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META-ANALYSIS

Mental health impact of the Middle East respiratory syndrome, SARS, and COVID-19: A comparative systematic review and meta-analysis

Gayathri Delanerolle, Yutian Zeng, Jian-Qing Shi, Xuzhi Yeng, Will Goodison, Ashish Shetty, Suchith Shetty, Nyla Haque, Kathryn Elliot, Sandali Ranaweera, Rema Ramakrishnan, Vanessa Raymont, Shanaya Rathod, Peter Phiri

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Abstract

BACKGROUND

Over the last few decades, 3 pathogenic pandemics have impacted the global population; severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV) and SARS-CoV-2. The global disease burden has attributed to millions of deaths and morbidities, with the majority being attributed to SARS-CoV-2. As such, the evaluation of the mental health (MH) impact across healthcare professionals (HCPs), patients and the general public would be an important facet to evaluate to better understand short, medium and long-term exposures.

AIM

To identify and report: (1) MH conditions commonly observed across all 3 pandemics; (2) Impact of MH outcomes across HCPs, patients and the general public associated with all 3 pandemics; and (3) The prevalence of the MH impact and clinical epidemiological significance.

METHODS

A systematic methodology was developed and published on PROSPERO (CRD42021228697). The databases PubMed, EMBASE, ScienceDirect and the Cochrane Central Register of Controlled Trials were used as part of the data extraction process, and publications from January 1, 1990 to August 1, 2021 were searched. MeSH terms and keywords used included *Mood disorders, PTSD, Anxiety, Depression, Psychological stress, Psychosis, Bipolar, Mental Health, Unipolar, Self-harm, BAME, Psychiatry disorders and Psychological distress*. The terms were expanded with a 'snowballing' method. Cox-regression and the Monte-Carlo simulation method was used in addition to I^2 and Egger's tests to determine heterogeneity and publication bias.

RESULTS

In comparison to MERS and SARS-CoV, it is evident SAR-CoV-2 has an ongoing MH impact, with emphasis on depression, anxiety and post-traumatic stress disorder.

CONCLUSION

It was evident MH studies during MERS and SARS-CoV was limited in comparison to SARS-CoV-2, with much emphasis on reporting symptoms of depression, anxiety, stress and sleep disturbances. The lack of comprehensive studies conducted during previous pandemics have introduced limitations to the "know-how" for clinicians and researchers to better support patients and deliver care with limited healthcare resources.

Key Words: COVID-19; Middle East respiratory syndrome; SARS-CoV; SARS-CoV-2; Mental health; Wellbeing; Psychiatry; Healthcare professionals; Patients; Physical health; Public health; Outbreaks and pandemics

Core Tip: Global research into exploring pandemics have been conducted for several decades. However, clinical research associated with mental health (MH) impact of Middle East respiratory syndrome, severe acute respiratory syndrome coronavirus (SARS-CoV) and SARS-CoV-2 was limited. This systematic review and meta-analysis is a comparison of the MH impact across, healthcare professionals, patients and the general public using the Monte-Carlo simulation method. Evaluated prevalence of multiple MH variables have been conducted using randomised controlled trials and cross-sectional studies. The study demonstrates the need to conduct comprehensive and longitudinal multi-morbid research to evaluate the true MH impact to aid better future pandemic preparedness. This systematic review and meta-analysis indicate a complex MH impact across all cohorts with the requirement for mechanistic relationships between physical and MH to be explored further.

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INTRODUCTION

Human civilisations have endeavoured various infectious diseases over centuries with multiple causatives, increases in population density, and increases in migration could attribute to increase in risk of emerging infectious diseases leading to global endemics and pandemics. Medicine in the modern era provide solutions to manage and mitigate infectious threats although there are many challenges associated with communicable and non-communicable diseases.

Fast forward to the 21st century, there have been three prominent outbreaks caused by novel coronaviruses[1]. The World Health Organisation (WHO) have classified two of these outbreaks as pandemics. Understanding the coronavirus family to prevent future pandemics would be useful.

The 2003 severe acute respiratory syndrome (SARS)-associated coronavirus (SARS-CoV) comprised of the Middle East respiratory syndrome coronavirus (MERS-CoV) which includes a family of enveloped, single-stranded and diverse RNA viruses consisting of four genera: alpha, beta, gamma and delta (*α*-, *β*-, *γ*- and *δ*-*CoV*). Of these, alpha and beta-coronaviruses appear to be more deadly due to its ability to transmit across animals and humans, leading to stronger pathogens. Coronaviruses were first identified in 1965[2]. The SARS-CoV was the first outbreak in 2012. Neither of the outbreaks reached a pandemic status. Genetically similar to SARS-CoV, the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), officially declared as a pandemic on March 11, 2020, continues to engulf global populations.

In comparison to the current SARS-CoV-2 pandemic, the SARS-CoV outbreak was effectively managed with aggressive public health measures amongst the countries affected[3]. Although, there are multi-factorial composites to consider to assess physical and mental health impact on the previous and current populations. For example, SARS-CoV reported an incidence and mortality of 8096 and 774 respectively across 29 countries[4].

In contrast, MERS-CoV outbreaks were reported across 27 countries between 2012-2019, mainly within the Middle East, with Saudi Arabia reporting majority of the cases based on WHO data[5]. However, incidence reporting of MERS-CoV over the last 7 years have been sporadic, indicating it is less contagious compared to the current SARS-CoV-2 infection. To date, there have been 2578 reported cases and 888 deaths due to MERS-CoV, with a crude mortality rate of around 34.4%[5]. Management of these infections primarily consist of public health measures to identify and isolate patients and effective infection control measures to reduce transmission rates[6]. Failures in effectively managing these outbreaks have primarily been attributed to the late identification of the disease. Secondary measures include quarantine failures due to non-disclosures by patients and poor communication between officials and the public[7,8].

Most patients with SARS-COV-2 are asymptomatic or develop mild symptoms[9]. However, for a small minority, they are likely to require admission to hospital with severe respiratory compromise which can lead to critical illness with respiratory failure and multiple organ failure[9]. These cases require high-level medical care within an intensive care unit (ICU) setting, including ventilatory support. Dexamethasone and Remdesivir are used alongside supportive measures and have proved effective in reducing mortality and hospital length of stay[10,11]. Interventions such as pruning, which has been recommended in the treatment of severe COVID-19 disease[12], have become common place in ICU settings, but is a labour-intensive procedure, putting further pressure on staff.

The global response to SARS-COV-2

The high degree of viral homology between SARS-COV-2 and previous coronavirus outbreaks directed the initial global response to the coronavirus disease 2019 (COVID-19) pandemic[13]. Given the relatively small population sizes involved in the first two novel coronavirus outbreaks, in addition to the geographical areas affected, the global understanding that shaped our response was probably limited in its scope. We recognise now it is in fact the differences, not the similarities, that have driven the rapid spread of the virus, including more prominent community spread and higher transmissibility of SARS-CoV-2, which includes asymptomatic and mildly symptomatic patients not seen in SARS-CoV [14].

The spread comparison between SARS-CoV, MERS-CoV and SARS-CoV-2

The characteristics of the emerging SARS-CoV-2 appears to be changing with the appearance of new variants, which is different to its predecessors, SARS-CoV and MERS-CoV. At the height of the SARS-CoV era, 140 new infections were reported *per* week, whilst current data suggest SARS-CoV-2 transmits approximately 100000 new infections *per* week during its peak period between February and May 2020 [15,16]. In addition to the common transmission network, viral shedding for SARS-CoV-2 in particular starts prior to symptom onset, which was the opposite with SARS-CoV. Therefore, quarantine measures would have been more effective during SARS-CoV in comparison to SARS-CoV-2.

The mental health impact of SARS-CoV-2

One of the long-term unknowns about the current pandemic is the physical manifestations and its impact on the mental health as well as the well-being of the public, patients and front-line healthcare professionals (HCPs). Experience from the previous novel coronavirus outbreaks suggests that the psychological impacts will be widespread and long-lasting. Significant psychological symptomatology has been reported in the acute and early recovery phases associated with SARS-CoV[17-22] and MERS-CoV[17,23] in all three groups considered in this review. Importantly, when considering the long-term effects of this pandemic, the impact of the SARS-CoV pandemic was still recorded amongst infected individuals over four years after the reported outbreak, and in some cases with deteriorating symptoms [13].

The morphological and demographic features of the 3 viruses are vital to understand the mental health impact. Physical manifestations drive the mental health impact, often interacting as a planarian.

MATERIALS AND METHODS

A systematic review protocol was designed, internally peer-reviewed and published on PROSPERO (CRD42021228697) with a comprehensive search strategy and data extraction method.

Research question/aims

This study has 3 primary aims of identifying and reporting: (1) Mental health (MH) conditions commonly observed across all 3 pandemics; (2) Impact of MH outcomes across HCPs, patients and the general public associated with all 3 pandemics; and (3) The prevalence of the MH impact and clinical epidemiological significance.

Data searches

Multiple databases of PubMed, EMBASE, ScienceDirect and the Cochrane Central Register of Controlled Trials were used to extract relevant data. MeSH terms and keywords used included *Mood disorders, PTSD, Anxiety, Depression, Psychological stress, Psychosis, Bipolar, Mental Health, Unipolar, Self-harm, BAME* (*Black, Asian and Minority Ethnic*), *Psychiatry disorders* and *Psychological distress*. The terms were expanded with a 'snowball' method that has been demonstrated with a PRISMA diagram. All publications that were peer-reviewed in English were included. The final dataset was reviewed independently before the analysis was conducted.

Data synthesis

The data synthesis is based on the statistical data extracted from the studies included based on the eligibility criteria developed. This includes data associated with the mean ± SD and median along with q_1 (25% quantile) and q_3 (75% quantile). Q1 and q_3 are novel estimation methods used to improve existing meta-analysis as demonstrated by Wan and colleagues[24]. Most of the studies identified reported multiple MH outcomes such as depression, anxiety and psychological distress among people who experienced MERS, SARS-CoV and SARS-CoV-2. For studies that reported the median along with q_1 and q_3, the mean ± SD of the studies were estimated from the median, q_1 and q_3. Therefore, the following equation was used to analyse the data, where the Φ^{-1} represented the inverse of the standard normal distribution, as described below.

Most MERS-CoV studies only reported SD. Some studies included the median only, and these were transformed to q_1 and q_3, where the mean ± SD were estimated using the Monte-Carlo simulation method, with the cut off scores of the MH assessments used within the studies. This data was assumed to be normally distributed. Random effects models were used to conduct the meta-analysis to estimate the pooled prevalence. MH assessments reported within the studies included the Impact of Event Scale-Revised (IES-R), Hospital Anxiety and Depression Scale (HADS), Patient Health Questionnaire (PHQ-9), Short Form 36 Health Survey (SF-36), General Anxiety Disorder (GAD-7) and State-Trait Anger Expression Inventory (STAXI). For this we assumed normal distribution of the data. A subgroup analysis was conducted to evaluate any identified heterogeneity. Funnel plots and Egger's tests were performed to demonstrate publication bias and a sensitivity analysis. A comparative analysis was conducted using the SAR-CoV and SARS-CoV-2 data published by Chau *et al*[25].

The full data analysis was conducted using the STATA 16.1 software application.

