

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of non-pharmaceutical interventions for reducing transmission of coronavirus disease 2019 [COVID-19]: A systematic review and meta-analysis protocol
AUTHORS	Regmi, Krishna; Lwin, Cho Mar

VERSION 1 – REVIEW

REVIEWER	Nick Jones University of Oxford, UK I have been working on a review of social distancing published on the University of Oxford Centre for Evidence Based Medicine rapid review site.
REVIEW RETURNED	06-Jul-2020

GENERAL COMMENTS	<p>Major</p> <ul style="list-style-type: none">- Definition of social distancing you are giving in the introduction is very broad and includes interventions which many would consider different to social distancing e.g. quarantine. The language is confusing, at times, school closure and case finding are also mentioned alongside types of distancing. The reference given (8) is for 'non pharmaceutical interventions', which is obviously different and broader to SDM. The intervention needs to be clearly defined and consistent throughout. This needs amending so that either the title / aim of the review changes to broader non-pharmaceutical interventions or the inclusion criteria reflect the title.- You also need to be clear in the introduction if you are focusing only on reviews of COVID-19/ SARS-CoV-2 or including other studies of social distancing e.g. SARS or MERS - seems the former but therefore be clear re; context when referring to other settings.- I would change title and objective to state this is about reducing transmission rather than prevention of COVID-19- Psychological distress, anxiety etc. included as secondary outcome measures yet not discussed in intro or justified. Nothing about anxiety/ depression or secondary outcome measures in the search. List of study types is limited and likely to miss studies.- Lots of detail in intro and discussion around health inequalities, yet nothing in the study design that covers this. Either needs greater focus within review e.g. subgroup analysis of studies of
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	<p>distancing in different socioeconomic groups - or rewrite abstract + discussion</p> <p>- Relying on peer-reviewed articles during COVID-19 will miss a lot of relevant material in pre-print form. Search should include engines such as MedRxiv + LitCovid if aiming to be comprehensive for COVID relevant literature. I would get a search specialist to help formulate this search + pilot it if you have not done so.</p> <p>- Low quality study is not usually an exclusion criteria - should be included but then run in sensitivity analysis with and without these data.</p> <p>- Multiple occasions where give definition of a test e.g. I2 for heterogeneity and describe how this applies in general - this isn't helpful to readers - what needs to be included is specific details relevant to this study question and how you will adapt these methods to reflect this. i.e one might anticipate a lot of variation based on the type of intervention or setting, would you consider a sub-group analysis in this scenario? What else might lead to variation etc etc? The section on sub-group analysis provides extremely limited information.</p> <p>Minor Abstract - first line suggest change to 'protect the public'. Methods - suggest 'systematic review and meta-analysis'</p> <p>Intro - line 3 - remove 'for us' after biggest challenge - change to globally or something similar - biggest in what sense? change or define. Suggest removed i.e. six deaths per 100 - percentage already reported. Abbreviations e.g. UK, US (which should be USA) need full text first time mentioned in article. Paragraph 2 - 'great equaliser' - again reference and explain more precisely - its a bit colloquial. Would reduce detail on COVID epidemiology. 'preliminary scan' usually called a 'scoping search' + this sentence does not make sense to me - 'very limited systematically reviewed'? Not reviewed? Not reviewed well?</p> <p>Methods - dont need to define what a systematic review or meta-analysis is. Dont need a blank PRISMA flow diagram included. Dont need to include a reproduction of a JBI checklist.</p> <p>Reporting bias - do you think Trim and Fill will be possible if studies are very heterogeneous? How will you handle this?</p> <p>Data analysis - I dont understand the 2nd paragraph - please rephrase.</p> <p>Missing data - what if authors dont provide?</p> <p>Risk of bias - would be very difficult 'to create row for every relevant type of potential bias' - state which tool you will use to assess ROB and why this chosen? Isn't this JBI? Why has this now changed to ROBINS-I and RoB2? If you are considering risk of bias across studies might want to consider eg. GRADE approach.</p> <p>Discussion - too long! Summarise the review in a single paragraph. Justification for review should be in the intro. Avoid sweeping and unsupported statements e.g. sentence beginning - 'need to completely change the way the economy....'</p>
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REVIEWER	Martin S Andersen University of North Carolina at Greensboro United States of America
REVIEW RETURNED	15-Jul-2020

