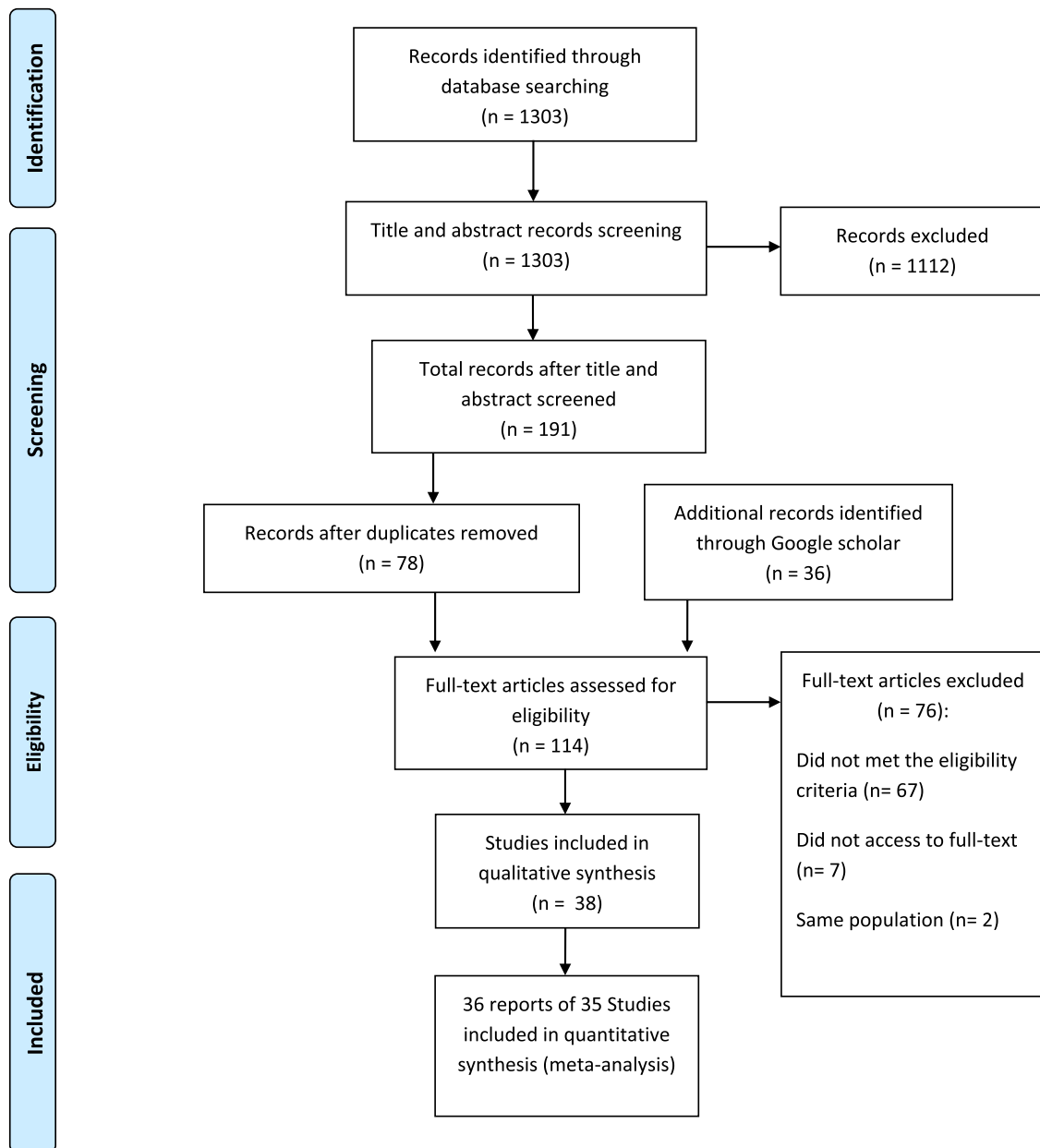
Figure 1. Flow chart of literature search

et al., 2010; K. K. Wu, Chan, & Ma, 2005a, 2005b), Singapore (n= 6) (Sim, Huak Chan, Chong, Chua, & Wen Soon, 2010; Sin & Huak, 2004; Tan et al., 2020; Chan and Huak, 2004; Tham et al., 2005; Kwek et al., 2006), Singapore and India (n= 1) (Chew et al., 2020), South Korea (n= 7) (S. H. Lee et al., 2019; S. M. Lee, Kang, Cho, Kim, & Park, 2018; Park et al., 2020; Shin et al., 2019; Um, Kim, Lee, & Lee, 2017; Jung et al., 2020), Spain (n= 1) (Gonzalez-Sanguino et al., 2020), and Taiwan (n= 3) (Su et al., 2007; Chen et al., 2005; Chong et al., 2004). Most included studies assessed the prevalence of PTSD symptoms during or after the SARS outbreak (n= 19) (Assar et al., 2010; Chan and Huak, 2004; C. S. Chen et al., 2005; Chong et al., 2004; Hawryluck et al., 2004; Hong et al., 2009; Kwek et al., 2006; Lancee et al., 2008; Lau, Yang, Tsui, Pang, & Wing, 2006; T. M. Lee, Chi, Chung, & Chou, 2006; Mak et al., 2010; Sim et al., 2010; Sin & Huak, 2004; Su et al., 2007; Tham et al., 2005; K. K. Wu et al., 2005a, 2005b; P. Wu et al., 2009; Hong et al., 2009); followed by COVID-19 (n= 12) (Chew et al., 2020; Gonzalez-Sanguino et al., 2020; Guo et al., 2020; Hao et al., 2020; Huang & Zhao, 2020; Liang et al., 2020; Liu et al., 2020; Sun et al., 2020; Tan et al., 2020; Tang et al.,

