Caring for critically ill patients is challenging in resource-limited settings, where the burden of disease and mortality from potentially treatable illnesses is higher than in resource-rich areas. Barriers to delivering quality critical care in these settings include lack of epidemiologic data and context-specific evidence for medical decision-making, deficiencies in health systems organization and resources, and institutional obstacles to implementation of life-saving interventions. Potential solutions include the development of common definitions for intensive care unit (ICU), intensivist, and intensive care to create a universal ICU organization framework; development of educational programs for capacity building of health care professionals working in resource-limited settings; global prioritization of epidemiologic and clinical research in resource-limited settings to conduct timely and ethical studies in response to emerging threats; adaptation of international guidelines to promote implementation of evidence-based care; and strengthening of health systems that integrates these interventions. This manuscript reviews the field of global critical care, barriers to safe high-quality care, and potential solutions to existing challenges. We also suggest a roadmap for improving the treatment of critically ill patients in resource-limited settings.

**Introduction**

Critical care is an important component of health care systems around the world (Figure 1). Caring for critically ill patients in resource-rich settings typically involves treatment in intensive care units (ICUs) staffed with highly specialized health care professionals, systematic monitoring and use of high-cost technology [1]. Unfortunately, these components are not always available in resource-limited settings [2, 3], where the burden of disease is greater [4], outcomes are poorer [5, 6], and local characteristics require context-specific approaches to the organization of critical care services.

Critical care delivery, education, and research require a global perspective based on epidemiologic considerations. The burden of critical illness in resource-limited settings is not well described, but the best available estimates suggest that it may be greater than in resource-rich settings [7, 8] due to deficiencies in access to health care, emergency triage, and lack of early recognition [9–11]. Mortality for adults with sepsis [5, 12, 13] and acute respiratory distress syndrome (ARDS) [14–16] in resource-limited settings is higher than in resource-rich settings, and decedents are usually young (mean age 35 years vs. 61 years in United States) [12, 17], which contributes to a greater negative downstream social and economic impact. Similarly, there is a higher burden of sepsis and respiratory infection mortality among children [18–21]. Recent epidemiological changes in global health have created a ‘double burden of disease’ to resource-limited settings [9, 22] due to an increase in the prevalence of non-communicable diseases combined with lack of improvement in the long-recognized higher burden of communicable diseases, maternal and child mortality, malnutrition, and human immunodeficiency virus (HIV)-related complications.

Health care professionals from resource-rich and resource-limited settings should take a global perspective on critical care for both ethical and practical reasons. Ethically, health care professionals, trainees, professional societies, non-governmental organizations (NGOs), and international organizations from resource-rich settings have the capacity of deploying resources to improve outcomes for critically ill patients in resource-limited settings [11, 23, 24]. Assistance can include financial help, knowledge exchange in the form of research and educational partnerships, and capacity building in operations and implementation science. From a practical point of view, supporting resource-limited settings is also important given that inter-related economies,
the consequences of pandemics, and conflicts driving mass migration [25–27] can all reach far beyond local borders [28–31]. In recent years, challenges arising from limitations of human, technological, infrastructure, and health system resources in resource-poor settings have been well documented [2, 3, 9, 12, 21, 22, 32, 33], but less attention has been given to potential solutions [34, 35]. In this article, we review the epidemiology and challenges of critical care in these settings and then focus on potential solutions and opportunities for improvement.

**Challenges to Critical Care in Resource-limited Settings**

**Gaps in Epidemiological Data**

Comparative epidemiological data on ICU capacity is important for rational allocation of health care resources and to deliver life-saving, cost-efficient intensive care services, especially in settings where resources are scarce [36, 37]. However, the burden of critical illness and its global variation are not well established, even by the Global Burden of Disease project [4, 9, 21, 38]. Accurate estimation of ICU outcomes depends on administrative records or representative epidemiologic studies with sufficient follow-up, both of which require a well-organized health care system and a robust research infrastructure that are usually underdeveloped in resource-limited settings. Additional challenges to identifying the burden of critical illness include vague and sometimes varying working definitions of ICUs and critically ill patients [1, 39] and inconsistent ICU admission criteria across different settings, usually primarily driven by availability of ICU beds [37, 40]. Moreover, the need for critical care is usually substantially underestimated due to barriers to access related to distance, lack of transportation, and cost [22, 41]. Population-based estimates of the burden of critical illness in resource-limited settings are lacking [9]. Epidemiologic studies are typically cross-sectional and, except for few studies, have limited longitudinal follow-up to assess survival outcomes [5, 15]. There is also limited data on ICU capacity in resource-limited settings [3, 33, 42], and only a few assessments are population based [12, 43, 44], precluding accurate national estimates of ICU capacity or the number ICU-treated critically ill patients.