GENERAL COMMENTS	<p>Referee Report: Impact of social distancing measures for preventing coronavirus disease 2019 [COVID-19]: A systematic review and meta-analysis protocol (BMJOPEN 2020-041383)</p> <p>Positives A rapid review of the effectiveness of social distancing measures at reducing Covid-19 transmission is of first-order important and I applaud the authors for proposing this study. It is difficult to imagine a field that has grown more rapidly than Covid-19 research and systematic reviews of the kind proposed by this protocol will be vital to assist policymakers and researchers in synthesizing a large and complex literature.</p> <p>Comments My main area of concern is the decision to limit the study to peer-reviewed articles. I understand the rationale for doing so, but the Covid literature on social distancing has mostly been in the grey literature given the lags in publication. The time lag imposed by the peerreview process also means that the review will be biased towards studies of countries and areas that were affected earlier.</p> <p>Related to the concern about the exclusion of peer-reviewed studies is the decision to exclude Google Scholar from the list of databases to be searched. The list that the authors presented does not, to my knowledge, cover preprint servers (medRxiv, bioRxiv, SSRN, etc.), but Google Scholar does. Given that the authors will still screen articles using the JBI, there is no reason to limit the set of databases in the manner that the authors propose. Lastly, I think it would be helpful to address some obvious issues with using the JBI in this context. There are several items in the JBI that are irrelevant to social distancing studies; for example, I do not think it is possible to conduct a blinded study of a social distancing measure. It would be helpful to acknowledge that some of the items will be irrelevant, and the authors should consider removing fully irrelevant items from Box 1.</p>
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VERSION 1 – AUTHOR RESPONSE

<p>Reviewer: 1</p> <p>Major</p> <p>- Definition of social distancing you are giving in the introduction is very broad and includes interventions which many would consider different to social distancing e.g. quarantine. The language</p>	<p>- Thanks for your suggestion. I have now revisited the definition of social distancing,</p>
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is confusing, at times, school closure and case finding are also mentioned alongside types of distancing. The reference given (8) is for 'non pharmaceutical interventions', which is obviously different and broader to SDM. The intervention needs to be clearly defined and consistent throughout. This needs amending so that either the title / aim of the review changes to broader non-pharmaceutical interventions or the inclusion criteria reflect the title.

- You also need to be clear in the introduction if you are focusing only on reviews of COVID-19/ SARS-CoV-2 or including other studies of social distancing e.g. SARS or MERS - seems the former but therefore be clear re; context when referring to other settings.

- I would change title and objective to state this is about reducing transmission rather than prevention of COVID-19

- Psychological distress, anxiety etc. included as secondary outcome measures yet not discussed in intro or justified. Nothing about anxiety/ depression or secondary outcome measures in the search. List of study types is limited and likely to miss studies.

- Lots of detail in intro and discussion around health inequalities, yet nothing in the study design that covers this. Either needs greater focus within review e.g. subgroup analysis of studies of distancing in different socioeconomic groups - or rewrite abstract + discussion

- Relying on peer-reviewed articles during COVID-19 will miss a lot of relevant material in pre-print form. Search should include engines such as MedRxiv + LitCovid if aiming to be comprehensive for COVID relevant literature. I would get a search specialist to help formulate this search + pilot it if you have not done so.

- Low quality study is not usually an exclusion criteria - should be included but then run in sensitivity analysis with and without these data.

- Multiple occasions where give definition of a test e.g. I2 for heterogeneity and describe how this

revisited the introduction, and 'non pharmaceutical interventions clearly defined and made consistent throughout (see p.5, paras 2 and 3). This has now reflected in the title / aim and the inclusion criteria. See p.1 (title), p.2 (title), p.6 (aim and review question) and p.7 (inclusion criteria)

-Clarified this in the introduction. See p.5, para 3

- Corrected. See p.1 (title), p.2 (title), p.6 (aim/objective)

- Added psychological impacts of COVID-19 e.g. distress, anxiety etc in the revised manuscript (See p.4, para 2). Also added relevant search terms in the search strategy. See Table 1

- Revisited (see p. 3-4, p. 7 – inclusion criteria) and also revised the subgroup analysis to reflect these aspects. See p. 13

- Revisited searching sources where I have added pre-print engines. See p.2 and p.7. Search strategy was developed in collaboration with departmental subject librarians from authors' universities and also piloted them (See p.8, para1).

applies in general - this isnt helpful to readers - what needs to be included is specific details relevant to this study question and how you will adapt these methods to reflect this. i.e one might anticipate a lot of variation based on the type of intervention or setting, would you consider a sub-group analysis in this scenario? What else might lead to variation etc etc? The section on sub-group analysis provides extremely limited information.

