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Title: A Systematic Review and Meta-analysis comparing the mental health impact on Healthcare Professionals, Patients, and the General public during MERS, SARS, and Covid-19

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2 Peer-review report

Reviewer #1:

1. I am confused with the sentences presented in the Methods in Abstract, please reshape.

Response: The methods section in the Abstract lists out the databases used to extract article list, mesh terms used, and analysis method used to work on the data. The complete methodology is published on PROSPERO. The sentences have now been slightly modified to make it clearer.

2. Please add references to paragraph 1, 2 and 3.

Response: The first paragraph is a generic statement; therefore no reference was necessary. The references have been added to the content in para. 2 and 3 (see page 3, line 109 and 118)

3. protocol was "peer reviewed"? it should be published in journals.

Response: The protocol was internally peer reviewed before submission. Therefore, in this instance peer review does not relate to a published journal. For clarity, we have added a word indicating this was internal review. See line 185. Protocol was published in the PROSPERO as stated in the abstract and methods sections.

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

4. Please provide all searches in Appendix files as required by PRISMA.

Response: It is our understating that PRISMA does not ask for all searches, however they do ask for the PRISMA diagram which we have provided in Figure 1.

5. Please provide a good-look chart.

Thank you for your suggestion of adding a good-look chart. We do appreciate that good-look charts are used to present data as part of data visualisation in big-data sets or pattern inferences. We however, are not aware of this being done for comparative meta-analysis.

6. “The authors have read the STROBE Statement”, why not “PRISMA”? moreover, please use PRISMA-2020.

Thank you for your comment, in this manuscript a modified PRISMA and STROBE has been used to fit into the research question and criteria; this is not a conventional Systematic Review /Meta-Analysis whereby either can be used.

Reviewer #2: This systematic review and meta-analysis presents a comprehensive evaluation about the negative impact of pandemics caused by coronaviruses on the mental health (MH) across healthcare professionals, patients and the general public. Such study is very important and timely, and should be published if the authors are willing to make the following minor revisions.

The following typos and grammatical errors should be corrected:

1) The name and acronym for healthcare professionals (HCPs) should be unified throughout the manuscript (for example: on page 2, line 57, it is HCPs; on page 13, line 418, it is changed to healthcare workers; on page 20, line 638, it is GCWs)

Response: Thank you for your comment. We have reworded healthcare workers to healthcare professionals in general sentences but retained at places where we are referring to works used in original articles.

2) Page 3, line 108, “it is vital to understand the coronavirus family is vital to develop...” should be “it is vital to understand the coronavirus family for the development of ...”

Response: Thank you. This has been amended accordingly (see line 109).

3) Page 3, line 110, "2003" should be "2003 Severe acute respiratory syndrome (SARS)-associated coronavirus (SARS-CoV)"; "(MERS-CoV), which Coronavirus is a family of ..." should be "(MERS-CoV) are a family of ..."

Response: Thanks; amended (see line 111).

4) Page 3, line 114, "adult" should be "acute";

Response: Thanks; amended (see line 116).

5) Page 3, line 115-116, "... was the first outbreak because of these coronaviruses was first identified in 2012." Should be "... was the first outbreak. Coronaviruses were first identified in 1968. [1]"

Response: Thanks; amended (line 117).

6) Page 4, line 122, "effected" should be "affected"; line 129, "SARS-CovV-2" should be "SARS-CoV-2"

Response: Thanks; amended (see lines 123 & 130).

7) Page 4, line 141, "ITU" should be "ICU"; line 144, "Severe SARS-CoV-2" should be "severe COVID-19 disease"

Response: Thanks; amended (see lines 142 & 145).