2020; C. Wang et al., 2020; Yin et al., 2020) and MERS (n= 7) (Jung et al., 2020; Kim et al., 2018; S. H. Lee et al., 2019; S. M. Lee et al., 2018; Park et al., 2020; Shin et al., 2019; Um et al., 2017); respectively. The IES-R (n= 17) (Chew et al., 2020; Hao et al., 2020; Hawryluck et al., 2004; Jung et al., 2020; Kim et al., 2018; S. H. Lee et al., 2019; S. M. Lee et al., 2018; T. M. Lee et al., 2006; Park et al., 2020; Reynolds et al., 2008; Sim et al., 2010; Tan et al., 2020; Um et al., 2017; C. Wang et al., 2020; K. K. Wu et al., 2005a, 2005b; P. Wu et al., 2009) and IES (n= 9) (Chan and Huak, 2004); C. S. Chen et al., 2005; Chong et al., 2004; Hong et al., 2009; Kwek et al., 2006; Lancee et al., 2008; Lau et al., 2006; Sin & Huak, 2004; Tham et al., 2005) were the most frequent measurement tools to diagnose PTSD related symptoms (Table 1). There were few studies with the same population reported the prevalence rates of PTSD symptoms in different time periods (Assar et al., 2010; Hong et al., 2009). In such cases, the highest prevalence rate was included in the meta-analysis.

Table 1
Characteristics of the included studies reported the prevalence of PTSD during and after the coronavirus outbreaks

ID	Quality score	First author, publication year (reference)	Continent (Country)	Study design (Study base)	Type of pandemics/ outbreaks	Time of measurement	Response rate, %	Total, n	Male, n	Female, n	Age (Mean; SD)	Instrument	PTSD/PTSS outcome/s Male, %	Female, %	Both, %	Mean (SD)
1a	17	Assar, N. 2010	North America (Canada)	Longitudinal study (Survivors)	SARS	1 year after the outbreak	-	40	5	35	20-65	Posttraumatic Stress Disorder Checklist-Civilian Version (PCL-C)	-	-	15.6	-
1b	17	Assar, N. 2010	North America (Canada)	Longitudinal study (Survivors)	SARS	4 years after the outbreak	-	40	5	35	20-65	Posttraumatic Stress Disorder Checklist-Civilian Version (PCL-C)	-	-	30	-
2	19	Chan, A. O. 2004	Asia (Singapore)	Cross-sectional study (Healthcare workers)	SARS	2 months after the outbreak	65.5	651	-	-	<25->51	Impact of Events Scale (IES)	-	-	19.5	-
3	25	Chen, C. S. 2005	Asia (Taiwan)	Cross-sectional study (Healthcare workers)	SARS	During the outbreak	69.5	128	0	128	- (26.5; 3.1)	Impact of Events Scale (IES)	-	11	-	17.8 (12.4)
4	23	Chew, N. W. S. 2020	Asia (Singapore and India)	Cross-sectional study (Healthcare workers)	COVID-19	During pandemic	90.6	906	323	583	25-35	Impact of Events Scale-Revised (IES-R)	-	-	7.4	-
5	21	Chong, M. Y. 2004	Asia (Taiwan)	Cross-sectional study (Healthcare workers)	SARS	During the outbreak	50.28	1257	238	1019	21-59 (31.8; 6.4)	Impact of Events Scale (IES)	-	-	-	34.8 (19.7)
6	23	Gonzalez-Sanguino, C. 2020	Europe (Spain)	Cross-sectional study (General population)	COVID-19	During pandemic	-	3480	870	2610	18-80 (37.92; -)	Post-traumatic Stress Disorder Checklist-Reduced version (PCL-C-2)	-	-	15.8	1.84 (1.42)
7a	18	Guo, Q. 2020	Asia (China)	Cross-sectional study (Patient population)	COVID-19	During pandemic	-	103	59	44	18-75 (42.5; 12.53)	The PTSD Checklist for DSM-5 (PCL-5)	-	-	1	-
7b	18	Guo, Q. 2020	Asia (China)	Cross-sectional study (General population)	COVID-19	During pandemic	-	103	54	49	18-75 (41.45; 13.09)	The PTSD Checklist for DSM-5 (PCL-5)	-	-	1.9	-
8	20	Hao, F. 2020	Asia (China)	Case-control study (General population)	COVID-19	During pandemic	83.8	109	41	68	≥18 (33.1; 11.2)	Impact of Event Scale-Revised (IES-R)	-	-	13.8	11.3 (10.1)

Table 1 (*continued*)

