# Prevalence of Depression, Anxiety, Delirium, and Post-Traumatic Stress Disorder Among COVID-19 Patients: Protocol for A Living Systematic Review

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**Protocol**

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# Abstract

### Background

Previous studies on the impact of COVID-19 on the mental health of the patients has been limited by the lack of relevant data. With the rapid and sustained growth of the publications on COVID-19 research, we will perform a living systematic review (LSR) to provide comprehensive and continuously updated data to explore the prevalence of depression, anxiety, delirium, and post-traumatic stress disorder (PTSD) among COVID-19 patients.

### Methods

We will perform a comprehensive search of the following databases: Cochrane library, PubMed, Web of Science, Embase, and Chinese Biomedicine Literature to identify relevant studies. We will utilize different tools to examine the bias risks (quality) regarding studies of varying design types, such as the revised Cochrane risk-of-bias tool (RoB 2) for randomized controlled trials (RCT), the Newcastle-Ottawa Scale (NOS) for cohort and case-control studies, etc. The literature searches would be updated every month. We will perform meta-analysis if any new eligible studies or data are obtained and resubmit an updated systematic review if any change in outcomes and heterogeneity is determined after the addition of the new studies. There will be no restrictions on language or year of publication.

### Discussion

This LSR would provide an in-depth and up-to-date summary of the psychological impact of COVID-19 diagnosis and treatment on the patients.

### Systematic review registration

**PROSPERO** CRD42020196610


# Background

The global outbreak of the COVID-19 has been designated as a pandemic that has affected more than ten million people, with more than half a million fatalities [1, 2]. Previous research focusing on pandemics confirmed that individuals who had experienced public health emergencies reported varying degrees of psychological disorders even after the event ended or they were cured and discharged from the hospital [3–6]. Patients with confirmed and suspected infections may suffer from repeated psychiatric and neuropsychiatric incidences due to multiple reasons, such as progression of the disease, adverse drug reaction, social isolation, uncertainty, and physical discomfort [7–9].

A recently published systematic review and meta-analysis indicated the incidence of delirium as a common occurrence amongst patients hospitalized due to severe coronavirus infections (SARS-CoV and MERS-CoV), whereas, PTSD, anxiety, depression, and fatigue were observed in the subsequent months [3].

There exists some preliminary/unpublished data showing psychiatric and neuropsychiatric presentations in COVID-19 patients [3]. Since the spread of COVID-19, there has been extensive research on the topic globally, translating into an unprecedented number of publications, approximately 59 articles per day, probably higher than observed for any other disease [10]. It is essential to collect continuously updated data to provide convincing evidence for patients, healthcare workers, and policy makers. A living systematic review (LSR) retains the benefits of a systematic review and accepts continual updating of the relevant data without compromising the methodological rigor [11–14].

The aim of this study is to provide a living systematic review for synthesizing rapid and continual updating of data on whether the common neuropsychiatric conditions observed in patients hospitalized for severe SARS-CoV or MERS-CoV are also prevalent in a different stage of COVID-19 patients.

# Methods/design

### Study design

This systematic review has been designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) statement and has been registered on PROSPERO (CRD42020196610) [15].

### Eligibility criteria

### Population

COVID-19 patients who were diagnosed with four types of psychiatric and neuropsychiatric syndromes (depression, anxiety, delirium, and PTSD). Studies that investigated the indirect effects of SARS-CoV-2 on family members, care providers, or isolated people who did not infect the prevalence of depression, anxiety, delirium, and PTSD will be excluded.

### Type of outcomes

### The primary outcomes

- Number of signs or symptom (depression, anxiety, delirium, and PTSD);
- The degree of diagnoses (depression, anxiety, delirium, and PTSD).

### The secondary outcomes:

- Symptom severity;
- Incidence of mortality in COVID-19 patients with depression, anxiety, delirium or PTSD;
- The measurement of health-related quality of life using a validated scale, such as the Short Form 36 Health Survey questionnaire.

## Studies design

We will include only peer-reviewed RCT, cohort/case-control/cross-sectional studies, case reports, case series, and qualitative studies. Conference abstracts and letters will be excluded because they lack adequate information for meta-analysis.