Unfortunately, the standard practice of extrapolating outcomes data from resource-rich to resource-limited settings is misleading. ICU mortality rates in resource-rich settings appear to be decreasing over the last decades [17, 45], but this trend is related to case mix, organizational factors, and clinician practices that may be different or inapplicable in resource-limited settings [40]. Thus, improving ICU outcomes globally will require a better understanding of the burden of critical illness and inequities in ICU capacity, with a focus on regional and local data about ICU processes and outcomes in resource-limited settings. An important concept that may guide future epidemiologic estimates is the notion that many patients in resource-limited settings who die of acute reversible illnesses can be assumed to be critically ill and would be offered treatment in an ICU, if it were available.

**Gaps in Evidence for Best Practices**

Given that data on treatment outcomes generated by local clinical trials is rarely available, health professionals
in resource-limited settings must rely on literature from developed countries. However, interventions that improve outcomes in patients from resource-rich settings may not always be relevant; prominent examples include the higher mortality of septic children and adults treated with aggressive fluid resuscitation in Africa [46–48].

Local characteristics require that bundles and protocols developed in resource-rich countries be adapted before implementation in resource-limited settings [49, 50]. For example, most sub-Saharan countries lack resources to implement all components of the Surviving Sepsis Campaign Guidelines, but local modification might allow the implementation of specific life-saving interventions [51]. New trials may also inform appropriate modifications to guidelines; for example, routine measurement of central venous pressure is no longer a recommendation in recent Surviving Sepsis guidelines [52], which may improve adherence to sepsis bundles where central venous catheters are not routinely used or available [53].

Mortality prediction scores to risk-adjust in research and quality improvement efforts must also be developed and validated in relevant populations [54, 55]. Region-specific equations or adaptations for resource-limited settings can improve performance and facilitate implementation [55–59]. Risk assessment tools, such as the Modified Early Warning Score, which might help triage critically patients and allocate resources [54] have shown conflicting results when applied in resource-limited settings and need additional modifications and validation [60, 61].

Selecting Allocation of Critical Care Resources
Triage decisions for ICU admission are required because demand commonly exceeds supply, even outside pandemics or mass casualty disasters [62, 63]. Importantly, these criteria should take into account patient autonomy, which may vary based on cultural and other local factors and should incorporate regional policies. Unfortunately, adequate tools for resource-limited settings are very limited. Even when evidence from resource-rich settings exists, implementation is challenging [65]. Barriers include lack of equipment (e.g., mechanical ventilators to support patients with acute respiratory failure), medications (e.g., antibiotics for multidrug resistant bacteria), diagnostics (e.g., equipment for repeated measurements of lactate and blood gases to guide treatment of sepsis or ARDS), trained personnel, and quality improvement systems. Therefore, clinical trials of novel therapeutic approaches and implementation strategies are required to ensure the ‘right solution for the right setting’.

Potential Solutions and Opportunities for Innovation
While challenges are formidable, many opportunities exist to improve critical care in resource-poor settings in the categories of ICU organization, clinical guidelines, education, research capacity, and health care system strengthening.