ID	Quality score	First author, publication year (reference)	Continent (Country)	Study design (Study base)	Type of pandemics/ outbreaks	Time of measurement	Response rate, %	Total, n	Male, n	Female, n	Age (Mean; SD)	Instrument	PTSD/PTSS outcome/s Male, %	Female, %	Both, %	Mean (SD)
9	16	Hawryluck, L. 2004	North America (Canada)	Cross-sectional study (General population)	SARS	During the outbreak	-	129	-	-	18- >66	Impact of Event Scale-Revised (IES-R)	-	-	28.9	15.2 (17.8)
10a	25	Hong, X. 2009	Asia (China)	Longitudinal study (Survivors)	SARS	Average of 53 days after hospital discharge	95.71	67	23	45	<30->45 (38.5; 12.3)	Impact of Event Scale (IES)	26	53.33	41.79	45.3 (16.6)
10b	25	Hong, X. 2009	Asia (China)	Longitudinal study (Survivors)	SARS	Average of 10 months after hospital discharge	81.42	57	-	-	<30->45 (38.5; 12.3)	Impact of Event Scale (IES)	-	-	38.6	46.7 (14.6)
10c	25	Hong, X. 2009	Asia (China)	Longitudinal study (Survivors)	SARS	Average of 20 months after hospital discharge	82.85	58	-	-	<30->45 (38.5; 12.3)	Impact of Event Scale (IES)	-	-	39.7	41.2 (16.6)
10d	25	Hong, X. 2009	Asia (China)	Longitudinal study (Survivors)	SARS	Average of 46 months after hospital discharge	81.42	57	-	-	<30->45 (38.5; 12.3)	Impact of Event Scale (IES)	-	-	42.1	39 (20.9)
11	17	Huang, J. Z. 2020	Asia (China)	Cross-sectional study (Healthcare workers)	COVID-19	During pandemic	93.5	230	43	187	20-59 (32.6; 6.2)	Post-Traumatic Stress Disorder Self-rating Scale (PTSD-SS)	18.6	29.41	27.39	42.92 (17.88)
12	24	Jung, H. 2020	Asia (South Korea)	Cross-sectional study (Healthcare workers)	MERS	After the pandemic; October 1 through November 30, 2015	49	147	0	147	-	Impact of Event Scale–Revised Korean version	-	25.1	-	-
13	21	Kim, Y. 2018	Asia (South Korea)	Cross-sectional study (Healthcare workers)	MERS	During the outbreak	97.39	112	13	99	22-42 (28.7; 4.43)	Impact of Event Scale–Revised Korean version	-	-	50	26.63 (12.96)
14	16	Kwek, S. K. 2006	Asia (Singapore)	Cross-sectional study (Survivors)	SARS	3 months post-discharge	40	63	13	50	21-65 (34.83; 10.49)	The Impact of Event Scale (IES)	-	-	41.7	21.8 (16.3)
15a	16	Lancee, W. J. 2008	North America (Canada)	Cross-sectional study (Healthcare workers)	SARS	13 to 22 months after discharge or die the last patient	-	448	64	384	- (41.3; 10.2)	Impact of Events Scale (IES)	-	-	-	12.8 (10.3)
15b	16	Lancee, W. J. 2008	North America (Canada)	Cross-sectional study (Healthcare workers)	SARS	13 to 22 months after the last patient was discharged or died	24	139	18	121	- (45; 9.6)	Clinician-Administered PTSD Scale (CAPS)	-	-	3	13.6 (9.9)
16	19	Lau, J. T. F. 2006			SARS		64.7	818	407	411	18-60		13.3	18	15.7	-

Table 1 (*continued*)

ID	Quality score	First author, publication year (reference)	Continent (Country)	Study design (Study base)	Type of pandemics/outbreaks	Time of measurement	Response rate, %	Total, n	Male, n	Female, n	Age (Mean; SD)	Instrument	PTSD/PTSS outcome/s			Mean (SD)
													Male, %	Female, %	Both, %	
			Asia (Hong Kong)	Cross-sectional study (General population)		May 27 to June 1, 2003, at the end phase of the epidemic						The Chinese version of Impact of event scale (IES)				
17a	19	Lee, S. H. 2019	Asia (South Korea)	Longitudinal study (Survivors)	MERS	12 months after the outbreak	35.13	52	32	20	- (49.7; 12)	Impact of Event Scale-Revised (IES-R)	-	-	42.3	25.83 (20.05)
17b	19	Lee, S. H. 2019	Asia (South Korea)	Longitudinal study (Survivors)	MERS	18 months after the outbreak	35.13	52	32	20	- (49.7; 12)	Impact of Event Scale-Revised (IES-R)	-	-	26.9	19.29 (21.03)
18	17	Lee, S. M. 2018	Asia (South Korea)	Cross-sectional study (Healthcare workers)	MERS	During the outbreak	19.94	359	65	294	20- ≥60	The Impact of Events Scale-Revised (IES-R) Korean version	-	-	51	26.3 (19.09)
19	21	Lee, T. M. 2006	Asia (Hong Kong)	Case-control study (General population)	SARS	Two months after the epidemic	31.6	146	-	-	≥35	Chinese version of the Impact of Event (Revised) scale (CIES-R)	-	-	8.9	-
20	19	Liang, L. 2020	Asia (China)	Cross-sectional study (General population)	COVID-19	During pandemic	95.7	584	223	361	14-35 (74.6% between 21 and 30 years)	The PTSD Checklist-Civilian Version (PCL-C)	-	-	14.4	-
21	23	Liu, N. 2020	Asia (China)	Cross-sectional study (General population)	COVID-19	During pandemic	95	285	130	155	>18	The PTSD Checklist for DSM-5 (PCL-5)	-	-	7	-
22	23	Mak, I. W. 2010	Asia (Hong Kong)	Longitudinal study (Survivors)	SARS	30 months after the outbreak	96.8	90	34	56	≥18 (41.1; 12.1)	The Chinese version of the Structured Clinical Interview for DSM-IV (SCID)	11.76	33.92	25.55	-
23	22	Park, H. Y. 2020	Asia (South Korea)	Longitudinal study (Survivors)	MERS	12 months after the outbreak	42.56	63	39	24	20-60 (49.2; 12.6)	The Impact of Event Scale-Revised Korean version (IES-R-K)	-	-	42.9	25.93 (20.01)
24	25	Reynolds, D. L. 2008	North America (Canada)	Longitudinal study (General population)	SARS	During the outbreak	55.3	1057	380	646	≥18 (49.2; 15.7)	Impact of Event Scale-Revised (IES-R)	-	-	14.6	8.9 (13.7)
25	20	Shin, J. 2019	Asia (South Korea)	Longitudinal study (Survivors)	MERS	1 year after the outbreak	-	63	39	24	20- ≥60 (49.2; 12.6)	The Korean-Symptom Check List 95 (KSCL 95)	-	-	36.5	-
26	21	Sim, K. 2010	Asia (Singapore)	Cross-sectional	SARS	16 weeks after the first	78	415	246	169	- (36.6; 13.9)		27.64	23.07	25.8	-