All literatures included in the Figures and Tables of the manuscript with detailed data cited from these literatures should be included as references for the easy check and verification of data by the readers. Beside the global rolling out of vaccination, the negative impact of this COVID-19 pandemic on mental health will be greatly relieved if a better understanding about infectious diseases can be communicated to the HCPs, patients, and the public in general. Basically, every one of us needs to get the knowledge that the real problem of this pandemic is not the SARS-CoV-2 viral infection, but the overnutrition state in the patients of severe cases of COVID-19 disease [2]. In talking about infectious diseases, it would be better if we distinguish infections from diseases. Infection is the presence of pathogen, which is not a sufficient condition for disease. [3] Like most of the other viral and bacterial infections, the SARS-COV-2 viral infection is self-limiting [4], due to the strong innate immune response (necrosis or necroptosis - an inflammation-inducing cell self-destruction) inside every human being [5] to destroy the infected cells as well as the virus particles in the infected cell. This inflammation-inducing cell self-destruction is a powerful immune response to stop the viral infection and to initiate tissue regeneration. Therefore, most of the COVID-19 cases are asymptomatic or very mild. Most of the common diseases are the overreaction of the strong and

violent immune response, as Sir William Osler stated more than 100 years ago: "Except on few occasions, the patient appears to die from the body's response to infection rather than from it. Sir William Osler (1904)". [6] As the human immune system also plays a virtual role in nutrition acquisition from the degradation of viral damaged epithelial cells, the transient nutrition surge coupled with the overnutrition state in some patients with obesity or metabolic syndromes may contribute to lipotoxicity and damage in non-adipose tissues, triggering hyperinflammation and cytokine storms observed in severe cases of COVID-19 [2]. So the SARS-CoV-2 viral infection is only the trigger, not the real cause for the severe cases of COVID-19 disease. A lot of reported evidences shows that severe cases of COVID-19 are autoimmune disorder caused by overnutrition and expressed in the form of hyperinflammation [7,8]. References: 1. Virology: Coronaviruses. Nature. 1968;220(5168):650. DOI: 10.1038/220650b0. 2. Al Kassaa I, El Omari S, Abbas N, Papon N, Drider D, Kassem II, et al. (2021) High association of COVID-19 severity with poor gut health score in Lebanese patients. PLoS ONE 16(10): e0258913. DOI: 10.1371/journal.pone.0258913 3. Humphries DL, Scott ME, Vermund SH (2021) Pathways linking nutritional status and infectious disease: causal and conceptual frameworks. In: Nutrition and infectious diseases, Shifting the Clinical Paradigm (eds DL Humphries, ME Scott, SH Vermund), pp. 3–22. Cham, Switzerland: Humana. DOI: 10.1007/978-3-030-56913-6_1 4. Zhu CC, Zhu J (2021) The effect of self-limiting on the prevention and control of the diffuse COVID-19 epidemic with delayed and temporal-spatial heterogeneous. BMC Infect Dis 21, 1145. DOI: 10.1186/s12879-021-06670-y 5. Nailwal, H., Chan, F.K.M. Necroptosis in anti-viral inflammation. Cell Death Differ 26, 4–13 (2019). DOI: 10.1038/s41418-018-0172-x 6. Dobson GP, Biro E, Letson HL and Morris JL (2021) Living in a Hostile World: Inflammation, New Drug Development, and Coronavirus. Front. Immunol. 11:610131. DOI: 10.3389/fimmu.2020.610131 7. Icenogle T (2020) COVID-19: Infection or Autoimmunity. Front. Immunol. 11:2055. doi: 10.3389/fimmu.2020.02055 8. Halpert G, Yehuda Shoenfeld Y (2020) SARS-CoV-2, the autoimmune virus. Autoimmunity Reviews 19(12):102695. DOI: 10.1016/j.autrev.2020.102695.

Response: Thank you for your review comments. The authors use, the term, Infectious disease, is the accurate clinical term to be used and appropriate for the context of this research where the scope is limited to evaluating the mental health impact due to the prevalence of mental health conditions endeavoured by 3 cohorts (i.e. patients, healthcare professionals and the general public) due to COVID-19. It is the process or "infectious disease" that causes the mental health impact. Any given individual acquiring a disease would be subjected to physiological changes which may alter the mental well-being at certain time points. To truly assess this, we need to conduct prospective studies with biological samples to evaluate changes in the state of biomarkers that are aligned to conditions such as depression or anxiety. However, our scope of the research does not include these aspects, given the aim of this study is to systematically review the published data to conclude the knowledge and practice gap that needs addressing. Thus, the content in our study is clinically and scientifically specific to the "process" of disease sequelae.

