

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Critical care service delivery across healthcare systems in low- and low-middle income countries: Protocol for a Systematic Review
AUTHORS	Lim, Andrew; Kivlehan, Sean; Losonczy, Lia; Murthy, Srinivas; Dippenaar, Enrico; Lowsby, Richard; Yang, Marc Li Chuan; Jaung, Michael; Stephens, P. Andrew; Benzoni, Nicole; Sefa, Nana; Bartlett, Emily; Chaffay, Brandon; Haridasa, Naeha; Velasco, Bernadett; Yi, Sojung; Contag, Caitlin; Rashed, Amir; McCarville, Patrick; Sonenthal, Paul; Shukur, Nebiyu; Bellou, Abdelouahab; Mickman, Carl; Ghatak-Roy, Adhiti; Ferreira, Allison; Adhikari, Neill; Reynolds, Teri

VERSION 1 – REVIEW

REVIEWER	Slusher, Tina University of Minnesota Academic Health Center, Pediatrics
REVIEW RETURNED	24-Feb-2021

GENERAL COMMENTS	This is an excellent description of an urgently needed systematic review. The only minor non-essential revision I would suggest is put the additional exclusions you mention in the paper in the hierarchy table i.e. OR only, military, etc.
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REVIEWER	Ma, Xiya University of Montreal
REVIEW RETURNED	03-Mar-2021

GENERAL COMMENTS	<p>I would like to thank the authors for the opportunity to review their protocol submission and to congratulate them on this work. Please find below my comments and suggestions:</p> <ol style="list-style-type: none">1) I recommend the authors to have a look and adjust according to the most recently updated list of the World Bank Classifications for countries, as quite a few have changed their status since 2016: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups2) While I agree with including all age groups, I suggest the authors make a clear distinction in their eventual data presentation and analysis to separate pediatric critical care facilities and adult ones, as the resources required (human, material, etc) is different in these two populations.3) I understand the authors aim to characterize critical care services in LLMICs before the pandemic, although could it be interesting to also look at papers published beyond January 2020 that may describe changes in critical care capacity in the last year?
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	4) Do the authors also plan to do calibration pilot exercises for full-text screening?
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REVIEWER	Murni, Indah Universitas Gadjah Mada
REVIEW RETURNED	12-Mar-2021

GENERAL COMMENTS	<p>Thank you for submitting this article to BMJ Open. I was pleased to review this paper.</p> <p>This study aimed to systematically review the previous published studies on determining the types of critical care services and interventions delivered in low- and middle-income countries. These are some of my observations:</p> <p>Searching for the studies</p> <ul style="list-style-type: none"> • Will the authors also aim to search multiple sources including manual searching, other sources for published studies such as individual journal archives, Cochrane library, and unpublished studies to have a complete picture of the investigated topic? <p>Selecting studies</p> <ul style="list-style-type: none"> • Selecting which studies are included in and excluded from the review might be the most important decision to make because this will determine the results of the review. Therefore, it is very important to minimise any possible bias in making these judgements. • How will the authors minimise this risk of bias in terms of training for the authors who will select the studies? Will all 21 reviewers select the studies? • It may be helpful to have one of the authors selecting studies not be a content expert, to avoid any preconceptions about particular studies or interventions. <p>Collecting data</p> <ul style="list-style-type: none"> • Will the authors also include types of included studies in the data collection form? • What is the relevant of collecting data on sample size in this type of review? Since the authors will not extract data on patient outcome. Will the numbers of bed at the ICU be important to collect? • What outcomes will the authors collect from the included studies? I suspect there will be much qualitative data included as well, such as the barriers or problems related to critical care in LMICs. Will the authors consider to do a qualitative systematic review as well? • Other items of interest including bibliographic information and contact details of the authors for each included study may be necessary to be collected in order to reach the authors when there is no full text available. These will ensure the complete picture of this review. <p>Risk of bias</p> <ul style="list-style-type: none"> • The authors need to consider doing the risk of bias analysis. These will depend on the type of included studies whether qualitative or quantitative. <p>Synthesis of data</p> <ul style="list-style-type: none"> • When there are circumstances when meta-analysis may not be possible, the authors may consider to synthesis the review without meta-analysis, namely narrative synthesis. These should be included in the protocol.
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	<ul style="list-style-type: none"> • Will a conceptual framework, logic model or taxonomy be possible for synthesizing? <p>Good luck with the study.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Tina Slusher, University of Minnesota Academic Health Center

Comments to the Author:

This is an excellent description of an urgently needed systematic review. The only minor non-essential revision I would suggest is put the additional exclusions you mention in the paper in the hierarchy table i.e. OR only, military, etc.