Table 1 (*continued*)

ID	Quality score	First author, publication year (reference)	Continent (Country)	Study design (Study base)	Type of pandemics/outbreaks	Time of measurement	Response rate, %	Total, n	Male, n	Female, n	Age (Mean; SD)	Instrument	PTSD/PTSS outcome/s			
													Male, %	Female, %	Both, %	Mean (SD)
				study (General population)		national outbreak						Impact of Event Scale-Revised (IES-R)				
27	17	Sin, S. S. 2004	Asia (Singapore)	Cross-sectional study (Healthcare workers)	SARS	2 months after the outbreak	85.45	47	-	-	<25- 50 (38.5; 12.3)	Impact of Event Scale (IES)	-	-	12.8	-
28	23	Su, T. P. 2007	Asia (Taiwan)	Longitudinal study (Healthcare workers)	SARS	During the outbreak	-	102	0	102	- (25.4; 3.7)	Chinese version of the Davidson Trauma Scale (DTS-C)	-	28.43	-	-
29	20	Sun, L. 2020	Asia (China)	Cross-sectional study (General population)	COVID-19	During pandemic	-	2091	819	1272	<18->=60	The PTSD Checklist for DSM-5 (PCL-5)	-	-	4.6	-
30	25	Tan, B. YQ. 2020	Asia (Singapore)	Cross-sectional study (Healthcare workers)	COVID-19	During pandemic	94	470	149	321	28-36	Impact of Event Scale-Revised (IES-R)	-	-	7.7	9.4 (10.08)
31	25	Tang, W. 2020	Asia (China)	Cross-sectional study (General population)	COVID-19	During pandemic	99.3	2485	960	1525	16-27 (19.81; 1.55)	PTSD CheckList-Civilian Version (PCL-C)	-	-	2.7	-
32	25	Tham, K.Y. 2005	Asia (Singapore)	Cross-sectional study (Healthcare workers)	SARS	After the outbreak; in the first two weeks of November 2003	77.4	96	30	66	>18	Impact of Event Scale (IES)	10	21.2	17.7	-
33	20	Um, D. H. 2017	Asia (South Korea)	Cross-sectional study (Healthcare workers)	MERS	After the pandemic was over	-	64	40	24	30-70	Impact of Event Scale-Revised (IES-R)	-	-	7.8	-
34	20	Wu, P. 2009	Asia (China)	Longitudinal study (Healthcare workers)	SARS	3 years after the outbreak	83	549	130	419	<=34->51	Impact of Event Scale-Revised (IES-R)	-	-	10	8.7
35a	22	Wu, K. K. 2005	Asia (Hong Kong)	Cross-sectional study (Survivors)	SARS	1 month after discharge	28	131	57	74	18-84 (41.82; 14.01)	Impact of Event Scale-Revised (IES-R)	-	-	4	-
35b	22	Wu, K. K. 2005	Asia (Hong Kong)	Cross-sectional study (Survivors)	SARS	3 months after discharge	28	131	57	74	18-84 (41.82; 14.01)	Impact of Event Scale-Revised (IES-R)	-	-	5	-
36	21	Wu, K. K. 2005	Asia (Hong Kong)	Cross-sectional	SARS	1 month after discharge	41	195	84	111			-	-	6	-

Table 1 (*continued*)