## Search strategy

A senior investigator (Y.G.) would examine the published and gray literature sources to extract the studies reporting the prevalence of depression, PTSD, anxiety, or delirium in COVID-19 patients. An experienced medical information specialist (J.H.T.) would further check and approve the search methodology. We will conduct a comprehensive search of Cochrane library, PubMed, Web of Science, Embase, and Chinese Biomedicine Literature to extract articles/abstracts published between the date of database initiation and July 5, 2020. There will be no restrictions on language or year of publication. An additional file, which would describe the complete search strategy for PubMed as well as other electronic databases will be provided. We will also thoroughly search the reference lists of the relevant reviews and research trials. We have presented the search strategy using PubMed as an example in Table 1. The search strategy will be adapted to fit other online databases as well.

## Update plan

We will perform identical search operations at regular pre-defined intervals to identify newly published data. There are no robust standards for the update frequency based on current research; however, due to the unprecedented number of publications on COVID-19, we will update the literature searches every month, and perform meta-analysis if any new eligible studies or data are obtained. We will submit an updated systematic review if we observe any changes in the outcomes and heterogeneity after the addition of new studies or provide data on additional outcomes [11, 12]. We chose this updating frequency to allow quick updates and to highlight the most recent information to the researchers, clinicians, nurses, and policy makers [11, 14, 16].

## Study selection

Original literature search records will be imported into Endnote X9 software tool (Thomson Reuters, New York, NY, USA) management software. Two authors (JYS and YG) will independently retrieve full-text of potentially studies after deduplication to assess their eligibility according to the abovementioned inclusion criteria. Any disagreement will be resolved by the third reviewer (JHT).

## Data extraction

Two independent reviewers (JYS and MMN) will be involved in data extraction; we will extract country of patients, population type (e.g., old people and children), age, study design (such as RCT/cohort/case-control), diagnostic criteria for the viral infection (such as WHO criteria), stage and severity of disease, length of follow-up, sample size (such as number of cohort, number of cases), and gender.

### Risk of bias (quality) assessment.

Two independent reviewers will use the following tools to examine the risk of bias in the included studies: the revised Cochrane risk-of-bias tool (RoB 2) for RCT [17], the Risk Of Bias In Non-randomized Studies of interventions (ROBINS-I Scale) for non-randomized controlled trials, the Newcastle-Ottawa Scale (NOS) for cohort and case-control studies, confidence in the Evidence from Reviews of Qualitative research for qualitative studies, and the Agency for Healthcare Research and Quality (AHRQ) for cross-sectional studies.

### Processing missing data

We will contact the corresponding or other primary authors to obtain missing data or insufficiently reported data after selecting the studies. Randomized controlled trials will be treated as cohort studies; all data from the control and experimental group will be extracted if they met our criteria. In addition, we will estimate missing data if they can be extracted from tables or figures. Trials with missing data that cannot be obtained will be excluded for reasons.

### Differences between the protocol and the final review

Any significant deviations between the protocol and final review will be reported clearly.

### Data analysis

The Stata (v13.0; StataCorp) and Revman 5 were used for statistical analysis. The statistical heterogeneity will be examined using the Cochran's Q and the $I^2$ statistic. An $I^2 > 50\%$, and a *p*-value < 0.05 will correspond to significant heterogeneity, and a random-effects model will be used for the subgroup analyses and pooled estimates. On the contrary, an $I^2 < 50\%$ and a *p*-value > 0.05 will correspond to insignificant heterogeneity, and the fixed-effect model shall be used for the subsequent meta-analysis. The effect size measures were mean difference with 95% CI (for severity of the symptoms and degree of diagnoses) and prevalence with 95% CI (number of psychiatric diagnoses (depression, anxiety, delirium, and PTSD); severity of depression, anxiety, delirium, and PTSD). The heterogeneity/publication bias will be examined using the Egger's test or the symmetry of the funnel plot. In the Egger's test, bias will be significant when *p*-value < 0.05.

### Subgroup analysis

The following subgroup analyses will be planned for main outcomes if data are sufficient: Age (< 60 vs. ≥ 60 years), symptom severity (mild vs. severe vs. ICU patients), high and middle-high vs. middle-low and low-income countries, databases (data from Chinese databases vs. data from English databases), study design (RCT, cross-sectional, non-randomized control trials, cohort-study case-control trials, and qualitative studies), and follow-up time (1, 3, 6 months of acute and post-illness for COVID-19 patients).

### Sensitivity analyses

We will exclude the studies with high risk-of-bias based on a sensitivity analysis.

### Quality of the evidence

The Grades of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group method will be used to examine the quality of the evidence for each outcome. We will assess each outcome based on each of the following five aspects: imprecision, inconsistency, limitations, indirectness, and publication bias. They will be rated as very-low, low, moderate, or high level [18].

## Discussion

Coronaviruses have resulted in two severe outbreaks of the severe acute respiratory syndrome (SARS); however, before SARS-CoV-2. Previous coronaviruses have been associated with delirium signs in the acute stage and fatigue, depression, PTSD, and anxiety in the post-illness stage [3]. However, the lack of adequate data on COVID-19 patients limited the previous study to investigate and conclude the effects of the SARS-CoV-2 infection on patients' mental health. Given that the rapid and sustained growth of publication of COVID-19 research, we will perform a LSR to comprehensive and continuous synthesis updated data to explore the prevalence of depression, anxiety, delirium, and PTSD in COVID-19 patients.

## Declarations

### Ethics approval and consent to participate

All authors are accountable for all aspects of this work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The present study will not involve any patients and/or the public. No ethical approve or informed consent is required for the purposes of the present study.

### Consent for publication

Not applicable.

### Availability of data and materials

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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### Authors’ contributions

(I) Conception and design: JYS and JHT; (II) Administrative support: None; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: YYL, LZ and YMC; (V) Data analysis and interpretation: YG, MMN and MLY; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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# References

1. Sahu KK, Mishra AK, Lal A. Trajectory of the COVID-19 pandemic: chasing a moving target. Ann Transl Med. 2020;8(11):694.
2. Available online. https://covid19.who.int.
3. Rogers JP, Chesney E, Oliver D, Pollak TA, McGuire P, Fusar-Poli P, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. Lancet Psychiat. 2020;7(7):611–27.
4. Greenberg N, Docherty M, Gnanapragasam S, Wessely S. Managing mental health challenges faced by healthcare workers during covid-19 pandemic. BMJ. 2020;368:m1211.
5. Xiang YT, Yang Y, Li W, Zhang L, Zhang Q, Cheung T, et al. Timely mental health care for the 2019 novel coronavirus outbreak is urgently needed. Lancet Psychiat. 2020;7(3):228–9.
6. Strahan EH, Brown RJ. A qualitative study of the experiences of patients following transfer from intensive care. Intens Crit Care Nur. 2005;21(3):160–71.
7. Talevi D, Socci V, Carai M, Carnaghi G, Faleri S, Trebbi E, et al. Mental health outcomes of the CoViD-19 pandemic. Riv Psichiatr. 2020;55(3):137–44.
8. Park SC, Park YC. Mental Health Care Measures in Response to the 2019 Novel Coronavirus Outbreak in Korea. Psychiat Invest. 2020;17(2):85–6.
9. Mak IW, Chu CM, Pan PC, Yiu MG, Ho SC, Chan VL. Risk factors for chronic post-traumatic stress disorder (PTSD) in SARS survivors. Gen Hosp Psychiat. 2010;32(6):590–8.
10. Tao Z, Zhou S, Yao R, Wen K, Da W, Meng Y, et al. COVID-19 will stimulate a new coronavirus research breakthrough: a 20-year bibliometric analysis. Ann Transl Med. 2020;8(8):528.
11. Garner P, Hopewell S, Chandler J, MacLehose H, Schünemann HJ, Akl EA, et al. When and how to update systematic reviews: consensus and checklist. BMJ. 2016;354:i3507.
12. Schünemann HJ, Khabsa J, Solo K, Khamis AM, Brignardello-Petersen R, El-Harakeh A, et al. Ventilation Techniques and Risk for Transmission of Coronavirus Disease, Including COVID-19: A Living Systematic Review of Multiple Streams of Evidence. Ann Intern Med 2020.
13. Thombs BD, Bonardi O, Rice DB, Boruff JT, Azar M, He C, et al. Curating evidence on mental health during COVID-19: A living systematic review. J Psychosom Res. 2020;133:110113.

14. Créquit P, Martin-Montoya T, Attiche N, Trinquart L, Vivot A, Ravaud P. Living network meta-analysis was feasible when considering the pace of evidence generation. J Clin Epidemiol. 2019;108:10–6.
15. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015;350:g7647.
16. Badgett RG, Vindhyal M, Stirnaman JT, Gibson CM, Halaby R. A Living Systematic Review of Nebulized Hypertonic Saline for Acute Bronchiolitis in Infants. JAMA Pediatr. 2015;169(8):788–9.
17. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898.
18. Ge L, Sadeghirad B, Ball GDC, da Costa BR, Hitchcock CL, Svendrovski A, et al. Comparison of dietary macronutrient patterns of 14 popular named dietary programmes for weight and cardiovascular risk factor reduction in adults: systematic review and network meta-analysis of randomised trials. BMJ. 2020;369:m696.

## Supplementary Files

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