ICU Organization
The World Federation of Societies of Intensive and Critical Care Medicine (WFSICCM) developed a common framework describing critically ill patients and critical care service, targeting policy-makers, clinicians, and patients, which has led to several consensus-based documents [1, 39, 62]. The task force proposed a three-tiered system of categorizing ICUs into: 1) level 1 units, capable of providing oxygen, noninvasive monitoring, and more intensive nursing care than a regular ward; 2) level 2 units, which have short-term ability of providing invasive monitoring and basic life support; and 3) level 3 units, capable of providing the full spectrum of monitoring and life support technologies, serving as a regional resource for the care of critically ill patients, and also playing an active role in research and education [1]. With these standardized definitions, different countries can create a more accurate inventory of their ‘ICU capacity’ allowing for meaningful comparisons across regions. In addition, the Global Intensive Care Working Group of the European Society of Critical Care Medicine has developed recommendations for infrastructure and ICU organization in resource-limited settings [64].

The WFSICCM guidelines also described the training needs, roles, and responsibilities of critical care specialists [39] and the need for uniform training pathways to ensure minimal standards and competencies. The report recommends adoption of existing competency-based training frameworks, such as the Competency-Based Training in Intensive Care Medicine program in Europe (CoBaTrICE) and the CanMEDS competencies of the Royal College of Physicians and Surgeons of Canada. These documents delineate competencies related to medical knowledge – such as diagnosis, monitoring, and treatment of patients with critical illnesses – and leadership, professionalism, end-of-life care, and communication, among others.

Finally, the WFSICCM task force emphasizes the importance of intensivist-led triage based on input from other clinicians and following institutional or regional policies, regardless of patients’ socioeconomic status, insurance coverage or ability to pay for care [62, 63].

Education and Capacity Building
Educational interventions to build critical care capacity in resource-limited settings are important because of the underrepresentation of relevant topics in medical school curricula, the lack of post-graduate, critical care training pathways, and limited access to continuing medical education [66, 67]. Interventions can range from short focused courses to longer-term programs based on academic partnerships between high- and low-income countries (including academic institutions, professional societies, and NGOs) that aim at training critical care specialists [66, 67]. Short courses (Table 1) cannot replace long-term clinical training but have the advantage of providing standardized education on specific topics to many clinicians, and can be implemented in response to acute needs. However, the impact of short courses on longer-term knowledge, bedside processes of care, and patient outcomes has not been well studied.

In contrast, longitudinal academic partnerships (Table 2) can provide knowledge exchange platforms and build local ICU faculty expertise, but these depend on continuous on-site mentorship and training by visiting
unknown. As a result, insights into critical care epidemiology of deaths due to respiratory failure and sepsis remain the leading cause of death in children less than five years of age in low-income countries [77]; however, number of deaths due to respiratory failure and sepsis remains unknown. As a result, insights into critical care epidemiology have relied on convenience samples of ICUs with more recent studies including more participants from low- and middle-income countries [5]. However, because most septic patients are not admitted to an ICU in resource-limited settings, methods of incidence estimation that rely on ICU-treated cases underestimate morbidity and mortality. Another approach to understand sepsis-related mortality would be to examine causes of death based on interviews of relatives using verbal autopsy methods, as done for surgical conditions and renal failure [78, 79].

**Research**

Opportunities for research in epidemiology, diagnostics, therapeutics, and implementation of critical care resources in resource-limited settings are vast. We outline areas of investigation with promising studies completed.

**Burden of Disease**

The Global Burden of Disease project, which has the goal of identifying risk factors and estimating the health impact of different diseases [77], does not directly address critical illnesses. For example, lower respiratory infections remain the leading cause of death in children less than five years of age in low-income countries [77]; however, number of deaths due to respiratory failure and sepsis remains unknown. As a result, insights into critical care epidemiology have relied on convenience samples of ICUs with

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**Table 1:** Examples of Short Critical Care Courses Available in Resource-limited Settings.