Response: Thank you for these comments. We have added the additional exclusions to the table.

Reviewer: 2

Dr. Xiya Ma, University of Montreal

Comments to the Author:

I would like to thank the authors for the opportunity to review their protocol submission and to congratulate them on this work. Please find below my comments and suggestions:

1) I recommend the authors to have a look and adjust according to the most recently updated list of the World Bank Classifications for countries, as quite a few have changed their status since 2016: <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups>

Response: Thank you for the recommendations. We use the 2016 World Bank classification from several years ago as a reference point of our study, since our articles range from 2008 to 2020. Therefore, the earlier classification is likely to capture more accurately the LICs and LMICs from which the included studies originate. We have added a sentence to clarify the reasoning to the methods (page 7): “We decided to use the 2016 World Bank classification as a reference point, as the earlier classification is likely to capture more accurately the LLMICs during the time period from which the included studies originate (2008-2020).”

2) While I agree with including all age groups, I suggest the authors make a clear distinction in their eventual data presentation and analysis to separate pediatric critical care facilities and adult ones, as the resources required (human, material, etc) is different in these two populations.

Response: Thank you; we agree with your assessment, although it is possible that critical care is delivered to both adults and children in similar settings in these LICs and LMICs. We have added a statement in the analysis that we will conduct a sensitivity analysis considering studies reporting only on adults and studies only on children separately (page 12): “We will conduct a sensitivity analysis to separately consider studies that report only on adults and studies only on children.”

3) I understand the authors aim to characterize critical care services in LLMICs before the pandemic, although could it be interesting to also look at papers published beyond January 2020 that may describe changes in critical care capacity in the last year?

Response: We agree that this would be a very interesting comparison, and including COVID-era publications was indeed a consideration. However, given that the vast majority of our papers were from the preceding decade, and given that much of the critical care literature following COVID is actively emerging, and may evolve over the coming months to years, we decided to keep the timeframe as outlined in the protocol. We anticipate that a future literature review including the COVID-era and beyond would make for an interesting cross-comparison. We have added this point to the limitations (page 11): “Our study does not include publications on critical care delivery during the COVID-19 pandemic, and characteristics of care delivery may have changed over that time.”

4) Do the authors also plan to do calibration pilot exercises for full-text screening?

Response: We agree that bias in study selection plays a potential significant role in our study, and we aim to mitigate bias with extensive training of the 21 reviewers involved. This training includes calibration pilot exercises of our inclusion/exclusion criteria and multiple group discussions (over virtual teleconferences or online discussion board forums) to ensure shared understanding of the study criteria. The conflict resolution step built into our selection process also ensures that a third reviewer arbitrates all disagreements, and that the rationale for inclusion/exclusion is also discussed via the Covidence platform that is available to the entire review team. We provide details of these methods on page 10.

Reviewer: 3

Dr. Indah Murni, Universitas Gadjah Mada

Comments to the Author:

Thank you for submitting this article to BMJ Open. I was pleased to review this paper.

This study aimed to systematically review the previous published studies on determining the types of critical care services and interventions delivered in low- and middle-income countries.

These are some of my observations:

Searching for the studies

- Will the authors also aim to search multiple sources including manual searching, other sources for published studies such as individual journal archives, Cochrane library, and unpublished studies to have a complete picture of the investigated topic?

Response: Thank you for your comments. Because of the large scope of our study, we will exclude study protocols, conference abstracts, and other unpublished studies without available full-text. We expect challenges in determining whether unpublished studies meet eligibility criteria and limited ability to extract data. In a pilot search, we identified a large number of peer-reviewed, published manuscripts meeting our inclusion criteria, and thus we feel that we will have sufficient studies to include to describe the range and characteristics of critical care services, suitable to our study objectives. In addition to searching standard electronic databases, we will search bibliographies of systematic reviews that have met inclusion criteria, as well as WHO intranet databases. We have clarified our approach on page 8-9.

Selecting studies

- Selecting which studies are included in and excluded from the review might be the most important decision to make because this will determine the results of the review. Therefore, it is very important to minimise any possible bias in making these judgements.
- How will the authors minimise this risk of bias in terms of training for the authors who will select the studies? Will all 21 reviewers select the studies?
- It may be helpful to have one of the authors selecting studies not be a content expert, to avoid

any preconceptions about particular studies or interventions.