ID	Quality score	First author, publication year (reference)	Continent (Country)	Study design (Study base)	Type of pandemics/ outbreaks	Time of measurement	Response rate, %	Total, n	Male, n	Female, n	Age (Mean; SD)	Instrument	PTSD/PTSS outcome/s Male, %	Female, %	Both, %	Mean (SD)
				study (Survivors)							18-88 (41.52; 13.98)	Impact of Event Scale-Revised (IES-R)				-
37	23	Yin, Q. 2020	Asia (China)	Cross-sectional study (Healthcare workers)	COVID-19	During pandemic	98.41	371	143	228	18-60 (35.3; 9.48)	The PTSD Checklist for DSM-5 (PCL-5)	2	4.80	3.8	-
38a	23	Wang, C. 2020	Asia (China)	Longitudinal study (General population)	COVID-19	During pandemic	92.7	1304	427	877	12-59	Impact of Event Scale-Revised (IES-R)	-	-	-	32.98 (16.34)
38b	23	Wang, C. 2020	Asia (China)	Longitudinal study (General population)	COVID-19	1 month after first survey	99.5	861	216	645	12-59	Impact of Event Scale-Revised (IES-R)	-	-	-	30.76 (15.42)

3.2. Meta-analysis

The total prevalence rate of 18% (95%CI: 15-20%; I^2: 97.52%) for PTSD related symptoms was estimated in coronavirus outbreaks (Figure 2). Subgroup analysis was performed and the variation in prevalence rates of PTSD symptoms by study characteristics was assessed (Supplement 2). PTSD symptoms were more frequent in cohort based studies (29%) compared to cross-sectional (15%) and case-control (11%) studies. Prevalence rates of PTSD in MERS (36%) outbreaks were also significantly higher than SARS (18%) and COVID-19 (9%) outbreaks.

To explore the source of heterogeneity, meta-regression was conducted. It was identified that the geographical location of study was the source of heterogeneity (R^2: 19.8%, P-value: 0.003) (Table 2). Analyses of publication bias for studies estimated the total prevalence of PTSD was performed and bias was found by both Begg`s test (z= 1.99; Pr= 0.047) and Egger`s test (p= 0.002) (Figure 3A).

3.3. Sensitivity analysis

By specifying $I^2 = 10\%$ and $tau^2 = 0.25$, sensitivity meta-analyses were performed to check the impact of heterogeneity on effect size and the effect size remained significant ($tau^2 = 0.25$: ES, 0.19 with the 95% CI of [.0258572, .3533172], SE, 0.084, p = 0.023, $I^2 = 99.9\%$; $I^2 = 10$: ES, 0.086 with the 95% CI of [.0811136, .0905173], SE, 0.002, p = 0.000, $tau^2 = 0.000$).

3.4. PTSD related symptoms among healthcare workers and meta-analysis

We found 15 studies estimated the prevalence of PTSD related symptoms among healthcare workers; including 5628 participants from Canada (n= 1) (Lancee et al., 2008), China (n= 3) (Huang & Zhao, 2020; P. Wu et al., 2009; Yin et al., 2020), Singapore (n= 4)(Chan and Huak, 2004; Sin & Huak, 2004; W. Tan et al., 2020; Tham et al., 2005), Singapore and India (n= 1) (Chew et al., 2020), South Korea (n= 4) (Jung et al., 2020; Kim et al., 2018; S. M. Lee et al., 2018; Um et al., 2017), and Taiwan (n= 2) (C. S. Chen et al., 2005; Su et al., 2007). One study only reported the mean and standard deviation of the IES score and was excluded from the meta-analysis (Chong et al., 2004).

The prevalence rate of PTSD related symptoms was estimated to be 18% among healthcare workers (95%CI: 13-24%; I^2: 97.21%) (Figure 4A). By conducting subgroup analysis, no significant differences were observed among variables of each subgroup (Suoolement 2).

We conducted analyses of publication bias for studies estimated the prevalence of PTSD among healthcare workers (Figure 3B). No evidence of publication bias was found by Begg`s test (z= 1.73; Pr= 0.083). Egger`s test, however, showed the significant publication bias (p= 0.011).

3.3. PTSD related symptoms among survivors of coronavirus and meta-analysis

There were 10 studies assessed the prevalence of PTSD related symtoms among survivors including 794 individuals from Canada (n= 1) (Assar et al., 2010), China (n= 2) (Guo et al., 2020; Hong et al., 2009), Hong Kong (n= 3) (Mak et al., 2010; K. K. Wu et al., 2005a, 2005b), Singapore (n= 1) (Kwek et al., 2006), and South Korea (n= 3) (S. H. Lee et al., 2019; Park et al., 2020; Shin et al., 2019). Two of these studies reported the overlapping samples and the study with larger sample size was included in the meta-analysis (K. K. Wu et al., 2005a, 2005b)