Minor

Abstract - first line suggest change to 'protect the public'. Methods - suggest 'systematic review and meta-analysis'

Intro - line 3 - remove 'for us' after biggest challenge - change to globally or something similar - biggest in what sense? change or define. Suggest removed i.e. six deaths per 100 - percentage already reported.

Abbreviations e.g. UK, US (which should be USA) need full text first time mentioned in article.

Paragraph 2 - 'great equaliser' - again reference and explain more precisely - its a bit colloquial. Would reduce detail on COVID epidemiology.

'preliminary scan' usually called a 'scoping search' + this sentence does not make sense to me - 'very limited systematically reviewed'? Not reviewed? Not reviewed well?

Methods - dont need to define what a systematic review or meta-analysis is. Dont need a blank PRISMA flow diagram included. Dont need to include a reproduction of a JBI checklist.

Reporting bias - do you think Trim and Fill will be possible if studies are very heterogeneous? How will you handle this?

- Deleted low quality study from exclusion criteria

- Revisited I2 for heterogeneity and necessary details were added (See p.12). Sub-group analysis also revised to reflect this. See p.13

Abstract - first line added 'protect the public'. Methods – also added 'systematic review and meta-analysis' (p.2)

- Removed them in the revised manuscript

- Provided full text for these abbreviations e.g. UK, US and EU (see p. 5, para 2, and also reduced some details of COVID epidemiology.

- Corrected. See p.5, last para

Methods - deleted these definitions (please see p.6, last para). Removed blank PRISMA flow diagram, and also removed the quality assessment checklist. Instead of using JBI, we

<p>Data analysis - I dont understand the 2nd paragraph - please rephrase.</p> <p>Missing data - what if authors dont provide?</p> <p>Risk of bias - would be very difficult 'to create row for every relevant type of potential bias' - state which tool you will use to assess ROB and why this chosen? Isnt this JBI? Why has this now changed to ROBINS-I and RoB2? If you are considering risk of bias across studies might want to consider eg. GRADE approach.</p> <p>Discussion - too long! Summarise the review in a single paragraph. Justification for review should be in the intro. Avoid sweeping and unsupported statements e.g. sentence beginning - ' need to completely change the way the economy....'</p>	<p>will be using Cochrane Collaboration's tool for assessing risk of bias for randomised controlled trials and the Newcastle Ottawa scale (NOS) for non-randomised studies as these are widely used for SR and Meta-analysis study and GRADE approach – considering risk of bias across studies (see p.10 and 11).</p> <p>- Revised and necessary corrections were made regarding data analysis. See p.12, para 3</p> <p>- Necessary details were added. See p.13</p> <p>- Thanks for your suggestion. Considering risk of bias across studies, we will be using GRADE approach. See p. 11, para 1</p> <p>Discussion – revised and provided the summary of the review in a single paragraph. See p.14</p>
<p>Reviewer: 2</p>	
<p>Positives</p> <p>A rapid review of the effectiveness of social distancing measures at reducing Covid-19 transmission is of first-order important and I applaud the authors for proposing this study. It is difficult to imagine a field that has grown more rapidly than Covid-19 research and systematic reviews of the kind proposed by this protocol will be vital to assist policymakers and researchers in synthesizing a large and complex literature.</p>	<p>Thank you!</p>
<p>Comments</p> <p>My main area of concern is the decision to limit the study to peer-reviewed articles. I understand the rationale for doing so, but the Covid literature on</p>	<p>- Revisited and now considered to expand our strategy covering ClinicalTrials.Gov for clinical trials on COVID-19, Cochrane Resources on</p>