Response: We agree that bias in study selection plays a potential significant role in our study, and we will mitigate bias with extensive training of the 21 reviewers involved.

This training includes calibration pilot exercises of our inclusion/exclusion criteria and multiple group discussions (over virtual teleconferences or online discussion board forums) to ensure shared understanding of the study criteria. The conflict resolution step built into our selection process also ensures that a third reviewer arbitrates all disagreements, and that the rationale for inclusion/exclusion is also discussed via the Covidence platform that is available to the entire review team.

The review authors represent a variety of training backgrounds, including medical students, residents, fellows, and attending physicians representing multiple specialties (including anesthesia, pediatrics, critical care, emergency medicine) to diversify our collective perspective on study interventions.

We provide details of these methods on page 10.

Collecting data

- Will the authors also include types of included studies in the data collection form?
- What is the relevant of collecting data on sample size in this type of review? Since the authors will not extract data on patient outcome. Will the numbers of bed at the ICU be important to collect?

Response: We will report on the types of included studies, categorized based on study design.

We will collect data on studies' sample size, where reported, to describe to the reader the aggregate number of patients for whom critical care service delivery was studied for a given population/country. We will not report on the number of ICU beds in a given study because many studies in LIC/LMIC critical care environments do not take place in traditional ICU settings, or have a flexible bed capacity over a variety of geographic locations, and thus these numbers would be difficult to interpret. We have clarified our approach on page 11.

- What outcomes will the authors collect from the included studies? I suspect there will be much qualitative data included as well, such as the barriers or problems related to critical care in LMICs. Will the authors consider to do a qualitative systematic review as well?

Response: The data we will collect include study design, LMIC country or countries involved, article identifiers, location(s) within the healthcare system that critical care service(s) were delivered, healthcare provider(s) providing the service(s), the critical care service(s) provided, critical illnesses addressed, sample size, and the age range of the study population (page 11). We agree that a qualitative review of barriers and facilitators of critical care would be of interest, and we intend to make our study database available to answer such questions that we are unable to address in this primary review.

- Other items of interest including bibliographic information and contact details of the authors for each included study may be necessary to be collected in order to reach the authors when there is no full text available. These will ensure the complete picture of this review.

Response: We agree. When authors' contact information is available, we will make concerted efforts to reach out to authors directly to acquire full text articles when not easily available online. We clarify our approach on page 10.

Risk of bias

- The authors need to consider doing the risk of bias analysis. These will depend on the type of included studies whether qualitative or quantitative.

Response: Thank you for your recommendation, and we have thoughtfully considered the inclusion of ROB analysis in our review. Risk of bias is crucial to assess when conducting a systematic review of therapy, diagnosis, natural history, prognosis, or clinical prediction; for each of these scenarios, an idealized study design and methodology exist that serves as a gold standard (for example a concealed blinded RCT with complete follow-up for therapy). For this study, we aim to describe the location of critical care delivery and the specific interventions delivered rather than assess associations between an exposure and outcome or describe prognosis or natural history. Although a complete sample of published literature within our timeframe of interest is crucial, we believe that assessing the risk of bias of each included study is not relevant to our intended review objectives. We have amended this line of argument on page 12.

If the reviewers and editors strongly believe that assessment of risk of bias should be included for this protocol and the subsequent systematic review, then we would invite suggestions for specific ROB frameworks/methods that align with our objectives.

Synthesis of data

- When there are circumstances when meta-analysis may not be possible, the authors may consider to synthesis the review without meta-analysis, namely narrative synthesis. These should be included in the protocol.
- Will a conceptual framework, logic model or taxonomy be possible for synthesizing?

Response: Thank you. We expect to be able to summarize the locations of critical care delivery, diseases and syndromes treated, and interventions delivered quantitatively, but we agree that for some aspects, narrative synthesis may be needed. We have added this consideration to page 12: "We anticipate that narrative synthesis may be required to summarise our study results."

It is possible that we may synthesize a conceptual framework from our results; however, as we are using existing diagnostic and service package frameworks from the WHO, we will likely center our discussion and analysis around those existing frameworks (see page 6, 11).

VERSION 2 – REVIEW

REVIEWER	Ma, Xiya University of Montreal
REVIEW RETURNED	22-Apr-2021
GENERAL COMMENTS	I would like to thank the authors for considering the reviewers' comments. I am satisfied with the responses and changes, and I am ready to recommend this manuscript for publication.
REVIEWER	Murni, Indah Universitas Gadjah Mada
REVIEW RETURNED	12-May-2021
GENERAL COMMENTS	Authors answered to all my comments and questions.