Risk of bias quality assessment

A quality assessment was performed using the Newcastle-Ottawa-Scale (NOS) for studies included systematically (Supplementary Table 1). The NOS is an eight-item scale with three quality parameters: (1) Selection; (2) Comparability; and (3) Outcome. We rated the quality of the studies (good, fair and poor) by allocating each domain with stars in this manner: (1) A Good quality score was awarded 3 or 4 stars in selection, 1 or 2 in comparability, and 2 or 3 stars in outcomes; (2) A Fair quality score was awarded 2 stars in selection, 1 or 2 stars in comparability, and 2 or 3 stars in outcomes; and (3) A Poor quality score was allocated 0 or 1 star(s) in selection, 0 stars in comparability, and 0 or 1 star(s) in outcomes domain.

RESULTS

The comprehensive multiple database literature search included publications from January 1, 1990 to August 1, 2021. The PRISMA diagram reflects the total yielded studies and systematic inclusions prior to the completion of the meta-analysis as shown in Figure 1.

MERS-CoV

A total of 58 studies were included in the systematic review for MERS as shown in Supplementary Table 2. The search for MERS-CoV yielded 14, 144 of which 152 articles met the inclusion criteria to be reviewed by title and abstract. Eleven duplicates were removed. A further 29 studies were excluded as these were not pertinent to the MERS-CoV demonstrating MH outcomes, and 38 studies were excluded due to the lack of statistical data. Fifteen articles that were not published in English was also excluded. Therefore, the meta-analysis was conducted on 21 studies as demonstrated in Table 1.

SARS-CoV

In relation to the SARS-CoV, the systematic review was conducted on 80 studies, as detailed in Supplementary Table 3, and the meta-analysis included 39 studies, as shown in Table 2.

SARS-CoV-2

A total of 513 studies were included in the systematic review for SARS-CoV-2, as shown in Supplementary Table 4. 287 of these studies are from the meta-analysis conducted by Phiri *et al*[26]. The meta-analysis was conducted on 188 studies, as demonstrated in Supplementary Table 5.

Meta-analysis

Anxiety: Eight studies reported the prevalence of anxiety during the MERS-CoV outbreak. As demonstrated by Figure 2, the pooled prevalence of anxiety was 17.35% with a 95% confidence interval (CI): 8.36-36.02. A heterogeneity of I^2 = 95.62% was identified.

The systematic review indicates 14 studies report the prevalence of anxiety during SARS-CoV, although only 9 report the mean ± SD. Twenty-three studies were included into the meta-analysis. Figure 3 indicates the prevalence of anxiety during SARS-CoV where the pooled prevalence was 25.2%, with a 95%CI of 18.41-34.5. A high heterogeneity of I^2 = 93.47% was identified.

The systematic review identified 175 studies that reported anxiety as an outcome due to SARS-CoV-2 where 40 studies provided mean and SD. By utilizing the Monte-Carlo simulation on the studies that only provide mean and SD, we obtained twenty-five studies that reported the prevalence of anxiety. As for the anxiety resulting from SARS-CoV-2, Figure 4 shows a pooled prevalence of 21.44% with a 95%CI of 18.69-24.61. However, a high heterogeneity of 99.77% was identified.

Based on these results, the prevalence of anxiety during SARS-CoV is more significant in comparison to MERS-CoV and SARS-CoV-2.

Depression

The systematic search for MERS-CoV yielded seven studies reporting depression. The meta-analysis is demonstrated in Figure 5 and shows a pooled prevalence of 33.65%. The 95%CI ranged between 22.02-51.42. A moderate heterogeneity of at I^2 = 69.86% was identified.

Thirty-eight studies reported the prevalence of depression during the SARS-CoV outbreak. Of these, 23 reported prevalence directly and 15 demonstrated the mean score and SD instead. By using the Monte-Carlo simulation method, thirty-eight results were meta-analysed as demonstrated in Figure 6. The pooled prevalence of depression during the pandemic of SARS-CoV was 23.1%, while the 95%CI was between 18.14-29.4. A high heterogeneity was calculated at I^2 = 95.03%.

One hundred and twenty-three studies reported on depression during SARS-CoV-2. Of these, 102 reported the prevalence of depression directly and 21 demonstrated mean and SD values only. Figure 7 indicates the pooled prevalence of depression during SARS-CoV-2 was 27.68%, with a 95%CI ranging from 24.67-31.06. A high heterogeneity of I^2 = 99.71% was identified.

Based on the analysis, MERS-CoV and SARS-CoV-2 appear to report the highest levels of depression based on the pooled prevalence of 27.64% and 33.65% respectively.

Post-traumatic stress disorder

Twenty-seven studies reported post-traumatic stress disorder (PTSD) during the MERS-CoV outbreak. Figure 8 demonstrated a pooled prevalence of 35.97%, with a relatively moderate to high heterogeneity of I^2 = 75.2% and a 95%CI ranging between 29.60-43.72.

Sixty-four of the studies identified had reported on the prevalence of PTSD during SARS-CoV. Of these, 48 studies reported on the prevalence directly, whilst 17 demonstrated the mean score and the corresponding SD. Figure 9 shows the pooled prevalence of PTSD was 18.2% with a CI of 14.94-22.18 and an elevated heterogeneity of I^2 = 91.37%.

Table 1 21 studies that are included in meta-analysis for Middle East respiratory syndrome

Study ID	Ref.	Study type	Sample size	Country	Exposure	Outcome	*P* value	Quality assessment (NOS)
1	Shin *et al*[36]	Quantitative	63	Korea	MERS patients	PTSD, Sleep problem, anxiety, depression, suicidality, phobic anxiety, addiction, aggression	Not specified	7
2	Um *et al*[37]	Quantitative	64	Korea	MERS patients and HCWs	PTSD, depression	Not specified	7
3	Abolfotouh *et al*[38]	Quantitative	1031	Saudi Arabia	HCWs	Level of Concern	Not specified	7
4	Jung *et al*[39]	Quantitative	147	Korea	HCWs	PTSD	Not specified	6
5	Ahn *et al*[40]	Quantitative	63	Korea	MERS Patients	Suicide, fatigue	Not specified	6
6	Lee *et al*[41]	Quantitative	52	Korea	MERS Patients	Depression, PTSD, fatigue	Not specified	6
7	Kim *et al*[42]	Quantitative	112	Korea	HCWs	PTSD, burnout	Not specified	7
8	Oh *et al*[43]	Quantitative	313	Korea	HCWs	Stress	Stress: 0.066	7
9	Seo *et al*[44]	Quantitative	171	Korea	HCWs	Burnout	Not specified	5
10	Son *et al*[45]	Quantitative	280	Korea	HCWs and general public	PTSD	Not specified	6
11	Park *et al*[46]	Quantitative	187	Korea	HCWs	Stress	Not specified	6
12	Jeong *et al*[24]	Qualitative	1692	Korea	MERS patients and general public	Anxiety	Not specified	7
13	Al-Rabiaah *et al*[47]	Quantitative	174	Saudi Arabia	General public	Anxiety	Not specified	7
14	Park *et al*[48]	Quantitative	63	Korea	MERS Patients	PTSD, depression	Not specified	7
15	Cho *et al*[49]	Quantitative	111	Korea	General public	PTSD	PTSD: 0.3	7
16	Kim *et al*[50]	Quantitative	27	Korea	General public	Depression	Not specified	5
17	Lee *et al*[51]	Quantitative	359	Korea	HCWs	PTSD	Not specified	6
18	Kim and Choi[52]	Quantitative	215	Korea	HCWs	Burnout, stress	Not specified	6
19	Bukhari *et al* [53]	Quantitative	386	Saudi Arabia	HCWs	Worry	Not specified	6
20	Mollers *et al* [54]	Quantitative	72	Netherlands	General public	PTSD	Not specified	5
21	Kim and Choi[52]	Quantitative	215	Korea	HCWs	PTSD: 0.017	PTSD: 0.017	6

PTSD: Post-traumatic stress disorder; MERS: Middle East respiratory syndrome; HCW: Healthcare worker.

Nineteen studies reported the prevalence of PTSD during SARS-CoV-2. Figure 10 indicates a pooled prevalence of PTSD of 25.03% with a 95%CI ranging between 18.15-34.51. A high heterogeneity of I^2 = 99.58% was identified.

Based on the findings, PTSD appears to have been reported for SARS-CoV-2, MERS-CoV and SARS-CoV.

A comparative analysis was completed for each MH variable identified and reported, as demonstrated within Tables 3-5.

Table 2 39 studies that are included in meta-analysis for severe acute respiratory syndrome

Study ID	Ref.	Study type	Sample size	Country/region	Exposure	*P* value	Quality assessment (NOS)
1	Kwek *et al*[20]	Cross-sectional	360	Singapore	SARS patients	PTSD: 0.79; Depression: 0.7; Anxiety: 0.51	7
2	Fang *et al*[55]	Cross-sectional	1278	China	SARS patients	Anxiety: 0.291; Depression: 0.705; PTSD: 0.2	8
3	Liang[56]	Prospective cohort	769	China, Taiwan	SARS patients	PTSD: > 0.05; Anxiety: > 0.05	7
4	Dang *et al*[57]	Cross-sectional	549	China	General public	Anxiety: < 0.00001; Depression: 0.000361	7
5	Yip[58]	Prospective cohort	218	China, Hong Kong	SARS patients	Not specified	6
6	Cheng *et al* [59]	Cross-sectional	10	China, Hong Kong	SARS patients	Anxiety: > 0.05; Depression: > 0.05	5
7	Wu *et al*[60]	Cross-sectional	286	China, Hong Kong	SARS patients	PTSD: < 0.001; Depression: < 0.05; Anxiety: < 0.01	6
8	MaK *et al*[61]	Retrospective cohort	126	China, Hong Kong	SARS patients	Not specified	5
9	Lee *et al*[62]	Cross-sectional	10511	China, Hong Kong	Were not HCWs	Not specified	7
10	Hong *et al*[63]	Cross-sectional	1050	China	SARS patients	PTSD: 0.0323	7
11	Wang[64]	Prospective cohort	22	China	SARS patients	Not specified	4
12	Hu *et al*[65]	Cross-sectional	763	China	Attended hospital for other reasons	Not specified	5
13	Chen *et al*[66]	Prospective cohort	325	China, Taiwan	Non-infected HCWs in the largest obligatory SARS hospital, with high SARS contact	Anxiety: 0.55 Depression: 0.93	6
14	Ko *et al*[67]	Cross-sectional	72	China, Taiwan	General public of outbreak area	Depression: 0.02	5
15	Lee *et al*[21]	Cross-sectional	114	China, Hong Kong	General public of outbreak area	Not specified	6
16	Hawryluck *et al*[68]	Cross-sectional	652	Canada, Toronto	General public of outbreak area	Depression: 0.85; PTSD: 0.82	7
17	Liu *et al*[69]	Cross-sectional	96	China, Beijing	Non-infected HCWs of SARS hospital	Depression: < 0.05	7
18	Su *et al*[70]	Prospective cohort	57	China, Taiwan	Non-infected HCWs in SARS outbreak region with high exposure risk *vs* low exposure risk	PTSD: > 0.05; Depression: < 0.05	7
19	Lam *et al*[71]	Retrospective cohort	116	China, Hong Kong	SARS patients	Not specified	6
20	Shi *et al*[72]	Prospective cohort	87	China, Beijing	SARS outbreak region	Not specified	5
21	Huang *et al* [73]	Cross-sectional	4481	China, Beijing	Were not HCWs	Not specified	6
22	Yu *et al*[74]	Prospective cohort	180	China, Hong Kong	General public of outbreak area	Not specified	5
23	Chang and Sivam[75]	Cross-sectional	146	Singapore	General public of outbreak area	Not specified	5
24	Moldofsky and Patcai[76]	Retrospective cohort	107	Canada, Toronto	SARS patients, who were HCWs	Not specified	6
25	Sun *et al*[77]	Prospective cohort	1557	China, Xianxi	SARS patients	PTSD: 0.67	7
26	Lau *et al*[78]	Cross-sectional	333	China, Hong Kong	General public of outbreak area	Not specified	5

27	Reynolds *et al* [79]	Cross-sectional	89	Canada	General public of outbreak area, quarantined; non-infected HCWs in SARS outbreak region, quarantined	Not specified	5
28	Lancee *et al* [80]	Cross-sectional	613	Canada, Toronto	Non-infected HCWs in SARS outbreak region	Not specified	6
29	Lin *et al*[81]	Cross-sectional	6280	China, Taiwan, Taichung	Non-infected HCWs in in region without major SARS outbreak	Not specified	6
30	Gao *et al*[82]	Prospective cohort	127	China, Tianjin	SARS patients	Not specified	5
31	Xu *et al*[83]	Cross-sectional	129	China, Xianxi	Non-infected HCWs in SARS hospital	PTSD: > 0.05	6
32	Wong *et al*[84]	Cross-sectional	0 (?)	China, Hong Kong	Non-infected HCWs from SARS hospitals	Not specified	4
33	Sim *et al*[85]	Cross-sectional	90	Singapore	Non-infected HCWs in SARS outbreak region	Not specified	5
34	Wu *et al*[19]	Cross-sectional	133	China, Beijing	Non-infected HCWs in SARS hospital	Not specified	6
35	Chen *et al*[86]	Cross-sectional	103	China, Taiwan, Kaohsiung	Non-infected HCWs in SARS hospital, with high SARS contact; non-infected HCWs in SARS hospital; with low SARS contact	Not specified	6
36	Tham *et al*[87]	Cross-sectional	90	Singapore	Non-infected HCWs in SARS hospital with extra risk of exposure	Not specified	5
37	Maunder *et al* [88]	Cross-sectional	90	Canada, Toronto	Non-infected HCWs of outbreak area, unspecified (mix of SARS affected and non SARS affected hospitals	PTSD: < 0.01	7
38	Mak *et al*[89]	Retrospective cohort	126	China, Hong Kong	SARS patient	Not specified	6
39	McAlonan *et al*[90]	Cross-sectional	0 (?)	China, Hong Kong	Non-infected HCWs in SARS outbreak region with high exposure risk *vs* low exposure risk	Not specified	3

PTSD: Post-traumatic stress disorder; MERS: Middle East respiratory syndrome; HCW: Healthcare worker; CI: Confidence interval; SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2.

Table 3 Pooled prevalence and confidence interval of anxiety across Middle East respiratory syndrome coronavirus, severe acute respiratory syndrome coronavirus and severe acute respiratory syndrome coronavirus-2

Anxiety	Prevalence (%)	95%CI	Heterogeneity I^2 (%)
MERS	17.35	8.36-36.02	95.62
SARS-CoV-2	21.48	18.68-24.71	99.76
SARS-CoV	25.20	18.41-34.5	93.47

CI: Confidence interval; MERS: Middle East respiratory syndrome; SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2.

Table 4 Pooled prevalence and confidence interval of depression across three diseases

Depression	Prevalence (%)	95%CI	Heterogeneity I^2 (%)
MERS	33.65	22.02-51.42	69.86
SARS-CoV-2	27.64	24.59-31.06	99.69
SARS-CoV	23.10	18.14-29.4	95.03

CI: Confidence interval; MERS: Middle East respiratory syndrome; SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2.

Subgroup analysis

Multiple subgroup analyses using age group, cohort and location were conducted as an aim to identify the causation of the heterogeneity reported throughout the meta-analyses.

Age

SARS-CoV-2: The subgroup analysis of age includes 10-19, 20-29, 30-39, 40-49, 50-59, 60-69 (Supplementary Figure 1). In particular, it can be seen from Supplementary Figure 2 that the pooled prevalence for 10–19 year-olds who are likely to have depression due to SARS-CoV-2 is 24.42%. The pooled prevalence for 60–69 years old, on the other hand, was 7.75% with a lower prevalence of depression. Therefore, the details from these analyses demonstrate the statistically reported heterogeneity could be due to the inclusion of multiple age groups.

This is further demonstrated in Supplementary Figure 3, where similar results are indicated for those reporting PTSD among young people, which appears to be higher than the older population (for instance, 32.40% for 20-29 group compared while 5.38% for 50-59 group). However, this is still reflective of a high heterogeneity which could be attributed to the differences in body mass index or race, although, to make a conclusion, further research data is required.

SARS-CoV: The subgroup analysis based on age for the SARS-CoV indicate the prevalence of mental health issues in different age groups during SARS. Supplementary Figure 4 demonstrated that people from 50 to 59 years of age appear to have a higher risk of anxiety (51.62%) in comparison to those between 30-39 (27.4%) as indicated in Supplementary Figure 5. The prevalence of PTSD (Supplementary Figure 6) indicates people within the 30-39 age group report a relatively high risk (32.13%) of PTSD in comparison to those of 60-69 years of age. However, the age group of 60-69 years was based on a single study.

Comparison: Based on the comparison between the 3 meta-analyses, the following results associated with MH outcomes are as indicated within Tables 6-8.

Cohort

SARS-CoV-2: Another facet of the subgroup analysis was based upon the cohorts included within this study, of HCPs, patients and the general public. The MH outcomes are demonstrated in Supplementary Figures 7-9. It is evident that healthcare workers (HCWs) have a higher prevalence of anxiety and depression compared to the general public. The exception to this appears to be the prevalence of PTSD, where the levels appear to be similar for the public and HCWs, at 24.83% and 25.16% respectively.

MERS: Supplementary Figure 10 demonstrates that the general public consists of a smaller pooled prevalence (6.04%) for the MH outcome of anxiety in comparison to patients who contracted MERS-CoV (33.95%), although some of these patients could very well be HCWs themselves. On the contrary, the pooled data for the general public and MERS-CoV survivors indicate a relatively high prevalence of depression (40.7% and 41.69%), while the HCWs appear less likely to have depression (20.52%), as indicated by Supplementary Figure 11. Mild heterogeneity was detected across these 2 groups, with I^2 scores of 41.71%, I^2 = 71.77%. Therefore, statistically, the data and subsequent results appear to be more conclusive and reliable. Supplementary Figure 12 indicated the prevalence of PTSD between HCWs and the general public. PTSD within the general public appears to be relatively low (19.02%) in comparison to depression. Additionally, depression amongst HCWs is more prevalent (49.87%). Moreover, the heterogeneity (I^2 = 0) of this subgroup analysis is negligible, which demonstrates the data are statistically reliable and the conclusions are therefore more conclusive.

SARS-CoV: The subgroup analysis within the SARS-CoV group demonstrated a much higher prevalence of anxiety within HCWs (98.44%) in comparison to the general public (26.19%), as indicated in Supplementary Figure 12. Supplementary Figure 13 indicates that HCWs have a higher prevalence of depression (25.42%) than general public (23.31%) and SARS-CoV patients (21.96%). In contrast, the prevalence of PTSD among HCWs appear to be relatively low (16.97%) in comparison to SARS-CoV patients (19.80%) as well as the general public (18.36%), as indicated in Supplementary Figure 14. However, the heterogeneity score I^2 remains high, thus there may be other potential factors that may affect the statistical findings.

Comparison: Based on the subgroup analysis above, Tables 9-11 showcase the prevalence of different MH outcomes among various cohorts. There are similarities and differences. The prevalence of anxiety within the general public during MERS (6.04%) is the lowest across the three outbreaks, while SARS-CoV demonstrates the largest prevalence of anxiety within general public (26.19%). Meanwhile, HCWs who experienced SARS-CoV were likely to have anxiety (98.44%). The prevalence of anxiety within MERS-CoV patients (33.95%) appear to be the most commonly reported MH outcome. MERS-CoV also demonstrates the highest prevalence of depression within the general public and patients, at 40.70% and 41.69% respectively. Based on the current data on SARS-CoV-2, HCWs are more likely to suffer from depression (37.97%). The highest levels of PTSD were found in HCWs during MERS-CoV and MERS-

Table 5 Pooled prevalence and confidence interval of post-traumatic stress disorder across three diseases

PTSD	Prevalence (%)	95%CI	Heterogeneity I^2 (%)
MERS	35.97	29.6-43.72	75.2
SARS-CoV-2	25.03	18.15-34.51	99.58
SARS-CoV	18.20	14.94-22.18	91.37

PTSD: Post-traumatic stress disorder; CI: Confidence interval; MERS: Middle East respiratory syndrome; SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2.

Table 6 Subgroup analysis on Middle East respiratory syndrome data based on different age groups

Subgroup-age	MERS			
		Prevalence (%)	95%CI	Heterogeneity I^2 (%)
Anxiety	10-19	-	-	-
	20-29	-	-	-
	30-39	-	-	-
	40-49	18.51	8.11-42.23	96.43
	50-59	-	-	-
Depression	20-29	-	-	-
	30-39	-	-	-
	40-49	38.45	25.81-57.26	60.55
	50-59	-	-	-
PTSD	20-29	49.70	38.2-64.67	0
	30-39	19.32	14.82-25.18	0
	40-49	26.69	13.21-53.91	80.63
	50-59	-	-	-
	60-69	17.87	12.4-25.74	0

MERS: Middle East respiratory syndrome; PTSD: Post-traumatic stress disorder; CI: Confidence interval.

CoV patients (49.87% and 37.7%). SARS-CoV-2 appears to demonstrate that PTSD was experienced by 24.83% the general public.

From Supplementary Figures 15-17 we can see that people who experience MERS are more likely to have depression and PTSD than those who experience SARS-CoV-2 and SARS-CoV (the area of the MERS triangles in Supplementary Figures 15 and 17 are larger than the area of the SARS-CoV-2 and SARS-CoV triangles) while people who experience SARS-CoV may have a higher possibility to have anxiety than the other two (the area of the SARS-CoV triangle in Supplementary Figure 16 is larger the area of the MERS and SARS-CoV2 triangles).

Occupation

SARS-CoV-2: Another facet of the subgroup analysis was based upon the occupation of the sample and the reporting of MH outcomes as demonstrated in Supplementary Figures 7-9. It is evident that HCWs have a higher prevalence of anxiety and depression compared to the general public. The exception to this appears to be the prevalence of PTSD, where the levels appear to be similar between the public and HCWs, at 24.83% and 25.16% respectively.

MERS: A subgroup analysis based upon the categories of HCWs, patients and the general public associated with the prevalence of MH outcomes further demonstrates variability. Supplementary Figure 10, for example, demonstrates that the general public is consistent with a smaller pooled prevalence (6.04%) for the MH outcome of anxiety in comparison to patients who contracted MERS-CoV (33.95%), although some of these patients could very well be HCWs themselves. On the contrary, the pooled data for the general public and MERS-CoV survivors indicate a relatively high level of

Table 7 Subgroup analysis on severe acute respiratory syndrome coronavirus-2 data based on different age groups

Subgroup-age	SARS-CoV-2			
		Prevalence (%)	95%CI	Heterogeneity I^2 (%)
Anxiety	10-19	34.40	33.17-35.68	0
	20-29	25.70	19.38-34.08	99.25
	30-39	22.86	17.86-29.26	99.64
	40-49	15.59	9.65-25.17	99.66
	50-59	20.13	10.43-38.84	99.42
	60-69	7.75	0.79-76.29	99.47
Depression	10-19	43.91	42.12-45.77	0
	20-29	31.03	24.04-40.04	99.12
	30-39	30.4	25.15-36.74	99.48
	40-49	20.0	13.26-30.18	99.4
	50-59	19.98	15.84-25.19	92.68
	60-69	4.93	3.45-7.05	90.00
PTSD	20-29	32.40	6.54-160.49	98.29
	30-39	21.96	12.77-37.78	99.33
	40-49	27.72	19.88-38.66	97.59
	50-59	5.38	3.76-7.69	0
	60-69	-	-	-

SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2; PTSD: Post-traumatic stress disorder; CI: Confidence interval.

Table 8 Subgroup analysis on severe acute respiratory syndrome coronavirus data based on different age groups

Subgroup-age	SARS-CoV			
		Prevalence (%)	95%CI	Heterogeneity I^2 (%)
Anxiety	10-19	-	-	-
	20-29	-	-	-
	30-39	24.60	13.29-45.55	85.81
	40-49	15.63	10.97-22.26	60.57
	50-59	51.62	38.53-69.16	0
Depression	20-29	-	-	-
	30-39	27.47	16.09-46.9	89.58
	40-49	20.30	13.36-30.85	81.57
	50-59	22.49	14.8-34.17	0
	60-69	25.85	17.69-37.75	0
PTSD	20-29	24.43	15.53-38.44	72.18
	30-39	32.13	23.1-44.68	89.33
	40-49	11.68	8.45-16.15	86.20
	50-59	67.80	43.57-100	0
	60-69	7.54	2.64-21.54	53.28

SARS-CoV: Severe acute respiratory syndrome coronavirus; PTSD: Post-traumatic stress disorder; CI: Confidence interval.

Table 9 Subgroup analysis on Middle East respiratory syndrome data based on different type of people

Subgroup-occupation	MERS			
		Prevalence (%)	95%CI	Heterogeneity I^2 (%)
Anxiety	General Public	6.04	2.86-12.79	93.9
	HCW	-	-	-
	Patient	33.95	20.65-55.82	68.57
Depression	General Public	40.70	18.89-87.71	0
	HCW	20.52	11.81-35.67	41.71
	Patient	41.69	23.73-73.22	71.77
PTSD	General Public	19.02	14.01-25.81	0
	HCW	49.87	45.09-55.16	0
	Patient	37.70	27.47-51.74	0

MERS: Middle East respiratory syndrome; HCW: Healthcare worker; PTSD: Post-traumatic stress disorder; CI: Confidence interval.

Table 10 Subgroup analysis on severe acute respiratory syndrome coronavirus-2 data based on different type of people

Subgroup-occupation	SARS-CoV-2			
		Prevalence (%)	95%CI	Heterogeneity I^2 (%)
Anxiety	General Public	21.18	17.88-25.09	99.82
	HCW	22.35	17.42-28.66	99.36
	Patient	-	-	-
Depression	General Public	27.6	23.36-32.24	99.8
	HCW	27.71	23.22-33.08	98.79
	Patient	-	-	-
PTSD	General Public	24.83	14.97-41.18	99.67
	HCW	25.16	16.62-38.08	99.33
	Patient	-	-	-

SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2; HCW: Healthcare worker; PTSD: Post-traumatic stress disorder; CI: Confidence interval.

prevalence (40.7% and 41.69%) of depression, while the HCWs appear less likely to have depression (20.52%), as indicated by Supplementary Figure 11. Mild heterogeneity was detected across these 2 groups, with I^2 scores of 41.71%, I^2 = 71.77%. Therefore, statistically, the data and subsequent results appear to be more conclusive and reliable. Supplementary Figure 12 indicated the prevalence of PTSD between HCWs and the general public. PTSD within the general public appears to be relatively low (19.02%) in comparison to depression. Additionally, depression is more prevalent in HCWs (49.87%). Moreover, the heterogeneity I^2 = 0 of this subgroup analysis is negligible, which demonstrates the data are statistically reliable and the conclusions are therefore more conclusive.

SARS-CoV: The subgroup analysis within the SARS-CoV group demonstrated a much higher prevalence of anxiety within HCWs (98.44%) in comparison to the general public (26.19%), as indicated in Supplementary Figure 13. Supplementary Figure 14 indicates that HCWs have a higher prevalence of depression (25.42%) than the general public (21.96%) and SARS-CoV patients (23.31%). In contrast, the prevalence of PTSD among HCWs appear to be relatively low (16.97%) in comparison to SARS-CoV patients (19.80%) as well as the general public (18.36%), as indicated in Supplementary Figure 15. However, the heterogeneity score I^2 remains high, thus there may be other potential factors that may affect the statistical findings.

It can be seen from Supplementary Figure 15 that it is less likely for people who experience SARS-CoV to have depression, while people who experience MERS are the most likely to suffer from depression. In particular, the general public and MERS patients have a greater risk of depression than

Table 11 Subgroup analysis on studies under severe acute respiratory syndrome coronavirus data based on different type of people

Subgroup-occupation	SARS-CoV			
		Prevalence (%)	95%CI	Heterogeneity I^2 (%)
Anxiety	General Public	26.19	11.93-57.48	98.22
	HCW	98.44	22.67-427.49	0
	Patient	24.21	17.34-33.79	85.16
Depression	General Public	23.31	14.64-37.11	97.97
	HCW	25.42	13.74-47.03	90.29
	Patient	21.96	16.86-28.6	78.1
PTSD	General Public	18.36	13.59-24.81	81.69
	HCW	16.97	12.28-23.45	91.8
	Patient	19.80	14.28-27.46	90.44

SARS-CoV: Severe acute respiratory syndrome coronavirus; HCW: Healthcare worker; PTSD: Post-traumatic stress disorder; CI: Confidence interval.

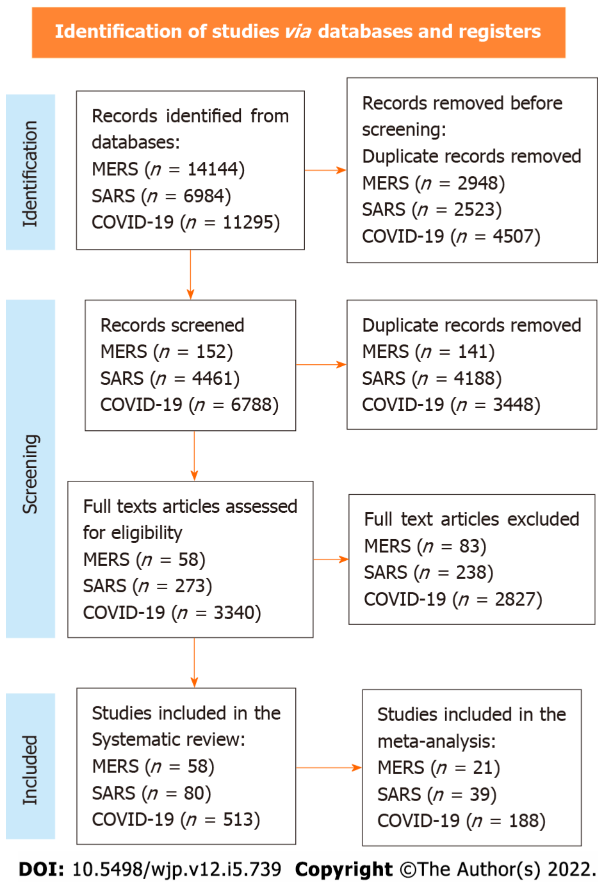

Figure 1 PRISMA flow diagram. MERS: Middle East respiratory syndrome; SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2; COVID-19: Coronavirus disease 2019.

those who experience SARS-CoV-2 and SARS-CoV. However, people in the outbreak of SARS-CoV are more likely to have anxiety than people in the outbreak of MERS and SARS-CoV-2 (Supplementary Figure 16). Moreover, it can be noted from Supplementary Figure 16 that HCWs, during the outbreak of SARS-CoV, endured a very high risk of having anxiety. When it comes to PTSD, Supplementary Figure 17 shows that MERS leads to the highest prevalence of PTSD in almost all the mental health diseases across the three pandemics. In particular, HCWs and MERS patients suffer from a serious risk of PSTD after MERS. On the other hand, SARS-CoV seems to lead a relative low risk on the prevalence of PTSD.

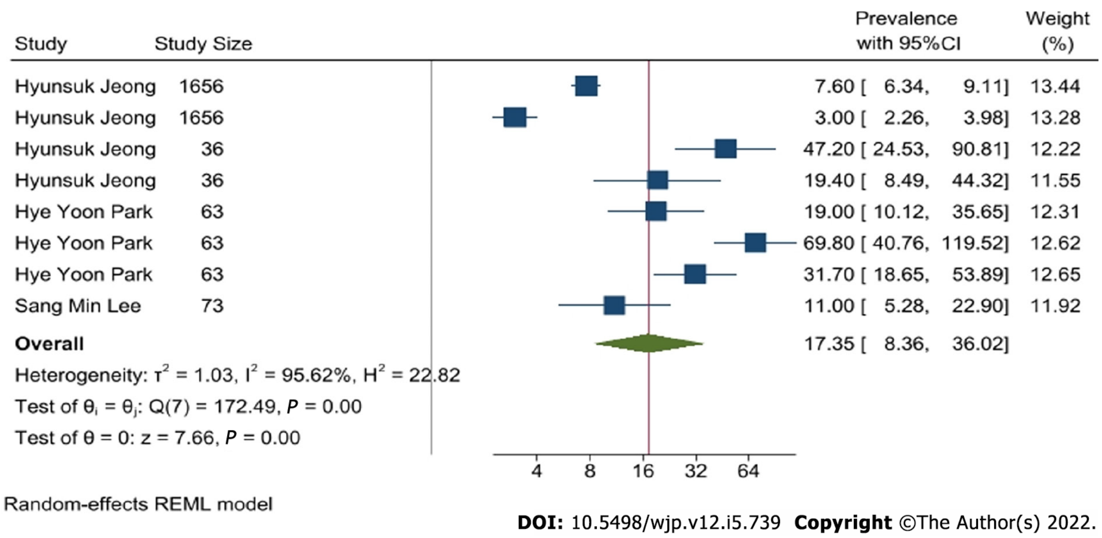

Figure 2 Forest plot of anxiety caused by Middle East respiratory syndrome.

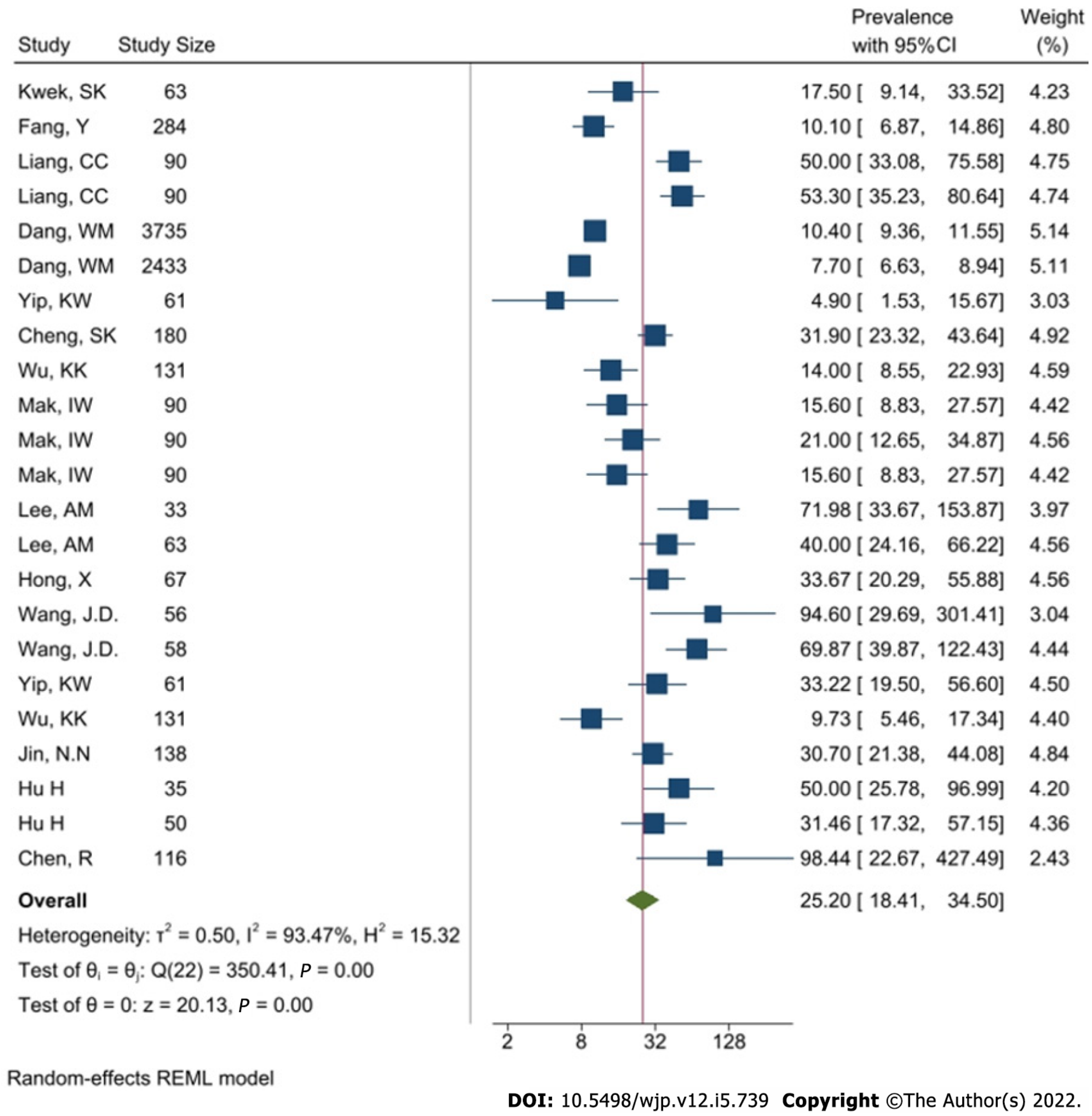

Figure 3 Forest plot of anxiety that is caused by severe acute respiratory syndrome coronavirus.

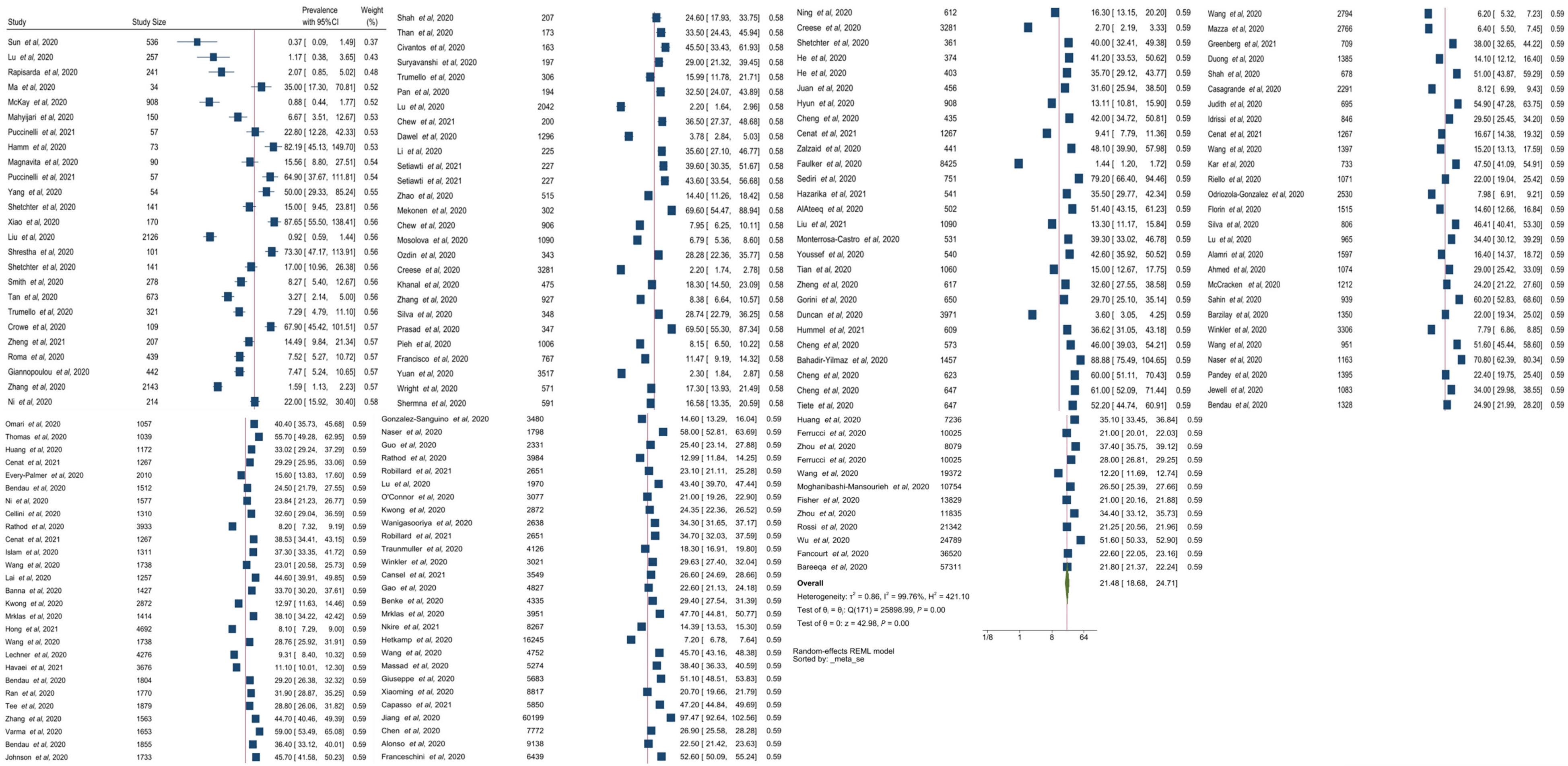

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Figure 4 Forest plot of anxiety caused by severe acute respiratory syndrome coronavirus-2 forest plot.

Geographical location

SARS-CoV-2: From Supplementary Figure 18-20, we can see that people in Canada are more likely to have anxiety (80.85%) and PTSD (83.99%) when they experience SARS-CoV-2, and they also showcase a relative high possibility of having depression (57.90%), while people in Palestine suffer from the highest prevalence of depression (88.38%). On the other hand, people in the United Kingdom have the lowest prevalence of depression (1.44%) among all the countries. And people in the United States and Australia have the lowest prevalence of PTSD (5.38%) and anxiety (3.78%) respectively.

Table 12 Sensitivity analysis for anxiety and depression studies under severe acute respiratory syndrome coronavirus-2

	Exposure	Outcome	Prevalence with 95%CI (before)	Prevalence with 95%CI (after)	*P* value
(g)	SARS-CoV-2	Anxiety	21.48 (18.66-24.71)	25.82 (23.98-27.8)	< 0.05
(h)	SARS-CoV-2	Depression	27.64 (24.59-31.06)	29.3 (26.98-31.81)	> 0.05

SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2; CI: Confidence interval.

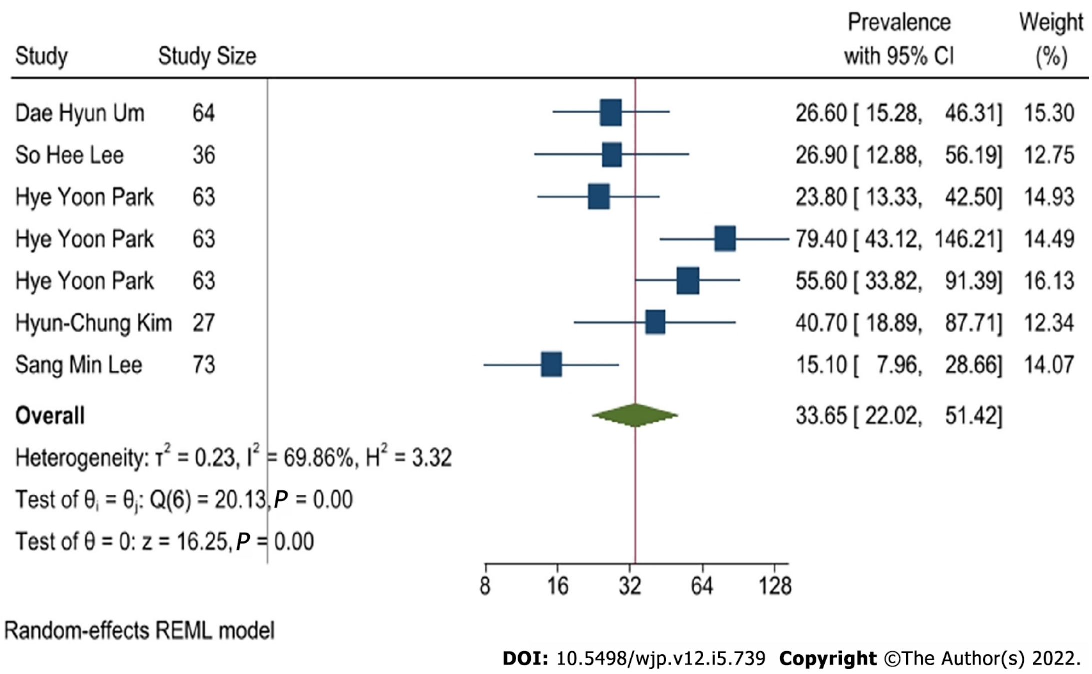


Figure 5 Forest plot of depression caused by Middle East respiratory syndrome.

MERS: A subgroup analysis was not conducted due to the studies taking place in South Korea only.

SARS-CoV: Supplementary Figure 21-23 indicate Taipei shows the highest prevalence of depression (38.36%) and anxiety (52.91%) during SARS-CoV. Moreover, people in Kaohsiung/Southern Taiwan also suffer from the highest prevalence of PTSD (45.52%) during SARS-CoV. This indicates that people in the Taiwan area may experience a serious mental health issue due to the outbreak of SARS-CoV. On the other hand, people in Toronto, Singapore and Beijing have the lowest prevalence of PTSD (13.01%), anxiety (17.5%) and depression (21.80%) respectively.

Publication bias and sensitivity analysis

The meta-analyses conducted indicate a high heterogeneity for depression, anxiety and PTSD. This could be due to differences in the reporting criteria and assessment tools used, geographical location and the difference in study designs, which had differing data collection time points. High heterogeneity could cause many studies to fall outside the 95%CI in the conventional funnel plot, which is based on the fixed effects model; therefore, we propose to use the funnel plot based on a random effects model. Both types of funnel plots were compared.

In the fixed effects model, the mean of the underlying model behind each study was fixed; therefore, the measure τ^2 for heterogeneity was 0. Since the random effects model assumes that the mean of each study comes from a normal distribution, the DerSimonian and Laird estimates τ^2 were calculated to show the heterogeneity between studies. The funnel plot based on the random effects model would include most of the studies and, therefore, make it easier to demonstrate publication bias. The pooled prevalence of the three mental health disorders and the 95%CI of the fixed (solid line) and random effects (dotted line) models were both plotted in Supplementary Figure 24 across all 3 pandemics.

When we looked at the funnel plots using the fixed effects model (solid line), most of the studies are located outside of the 95%CI. It is therefore difficult to find the sign of publication bias. They are masked by the widespread studies. By contrast, most of studies are well located within the 95%CI in the funnel plots using the random effects model (dotted line) except sub figs. Supplementary Figure 25A and B. Supplementary Figure 25C and D are typical examples. The large values of τ^2, 1.1110 and 0.4574

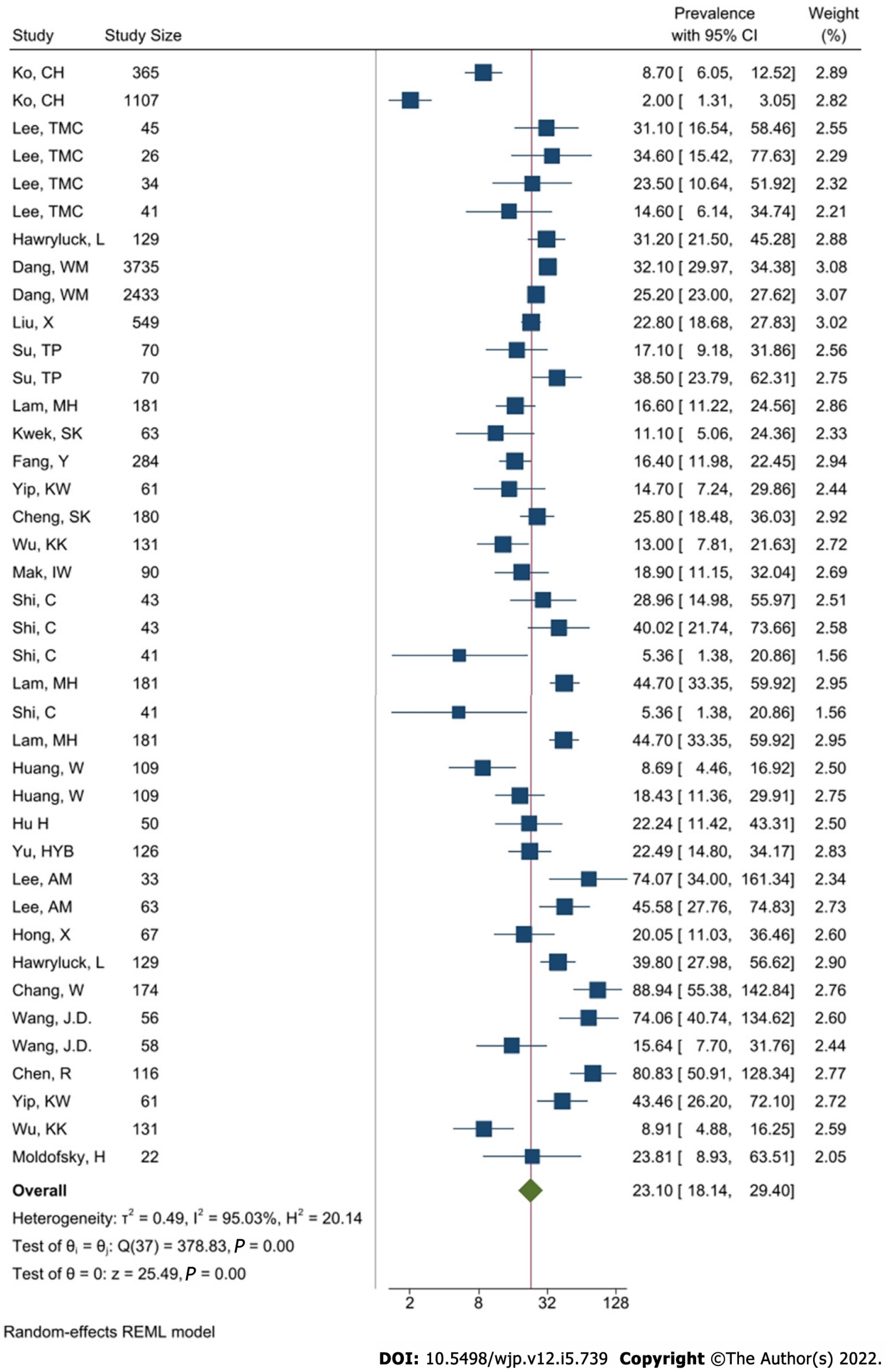
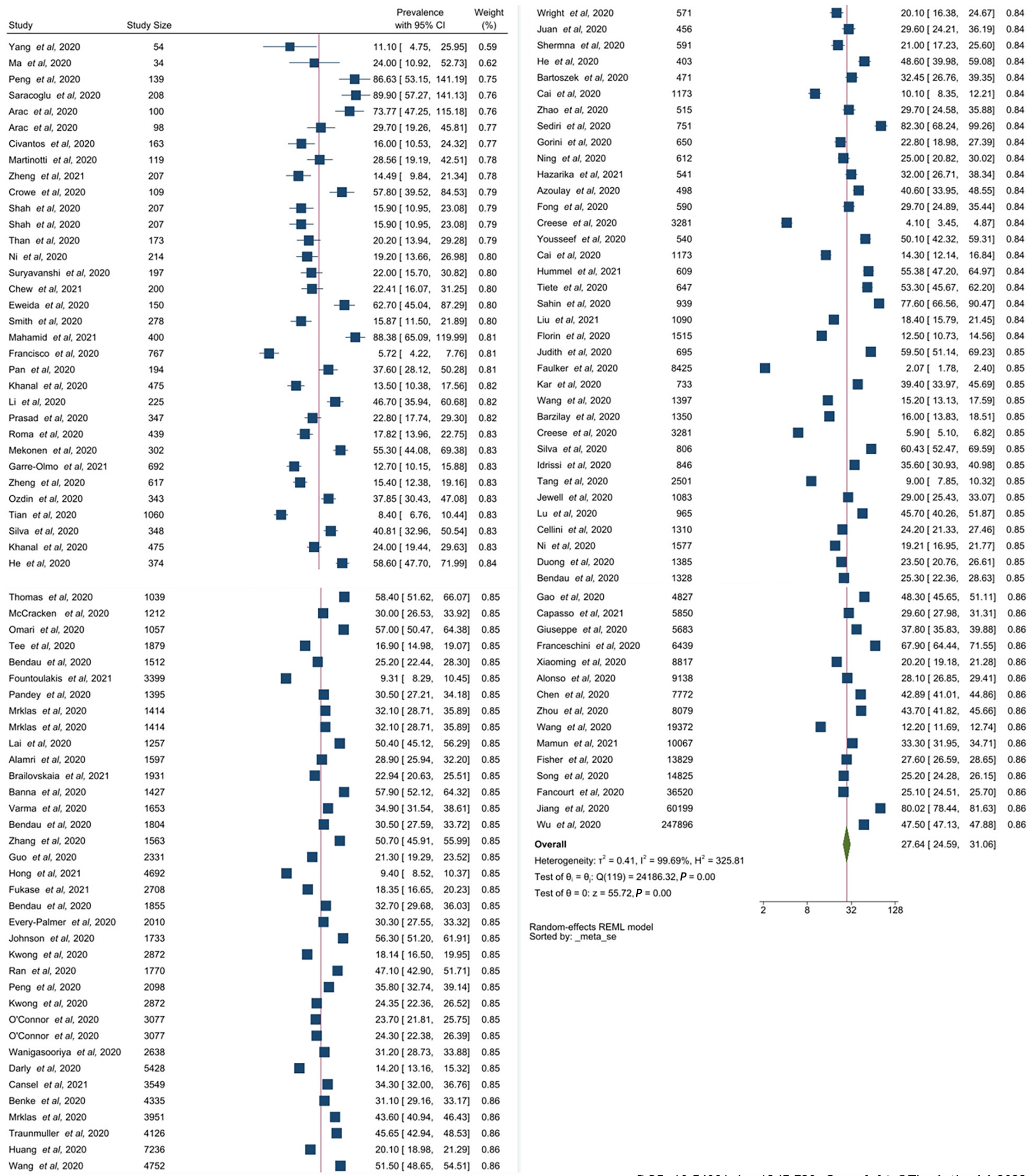


Figure 6 Forest plot of depression that is caused by severe acute respiratory syndrome coronavirus.

confirm the severe heterogeneity, and the random effects model we used addresses this problem well. We can therefore focus on the problem of publication bias.

Based on the 95%CI of the random effects model (dotted line), there is little sign of publication bias in Supplementary Figure 25C-F; the *P* values of Egger's test of 0.082, 0.589, 0.146 and 0.539 echo the findings (Table 7). In Supplementary Figure 25G-I, however, there is a sign of publication bias and the *P* values of the Egger's test are all less than 0.05, confirming the findings (Table 11).

Even if we used the funnel plot based on the random effects model, many studies in Supplementary Figure 25A and B still fall outside the 95%CI, meaning the random effects model cannot address the problem of heterogeneity well. Further investigation is required. The sign of publication



DOI: 10.5498/wjp.v12.i5.739

Figure 7 Forest plot of depression caused by severe acute respiratory syndrome coronavirus-2.

bias is not clear; the *P* values of Egger's test are 0.085 and 0.000 respectively for Supplementary Figure 25A and B.

To reduce the unclear impact of studies that fall outside the 95%CI of random effects model in Supplementary Figure 25A and B, further sensitivity analyses, by removing the studies external to the 95%CI range, was demonstrated in Table 12.

The prevalence of anxiety and depression under SARS-COV-2 (Supplementary Figure 25A and B) are significantly higher after removing the studies external to the 95%CI, with the result changing from 21.44% (18.69-24.61) to 25.54% (23.28-28.02) and 27.68% (24.67-31.06) to 29.7% (27.25-32.39) respectively. It means that factors associated with heterogeneity, say, the design, population and quality of those studies, may have some impact on the conclusion and a further inspection of the study quality and other factors are needed.

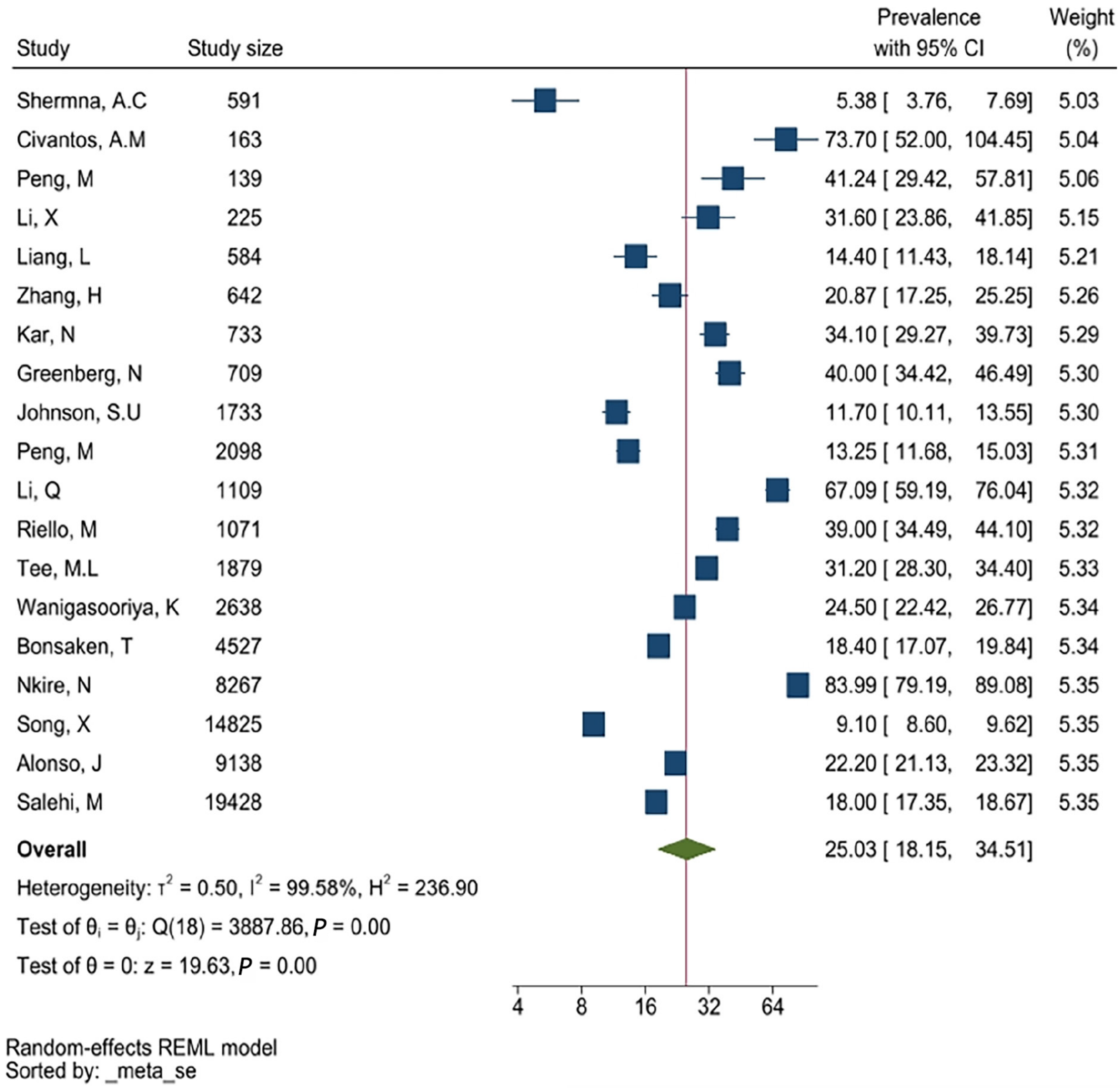


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Figure 8 Forest plot of post-traumatic stress disorder that is caused by Middle East respiratory syndrome.

DISCUSSION

The prevalence of anxiety, depression and PTSD was common across HCWs, patients and the general public. It could be argued HCWs experience psychological burden more profoundly than patients and the general public given that the exposure to negative thoughts would be higher within their work environment. Patients equally could experience a high psychological burden with the exacerbation of their conditions due to a number of factors such as isolation. The general public could equally experience a decline in their mental health due to the lockdown situation in some parts of the world more extensively than others, especially with SARS-CoV-2 as a number of national level lock-downs were imposed in different countries.

The incidence of anxiety across all groups during SARS-CoV-2 (33.16%) was higher in comparison to MERS (17.35%) and SARS-CoV (25.2%). MERS and SARS-CoV-2 demonstrated higher depressive symptoms, at 33.65% and 31.35% respectively, in comparison to SARS-CoV, which reported 23.1%. PTSD was much higher during MERS (35.9%) than SARS-CoV-2 (25.03%) and SARS-CoV (18.2%).

The prevalence of PTSD among HCWs during MERS was 49.87%. The highest prevalence of anxiety for HCWs was during SARS-CoV at 98.44%. Among HCWs, the highest reported prevalence thus far during SARS-CoV-2 appear to be depression and insomnia, at 37.97% and 35.16% respectively. The identified prevalence rates could be influenced directly and indirectly by stigmatisation being an attributor. Stigmatisation within this context could include social processes to discriminate or separate the usual life changes and opportunities. This issue could present a significant barrier in managing access to equitable and quality services. Individual or social construct based beliefs and behaviours could promote social discrimination and moral discredit that may aggravate mental health implications to worsen health outcomes[27]. Interestingly, Dye and colleagues indicated HCWs were unlikely to follow social distancing protocols compared to non-HCWs. This could be associated with bullying as

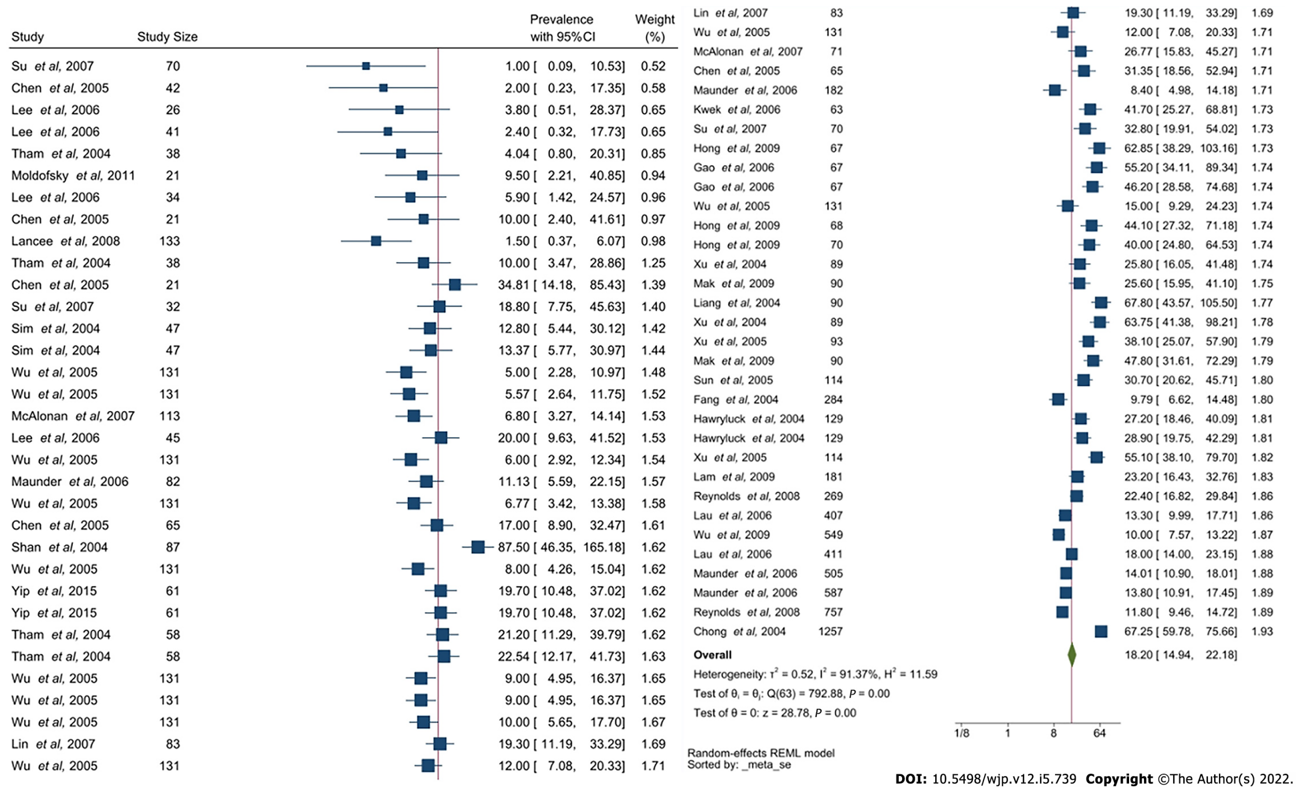

Figure 9 Forest plot of post-traumatic stress disorder that is caused by severe acute respiratory syndrome coronavirus.

demonstrated by Dye *et al*[27] Verbal and physical violence was also associated with bullying or harassment scenarios in comparison to MERS or SARS-CoV. This could be further purported with an influx of patients and workload that exacerbates fatigue and insomnia. This finding is consistent with MERS; therefore, it likely to occur with SARS-CoV-2.

Our results indicated age appear to play a role in mental illness manifestations during SARS-CoV-2, although there was insufficient data during MERS and SARS-CoV to conduct a comparative analysis. The pooled prevalence for ages between 20-29 years appear to demonstrate PTSD at 49.7% during MERS and 32.4% in SARS-CoV-2. Other mental illnesses during SARS-CoV-2 appear to be associated with 10 to 19 years of age with a significant prevalence of anxiety of 35.84% and insomnia (23.3%). In addition, depression was reported at 40.94% within the 30-39 age group.

The indirect influence of SARS-CoV-2 is widespread, especially among young people under 40 years old. For children and teenagers, the social isolation and loneliness of being unable to meet with friends will increase the anxiety. Students worry that the epidemic would limit their future choices and future education, employment and housing. Young workers have a higher rate of unemployment because of their immature skills. During MER-CoV, suicidality was reported at 16.62% with a 95%CI of 10.73-25.75, although the age range associated was non-specific.

Studies relating to SARS-CoV and MERs-COV are limited by several aspects, including the geographical constraints and sample sizes. The majority of studies were published in languages other than English. Psychological symptomatologies associated with depression, anxiety, distress, insomnia and fatigue, as well as comorbidities such as PTSD and neuro-psychiatric syndromes such as psychosis, have been reported in patients and HCWs more during the SARS-CoV-2 pandemic[28,29] which could be due to the scope and scale of the incidence and high transmission rates. The effects of mass lock-downs, economic downturns and mass uncertainty and fear within the general population are harder to characterise and assess, but early evidence suggests that rates of mental health disorders within the population will be higher during and following the pandemic[30,31]. More significant findings of severe psychological disorders including post-traumatic stress disorder and suicidal ideation amongst health care workers have been reported at levels greater than or expected to be seen in military veterans[32] or amongst victims of natural disasters[33]. Within the three groups there is likely to be variations in the levels of mental health disorders based on age, race and socio-economic status due to differences in the risk of mortality[34,35].

Non-specific use of MH interventions to support HCPs during each of the coronavirus disease outbreaks demonstrate the lack of preparedness global healthcare systems appeared to have had. Thereby, the ongoing SARS-CoV-2 will continue to impact their MH and overall well-being due to the lack of protective factors and assessments to identify specific risk factors. The available evidence demonstrates safeguarding measures should be considered by healthcare systems to better strategize

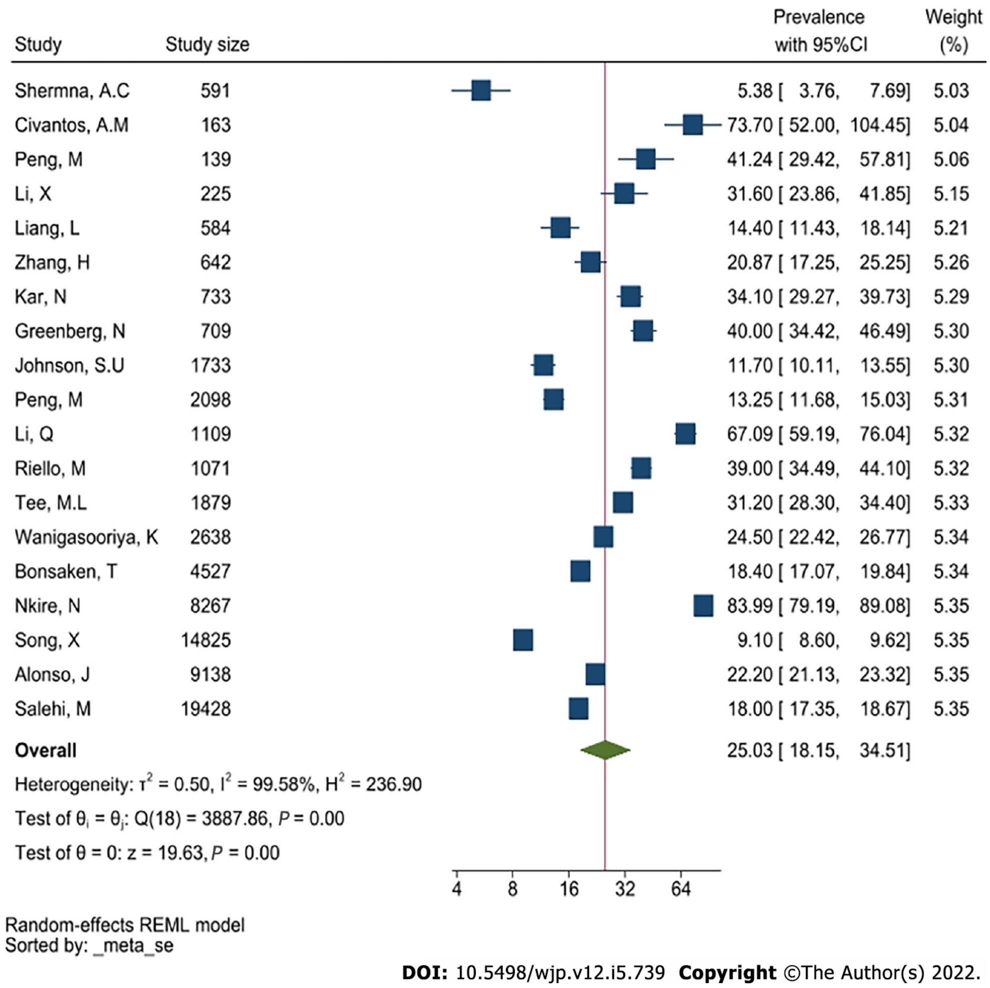

Figure 10 Forest plot of post-traumatic stress disorder caused by severe acute respiratory syndrome coronavirus-2. CI: Confidence interval.

both collegial support and control steps to support all HCPs.

Limitations

Several factors, including communication and country, as well as regional directives and their differences, were paramount to the inclusion and exclusion of the evidence within this study. All 3 cohorts included within this study reported their mental health impact differently. Multiple mental health assessments were used; thus, cut-off scores were used to better evaluate and inform the statistical analysis conducted. Unified approaches for the assessment of pandemic-specific or related mental health among HCPs, patients and the public should be considered in the future. This is another factor that led to the observations of high variation in outcomes and risks to medium- to long-term mental health impact.

CONCLUSION

As vaccines are rolled out globally, it is hoped that pressures on acute medical services due to the SARS-CoV-2 will slowly improve. The aim of this study is to understand and build on our knowledge of the viruses' impact on mental health, both previously and now, so that we may better manage and prepare to deal with the hidden consequences of this and any future outbreaks. Whilst there are cultural, economic and environmental differences between the countries affected in each pandemic, drawing similarities between the lasting effects on mental health will be important in highlighting where resources and support are needed as we contemplate our recovery–physically, mentally and socially–from this pandemic. The mortality impact of seasonal influenza and a pandemic on the mental health of the general public, patients and HCPs vary.

This study analysed the prevalence of mental health outcomes during the MERS, SARS-CoV and SARS-CoV-2 across multiple cohorts. In terms of mental illness like anxiety, depression and PTSD, the prevalence of depression (33.65% with 95%CI: 22.02-51.42) and PTSD (35.97% with 95%CI: 29.6-43.72) is higher during MERS, while the prevalence of anxiety (33.16% with 95%CI: 25.99-34.5) is higher during

SARS-CoV-2. Patients and HCWs are the first and second most likely groups to suffer from mental health problems. Young people are more likely to be caught up in depressive and anxiety emotions than older people.

Developing evidence-based and cohort-specific MH interventions could be a useful way to optimise MH support. HCPs in particular may benefit from this as it could promote better well-being for staff, increasing the efficiency within the work environment.

ARTICLE HIGHLIGHTS

Research background

The severe acute respiratory syndrome (SARS) virus has been present for centuries in different forms. Whilst civilisation has evolved, so has the virus, including its' ability to transmit. Thus, the comparison of the three most recent severe acute respiratory syndrome coronavirus (SARS-CoV) viruses in terms of the mental health implications infused to patients, healthcare professionals (HCPs) and patients is an important facet both clinically and scientifically. As a result, our study explores an important component that hasn't been addressed from a potential disease sequalae perspective.

Research motivation

Our motivation was to demonstrate the trends associated with the mental health prevalence in terms of specific conditions due to the last three virulent strands of SARS-CoV across patient, HCPs and the general public. The specified cohorts have specific behavioural patterns and differing levels of exposure to the virus, thus the risk of infection varies that influences the mental health impact. This would aid in assessing the true mental health impact that health care systems require to support those needing mental health support. The comparison also allows us to predict the trends in mental health impact due to infectious transmissions which ultimately should be addressed as a public health hazard, globally.

Research objectives

The study has three primary aims of identifying and reporting: (1) Mental health conditions commonly observed across all three pandemics; (2) Impact of mental health outcomes across patients, the general public and HCPs associated with all 3 pandemics; and (3) The prevalence of the mental health impact and clinical epidemiological significance.

Research methods

A systematic methodology was developed and published on PROSPERO (CRD42021228697). The databases PubMed, EMBASE, ScienceDirect and the Cochrane Central Register of Controlled Trials were used as part of the data extraction process, and publications from January 1, 1990 to August 1, 2021 were searched. MeSH terms and keywords used included *Mood disorders, PTSD, Anxiety, Depression, Psychological stress, Psychosis, Bipolar, Mental Health, Unipolar, Self-harm, BAME, Psychiatry disorders and Psychological distress*. The terms were expanded with a 'snowballing' method. Cox-regression and the Monte-Carlo simulation method was used in addition to I^2 and Egger's tests to determine heterogeneity and publication bias.

Research results

The results indicated that there is a mental health impact observed among patients, HCPs and the general public at varying levels. This study analysed the prevalence of some mental health outcomes to the outbreaks of Middle East respiratory syndrome (MERS), SARS-CoV and SARS-CoV-2 and compared the prevalence of the participants and the prevalence of different occupational groups and age groups. In terms of mental illness like anxiety, depression and post-traumatic stress disorder (PTSD), the prevalence of depression [33.65% with 95% confidence interval (CI): 22.02-51.42] and PTSD (35.97% with 95%CI: 29.6-43.72) is higher during MERS, while the prevalence of anxiety (33.16% with 95%CI: 25.99-34.5) is higher during SARS-CoV-2. Patients and healthcare workers are the first and second most likely groups to suffer from mental health problems. Young people are more likely to be caught up in depressive and anxiety emotions than older people.

Research conclusions

Developing evidence-based and cohort-specific mental health (MH) interventions could be a useful way to optimise MH support. HCPs in particular may benefit from this as it could promote better well-being for staff, increasing the efficiency within the work environment. As vaccines are rolled out globally, it is hoped that pressures on acute medical services due to the SARS-CoV-2 will slowly improve. The aim of this study is to understand and build on our knowledge of the viruses' impact on mental health, both previously and now, so that we may better manage and prepare to deal with the hidden consequences of this and any future outbreaks. Whilst there are cultural, economic and environmental differences between the countries affected in each pandemic, drawing similarities between the lasting effects on mental health will be important in highlighting where resources and support are needed as we contemplate our recovery–physically, mentally and socially–from this pandemic. The mortality impact of seasonal influenza and a pandemic on the mental health of the general public, patients and HCPs vary.

Research perspectives

Studies relating to SARS-CoV and MERS-CoV are limited by several aspects, including the geographical constraints and sample sizes. The majority of studies were published in languages other than English. Psychological symptomatologies associated with depression, anxiety, distress, insomnia and fatigue, as well as comorbidities such as PTSD and neuro-psychiatric syndromes such as psychosis, have been reported in patients and HCWs more during the SARS-CoV-2 pandemic which could be due to the scope and scale of the incidence and high transmission rates. The effects of mass lock-downs, economic downturns and mass uncertainty and fear within the general population are harder to characterise and assess, but early evidence suggests that rates of mental health disorders within the population will be higher during and following the pandemic. We need more comprehensive and longitudinal studies to be conducted to determine the mental health impact in multiple populations globally. This would also aid us to develop better pandemic preparedness frameworks and policies within healthcare systems.

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FOOTNOTES

Author contributions: Delanerolle G and Phiri P developed the systematic review protocol and embedded this within the EPIC project's evidence synthesis phase; Delanerolle G and Goodison W wrote the first draft of the manuscript; The statistical analysis plan was developed by Delanerolle G and was conducted by Shi JQ, Yeng X and Zeng Y; The data was critically appraised by Shetty A, Phiri P, Zeng Y, Yeng X, Shi JQ, Goodison W, Ramakrishnan R, Ranaweera S and Raymont V; The SARS-CoV data was extracted by Chau SWH and his team; The SARS-CoV-2 data was extracted by Phiri P/Delanerolle G and their team; Yeng X and Zeng Y extracted the MERS dataset which was reviewed by Delanerolle G, Phiri P, Shetty S, Shi JQ and Shetty A; Yeng X, Zeng Y and Shi JQ conducted the analysis; Shetty S designed and developed the original illustration; Delanerolle G, Phiri P, Shetty A, Zeng Y, Yeng X, Shetty S, Shi JQ, Goodison W, Ramakrishnan R, Elliot K, Ranaweera S and Raymont V critically appraised and finalised the manuscript; All authors approved the final version of the manuscript.

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