(Reference the of infectious disease <https://www.britannica.com/science/infectious-disease>)

The references are of interest although the scope and implications are not relevant to this study, nor clinically.

Therefore, most of the COVID-19 cases are asymptomatic or very mild.

Our response: We would argue that this comment is a misrepresentation of the deaths incurred due to COVID-19. This was deemed a pandemic due to the high transmission and mortality rates as such, we will not be claiming COVID-19 to have mild symptoms. Equally, patients that had Covid had a variety of symptoms. Whether the symptoms are mild or strong is dependent on the viral load, the given individual's immune system and various other factors. However, this information is still being explored and continued to be done so longitudinally to obtain a comprehensive understanding of the condition moving forward. Our aim is to report the evidence relevant to our research question.

<https://coronavirus.data.gov.uk/>

Reviewer #3: SARS-CoV, MERS-CoV and SARS-CoV-2 were 3 pathogenic pandemics impacted the global population over the last few decades. This study analysed the prevalence of some mental health outcomes to the outbreaks of 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 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 healthcare workers are the first and second most likely groups to suffer from mental health problem. Young people are more likely to be caught up in depressive and anxiety emotions than old people. In comparison to MERS and SARS-CoV, it is evident SAR-CoV-2 has an ongoing mental health impact with emphasis on depression, anxiety and PTSD. The limited of this results is having a high heterogeneity for depression, anxiety and PTSD in different studys that 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.

Response: Thank you for your review

Reviewer #4: Delanerolle et al.

5 ABBREVIATIONS

In general, do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/ definition. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, and mAb, do not need to be defined and can be used directly.

The basic rules on abbreviations are provided here:

- (1) **Title:** Abbreviations are not permitted. Please spell out any abbreviation in the title.

Title amended accordingly

- (2) **Running title:** Abbreviations are permitted. Also, please shorten the running title to no more than 6 words.

thanks

6 EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) *Science editor:*

This systematic review and meta-analysis intended to compare the mental health impact on healthcare professionals, patients, and the general public during MERS, SARS, and Covid-19. The manuscript is well-written and informative. The reviewers raised some issues, which should be addressed by the authors further. The format style of the references does not conform to the requirements of the WJP, please revise also.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

Reviewers' comments addressed accordingly

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Psychiatry, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.

We have provided decomposable figures where feasible

Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden.

We have amended tables as required

The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Step 4: References

Please revise the references according to the [Format for References Guidelines](#), and be sure to edit the reference using the reference auto-analyser.

Auto analyser used to edit and generate references according to journal specification

Reminder: It is unacceptable to have more than 3 references from the same journal. To resolve this issue and move forward in the peer-review/publication process, please revise your reference list accordingly.

No issue identified here

Step 5: Footnotes and Figure Legends

(1) Requirements for Figures: Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file, and submit as “72809-Figures.pptx” on the system. The figures should be uploaded to the file destination of “Image File”.

Image File submitted accordingly

(2) Requirements for Tables: Please provide decomposable Tables (in which all components are movable and editable), organize them into a single Word file, and submit as “72809-Tables.docx” on the system. The tables should be uploaded to the file destination of “Table File”.

Table file submitted accordingly

Step 7: Upload the Revision Files

For all required accompanying documents (listed below), you can begin the uploading process *via* the F6Publishing system. Then, please download all the uploaded documents to ensure all of them are correct.

- (1) 72809-Answering Reviewers -submitted
- (2) 72809-Audio Core Tip - submitted
- (3) 72809-Biostatistics Review Certificate - submitted
- (4) 72809-Conflict-of-Interest Disclosure Form - submitted
- (5) 72809-Copyright License Agreement - submitted
- (9) 72809-Image File -submitted

(10) 72809-Table File - **submitted**

(11) 72809-PRISMA 2009 Checklist - no changes

(12) 72809-Supplementary Material - **submitted**

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9 CONFLICT-OF-INTEREST DISCLOSURE FORM - submitted

Thank you for your review and comments, much appreciated.

Kind Regards,

Dr Peter Phiri, PhD
Corresponding Author