<p>social distancing has mostly been in the grey literature given the lags in publication. The time lag imposed by the peer-review process also means that the review will be biased towards studies of countries and areas that were affected earlier. Related to the concern about the exclusion of peer-reviewed studies is the decision to exclude Google Scholar from the list of databases to be searched. The list that the authors presented does not, to my knowledge, cover preprint servers (medRxiv, bioRxiv, SSRN, etc.), but Google Scholar does. Given that the authors will still screen articles using the JBI, there is no reason to limit the set of databases in the manner that the authors propose.</p> <p>Lastly, I think it would be helpful to address some obvious issues with using the JBI in this context. There are several items in the JBI that are irrelevant to social distancing studies; for example, I do not think it is possible to conduct a blinded study of a social distancing measure. It would be helpful to acknowledge that some of the items will be irrelevant, and the authors should consider removing fully irrelevant items from Box 1.</p>	<p>Coronavirus (COVID-19), Oxford COVID-19 Evidence Service, Google Scholar for published and unpublished literatures on COVID-19 including pre-print engines such as medRxiv, bioRxiv, LitCovid and SSRN for unpublished studies on COVID-19. See p.2 and P.7</p> <p>- Instead of JBI, we will be using GRADE approach to assess the certainty of the evidence across studies. I have also added that some items or questions in these quality assessments e.g. blinded study, are irrelevant to social distancing studies; we therefore consider removing them. See p. 10, last para.</p>
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VERSION 2 – REVIEW

REVIEWER	Nick Jones University of Oxford, UK I have published a narrative review of physical distancing published on the University of Oxford CEBM COVID-19 Evidence Service site and have a linked analysis piece accepted for publication in the BMJ.
REVIEW RETURNED	13-Aug-2020
GENERAL COMMENTS	<p>Thank you for your amendments to this paper. The topic is clearly relevant at the current time. My major concerns are 1) the scope of the review, which is extremely broad and likely to include very heterogeneous data 2) analysis plan, which is reported as being both a thematic analysis and narrative review as well as a meta-analysis and 3) seems to be a plan to include also the psychological impact of these interventions, though this aim does not seem to be fully developed. This ambitious plan for the research questions and analysis makes it a very extensive introduction and makes it difficult to follow the thought process as to which parts of the analysis link to which review questions and outcome measures.</p> <p>Major</p>

	<p>- described as first SR to measure impact of these NPIs in COVID19 - what about Chu systematic review including physical distancing published in the Lancet?</p> <p>- the introduction is very long and not always focused on the question in hand, i.e. non-pharmaceutical interventions. For example, there is an extended discussion at the start of the piece regarding risks of COVID19 in BAME populations. It's interesting but as not the objective of the review, suggest shortening this significantly. The link to psychological effects of COVID-19 in this context also not really clear - are you introducing this at this stage as one of the possible negative consequences of NPI?</p> <p>- Research question is extremely broad for a single review. Three types of intervention and specifically looking also at different settings e.g healthcare workers using any study design and also two main (both big) outcome measures - impact on reducing transmission and the psychological impact of these interventions. I think you might find there is an enormous amount of very heterogeneous data taking this approach - might it be better to split into two or three separate focused reviews?</p> <p>- Analysis plan as written is confusing. Describe first a narrative synthesis and thematic analysis (appropriate for qualitative research) and then also a plan for a quantitative meta-analysis. Is this a plan to do completely different analysis types in the same review?</p> <p>- Would be helpful to see planned list of data items to be extracted.</p> <p>- Tends to be explanations of the methods (e.g. what trim and fill is or how to calculate I2 / Q-value) whereas what is needed is a justification of why these methods are appropriate in this review, given the expected overall analysis plan and data to be used. Dont think you need to state e.g. how i2 is calculated - can assume readers know and just reference a relevant source.</p> <p>Minor</p> <p>- Page 4, Line 31-33 - this doesn't seem to run on from last paragraph as written.</p> <p>- Are lines 43-50 Page 4 re; survey in Canada a direct quote? Add quotations if so. Remove paragraph indent if not.</p> <p>Page 4, Line 53- 'It is difficult to predict an exact future' - Im not sure what this means? Doesnt seem to fit with reported global mortality figure in 2nd half of sentence.</p> <p>Page 5 line 10 - do you need separate abbreviations for social distancing measure and social distancing? suggest pick one and be consistent</p> <p>Page 5 line 53 - language is still colloquial for a BMJ article e.g. 'quick Google Scholar search'</p> <p>page 10 line 30-31 - all studies will be screened twice? Do you mean done in two stages or screened by two independent reviewers (or both)?</p>
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REVIEWER	Martin Andersen University of North Carolina at Greensboro, United States of America
REVIEW RETURNED	29-Aug-2020
GENERAL COMMENTS	I have no further comments and thank the authors (again) for proposing what I hope will be a useful paper on NPIs to address the Covid-19 pandemic.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Major

- described as first SR to measure impact of these NPIs in COVID19 - what about Chu systematic review including physical distancing published in the Lancet?