We estimated the prevalence rate of 29% for PTSD related symptoms among survivors of coronavirus (CI: 18-39%; I^2: 96.14%) (Figure 4B). Subgroup analysis showed that prevalence rate of PTSD or PTSD related symptoms in longitudinal studies and during outbreaks was statistically higher than cross-sectional studies and after outbreaks; respectively
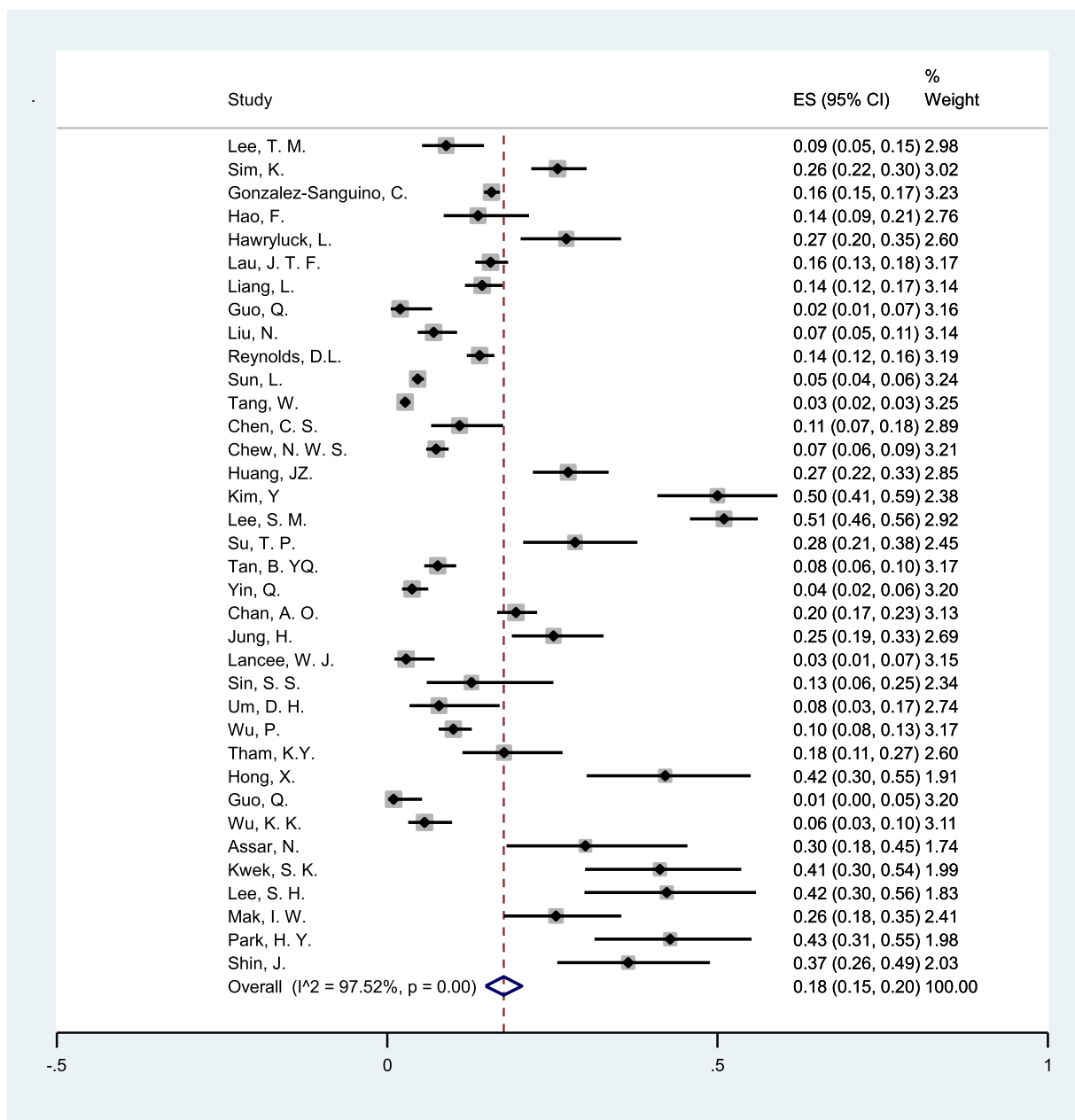
Figure 2. The prevalence of PTSD based on all included studies

Table 2
Meta-regression of studies to find heterogeneity

Moderator	No. of observations	Meta-regression				The proportion of total between-study variance explained
		Coef.	SE	z	P	R^2
Geographic location (Country)	36	.0338564	.01147	2.95	**0.003**	19.80
Publication year	36	-.0007586	.0035984	-0.21	0.833	0.00
Quality	36	-.0067987	.0081177	-0.84	0.402	0.00
Setting	36	.0154198	.0176116	0.88	0.381	0.00
hCoV type	36	-.0416724	.0256283	-1.63	0.104	4.98
Sample size	36	-.0000499	.0000307	-1.63	0.104	4.04
Age	18	.0014586	.0089933	0.16	0.871	0.00
Mean age	21	.002664	.004295	0.62	0.535	0.00

(Supplement 2).

Analyses of publication bias showed no evidence of publication bias by both Begg`s test (z= 0.00; Pr= 1.00) and Egger`s test (p= 0.59) (Figure 3C).