| Course                                                                 | Description                                                                 |
|------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| The Basic Assessment and Support in Intensive Care (BASIC) course,     | This is a short, intensive course that is widely available and free, with    |
| Chinese University of Hong Kong [70]                                   | standardized training material that covers a broad range of intensive care   |
|                                                                        | topics [66]. Its target audience includes critical care physician trainees,  |
|                                                                        | critical care nurses, non-intensivist physicians, and allied health workers.|
|                                                                        | Dissemination has relied on a train-the-trainers approach, with cascade      |
|                                                                        | trainings within countries by local facilitators.                           |
| World Health Organization short course on the critical care management | This course is designed to respond to outbreaks of severe respiratory infections |
| of Severe Acute Respiratory Infection (SARI) [71]                      | and has trained over 1000 intensive care unit doctors from 13 countries,     |
|                                                                        | focusing on clinical management of patients with severe pneumonia, sepsis,   |
|                                                                        | and acute respiratory distress syndrome. It is a collaborative effort between |
|                                                                        | local health authorities, the WHO regional offices, and the WHO expert      |
|                                                                        | clinical network.                                                           |
| Network for Intensive Care Skills Training (NICST), Sri Lanka          | NICST is a non-profit, international organization that provides training for |
|                                                                        | critical care nurses [72, 73] in Sri Lanka with a train-the-trainers approach.|
|                                                                        | An assessment found improvement of immediate knowledge and high levels of    |
|                                                                        | participant satisfaction [74].                                              |
| American Thoracic Society (ATS) Methods in Epidemiologic, Clinical,    | This series of courses is sponsored by the ATS and local respiratory societies|
| and Operations Research (MECOR) course                                | and has trained over 1000 health professionals in 24 countries in research  |
|                                                                        | methodology [75].                                                          |

**Table 2:** Examples of Academic Partnerships.

- **The East African Training Initiative:** A two-year fellowship program in pulmonary and critical care medicine hosted by the Tikur Anbessa (Black Lion) Teaching Hospital of Addis Ababa University (AAU) School of Medicine in Ethiopia. This is a collaborative effort between the health ministry, the AAU, international faculty, the World Lung Foundation and the Swiss Lung Foundation [69] and had graduated nine specialists as of January 2019.

- **The Rwanda Human Resources for Health (HRH) Program:** A partnership between 25 American institutions and the Rwandan Ministry of Health. It aims to increase capacity to 500 specialist-trained physicians within the seven years of its funding and includes critical care [76].

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and lung ultrasound and applied this classification to estimate incidence and mortality of ARDS in one hospital in Rwanda [14]. Such modified criteria, after additional validation, could be used to enhance our understanding of epidemiology and design clinical trials.

Septic shock also remains a major cause of mortality in adults and children globally [82], and it is clear that early recognition and treatment save lives [83]. Increasing attention to this condition has grown after the establishment of the World Sepsis Day [84] and the related 2017 World Health Assembly resolution [85]. However, trials of fluid resuscitation in sepsis in sub-Saharan Africa showed increased mortality in children [46] and adults [47, 48] illustrating the challenges of applying well-accepted resuscitation algorithms from resource-rich settings (that assume mechanical ventilation availability and intensive care capacity) in resource-limited settings. Defining safe fluid resuscitation approaches for resource-limited settings is a major research priority and reinforces the need for clinical trials that include rules for stopping therapy and that minimize risk of adverse effects by integrating local ICU practices [86].

Quality Improvement and Behavior Change
Quality improvement (QI) is an essential tool for making health care safer and more effective and another promising research area for resource-limited settings. Due to local site practices, there can be substantial differences in the effectiveness of QI interventions. Prominent examples are from Brazil, and include a before-after study of a multi-faceted QI intervention including screening strategies, multidisciplinary educational sessions, case management, and continuous performance assessment, resulting in improved adherence to the Surviving Sepsis Campaign 6h-bundle and lower mortality [87]. A cluster randomized trial in 118 Brazilian ICUs compared routine care to a another multi-faceted QI strategy that included a daily checklist, goal setting during multidisciplinary rounds, and clinician prompting for 11 care processes and found no effect on mortality and variable impact on processes of care [88]. Another ongoing project is testing a checklist for early recognition and treatment of acute illness (CERTAIN), a decision support tool for initial and follow-up management of critical illness syndromes currently under evaluation in resource-rich and resource-poor settings [89]. Conducting local QI projects in resource-limited settings, using small samples to test changes in outcomes and measuring impact on processes of care, is essential. Sharing successes and failures can inspire colleagues to test innovative approaches to behavior change leading to improved implementation of evidence-based interventions.