Author (KR): Thanks for your comments. Yes, I agree with you that Chu and colleagues did this study capturing data from 172 studies across 16 countries and six continents as of 26 March 2020, but none of the included studies was an RCT; therefore, their findings might suffer from both recall and measurement biases. Second, their focus was more on physical distance, face masks and eye protection, not the overall impact of NPS on reducing COVID infection. From that ground, I would still claim that as far as we authors are aware, this might still be the first SR at the point of writing this manuscript (see p.5, last para).

- the introduction is very long and not always focused on the question in hand, i.e. non-pharmaceutical interventions. For example, there is an extended discussion at the start of the piece regarding risks of COVID19 in BAME populations. It's interesting but as not the objective of the review, suggest shortening this significantly. The link to psychological effects of COVID-19 in this context also not really clear - are you introducing this at this stage as one of the possible negative consequences of NPI?

Author (KR): As per your suggestion, we revisited the introduction section and shortened this. In addition, the psychological effects of COVID-19 have been appropriately removed as we agreed with the reviewer that though these aspects are still interesting/important, this is not the objective of the review. I also revised the psychological effects of COVID-19 and deleted unrelated information including the quote from the survey study conducted in Canada.

- Research question is extremely broad for a single review. Three types of intervention and specifically looking also at different settings e.g healthcare workers using any study design and also two main (both big) outcome measures - impact on reducing transmission and the psychological impact of these interventions. I think you might find there is an enormous amount of very heterogeneous data taking this approach - might it be better to split into two or three separate focused reviews?

Author (KR): We believe that the proposed research question and methods are valid, therefore we would like to politely decline your suggestion. Similarly, the nature of NPIs is really complex as several countries across the world under WHO policy direction adopted social distancing measures, including all these three interventions (social distancing, quarantine and isolation) as a package. Therefore it is difficult to examine one particular effect of the intervention (e.g. social distancing) in relation to preventing or controlling COVID-19, which has already been highlighted in the sub-group analysis (p.14). If we come across any suitable studies published on the specific type of intervention and its effect on COVID, then we will certainly consider looking at that aspect in the next phase of the study

- Analysis plan as written is confusing. Describe first a narrative synthesis and thematic analysis (appropriate for qualitative research) and then also a plan for a quantitative meta-analysis. Is this a plan to do completely different analysis types in the same review?

Author (KR): Analysis plan for qualitative data has been revisited (p.13, para. 1).

- Would be helpful to see planned list of data items to be extracted.

Author (KR): Potential list of data items for extraction has been provided (p.13, para 2, under the sub-heading of 'Data extraction and data items').

- Tends to be explanations of the methods (e.g. what trim and fill is or how to calculate I2 / Q-value) whereas what is needed is a justification of why these methods are appropriate in this review, given the expected overall analysis plan and data to be used. Dont think you need to state e.g. how i2 is calculated - can assume readers know and just reference a relevant source.

Author (KR): Revisited this and provided some explanations of why these methods are appropriate in this review (see p.11, last para, and p.12, last para).

Minor

- Page 4, Line 31-33 - this doesn't seem to run on from last paragraph as written.

Author (KR): Corrected (see p.4, para. 2).

- Are lines 43-50 Page 4 re; survey in Canada a direct quote? Add quotations if so. Remove paragraph indent if not.

Author (KR): Based on your suggestion, we deleted this (also refer to major comment, point 2).

Page 4, Line 53- 'It is difficult to predict an exact future' - Im not sure what this means? Doesnt seem to fit with reported global mortality figure in 2nd half of sentence.

Author (KR): Deleted this line.

Page 5 line 10 - do you need separate abbreviations for social distancing measure and social distancing? suggest pick one and be consistent

Author (KR): Corrected (see p.4, last para, line 2).

Page 5 line 53 - language is still colloquial for a BMJ article e.g. 'quick Google Scholar search'

Author (KR): Corrected (see p.5, para. 3, first few lines).

page 10 line 30-31 - all studies will be screened twice? Do you mean done in two stages or screened by two independent reviewers (or both)?

Author (KR): Corrected (see p.10, under the sub-heading of 'Selection of studies').

Reviewer: 2

I have no further comments and thank the authors (again) for proposing what I hope will be a useful paper on NPIs to address the Covid-19 pandemic.

Author (KR): Thank you!

I have also attached the 'response table' for your information. Thank you again. I look forward to hearing from your decisions regarding publication. Should you have questions about my resubmission or need further information, please get in touch with me.