3.4. PTSD related symptoms among general population and meta-analysis

We found 12 studies estimated the prevalence of PTSD or PTSD related symptoms among general population including 13006
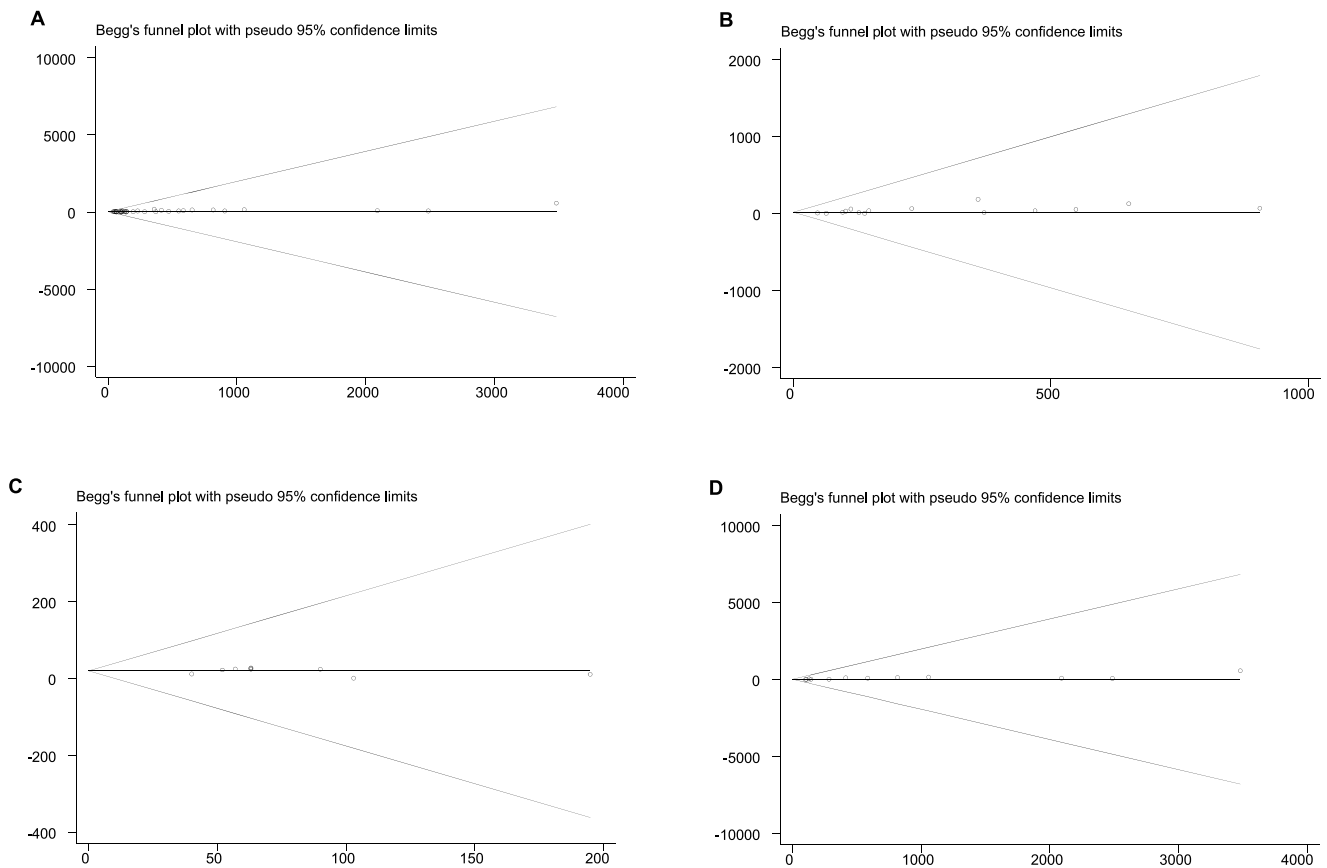
Figure 3. (A) Publication bias for prevalence of PTSD symptoms in all included studies (B) Publication bias for PTSD symptoms among healthcare workers (C) Publication bias for PTSD symptoms among survivors (D) Publication bias for PTSD symptoms among general population
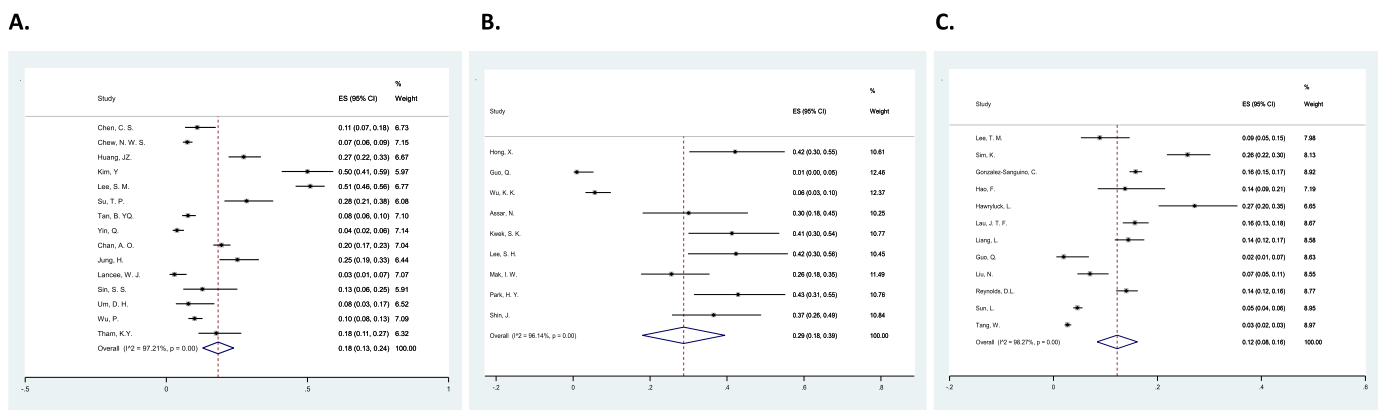

Figure 4. (A) Prevalence of PTSD symptoms among healthcare workers. (B) Prevalence of PTSD symptoms among survivors of coronavirus infection. (C) Prevalence of PTSD symptoms among general population.

participants from Canada (n= 2) (Hawryluck et al., 2004; Reynolds et al., 2008), China (n= 6) (Guo et al., 2020; Hao et al., 2020; Liang et al., 2020; Liu et al., 2020; Sun et al., 2020; Tang et al., 2020), Hong Kong (n= 2) (Lau et al., 2006; T. M. Lee et al., 2006), Singapore (n= 1) (B. Y. Tan et al., 2020), and Spain (n= 1) (Gonzalez-Sanguino et al., 2020). One study only reported the mean and standard deviation of the scores and thus was excluded from the meta-analysis (C. Wang et al., 2020); One study assessed the prevalence rates in two different populations (general population and survivors) and both were included in the meta-analysis (Guo et al., 2020).

The prevalence rates of 12% were estimated for PTSD related symptoms among general population (95%CI: 8-16%; I^2: 98.27%)

(Figure 4C). By conducting subgroup analysis, no significant differences were observed among variables of each subgroup (Supplement 2).

Analyses of publication bias were performed for studies estimated the prevalence of PTSD related symptoms among general population (Figure 3D). No evidence of publication bias was found by Begg`s test (z= 1.51; Pr= 0.13) but Egger`s test indicated the significant publication bias (p= 0.006).

4. Discussion

To our knowledge, this is the first systematic review and meta-analysis assessed the prevalence of PTSD or PTSD related symptoms

among different populations across the three most recent coronavirus outbreaks. Our meta-analysis showed that about three in every ten survivors of coronavirus infection, about two in every ten healthcare workers, and about one in every ten individuals of general population were reported to have a diagnosis of PTSD or PTSD related symptoms during and/or after outbreaks. Most studies included in this systematic-review were about epidemic SARS outbreaks that affected approximately 8100 individuals worldwide. We are now in the middle of pandemic COVID-19 outbreak with over 43 million diagnosed cases and more than 1 million deaths, as of October 2020. This can be a great warning to all of us that people will be in great risk of developing psychiatric disorders including PTSD. Mental care should not be, therefore, underestimated at the present time; especially for the survivors of the disease.

PTSD is an anxiety disorder that can significantly affect the quality of lives of people. It was estimated that the global prevalence of this condition was 1.1% in 2014 (Karam et al., 2014). Our study showed that infectious disease outbreaks could significantly increase the prevalence rate of PTSD. For years, the burden of anxiety disorders was underestimated due to limited numbers of surveys in this field. It is now found that anxiety disorders are the sixth leading cause of years with life disabilities in high and middle to low income countries (Baxter et al., 2014). Studies showed that PTSD was associated with higher risk of future physical and psychiatric co-morbidities. Depression, substance use, suicide, and chronic illness are more common among these individuals (Karatzias et al., 2019). A four-year follow-up study in China reported that patients that survived from SARS outbreak and were diagnosed with PTSD had severe and persistent psychiatric symptoms that affected both mental and physical health (Hong et al., 2009).

Some studies assessed the risk factors of developing PTSD in coronavirus outbreaks. Among healthcare workers, level of exposure to the infectious disease and duration of contacts with infected people were important risk factor (Carmassi et al., 2020) . Two case-control studies during SARS outbreaks in China and Taiwan reported that staff of emergency departments were at up to 3 times increased risk of PTSD development compared to healthcare workers of non-emergency departments (Lin et al., 2007; P. Wu et al., 2009). Another study conducted in Toronto, Canada, showed that SARS outbreaks had higher impact on nurses and they had higher IES score compared to other hospital workers. This could be due to longer contacts with infected people (Maunder et al., 2003). Quarantine and previous psychiatric disorders were other reported risk factors of PTSD among healthcare workers (Carmassi et al., 2020). Among general population, one study during COVID-19 outbreak on 2485 university students, showed that being an only child, short sleep duration, living in the worst-hit areas, and students who were in the final year of university were significantly at higher risk of developing PTSD (Tang et al., 2020).

There were some limitations to our study. High heterogeneity was seen between studies and about half of the studies had low quality. These factors can make interpretation and generalization of results challenging. Objective assessment of PTSD symptoms is limited and the diagnosis is reliant on reports of individuals and self-report rating scales that can lead to information bias in our included studies. Numbers of published papers about the association between COVID-19 outbreaks and risk of developing PTSD were limited until the date we searched. Future systematic-reviews should assess this correlation. Risk factors and predictors of PTSD development were not evaluated in our study that should be resolved in future studies. Observational studies with long-term follow-up periods should also be conducted to show the prognosis and risk of developing future mental and physical co-morbidities.

In conclusion, PTSD or PTSD related symptoms were shown to be common in coronavirus outbreaks in the last two decades. Mental health care should be considered to prevent this condition during and after pandemic COVID-19 outbreaks.

Author statement

Manuscript Title: The Prevalence of Post-Traumatic Stress Disorder Related Symptoms in Coronavirus Outbreaks: A Systematic-Review and Meta-Analysis

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Mohammadreza Mohammadi: Conception and design of the study; Revising the manuscript critically for important intellectual content

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Declaration of Competing Interest

All authors declare no conflict of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2020.12.188.

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