Ethics
The requirements for conducting critical care research in resource-limited settings need improvement to enable timely completion while ensuring protection of the rights of research participants and academic recognition to investigators in low- and middle-income countries. Unfortunately, currently prevailing models prioritize ‘blockbuster products’ that do not necessarily recognize a health rights framework or public health approach, and grossly fail to address population needs, especially for resource-limited settings, and are poorly suited for timely response to outbreak conditions [31]. Folayan et al. describe four major processes required to conduct research in resource-limited settings during outbreak conditions, including local access to products developed as a result of the research, capacity transfer to local researchers, development of competent local ethics committees, and empowerment of community members to actively engage in research design and implementation [90]. Public health organizations should work with the academic community to guide research priorities by taking into account the public health impact. In response to previous global health emergencies, the World Health Organization (WHO) and the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) have collaborated to develop modular standard case report forms that can be used in multiple settings to promote faster data collection during infectious disease outbreaks [91]. A severe acute respiratory infection (SARI) observational study is being conducted globally in collaboration with ISARIC, the International Forum of Acute Care Trialists and the Platform for European Preparedness Against (Re-)emerging Epidemics to test the global research response capacity, estimate global SARI incidence, and understand barriers to the research processes [92].

Clinical Guidelines
Until sufficient research from resource-limited settings drives locally generated clinical guidelines, adaptation of existing guidelines [52, 93, 94] is essential to bring safe, feasible, and effective practices to the bedside. For example, the European Society of Intensive Care Medicine Global Health Working group, including experts from both resource-rich and resource-limited settings, developed adapted recommendations for the management of sepsis in resource-limited settings. Topics covered include ventilatory support [95], sepsis recognition [96], and sepsis management in adults [20] and children [19]. These papers highlight the lack of primary evidence from resource-limited settings and advocate that future guidelines should be based on locally produced evidence and use GRADE-adherent processes. Similarly, the WHO has published clinical management guidelines for severely ill children [97–99], adolescents, and adults [100] in austere environments and more recently for dengue [101], malaria [102], and viral hemorrhagic fever [103]. Although these guidelines do not include mechanical ventilation or other ICU technologies, they do address triage and emergency treatments. Implementation of pediatric triage has been associated with improved outcomes in Sierra Leone [104], and a single center, pilot study in Haiti evaluating the Integrated Manual for Adult and Adolescent Illness (IMAI) protocol for severe sepsis demonstrated increased sepsis recognition, greater volume of fluid resuscitation, and increased frequency of vital signs monitoring [105].

Strengthening Health Systems
To improve critical care service delivery in resource-limited settings, decision-makers must accept that high-quality, equitable intensive care services are necessary to achieve
Conclusions
Caring for critically ill patients in resource-limited settings is challenging due to the high burden of disease and high mortality rates from potentially treatable critical illnesses. Despite the lack of epidemiologic data, deficiencies in health systems organization and resources, and institutional obstacles to implementation of effective interventions, many potential solutions are emerging. We suggest the following roadmap for the improvement of care for critically ill patients in resource-poor settings:

1. International organizations must recognize that the delivery of safe, equitable, and high-quality critical care in resource-limited settings is a priority for international health security.
2. Education and research activities must be integrated into national healthcare priorities.
3. Critical care education should be expanded in a uniform, sustainable fashion, including short courses to improve general knowledge as well as comprehensive, competency-based specialty training.
4. Research in resource-limited settings must take into account the public health impact and be prioritized to include epidemiologic investigations of burden of disease and access to critical care, evaluation of diagnostic and therapeutic interventions, quality improvement, and cost-effectiveness.

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Competing Interests
The authors have no competing interests to declare.

Author Contribution
Drs. Ferreira and Diaz contributed equally to the manuscript.

We confirm that all authors contributed significantly to the manuscript and have had access to all data and final version.

References
1. Marshall JC, Bosco L, Adhikari NK, et al. What is an intensive care unit? A report of the task force of the World Federation of Societies of Intensive and Critical Care Medicine. J Crit Care. 2017; 37: 270–276. DOI: https://doi.org/10.1016/j.jcrc.2016.07.015
2. Fowler RA, Adhikari NKJ and Bhagwanjee S. Clinical review: critical care in the global context—disparities in burden of illness, access, and economics. Crit Care. 2008; 12(5): 225. DOI: https://doi.org/10.1186/cc6984
3. Vukoja M, Riviello E, Gavrilovic S, et al. A survey on critical care resources and practices in low-and middle-income countries. Glob Heart. 2014; 9(3): 337–42.e5. DOI: https://doi.org/10.1016/j.gheart.2014.08.002
4. Adhikari NKJ, Fowler RA, Bhagwanjee S and Rubenfeld GD. Critical care and the global burden of critical illness in adults. Lancet. 2010; 376(9749): 1339–1346. DOI: https://doi.org/10.1016/S0140-6736(10)60446-1
5. Vincent J-L, Marshall JC, Namendys-Silva SA, et al. Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. Lancet Respir Med. 2014; 2(5): 380–386. DOI: https://doi.org/10.1016/S2213-2600(14)70061-X
6. Riviello ED, Sugira V and Twagirumugabe T. Sepsis research and the poorest of the poor. Lancet Infect Dis. 2015; 15(5): 501–503. DOI: https://doi.org/10.1016/S1473-3099(15)70148-9
7. Ferreira JC, Medeiros P, Rego FM and Caruso P. Risk factors for noninvasive ventilation failure in cancer patients in the intensive care unit: A retrospective cohort study. J Crit Care. 2015; 30(5): 1003–1007. DOI: https://doi.org/10.1016/j.jcrc.2015.04.121
8. Duggal A, Pinto R, Rubenfeld G and Fowler RA. Global variability in reported mortality for critical illness during the 2009–10 influenza A(H1N1) pandemic: A systematic review and meta-regression to guide reporting of outcomes during disease outbreaks. Cowling BJ (ed.), PLoS One. 2016; 11(5): e0155044. DOI: https://doi.org/10.1371/journal.pone.0155044
9. Dünser MW, Baelani I and Ganbold L. A review and analysis of intensive care medicine in the least developed countries. Crit Care Med. 2006; 34(4): 1234–1242. DOI: https://doi.org/10.1097/01.CCM.0000208360.70835.87
10. Murthy S and Adhikari NK. Global health care of the critically ill in low-resource settings. Ann Am Thorac Soc. 2013; 10(5): 509–513. DOI: https://doi.org/10.1513/AnnalsATS.201307-246OT
11. Mendsaikhan N, Begjav T, Lundeg G and Dünser MW. Potentially Preventable Deaths by Intensive Care Medicine in Mongolian Hospitals. Crit Care Res Pract. 2016; 2016: 8624035. DOI: https://doi.org/10.1155/2016/8624035
12. Kwizera A, Dünser M and Nakibuuka J. National intensive care unit bed capacity and ICU patient characteristics in a low income country. BMC
13. Papali A, Verceles AC, Augustin ME, et al. Sepsis in Haiti: Prevalence, treatment, and outcomes in a Port-au-Prince referral hospital. J Crit Care. 2017; 38: 35–40. DOI: https://doi.org/10.1016/j.jcrc.2016.09.031
14. Riviello ED, Kiviri W, Twagirumugabe T, et al. Hospital Incidence and Outcomes of the Acute Respiratory Distress Syndrome Using the Kigali Modification of the Berlin Definition. Am J Respir Crit Care Med. 2016; 193(1): 52–59. DOI: https://doi.org/10.1164/rcrm.201503-0584OC
15. Azevedo LCP, Park M, Salluh JIF, et al. Clinical outcomes of patients requiring ventilatory support in Brazilian intensive care units: A multicenter, prospective, cohort study. Crit Care. 2013; 17(2): R63. DOI: https://doi.org/10.1186/cc12594
16. Barreira ER, Munoz GOC, Cavalheiro PO, et al. Epidemiology and outcomes of acute respiratory distress syndrome in children according to the Berlin definition: A multicenter prospective study. Crit Care Med. 2015; 43(5): 947–953. DOI: https://doi.org/10.1097/CCM.0000000000000866
17. Zimmerman JE, Kramer AA and Knaus WA. Changes in hospital mortality for United States intensive care unit admissions from 1988 to 2012. Crit Care. 2013; 17(2): R81. DOI: https://doi.org/10.1186/cc12695
18. Ballot DE, Davies VA, Cooper PA, Chirwa T, Argent A and Mer M. Retrospective cross-sectional review of survival rates in critically ill children admitted to a combined paediatric/neoanatal intensive care unit in Johannesburg. South Africa, 2013–2015. BMJ Open. 2016; 6(6): e010850. DOI: https://doi.org/10.1136/bmjopen-2015-010850
19. Musa N, Murthy S and Kissoon N. Pediatric sepsis and septic shock management in resource-limited settings. Intensive Care Med. 2016; 42(12): 2037–2039. DOI: https://doi.org/10.1007/s00134-016-4382-8
20. Dùnser MW, Festic E, Dondorp A, et al. Recommendations for sepsis management in resource-limited settings. Intensive Care Med. 2012; 38(4): 557–574. DOI: https://doi.org/10.1007/s00134-012-2468-5
21. Baker T. Critical care in low-income countries. Trop Med Int Heal. 2009; 14(2): 143–148. DOI: https://doi.org/10.1111/j.1365-3156.2008.02202.x
22. Stafford RE, Morrison CA, Godfrey G and Mahalu W. Challenges to the provision of emergency services and critical care in resource-constrained settings. Glob Health. 2014; 9(3): 319–323. DOI: https://doi.org/10.1016/j.ghet.2014.08.005
23. United Nations. United Nations Sustainable Development Goals. https://www.who.int/sdg/en/Published 2018.
24. Gostin LO. Why rich countries should care about the world’s least healthy people. JAMA. 2007; 298(1): 89–92. DOI: https://doi.org/10.1001/jama.298.1.89
25. Nic Carthaigh N, De Gryse B, Esmati AS, et al. Patients struggle to access effective health care due to ongoing violence, distance, costs and health service performance in Afghanistan. Int Health. 2015; 7(3): 169–175. DOI: https://doi.org/10.1093/inthealth/iht086
26. Burnham G, Malik S, Al-Shibli ASD, et al. Understanding the impact of conflict on health services in Iraq: information from 401 Iraqi refugee doctors in Jordan. Int J Health Plann Manage. 2012; 27(1): e51–64. DOI: https://doi.org/10.1002/hpm.1091
27. Suphanchaimat R, Kantamaturapoju K, Puthasiri W and Prakongsai P. Challenges in the provision of healthcare services for migrants: A systematic review through providers’ lens. BMC Health Serv Res. 2015; 15: 390. DOI: https://doi.org/10.1186/s12913-015-1065-z
28. Cowling BJ and Yu H. Ebola: Worldwide dissemination risk and response priorities. Lancet. 2015; 385(9962): 7–9. DOI: https://doi.org/10.1016/S0140-6736(14)61895-X
29. Fineberg HV. Pandemic preparedness and response – Lessons from the H1N1 influenza of 2009. N Engl J Med. 2014; 370(14): 1335–1342. DOI: https://doi.org/10.1056/NEJMra1208802
30. Poutanen SM, Low DE, Henry B, et al. Identification of severe acute respiratory syndrome in Canada. N Engl J Med. 2003; 348(20): 1995–2005. DOI: https://doi.org/10.1056/NEJMoa030634
31. Heymann DL, Chen L, Takemi K, et al. Global health security: The wider lessons from the West African Ebola virus disease epidemic. Lancet. 2015; 385(9980): 1884–1901. DOI: https://doi.org/10.1016/S0140-6736(15)60858-3
32. Belle J, Cohen H, Shindo N, et al. Influenza preparedness in low-resource settings: A look at oxygen delivery in 12 African countries. J Infect Dev Ctries. 2010; 4(7): 419–424. DOI: https://doi.org/10.3855/jidc.859
33. Murthy S, Leligdowicz A and Adhikari NKJ. Intensive care unit capacity in low-income countries: A systematic review. PLoS One. 2015; 10(1): e0116949. DOI: https://doi.org/10.1371/journal.pone.0116949
34. Riviello ED, Letchford S, Achieng L and Newton MW. Critical care in resource-poor settings: Lessons learned and future directions. