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# BMJ Open

## Critical care service delivery across healthcare systems in low- and low-middle income countries: Protocol for a Systematic Review

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**Title:** Critical care service delivery across healthcare systems in low- and low-middle income countries: Protocol for a Systematic Review

In accordance with the guidelines, our systematic review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 29 October, 2019 and was last updated on 21 April, 2020 (registration number CRD42019146802). In the event of protocol amendments, the date of each amendment will be accompanied by a description of the change and the rationale.

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31 (IFEM), and the IFEM Special Interest Group for Critical Care in Emergency Medicine.

## Abstract

**Introduction:** Critical care in low- and low-middle income countries (LLMICs) is an underdeveloped component of the healthcare system. Given the increasing growth in demand for critical care services in LLMICs, understanding the current capacity to provide critical care is imperative to inform policy on service expansion. Thus, our aim is to describe the provision of critical care in LLMICs with respect to patients, providers, location of care, and services and interventions delivered.

**Methods & Analysis:** We will search PubMed/MEDLINE, Web of Science, and EMBASE for full-text original research articles available in English describing critical care services that specify the location of service delivery and describe patients and interventions. We will restrict our review to populations from LLMICs (using 2016 World Bank classifications) and published from January 1, 2008 to January 1, 2020. Two-reviewer agreement will be required for both title/abstract and full text review stages, and rate of agreement will be calculated for each stage. We will extract data regarding the location of critical care service delivery, the training of the healthcare professionals providing services, and the illnesses treated according to classification by the World Health Organization (WHO) Universal Health Coverage (UHC) Compendium.

**Ethics & Dissemination:** Reviewed and exempted by the Stanford University Office for Human Subjects Research and IRB on May 20, 2020. The results of this review will be disseminated through scholarly publication and presentation at regional and international conferences. This review is designed to inform broader WHO, IFEM and partner efforts to strengthen critical care globally.

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3 **Registration:** Registered with the International Prospective Register of Systematic Reviews  
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5 (PROSPERO) on 29 October, 2019 and last updated on 21 April, 2020 (registration number  
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7 CRD42019146802).  
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### Article Summary: (Strengths and Limitations of this Study)

- To our knowledge, this will be the first systematic review of published literature describing critical care services in healthcare settings across all low and lower-middle income countries (LLMICs).
- The scope of the review question is large, which will help to inform public policy but does not allow for meta-analysis to answer a focused clinical question.
- We used standard methods (comprehensive search, training exercises for reviewers, iterative process for conflict resolution) to maximize the rigour of this review.
- A multidisciplinary and multinational team identified through the World Health Organization (WHO) and International Federation for Emergency Medicine (IFEM) networks will conduct this review.

## Introduction

Acute illness can occur at any point in the healthcare system, and requires recognition, resuscitation and stabilization, along with definitive care. The WHO Emergency Care Systems Framework (ECSF) characterizes acute illness as disease or injury processes in which delays can “...worsen prognosis or render care less effective”. [1] This broad scope requires multiple healthcare partners in an integrated system to triage acuity, transport patients, and manage acute illness with infrastructure and personnel. Patients with acute illness often receive critical care, which includes interventions to support failing organ systems and prevent further deterioration while the underlying disease is treated. [2] Critical care interventions vary in technical complexity and location of delivery. Although mechanical ventilation in an intensive care unit (ICU) is a classic example, supplemental oxygen, intravenous fluids, and close monitoring and assessment by nurses and physicians all contribute to the maintenance of basic physiologic functions. [3, 4]

### *Critical care services in low-resource settings*

Critical illness is thought to have a higher incidence and mortality in low and low-middle income countries (LLMICs) [5-7], as shown recently with Global Burden of Disease data for sepsis [8]. The burden is expected to grow because of increasing urbanization, incidence of non-communicable disease and injury, and population life expectancy. The higher burden of critical illness in LLMICs is not matched by capacity in equipment, infrastructure, and healthcare workforce number and education [9-15] leading to excess mortality [16] that is not well-documented because of poor epidemiologic data and clinical research [17, 18]. Because of the lack of ICU capacity, critically ill patients may be managed in non-traditional environments, including hospital wards, emergency care units, or in pre-hospital settings.

## *Objectives*

The primary objective of our systematic review is to characterize the range of critical care services and interventions delivered across the healthcare system in LLMICs by reviewing reports published from January 1, 2008 to January 1, 2020. We aim to characterize the health service location in which these services or interventions are delivered, the healthcare professionals involved, and the conditions being treated.

## **Methods**

### *Eligibility criteria*

Studies will be eligible for inclusion if they meet the following criteria:

1) Study design: original, peer reviewed research articles (including cross-sectional, case-control, and cohort studies, randomized controlled trials, qualitative methods, and mixed methods studies) and systematic reviews that describe critical care services as defined below. We will exclude case reports and series, study protocols, and studies available only as abstracts (e.g. conference abstracts, poster presentations, etc.). We will only include studies with online full-text availability.

2) Setting: LLMICs, as per the 2016 World Bank classification (Table 1). Within LLMICs, we will include studies that describe the location of delivery of critical care services delivered by health care professionals in any setting. We will exclude studies describing out-of-hospital settings where care is delivered by lay providers, and critical care delivered in operating rooms as part of a surgical procedure (but will include studies on critical care in pre- or post-operative care environments). Our rationale is that critical care delivered as part of surgical anaesthesia is

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2  
3 often linked to the need for anaesthesia itself rather than to any critical illness. We will exclude  
4 studies of military health operations by high or high-middle income country armed forces  
5  
6 operating in LLMICs whose treatment populations exclusively consist of military personnel.  
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10 3) Participants: any age group.

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12 4) Interventions: critical care services, including medical interventions, diagnostic modalities  
13 (including radiology, laboratory testing, and microbiology) for the diagnosis or prognostication  
14 of critical illness states, pharmaceutical services, and healthcare systems-based processes  
15 (including advance care planning; coordination of specialist services, critical care triage or care  
16 pathways; crisis, surge, mass casualty, and disaster management (Table 2). This list reflects a  
17 broad perspective of critical care services and is informed by the World Health Organization  
18 (WHO) Emergency and Critical Care Services Framework (ECSF) [19].  
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28 We will include studies that describe critical care service utilization as a study intervention,  
29 exposure, or outcome, including studies of capacity building or education if they also involve  
30 service delivery for patients. We will exclude simulated interventions.  
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35 5) Timing: studies published from January 1, 2008 to January 1, 2020. This date range  
36 encompasses the contemporaneous provision of critical care before the onset of the global  
37 COVID-19 pandemic.  
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42 6) Language: studies available in English language through search filters.  
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#### 47 *Information sources*

48  
49 Our databases include PubMed/MEDLINE, EMBASE, and Web of Science, supplemented by  
50 scanning of reference lists of relevant systematic reviews and searches of WHO intranet  
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3 databases. We will not consider grey literature due to the large scope of the review question and  
4  
5 desire to focus on peer reviewed studies.  
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### 10 *Search strategies*

11  
12 Literature search strategies were developed by the authors in conjunction with a Stanford  
13  
14 University Health Sciences librarian (CDS) with expertise in systematic review searching, with  
15  
16 technical support from WHO Library services (TA). We used controlled vocabulary terms and  
17  
18 text words related to critical care in LLMICs (see Appendix 1 for PubMed/MEDLINE search  
19  
20 strategy, subsequently adapted to EMBASE and Web of Science). We also searched PROSPERO  
21  
22 for ongoing or recently completed systematic reviews. We restricted search results to citations in  
23  
24 English pertaining to humans, published from January 1, 2008 to January 1, 2020.  
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### 31 *Study records*

32  
33 Literature search results will be uploaded to Covidence (Covidence ©, Melbourne, Australia), a  
34  
35 web-based online platform that facilitates collaboration among reviewers during systematic  
36  
37 review study selection. Full text articles will be uploaded to Covidence during the full-text  
38  
39 review phase.  
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### 45 *Selection Process*

46  
47 Reviewers will be unblinded to author and institution details of citations. To maximize  
48  
49 consistency in assessing inclusion and exclusion criteria among 21 reviewers, we plan calibration  
50  
51 pilot exercises for title and abstract screening and group discussions using a Google forum  
52  
53 group. This training will emphasize the need for sensitivity in citation selection in the title and  
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3 abstract phase. Independently and in duplicate, reviewers will screen titles and abstracts for  
4  
5 potentially relevant studies using Covidence. Because of the anticipated very large number of  
6  
7 potentially relevant citations, the agreement of two members of the review team will be required  
8  
9 for citation selection at the title and abstract phase; disagreements will be adjudicated by a third  
10  
11 reviewer.  
12

13  
14 Full-text versions of citations included at the title and abstract screening phase will be retrieved  
15  
16 and reviewed by the same team of reviewers. If full-text is not retrievable by at least two  
17  
18 reviewers, the study will be excluded as unavailable. If retrieved citations are found to be  
19  
20 abstract-only, they will be excluded, but we will search for any subsequent peer-reviewed journal  
21  
22 publications not already captured by our search. The agreement of two reviewers will be required  
23  
24 for inclusion of the full-text study in the systematic review, with conflicts resolved by a third  
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26 reviewer experienced with this review process. Reasons for full-text exclusion will be recorded  
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28 (Table 3).  
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### 35 *Data Extraction*

36  
37 Individual reviewers will extract data from selected articles using Excel (Microsoft, Redmond,  
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39 Washington, U.S.A.). The data sheet underwent multiple iterations, informed by pilot testing on  
40  
41 selected articles and group discussion. A review group member will review each cluster of data  
42  
43 entry for consistency of data extraction.  
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47 We will extract data on the study design, LLMIC country or countries involved, article  
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49 identifiers, location(s) within the healthcare system that critical care service(s) were delivered,  
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51 healthcare provider(s) providing the service(s), the critical care service(s) provided, critical  
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53 illnesses addressed, sample size, and the age range of the study population. Given the clinical  
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3 heterogeneity of patient populations and interventions, we will not extract data on patient  
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5 outcomes.  
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8 Critical care services will be identified using international professional society definitions and  
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10 the scope of critical care functions in the WHO ECSF. Services will be subsequently classified  
11  
12 based on the categories in the WHO UHC Compendium [20]. We will use the top level  
13  
14 architecture of the compendium to categorize services broadly into foundations of care,  
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16 reproductive and sexual health, nutrition, end-of-life and palliative care issues, violence and  
17  
18 injury, non-communicable diseases (including diseases of the cardiovascular, respiratory,  
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20 neurologic, endocrine/metabolic, immunologic, digestive, hematologic, genitourinary, and other  
21  
22 systems) and communicable diseases.  
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### 28 *Risk of Bias*

29  
30 A potential overall source of bias in this review is the large number of reviewers involved in  
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32 article selection, such that the threshold for inclusion of studies in the review may vary by  
33  
34 reviewer pair and may lead to underestimate of the locations or types of critical care services  
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36 delivered . We have attempted to mitigate this by extensive training of reviewers. Given the  
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38 broad scope of the review, anticipated heterogeneous studies (regarding design, population,  
39  
40 methods, and outcomes), and lack of planned meta-analyses to calculate summary effects, we  
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42 will not assess the risk of bias of individual studies.  
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### 49 *Data analysis*

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51 We will calculate summary descriptive statistics, using counts and proportions for categorical  
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53 data and means (SD) or median (Q1, Q3) for continuous data. We will describe the number of  
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3 publications by year, types of services delivered, health care provider type, location of service  
4 delivery, study population age-group, and critical illness category (based on the WHO UHC  
5 Compendium), stratified by World Bank income class and WHO region. Due to the descriptive  
6 nature of the study question and expected heterogeneity of patients and interventions, no meta-  
7 analyses of effects on patient outcomes are planned.  
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12 Subsequent ancillary reviews based on this dataset of studies may investigate specific age-group  
13 populations, continents/regions, World Bank classes, critical care intervention clusters, disease  
14 groups, locations, or healthcare professionals involved.  
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### 24 *Ethics*

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26 The study protocol was reviewed and exempted by the Stanford University Office for Human  
27 Subjects Research and IRB on May 20, 2020.  
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### 31 *Patient and Public Involvement*

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33 No patients involved.  
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### 39 **Conclusion**

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41 We anticipate that the results of this comprehensive review will describe the current scope of  
42 critical care services, providers, and location of service delivery in LLMICs, and will provide a  
43 database of pertinent literature for future studies. The results of the review will be instrumental  
44 for planners and policy makers in developing critical care service infrastructure, funding  
45 priorities, and capacity-building interventions, and will highlight gaps in current knowledge of  
46 critical care service delivery in LLMICs.  
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3 Tables  
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6 **Table 1: List of World Bank Low to Lower-middle income countries - July 2016**

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Country	Region	World Bank Class
Afghanistan	South Asia	Low income
Armenia	Europe & Central Asia	Lower middle income
Bangladesh	South Asia	Lower middle income
Benin	Sub-Saharan Africa	Low income
Bhutan	South Asia	Lower middle income
Bolivia	Latin America & Caribbean	Lower middle income
Burkina Faso	Sub-Saharan Africa	Low income
Burundi	Sub-Saharan Africa	Low income
Cabo Verde	Sub-Saharan Africa	Lower middle income
Cambodia	East Asia & Pacific	Lower middle income
Cameroon	Sub-Saharan Africa	Lower middle income
Central African Republic	Sub-Saharan Africa	Low income
Chad	Sub-Saharan Africa	Low income
Comoros	Sub-Saharan Africa	Low income
Congo, Dem. Rep.	Sub-Saharan Africa	Low income
Congo, Rep.	Sub-Saharan Africa	Lower middle income
Côte d'Ivoire	Sub-Saharan Africa	Lower middle income
Djibouti	Middle East & North Africa	Lower middle income
Egypt, Arab Rep.	Middle East & North Africa	Lower middle income
El Salvador	Latin America & Caribbean	Lower middle income
Eritrea	Sub-Saharan Africa	Low income
Ethiopia	Sub-Saharan Africa	Low income
Gambia, The	Sub-Saharan Africa	Low income
Ghana	Sub-Saharan Africa	Lower middle income
Guatemala	Latin America & Caribbean	Lower middle income
Guinea	Sub-Saharan Africa	Low income
Guinea-Bissau	Sub-Saharan Africa	Low income
Haiti	Latin America & Caribbean	Low income
Honduras	Latin America & Caribbean	Lower middle income
India	South Asia	Lower middle income

Indonesia	East Asia & Pacific	Lower middle income
Kenya	Sub-Saharan Africa	Lower middle income
Kiribati	East Asia & Pacific	Lower middle income
Korea, Dem. People's Rep.	East Asia & Pacific	Low income
Kosovo	Europe & Central Asia	Lower middle income
Kyrgyz Republic	Europe & Central Asia	Lower middle income
Lao PDR	East Asia & Pacific	Lower middle income
Lesotho	Sub-Saharan Africa	Lower middle income
Liberia	Sub-Saharan Africa	Low income
Madagascar	Sub-Saharan Africa	Low income
Malawi	Sub-Saharan Africa	Low income
Mali	Sub-Saharan Africa	Low income
Mauritania	Sub-Saharan Africa	Lower middle income
Micronesia, Fed. Sts.	East Asia & Pacific	Lower middle income
Moldova	Europe & Central Asia	Lower middle income
Mongolia	East Asia & Pacific	Lower middle income
Morocco	Middle East & North Africa	Lower middle income
Mozambique	Sub-Saharan Africa	Low income
Myanmar	East Asia & Pacific	Lower middle income
Nepal	South Asia	Low income
Nicaragua	Latin America & Caribbean	Lower middle income
Niger	Sub-Saharan Africa	Low income
Nigeria	Sub-Saharan Africa	Lower middle income
Pakistan	South Asia	Lower middle income
Papua New Guinea	East Asia & Pacific	Lower middle income
Philippines	East Asia & Pacific	Lower middle income
Rwanda	Sub-Saharan Africa	Low income
Samoa	East Asia & Pacific	Lower middle income
São Tomé and Príncipe	Sub-Saharan Africa	Lower middle income
Senegal	Sub-Saharan Africa	Low income
Sierra Leone	Sub-Saharan Africa	Low income
Solomon Islands	East Asia & Pacific	Lower middle income
Somalia	Sub-Saharan Africa	Low income

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4	South Sudan	Sub-Saharan Africa	Low income
5	Sri Lanka	South Asia	Lower middle income
6			
7	Sudan	Sub-Saharan Africa	Lower middle income
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9	Swaziland	Sub-Saharan Africa	Lower middle income
10	Syrian Arab Republic	Middle East & North Africa	Lower middle income
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12	Tajikistan	Europe & Central Asia	Lower middle income
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14	Tanzania	Sub-Saharan Africa	Low income
15	Timor-Leste	East Asia & Pacific	Lower middle income
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17	Togo	Sub-Saharan Africa	Low income
18	Tonga	East Asia & Pacific	Lower middle income
19			
20	Tunisia	Middle East & North Africa	Lower middle income
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22	Uganda	Sub-Saharan Africa	Low income
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24	Ukraine	Europe & Central Asia	Lower middle income
25	Uzbekistan	Europe & Central Asia	Lower middle income
26			
27	Vanuatu	East Asia & Pacific	Lower middle income
28	Vietnam	East Asia & Pacific	Lower middle income
29			
30	West Bank and Gaza	Middle East & North Africa	Lower middle income
31	Yemen, Rep.	Middle East & North Africa	Lower middle income
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33	Zambia	Sub-Saharan Africa	Lower middle income
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35	Zimbabwe	Sub-Saharan Africa	Low income
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**Table 2: Critical Care Service Delivery/ Interventions List**

*Monitoring/nursing*

Frequent monitoring/ surveillance and recording of clinical parameters [vital signs, pulse oximetry, capnography, etc.]

Acuity-based triage / performance of focused assessment for the critically ill [including shock, altered mental status, difficulty breathing, polytrauma, etc.]

Critical care nursing services [including implementation of higher than floor/ward-level care or nurse:patient ratio]

Frequent monitoring/ surveillance of fetus [fetal heart monitoring, tocometry, etc.]

*Interventions for hemodynamic instability/ organ dysfunction*

Support of hemodynamic instability and management of acute life threatening organ dysfunction

Titration of advanced parenteral therapeutics

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4	Intravenous fluid resuscitation
5	Blood products transfusion
6	Administration of advanced blood replacement therapies [e.g. plasmapheresis]
7	Massive hemorrhage control [including tourniquet application, hemostatic agents, pelvic binding]
8	Targeted temperature management and hyperthermia / hypothermia management
9	Vasopressor/ inotrope administration
10	Anti-arrhythmic medication administration for the critically ill
11	Cardio-pulmonary resuscitation, basic only [chest compressions in the absence of invasive procedures]
12	Advanced cardiac life-support resuscitation [include emergent pacing, defibrillation, cardioversion]
13	Spinal immobilization
14	Extracorporeal membrane oxygenation (ECMO) / extracorporeal life support (ECLS)
15	Advanced trauma resuscitation / Advanced Trauma Life Support® (ATLS®) / WHO Trauma Care Checklist use
16	
17	
18	<i>Respiratory interventions</i>
19	Support of respiratory insufficiency/ failure
20	Oxygen delivery, simple [face mask, nasal prongs]
21	Oxygen delivery, high flow [> 15 L/min]
22	Mechanical ventilation, non-invasive [including continuous positive airway pressure (CPAP)]
23	Mechanical ventilation, invasive
24	Non-invasive airway management [basic airway opening maneuvers, bag mask ventilation, oro- or nasopharyngeal airway placement, etc.]
25	Advanced invasive airway management, non-surgical [tracheal intubation, laryngeal mask airway placement, bougie, airway exchange catheters, etc.]
26	Advanced surgical airway management [tracheostomy, cricothyrotomy performed outside the operating room/theatre]
27	
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30	<i>Other invasive procedures</i>
31	Peripheral venous cannulation for the critically ill
32	Advanced vascular access [arterial lines, central venous / pulmonary artery catheters, intra-osseous access]
33	Thoracic invasive procedures for the critically ill [thoracostomy, pleural drain placement, thoracentesis, pericardiocentesis, emergent thoracotomy performed outside of the operating room/theatre]
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37	<i>Additional targeted therapies</i>
38	Early antibiotic administration for the critically ill
39	Treatment of severe infections/ inflammation / sepsis [steroids and other adjuncts]
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4	Renal replacement therapy / hemodialysis or peritoneal dialysis
5	Monitoring and treatment of critical electrolyte/ metabolic/ acid base derangements
6	
7	Nutrition management for the critically ill / injured
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9	Provision of prophylaxis associated with critical illness [including alimentary, venous thromboembolism]
10	
11	Advanced burn care for the critically ill
12	
13	Emergent poisoning detoxification/ antidote
14	
15	Acute reperfusion therapy: medical or interventional [cardiac/coronary arteries]
16	
17	Acute reperfusion therapy: medical or interventional [pulmonary embolism, or other acute thromboembolism]
18	
19	<i>Neurological interventions</i>
20	Acute medical stabilization of critical neurologic illness / provision of neuroprotection for the critically ill [e.g. seizure management]
21	
22	Acute surgical stabilization of critical neurologic illness [e.g. emergent craniotomy, ventricular drain, intracranial pressure monitor performed outside the operating room/theatre]
23	
24	Acute management of agitation/ delirium
25	
26	Acute reperfusion therapy: medical or interventional [neurovascular procedures for cerebrovascular pathology such as stenting, coiling performed outside the operating room/theatre]
27	
28	Analgesia and sedation [sedative infusions, moderate / conscious sedation, up to general anesthesia, performed outside the operating room/theatre]
29	
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32	<i>Obstetrical critical care services</i>
33	Obstetric critical care management [induction, tocolytic, high-risk labor, emergent/complex delivery, perimortem cesarean section performed outside the operating room/theatre]
34	
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38	<i>Diagnostic modalities</i>
39	Utilization of targeted diagnostic strategy to establish timely etiology for the critically ill
40	
41	Basic radiography
42	
43	Computed tomography
44	
45	Magnetic resonance imaging
46	
47	Critical care ultrasound, including point-of-care trans-thoracic / trans-oesophageal echocardiography
48	Laboratory and other rapid results reporting including point-of-care diagnostics [arterial blood gas, glucometry, chemistry, hematology]
49	
50	Microbiology and other infectious rapid results reporting
51	
52	
53	<i>Multi-system processes related to critical care service delivery</i>
54	Prognosis-based advance care planning [critical care level hospice/palliative, goals of care discussions, plan for de-escalation of care and transition to post-critical care needs appropriate to context]
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4	Coordination of specialist services for multisystem illness [managing communication between, and coordination
5	of, various health care personnel caring for patient detailing diagnosis, treatment given, and disposition]
6	Critical care triage / care pathways systems / clinical illness severity and/or risk stratification
7	Critical care level crisis management [surge response, disaster management, multiple casualty incident]
8	
9	Health information systems, medical records
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12	<i>Other critical care services</i>
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14	Critical care pharmacy services
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16	Critical care education and capacity building [must have clinical service delivery component]
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18	Other critical care intervention/ service delivery
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<b>Table 3: Hierarchy of Exclusion for Full Text</b>	
<b>1</b>	Not published from Jan 1 2008 - Jan 1 2020
<b>2</b>	Is not a study on living humans, or is not related to health aspects of living humans (exclude animal or forensic studies)
<b>3</b>	Does not address Low- or Low-middle income country (per World Bank Class 2016)
<b>4</b>	Does not address critical care service/interventions (per list in this spreadsheet)
<b>5</b>	Not Original Research, Systematic Review, or Brief Report
<b>6</b>	Does not describe where in healthcare setting critical care service/intervention is delivered
<b>7</b>	Addresses exclusively peri-operative care that occurs in the operating room/theatre
<b>8</b>	Does not address care by healthcare professionals
<b>9</b>	Abstract-only, full text non-existent (for conference, poster/presentation, etc.)
<b>10</b>	Full text not available online

Contributorship Statement:

AL is the guarantor, drafted, prepared, and submitted the manuscript, contributed to the development of the selection criteria, methodology, data extraction criteria and forms, developed and executed the search strategy, provided teaching and guidance of review process to review group.

NA, SM, SK, LL, ED, BC, NB, AB, MJ, PDS and TR provided comments and critical revisions to the manuscript, made substantial contributions to the conception and design of the review methodology and planned analysis.

ED, SK, PAS, MY, BC, PDS, MJ, RL, AR, CC, NB, NH, NS, PM, BV, NS, AB, CM, AGR, EB, AF, SY made key contributions to the conception, design and execution of eligibility criteria and methodology, participated in the acquisition and interpretation of reference data for screening phases, provided feedback on full text data extraction forms, and provided critical edits to the intellectual content of the manuscript.

All authors read, provided feedback and approved the final manuscript, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Thus, all authors have met the four ICMJE criteria recommended for authorship.

Competing Interests Statement:

None declared.

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4 support for paediatric emergency care in sub-Saharan Africa. *Afr J Emerg Med* 2017;7:10-19.  
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27 <https://www.who.int/universal-health-coverage/compendium>  
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## Appendix 1: Example search strategy: Pubmed/Medline

(((("Critical Care"[Mesh] OR "critical care"[tw] OR "Critical Illness"[Mesh] OR "Critical Illness"[tw] OR "Critical Care Nursing"[Mesh] OR "Critical Care Outcomes"[Mesh] OR "intensive care"[tw] OR "Intensive Care Units"[Mesh] OR "intermediate care unit"[tw] OR "step down unit"[tw] OR "Shock"[Mesh] OR "Cardiac Arrest"[tw] OR "heart arrest"[MeSH] OR "Respiratory Arrest"[tw] OR "Emergency Medicine"[Mesh] OR "Evidence-Based Emergency Medicine"[Mesh] OR "Emergency Nursing"[Mesh] OR "Emergency Treatment"[mh:noexp] OR "Advanced Trauma Life Support Care"[mesh] OR "Resuscitation"[mesh] OR "cardiopulmonary resuscitation"[tw] OR "Cardiopulmonary Resuscitation"[mesh] OR "Heart Massage"[mesh] OR "Respiration, Artificial"[mesh] OR ventilator\*[ti] OR icu[ti] OR picu[ti] OR nicu[ti] OR cu[ti] OR cpr[ti] OR "ambulances"[Mesh] OR "Emergency Service, Hospital"[mesh] OR "Poison Control Centers"[mesh] OR "Triage"[mh:noexp] OR "Hospital Rapid Response Team"[Mesh])) AND (((("Developing Countries"[Mesh] OR "Medically Underserved Area"[Mesh] OR "developing country"[tw] OR "developing countries"[tw] OR "developing nation"[tw] OR "developing nations"[tw] OR "developing population"[tw] OR "developing populations"[tw] OR "developing world"[tw] OR "less developed country"[tw] OR "less developed countries"[tw] OR "less developed nation"[tw] OR "less developed nations"[tw] OR "less developed population"[tw] OR "less developed populations"[tw] OR "less developed world"[tw] OR "lesser developed country"[tw] OR "lesser developed countries"[tw] OR "lesser developed nation"[tw] OR "lesser developed nations"[tw] OR "lesser developed population"[tw] OR "lesser developed populations"[tw] OR "lesser developed world"[tw] OR "under developed country"[tw] OR "under developed countries"[tw] OR "under developed nation"[tw] OR "under developed nations"[tw] OR "under developed population"[tw] OR "under developed populations"[tw] OR "under developed world"[tw] OR "underdeveloped country"[tw] OR "underdeveloped 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countries"[tw] OR "under served nation"[tw] OR "under served nations"[tw] OR "under served population"[tw] OR "under served populations"[tw] OR "under served world"[tw] OR "deprived country"[tw] OR "deprived countries"[tw] OR "deprived nation"[tw] OR "deprived nations"[tw] OR "deprived population"[tw] OR "deprived populations"[tw] OR "deprived world"[tw] OR "poor country"[tw] OR "poor countries"[tw] OR "poor nation"[tw] OR "poor nations"[tw] OR "poor population"[tw] OR "poor populations"[tw] OR "poor world"[tw] OR "poorer country"[tw] OR "poorer countries"[tw] OR "poorer nation"[tw] OR "poorer nations"[tw] OR "poorer population"[tw] OR "poorer populations"[tw] OR "poorer world"[tw] OR "developing economy"[tw] OR "developing economies"[tw] OR "less developed economy"[tw] OR "less developed economies"[tw] OR "lesser developed economy"[tw] OR "lesser developed economies"[tw] OR "under developed economy"[tw] OR "under developed economies"[tw] OR "underdeveloped economy"[tw] OR 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8 OR "Solomon Islands"[tw] OR Somalia[tw] OR "South Sudan"[tw] OR "Sri Lanka"[tw] OR Sudan[tw] OR  
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10 Tunisia[tw] OR Uganda[tw] OR Ukraine[tw] OR Uzbekistan[tw] OR Vanuatu[tw] OR Vietnam[tw] OR "West  
11 Bank"[tw] OR Yemen[tw] OR Zambia[tw] OR Zimbabwe[tw] OR Kyrgyz[tw] OR Syrian[tw] OR "lao pdr"[tw]  
12 OR Burma[tw] OR gaza[tw] OR "ivory coast"[tw] OR Afghanistan[mesh] OR "guatemala" [mesh] OR "samoa"  
13 [mesh] OR tonga OR "cape verde" [mesh] OR Armenia [mesh] OR Bangladesh[mesh] OR Benin[mesh] OR  
14 Bhutan[mesh] OR Bolivia[mesh] OR "Burkina Faso"[mesh] OR Burundi[mesh] OR "Cabo Verde"[mesh] OR  
15 Cambodia[mesh] OR Cameroon[mesh] OR "Central African Republic"[mesh] OR Chad[mesh] OR  
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17 Salvador"[mesh] OR Eritrea[mesh] OR Ethiopia[mesh] OR Gambia[mesh] OR Ghana[mesh] OR Guinea[mesh]  
18 OR "Guinea-Bissau"[mesh] OR Haiti[mesh] OR Honduras[mesh] OR India[mesh] OR Indonesia[mesh] OR  
19 Kenya[mesh] OR Kiribati[mesh] OR "Democratic People's Republic of Korea"[mesh] OR Kosovo[mesh] OR  
20 Kyrgyzstan[mesh] OR laos[mesh] OR Lesotho[mesh] OR Liberia[mesh] OR Madagascar[mesh] OR  
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27 Leste"[mesh] OR Togo[mesh] OR Tunisia[mesh] OR Uganda[mesh] OR Ukraine[mesh] OR Uzbekistan[mesh]  
28 OR Vanuatu[mesh] OR Vietnam[mesh] OR Yemen[mesh] OR Zambia[mesh] OR Zimbabwe[mesh])) NOT  
29 ("Emergency Services, Psychiatric"[Mesh] OR "Addresses"[pt] OR "Autobiography"[pt] OR "Bibliography"[pt]  
30 OR "Biography"[pt] OR "Case Reports"[pt] OR "Comment"[pt] OR "Congresses"[pt] OR "Consensus  
31 Development Conference"[pt] OR "Consensus Development Conference, NIH"[pt] OR "Dictionary"[pt] OR  
32 "Directory"[pt] OR "Editorial"[pt] OR "Electronic Supplementary Materials"[pt] OR "Festschrift"[pt] OR  
33 "Historical Article"[pt] OR "Interactive Tutorial"[pt] OR "Interview"[pt] OR "Lectures"[pt] OR "Legal  
34 Cases"[pt] OR "Legislation"[pt] OR "Letter"[pt] OR "News"[pt] OR "Newspaper Article"[pt] OR "Overall"[pt]  
35 OR "Patient Education Handout"[pt] OR "Periodical Index"[pt] OR "Personal Narratives"[pt] OR  
36 "Portraits"[pt] OR "Practice Guideline"[pt] OR "Published Erratum"[pt] OR "Retracted Publication"[pt] OR  
37 "Retraction of Publication"[pt] OR "Technical Report"[pt] OR "Video-Audio Media"[pt] OR "Webcasts"[pt] OR  
38 "case report"[ti] OR bystand\*[ti])) AND english[lang] NOT ("animals"[mesh] NOT "humans"[mesh]) AND  
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**PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\***

Section and topic	Item No	Checklist item	Completed?
<b>ADMINISTRATIVE INFORMATION</b>			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	X
	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	X
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	X
	3b	Describe contributions of protocol authors and identify the guarantor of the review	X
Contributions	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	X
Sponsor	5b	Provide name for the review funder and/or sponsor	X
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	X
<b>INTRODUCTION</b>			
Rationale	6	Describe the rationale for the review in the context of what is already known	X
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	X
<b>METHODS</b>			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	X
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	X
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	X
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	X
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	X

Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	X
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	X
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	X
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	X
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	N/A
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as $I^2$ , Kendall's $\tau$ )	N/A
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	N/A
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	X
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	N/A

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

*From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.*

# BMJ Open

## Critical care service delivery across healthcare systems in low- and low-middle income countries: Protocol for a Systematic Review

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-048423.R1
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Date Submitted by the Author:	22-Apr-2021
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3 1 **Title:** Critical care service delivery across healthcare systems in low- and low-middle income  
4 2 countries: Protocol for a Systematic Review  
5 3

6 4 In accordance with the guidelines, our systematic review protocol was registered with the  
7 5 International Prospective Register of Systematic Reviews (PROSPERO) on 29 October, 2019  
8 6 and was last updated on 21 April, 2020 (registration number CRD42019146802). In the event of  
9 7 protocol amendments, the date of each amendment will be accompanied by a description of the  
10 8 change and the rationale.  
11 9

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27 64 Review Consortium (IFEM-CCRC)  
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52 78 (IFEM), and the IFEM Special Interest Group for Critical Care in Emergency Medicine.  
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60 82

## Abstract

**Introduction:** Critical care in low- and low-middle income countries (LLMICs) is an underdeveloped component of the healthcare system. Given the increasing growth in demand for critical care services in LLMICs, understanding the current capacity to provide critical care is imperative to inform policy on service expansion. Thus, our aim is to describe the provision of critical care in LLMICs with respect to patients, providers, location of care, and services and interventions delivered.

**Methods & Analysis:** We will search PubMed/MEDLINE, Web of Science, and EMBASE for full-text original research articles available in English describing critical care services that specify the location of service delivery and describe patients and interventions. We will restrict our review to populations from LLMICs (using 2016 World Bank classifications) and published from January 1, 2008 to January 1, 2020. Two-reviewer agreement will be required for both title/abstract and full text review stages, and rate of agreement will be calculated for each stage. We will extract data regarding the location of critical care service delivery, the training of the healthcare professionals providing services, and the illnesses treated according to classification by the World Health Organization (WHO) Universal Health Coverage (UHC) Compendium.

**Ethics & Dissemination:** Reviewed and exempted by the Stanford University Office for Human Subjects Research and IRB on May 20, 2020. The results of this review will be disseminated through scholarly publication and presentation at regional and international conferences. This review is designed to inform broader WHO, IFEM and partner efforts to strengthen critical care globally.

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3 107 **Registration:** Registered with the International Prospective Register of Systematic Reviews  
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5 108 (PROSPERO) on 29 October, 2019 and last updated on 21 April, 2020 (registration number  
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7 109 CRD42019146802).  
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For peer review only

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3 112 **Strengths and Limitations of this Study:**  
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- 5 113 • To our knowledge, this will be the first systematic review of published literature to  
6  
7 114 comprehensively describe the spectrum of critical care services in healthcare settings  
8  
9 115 across low and lower-middle income countries (LLMICs).  
10  
11 116 • We will use standard methods (comprehensive search, training exercises for reviewers,  
12  
13 117 iterative process for conflict resolution) to maximise the rigour of this review.  
14  
15 118 • A multidisciplinary and multinational team identified through World Health Organization  
16  
17 119 (WHO) and International Federation for Emergency Medicine (IFEM) networks will  
18  
19 120 conduct this review.  
20  
21 121 • The scope of the review question is large, which will help to inform public policy but  
22  
23 122 does not allow for meta-analysis to answer a focused clinical question.  
24  
25 123 • There is a large number of reviewers involved in article selection, such that the threshold  
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27 124 for inclusion of studies in the review may vary by reviewer pair and may lead to  
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29 125 underestimation of the types or characteristics of critical care services delivered.  
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## 127 **Introduction**

128 Acute illness can occur at any point in the healthcare system, and requires recognition,  
129 resuscitation and stabilisation, along with definitive care. The WHO Emergency Care Systems  
130 Framework (ECSF) characterises acute illness as disease or injury processes in which delays can  
131 “...worsen prognosis or render care less effective”. [1] This broad scope requires multiple  
132 healthcare partners in an integrated system to triage acuity, transport patients, and manage acute  
133 illness with infrastructure and personnel. Patients with acute illness often receive critical care,  
134 which includes interventions to support failing organ systems and prevent further deterioration  
135 while the underlying disease is treated. [2] Critical care interventions vary in technical  
136 complexity and location of delivery. Although mechanical ventilation in an intensive care unit  
137 (ICU) is a classic example, supplemental oxygen, intravenous fluids, and close monitoring and  
138 assessment by nurses and physicians all contribute to the maintenance of basic physiologic  
139 functions. [3, 4]

140

### 141 *Critical care services in low-resource settings*

142 Critical illness is thought to have a higher incidence and mortality in low and low-middle income  
143 countries (LLMICs) [5-7], as shown recently with Global Burden of Disease data for sepsis [8].  
144 The burden is expected to grow because of increasing urbanisation, incidence of non-  
145 communicable disease and injury, and population life expectancy. The higher burden of critical  
146 illness in LLMICs is not matched by capacity in equipment, infrastructure, and healthcare  
147 workforce number and education [9-15] leading to excess mortality [16] that is not well-  
148 documented because of poor epidemiologic data and clinical research [17, 18]. Because of the  
149 lack of ICU capacity, critically ill patients may be managed in non-traditional environments,  
150 including hospital wards, emergency care units, or in pre-hospital settings.

151

152 *Objectives*

153 The primary objective of our systematic review is to characterise the range of critical care  
154 services and interventions delivered across the healthcare system in LLMICs by reviewing  
155 reports published from January 1, 2008 to January 1, 2020. We aim to characterise the health  
156 service location in which these services or interventions are delivered, the healthcare  
157 professionals involved, and the conditions being treated.

158

159 **Methods**160 *Eligibility criteria*

161 Studies will be eligible for inclusion if they meet the following criteria:

162 1) Study design: original, peer reviewed research articles (including cross-sectional, case-control,  
163 and cohort studies, randomised controlled trials, qualitative methods, and mixed methods  
164 studies) and systematic reviews that describe critical care services as defined below. We will  
165 exclude case reports and series, study protocols, studies available only as abstracts (e.g.  
166 conference abstracts, poster presentations, etc.), and other unpublished studies. We will only  
167 include studies with online full-text availability.

168 2) Setting: LLMICs, as per the 2016 World Bank classification (Table 1). We decided to use the  
169 2016 World Bank classification as a reference point, as the earlier classification is likely to  
170 capture more accurately the LLMICs during the time period from which the included studies  
171 originate (2008-2020). Within LLMICs, we will include studies that describe the location of  
172 delivery of critical care services delivered by health care professionals in any setting. We will  
173 exclude studies describing out-of-hospital settings where care is delivered by lay providers, and



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3 174 critical care delivered in operating rooms as part of a surgical procedure (but will include studies  
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5 175 on critical care in pre- or post-operative care environments). Our rationale is that critical care  
6  
7 176 delivered as part of surgical anaesthesia is often linked to the need for anaesthesia itself rather  
8  
9 177 than to any critical illness. We will exclude studies of military health operations by high or high-  
10  
11 178 middle income country armed forces operating in LLMICs whose treatment populations  
12  
13 179 exclusively consist of military personnel.

14  
15 180 3) Participants: any age group.

16  
17 181 4) Interventions: critical care services, including medical interventions, diagnostic modalities  
18  
19 182 (including radiology, laboratory testing, and microbiology) for the diagnosis or prognostication  
20  
21 183 of critical illness states, pharmaceutical services, and healthcare systems-based processes  
22  
23 184 (including advance care planning; coordination of specialist services, critical care triage or care  
24  
25 185 pathways; crisis, surge, mass casualty, and disaster management (Table 2). This list reflects a  
26  
27 186 broad perspective of critical care services and is informed by the World Health Organization  
28  
29 187 (WHO) Emergency and Critical Care Services Framework (ECSF) [19].

30  
31 188 We will include studies that describe critical care service utilisation as a study intervention,  
32  
33 189 exposure, or outcome, including studies of capacity building or education if they also involve  
34  
35 190 service delivery for patients. We will exclude simulated interventions.

36  
37 191 5) Timing: studies published from January 1, 2008 to January 1, 2020. This date range  
38  
39 192 encompasses the contemporaneous provision of critical care studied before the onset of the  
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41 193 global COVID-19 pandemic.

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43 194 6) Language: studies available in English language through search filters.

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3 196 *Information sources*  
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5 197 Our databases include PubMed/MEDLINE, EMBASE, and Web of Science, supplemented by  
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7 198 scanning of reference lists of relevant systematic reviews and searches of WHO intranet  
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10 199 databases. We will not consider grey literature due to the large scope of the review question and  
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12 200 the desire to focus on peer reviewed studies.  
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17 202 *Search strategies*  
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19 203 Literature search strategies were developed by the authors in conjunction with a Stanford  
20  
21 204 University Health Sciences librarian (CDS) with expertise in systematic review searching, with  
22  
23 205 technical support from WHO Library services (TA). We used controlled vocabulary terms and  
24  
25 206 text words related to critical care in LLMICs (see Appendix 1 for PubMed/MEDLINE search  
26  
27 207 strategy, subsequently adapted to EMBASE and Web of Science). We also searched PROSPERO  
28  
29 208 for ongoing or recently completed systematic reviews. We restricted search results to citations in  
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31 209 English pertaining to humans, published from January 1, 2008 to January 1, 2020.  
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37 211 *Study records*  
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39 212 Literature search results will be uploaded to Covidence (Covidence ©, Melbourne, Australia), a  
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41 213 web-based online platform that facilitates collaboration among reviewers during systematic  
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43 214 review study selection. Full text articles will be uploaded to Covidence during the full-text  
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45 215 review phase.  
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49 217 *Selection Process*  
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3 218 Reviewers will be unblinded to author and institution details of citations. To maximise  
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5 219 consistency in assessing inclusion and exclusion criteria among 21 reviewers, we plan calibration  
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7 220 pilot exercises for title and abstract screening and group discussions using Google Groups  
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10 221 (Google ©, Mountain View, California, U.S.A.) and online group videoconferencing. This  
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12 222 training will emphasise the need for sensitivity in citation selection in the title and abstract phase.  
13  
14 223 Independently and in duplicate, reviewers will screen titles and abstracts for potentially relevant  
15  
16 224 studies using Covidence. Because of the anticipated very large number of potentially relevant  
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18 225 citations, the agreement of two members of the review team will be required for citation  
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20 226 selection at the title and abstract phase; disagreements will be adjudicated by a third reviewer.  
21  
22 227 Full-text versions of citations included at the title and abstract screening phase will be retrieved  
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24 228 and reviewed by the same team of reviewers. If full-text is not retrievable by at least two  
25  
26 229 reviewers, including efforts to contact the study authors directly, the study will be excluded as  
27  
28 230 unavailable. If retrieved citations are found to be abstract-only, they will be excluded, but we  
29  
30 231 will search for any subsequent peer-reviewed journal publications not already captured by our  
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32 232 search. The agreement of two reviewers will be required for inclusion of the full-text study in the  
33  
34 233 systematic review, with conflicts resolved by a third reviewer experienced with this review  
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36 234 process. Reasons for full-text exclusion will be recorded (Table 3).  
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#### 44 236 *Data Extraction*

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46 237 Individual reviewers will extract data from selected articles using Excel (Microsoft ©, Redmond,  
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48 238 Washington, U.S.A.). The data sheet underwent multiple iterations, informed by pilot testing on  
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50 239 selected articles and group discussion. A review group member will review each cluster of data  
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52 240 entry for consistency of data extraction.  
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3 241 We will extract data on the study design, LLMIC country or countries involved, article  
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5 242 identifiers, location(s) within the healthcare system that critical care service(s) were delivered,  
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7 243 healthcare provider(s) providing the service(s), the critical care service(s) provided, critical  
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9 244 illnesses addressed, sample size, and the age range of the study population. Given the clinical  
10  
11 245 heterogeneity of patient populations and interventions, we will not extract data on patient  
12  
13 246 outcomes or the number of critical care beds in a given study facility.  
14  
15 247 Critical care services will be identified using international professional society definitions and  
16  
17 248 the scope of critical care functions in the WHO ECSF. Services will be subsequently classified  
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19 249 based on the categories in the WHO UHC Compendium [20]. We will use the top level  
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21 250 architecture of the compendium to categorise services broadly into foundations of care,  
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23 251 reproductive and sexual health, nutrition, end-of-life and palliative care issues, violence and  
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25 252 injury, non-communicable diseases (including diseases of the cardiovascular, respiratory,  
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27 253 neurologic, endocrine/metabolic, immunologic, digestive, haematologic, genitourinary, and other  
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29 254 systems) and communicable diseases.  
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### 36 37 256 *Limitations*

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39 257 A potential overall source of bias in this review is the large number of reviewers involved in  
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41 258 article selection, such that the threshold for inclusion of studies in the review may vary by  
42  
43 259 reviewer pair and may lead to an underestimation of the locations or types of critical care  
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45 260 services delivered. We have attempted to mitigate this bias by extensive training of reviewers as  
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47 261 described above.  
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51 262 Our study does not include publications on critical care delivery during the COVID-19  
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53 263 pandemic, and characteristics of care delivery may have changed over that time.  
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5 265 *Risk of Bias*

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8 266 Given the broad scope of the review, anticipated heterogeneous studies (regarding design,  
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10 267 population, methods, and outcomes), and lack of planned meta-analyses to calculate summary  
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12 268 effects of associations between exposures and outcomes, we will not assess the risk of bias  
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14 269 (ROB) of individual studies. ROB of included studies is crucial to assess when conducting a  
15  
16 270 systematic review of therapeutic outcomes, diagnosis, natural history, prognosis, or clinical  
17  
18 271 prediction. However, for this study, we aim to describe the location of critical care delivery and  
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20 272 the specific services and interventions delivered. Although a complete sample of published  
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22 273 literature within our timeframe of interest is crucial, we believe that assessing the risk of bias of  
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24 274 each included study is not relevant to our intended review objectives.  
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31 276 *Data analysis*

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33 277 We will calculate summary descriptive statistics, using counts and proportions for categorical  
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35 278 data and means (SD) or median (Q1, Q3) for continuous data. We will describe the number of  
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37 279 publications by year, types of services delivered, health care provider type, location of service  
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39 280 delivery, study population age-group, and critical illness category (based on the WHO UHC  
40  
41 281 Compendium), stratified by World Bank income class and WHO region. Due to the descriptive  
42  
43 282 nature of the study question and expected heterogeneity of patients and interventions, no meta-  
44  
45 283 analyses of effects on patient outcomes are planned. We anticipate that narrative synthesis may  
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47 284 be required to summarise our study results. We will conduct a sensitivity analysis to separately  
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49 285 consider studies that report only on adults and studies only on children.  
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3 286 Subsequent ancillary reviews based on this dataset of studies may investigate specific age-group  
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5 287 populations, continents/regions, World Bank classes, critical care intervention clusters, disease  
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7 288 groups, locations, or healthcare professionals involved.  
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## 11 12 290 **Ethics & Dissemination**

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14 291 The study protocol was reviewed and exempted by the Stanford University Office for Human  
15  
16 292 Subjects Research and IRB on May 20, 2020. The results of this review will be disseminated  
17  
18 293 through scholarly publication and presentation at regional and international conferences. This  
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20 294 review is designed to inform broader WHO, IFEM and partner efforts to strengthen critical care  
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22 295 globally.  
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26 296 We anticipate that the results of this comprehensive review will describe the current scope of  
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28 297 critical care services, providers, and location of service delivery in LLMICs, and will provide a  
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30 298 database of pertinent literature for future studies. The results of the review will be instrumental  
31  
32 299 for planners and policy makers in developing critical care service infrastructure, funding  
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34 300 priorities, and capacity-building interventions, and will highlight gaps in current knowledge of  
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36 301 critical care service delivery in LLMICs.  
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### 41 304 *Patient and Public Involvement*

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43 305 No patients were involved in this study.  
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310 Tables

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**Table 1: List of World Bank Low to Lower-middle income countries - July 2016**

Country	Region	World Bank Class
Afghanistan	South Asia	Low income
Armenia	Europe & Central Asia	Lower middle income
Bangladesh	South Asia	Lower middle income
Benin	Sub-Saharan Africa	Low income
Bhutan	South Asia	Lower middle income
Bolivia	Latin America & Caribbean	Lower middle income
Burkina Faso	Sub-Saharan Africa	Low income
Burundi	Sub-Saharan Africa	Low income
Cabo Verde	Sub-Saharan Africa	Lower middle income
Cambodia	East Asia & Pacific	Lower middle income
Cameroon	Sub-Saharan Africa	Lower middle income
Central African Republic	Sub-Saharan Africa	Low income
Chad	Sub-Saharan Africa	Low income
Comoros	Sub-Saharan Africa	Low income
Congo, Dem. Rep.	Sub-Saharan Africa	Low income
Congo, Rep.	Sub-Saharan Africa	Lower middle income
Côte d'Ivoire	Sub-Saharan Africa	Lower middle income
Djibouti	Middle East & North Africa	Lower middle income
Egypt, Arab Rep.	Middle East & North Africa	Lower middle income
El Salvador	Latin America & Caribbean	Lower middle income
Eritrea	Sub-Saharan Africa	Low income
Ethiopia	Sub-Saharan Africa	Low income
Gambia, The	Sub-Saharan Africa	Low income
Ghana	Sub-Saharan Africa	Lower middle income
Guatemala	Latin America & Caribbean	Lower middle income
Guinea	Sub-Saharan Africa	Low income
Guinea-Bissau	Sub-Saharan Africa	Low income
Haiti	Latin America & Caribbean	Low income
Honduras	Latin America & Caribbean	Lower middle income
India	South Asia	Lower middle income

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4	Indonesia	East Asia & Pacific	Lower middle income
5	Kenya	Sub-Saharan Africa	Lower middle income
6			
7	Kiribati	East Asia & Pacific	Lower middle income
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9	Korea, Dem. People's Rep.	East Asia & Pacific	Low income
10	Kosovo	Europe & Central Asia	Lower middle income
11			
12	Kyrgyz Republic	Europe & Central Asia	Lower middle income
13			
14	Lao PDR	East Asia & Pacific	Lower middle income
15	Lesotho	Sub-Saharan Africa	Lower middle income
16			
17	Liberia	Sub-Saharan Africa	Low income
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19	Madagascar	Sub-Saharan Africa	Low income
20	Malawi	Sub-Saharan Africa	Low income
21			
22	Mali	Sub-Saharan Africa	Low income
23			
24	Mauritania	Sub-Saharan Africa	Lower middle income
25	Micronesia, Fed. Sts.	East Asia & Pacific	Lower middle income
26			
27	Moldova	Europe & Central Asia	Lower middle income
28	Mongolia	East Asia & Pacific	Lower middle income
29			
30	Morocco	Middle East & North Africa	Lower middle income
31	Mozambique	Sub-Saharan Africa	Low income
32			
33	Myanmar	East Asia & Pacific	Lower middle income
34			
35	Nepal	South Asia	Low income
36	Nicaragua	Latin America & Caribbean	Lower middle income
37			
38	Niger	Sub-Saharan Africa	Low income
39			
40	Nigeria	Sub-Saharan Africa	Lower middle income
41	Pakistan	South Asia	Lower middle income
42			
43	Papua New Guinea	East Asia & Pacific	Lower middle income
44	Philippines	East Asia & Pacific	Lower middle income
45			
46	Rwanda	Sub-Saharan Africa	Low income
47			
48	Samoa	East Asia & Pacific	Lower middle income
49	São Tomé and Príncipe	Sub-Saharan Africa	Lower middle income
50			
51	Senegal	Sub-Saharan Africa	Low income
52			
53	Sierra Leone	Sub-Saharan Africa	Low income
54	Solomon Islands	East Asia & Pacific	Lower middle income
55			
56	Somalia	Sub-Saharan Africa	Low income
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South Sudan	Sub-Saharan Africa	Low income
Sri Lanka	South Asia	Lower middle income
Sudan	Sub-Saharan Africa	Lower middle income
Swaziland	Sub-Saharan Africa	Lower middle income
Syrian Arab Republic	Middle East & North Africa	Lower middle income
Tajikistan	Europe & Central Asia	Lower middle income
Tanzania	Sub-Saharan Africa	Low income
Timor-Leste	East Asia & Pacific	Lower middle income
Togo	Sub-Saharan Africa	Low income
Tonga	East Asia & Pacific	Lower middle income
Tunisia	Middle East & North Africa	Lower middle income
Uganda	Sub-Saharan Africa	Low income
Ukraine	Europe & Central Asia	Lower middle income
Uzbekistan	Europe & Central Asia	Lower middle income
Vanuatu	East Asia & Pacific	Lower middle income
Vietnam	East Asia & Pacific	Lower middle income
West Bank and Gaza	Middle East & North Africa	Lower middle income
Yemen, Rep.	Middle East & North Africa	Lower middle income
Zambia	Sub-Saharan Africa	Lower middle income
Zimbabwe	Sub-Saharan Africa	Low income

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<b>Table 2: Critical Care Service Delivery/ Interventions List</b>
<i>Monitoring/nursing</i>
Frequent monitoring/ surveillance and recording of clinical parameters [vital signs, pulse oximetry, capnography, etc.]
Acuity-based triage / performance of focused assessment for the critically ill [including shock, altered mental status, respiratory distress, polytrauma, etc.]
Critical care nursing services [including implementation of higher than floor/ward-level care or nurse:patient ratio]
Frequent monitoring/ surveillance of fetus [fetal heart monitoring, tocometry, etc.]
<i>Interventions for haemodynamic instability/ organ dysfunction</i>
Support of haemodynamic instability and management of acute life threatening organ dysfunction
Titration of advanced parenteral therapeutics
Intravenous fluid resuscitation
Blood products transfusion
Administration of advanced blood replacement therapies [e.g. plasmapheresis]
Massive haemorrhage control [including tourniquet application, haemostatic agents, pelvic binding]
Targeted temperature management and hyperthermia / hypothermia management
Vasopressor/ inotrope administration
Anti-arrhythmic medication administration for the critically ill
Cardio-pulmonary resuscitation, basic only [chest compressions in the absence of invasive procedures]
Advanced cardiac life-support resuscitation [include emergent pacing, defibrillation, cardioversion]
Spinal immobilisation
Extracorporeal membrane oxygenation (ECMO) / extracorporeal life support (ECLS)
Advanced trauma resuscitation / Advanced Trauma Life Support® (ATLS®) / WHO Trauma Care Checklist use
<i>Respiratory interventions</i>
Support of respiratory insufficiency/ failure
Oxygen delivery, simple [face mask, nasal prongs]
Oxygen delivery, high flow [> 15 L/min]
Mechanical ventilation, non-invasive [including continuous positive airway pressure (CPAP)]
Mechanical ventilation, invasive
Non-invasive airway management [basic airway opening maneuvers, bag mask ventilation, oro- or naso-pharyngeal airway placement, etc.]

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3	Advanced invasive airway management, non-surgical [tracheal intubation, laryngeal mask airway placement,
4	bougie, airway exchange catheters, etc.]
5	Advanced surgical airway management [tracheostomy, cricothyrotomy performed outside the operating
6	room/theatre]
7	
8	
9	
10	<i>Other invasive procedures</i>
11	Peripheral venous cannulation for the critically ill
12	
13	Advanced vascular access [arterial lines, central venous / pulmonary artery catheters, intra-osseous access]
14	Thoracic invasive procedures for the critically ill [thoracostomy, pleural drain placement, thoracentesis,
15	pericardiocentesis, emergent thoracotomy performed outside of the operating room/theatre]
16	
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18	<i>Additional targeted therapies</i>
19	
20	Early antibiotic administration for the critically ill
21	
22	Treatment of severe infections/ inflammation / sepsis [steroids and other adjuncts]
23	
24	Renal replacement therapy / haemodialysis or peritoneal dialysis
25	
26	Monitoring and treatment of critical electrolyte/ metabolic/ acid base derangements
27	
28	Nutrition management for the critically ill / injured
29	
30	Provision of prophylaxis associated with critical illness [including alimentary, venous thromboembolism]
31	
32	Advanced burn care for the critically ill
33	
34	Emergent poisoning detoxification/ antidote
35	
36	Acute reperfusion therapy: medical or interventional [cardiac/coronary arteries]
37	
38	Acute reperfusion therapy: medical or interventional [pulmonary embolism, or other acute thromboembolism]
39	
40	
41	<i>Neurological interventions</i>
42	
43	Acute medical stabilisation of critical neurologic illness / provision of neuroprotection for the critically ill [e.g.
44	seizure management]
45	
46	Acute surgical stabilisation of critical neurologic illness [e.g. emergent craniotomy, ventricular drain, intracranial
47	pressure monitor performed outside the operating room/theatre]
48	
49	Acute management of agitation/ delirium
50	
51	Acute reperfusion therapy: medical or interventional [neurovascular procedures for cerebrovascular pathology such
52	as stenting, coiling performed outside the operating room/theatre]
53	
54	Analgesia and sedation [sedative infusions, moderate / conscious sedation, up to general anaesthesia, performed
55	outside the operating room/theatre]
56	
57	
58	<i>Obstetrical critical care services</i>
59	
60	Obstetric critical care management [induction, tocolytic, high-risk labor, emergent/complex delivery, perimortem
	cesarean section performed outside the operating room/theatre]

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4	<i>Diagnostic modalities</i>
5	Utilisation of targeted diagnostic strategy to establish timely aetiology for the critically ill
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7	Basic radiography
8	
9	Computed tomography
10	
11	Magnetic resonance imaging
12	Critical care ultrasound, including point-of-care trans-thoracic / trans-oesophageal echocardiography
13	Laboratory and other rapid results reporting including point-of-care diagnostics [arterial blood gas, glucometry, chemistry, haematology]
14	
15	Microbiology and other infectious rapid results reporting
16	
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18	
19	<i>Multi-system processes related to critical care service delivery</i>
20	Prognosis-based advance care planning [critical care level hospice/palliative, goals of care discussions, plan for de-escalation of care and transition to post-critical care needs appropriate to context]
21	
22	Coordination of specialist services for multisystem illness [managing communication between, and coordination of, various healthcare personnel caring for patient detailing diagnosis, treatment given, and disposition]
23	
24	
25	Critical care triage / care pathways systems / clinical illness severity and/or risk stratification
26	
27	Critical care level crisis management [surge response, disaster management, multiple casualty incident]
28	
29	Health information systems, medical records
30	
31	<i>Other critical care services</i>
32	
33	Critical care pharmacy services
34	
35	Critical care education and capacity building [must have clinical service delivery component]
36	
37	Other critical care intervention/ service delivery

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<b>Table 3: Hierarchy of Exclusion for Full Text</b>	
<b>1</b>	Not published from Jan 1 2008 - Jan 1 2020
<b>2</b>	Is not a study on living humans, or is not related to health aspects of living humans (exclude animal or forensic studies)
<b>3</b>	Does not address Low- or Low-middle income country (per World Bank Class 2016)
<b>4</b>	Does not address critical care service/interventions (per Table 2)
<b>5</b>	Not Original Research, Systematic Review, or Brief Report
<b>6</b>	Does not describe where in healthcare setting critical care service/intervention is delivered
<b>7</b>	Addresses exclusively peri-operative care that occurs in the operating room/theatre
<b>8</b>	Does not address care by healthcare professionals
<b>9</b>	Addresses care performed exclusively by or for High Income Country / High-Middle Income Country military personnel
<b>10</b>	Abstract-only, full text non-existent (for conference, poster/presentation, etc.)
<b>11</b>	Full text not available in English
<b>12</b>	Full text not available online

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3 323 Authors' Contributions:

4 324 AL is the guarantor, drafted, prepared, and submitted the manuscript, contributed to the  
5 325 development of the selection criteria, methodology, data extraction criteria and forms, developed  
6 326 and executed the search strategy, provided teaching and guidance of review process to review  
7 327 group.  
8 328

9 329 NA, SM, SK, LL, ED, BC, NB, AB, MJ, PDS and TR provided comments and critical revisions  
10 330 to the manuscript, made substantial contributions to the conception and design of the review  
11 331 methodology and planned analysis.  
12 332

13 333 ED, SK, PAS, MY, BC, PDS, MJ, RL, AR, CC, NB, NH, NS, PM, BV, NS, AB, CM, AGR, EB,  
14 334 AF, SY made key contributions to the conception, design and execution of eligibility criteria and  
15 335 methodology, participated in the acquisition and interpretation of reference data for screening  
16 336 phases, provided feedback on full text data extraction forms, and provided critical edits to the  
17 337 intellectual content of the manuscript.  
18 338

19 339 All authors read, provided feedback and approved the final manuscript, and agree to be  
20 340 accountable for all aspects of the work in ensuring that questions related to the accuracy or  
21 341 integrity of any part of the work are appropriately investigated and resolved. Thus, all authors  
22 342 have met the four ICMJE criteria recommended for authorship.  
23 343

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27 347

28 348 Competing Interests Statement:

29 349 There are no competing interests to declare for this research.  
30 350

31 351 Word Count:

32 352 3975 (includes abstract)  
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## Appendix 1: Example search strategy: Pubmed/Medline

(((("Critical Care"[Mesh] OR "critical care"[tw] OR "Critical Illness"[Mesh] OR "Critical Illness"[tw] OR "Critical Care Nursing"[Mesh] OR "Critical Care Outcomes"[Mesh] OR "intensive care"[tw] OR "Intensive Care Units"[Mesh] OR "intermediate care unit"[tw] OR "step down unit"[tw] OR "Shock"[Mesh] OR "Cardiac Arrest"[tw] OR "heart arrest"[MeSH] OR "Respiratory Arrest"[tw] OR "Emergency Medicine"[Mesh] OR "Evidence-Based Emergency Medicine"[Mesh] OR "Emergency Nursing"[Mesh] OR "Emergency Treatment"[mh:noexp] OR "Advanced Trauma Life Support Care"[mesh] OR "Resuscitation"[mesh] OR "cardiopulmonary resuscitation"[tw] OR "Cardiopulmonary Resuscitation"[mesh] OR "Heart Massage"[mesh] OR "Respiration, Artificial"[mesh] OR ventilator\*[ti] OR icu[ti] OR picu[ti] OR nicu[ti] OR cu[ti] OR cpr[ti] OR "ambulances"[Mesh] OR "Emergency Service, Hospital"[mesh] OR "Poison Control Centers"[mesh] OR "Triage"[mh:noexp] OR "Hospital Rapid Response Team"[Mesh])) AND (((("Developing Countries"[Mesh] OR "Medically Underserved Area"[Mesh] OR "developing country"[tw] OR "developing countries"[tw] OR "developing nation"[tw] OR "developing nations"[tw] OR "developing population"[tw] OR "developing populations"[tw] OR "developing world"[tw] OR "less developed country"[tw] OR "less developed countries"[tw] OR "less developed nation"[tw] OR "less developed nations"[tw] OR "less developed population"[tw] OR "less developed populations"[tw] OR "less developed world"[tw] OR "lesser developed country"[tw] OR "lesser developed countries"[tw] OR "lesser developed nation"[tw] OR "lesser developed nations"[tw] OR "lesser developed population"[tw] OR "lesser developed populations"[tw] OR "lesser developed world"[tw] OR "under developed country"[tw] OR "under developed countries"[tw] OR "under developed nation"[tw] OR "under developed nations"[tw] OR "under developed population"[tw] OR "under developed populations"[tw] OR "under developed world"[tw] OR "underdeveloped country"[tw] OR "underdeveloped 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3 People's Republic of Korea"[tw] OR "north korea"[tw] OR Kosovo[tw] OR Kyrgyzstan[tw] OR laos[tw] OR  
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5 Micronesia[tw] OR Moldova[tw] OR Mongolia[tw] OR Morocco[tw] OR Mozambique[tw] OR Myanmar[tw] OR  
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8 OR "Solomon Islands"[tw] OR Somalia[tw] OR "South Sudan"[tw] OR "Sri Lanka"[tw] OR Sudan[tw] OR  
9 Swaziland[tw] OR syria[tw] OR Tajikistan[tw] OR Tanzania[tw] OR "Timor-Leste"[tw] OR Togo[tw] OR  
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11 Bank"[tw] OR Yemen[tw] OR Zambia[tw] OR Zimbabwe[tw] OR Kyrgyz[tw] OR Syrian[tw] OR "lao pdr"[tw]  
12 OR Burma[tw] OR gaza[tw] OR "ivory coast"[tw] OR Afghanistan[mesh] OR "guatemala" [mesh] OR "samoa"  
13 [mesh] OR tonga OR "cape verde" [mesh] OR Armenia [mesh] OR Bangladesh[mesh] OR Benin[mesh] OR  
14 Bhutan[mesh] OR Bolivia[mesh] OR "Burkina Faso"[mesh] OR Burundi[mesh] OR "Cabo Verde"[mesh] OR  
15 Cambodia[mesh] OR Cameroon[mesh] OR "Central African Republic"[mesh] OR Chad[mesh] OR  
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17 Salvador"[mesh] OR Eritrea[mesh] OR Ethiopia[mesh] OR Gambia[mesh] OR Ghana[mesh] OR Guinea[mesh]  
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27 Leste"[mesh] OR Togo[mesh] OR Tunisia[mesh] OR Uganda[mesh] OR Ukraine[mesh] OR Uzbekistan[mesh]  
28 OR Vanuatu[mesh] OR Vietnam[mesh] OR Yemen[mesh] OR Zambia[mesh] OR Zimbabwe[mesh])) NOT  
29 ("Emergency Services, Psychiatric"[Mesh] OR "Addresses"[pt] OR "Autobiography"[pt] OR "Bibliography"[pt]  
30 OR "Biography"[pt] OR "Case Reports"[pt] OR "Comment"[pt] OR "Congresses"[pt] OR "Consensus  
31 Development Conference"[pt] OR "Consensus Development Conference, NIH"[pt] OR "Dictionary"[pt] OR  
32 "Directory"[pt] OR "Editorial"[pt] OR "Electronic Supplementary Materials"[pt] OR "Festschrift"[pt] OR  
33 "Historical Article"[pt] OR "Interactive Tutorial"[pt] OR "Interview"[pt] OR "Lectures"[pt] OR "Legal  
34 Cases"[pt] OR "Legislation"[pt] OR "Letter"[pt] OR "News"[pt] OR "Newspaper Article"[pt] OR "Overall"[pt]  
35 OR "Patient Education Handout"[pt] OR "Periodical Index"[pt] OR "Personal Narratives"[pt] OR  
36 "Portraits"[pt] OR "Practice Guideline"[pt] OR "Published Erratum"[pt] OR "Retracted Publication"[pt] OR  
37 "Retraction of Publication"[pt] OR "Technical Report"[pt] OR "Video-Audio Media"[pt] OR "Webcasts"[pt] OR  
38 "case report"[ti] OR bystand\*[ti])) AND english[lang] NOT ("animals"[mesh] NOT "humans"[mesh]) AND  
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**PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\***

Section and topic	Item No	Checklist item	Completed?	(Page, Line)
<b>ADMINISTRATIVE INFORMATION</b>				
Title:				
Identification	1a	Identify the report as a protocol of a systematic review	X	1, 1
	Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	X	1, 6
Authors:				
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	X	1, 10
	Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	X
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A	
Support:				
Sources	5a	Indicate sources of financial or other support for the review	X	1, 75
Sponsor	5b	Provide name for the review funder and/or sponsor	X	21, 407
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	X	1, 75
<b>INTRODUCTION</b>				
Rationale	6	Describe the rationale for the review in the context of what is already known	X	6, 150
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	X	7, 175
<b>METHODS</b>				
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	X	7, 160
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	X	9, 196
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	X	appx. 1
Study records:				
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	X	9, 211

Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	X	9, 217
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	X	10, 236
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	X	10, 241
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	X	11, 247
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	X	12, 265
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	X	12, 276
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as $I^2$ , Kendall's $\tau$ )	X	12, 276
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	X	12, 276
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	X	12, 276
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	N/A	
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	N/A	

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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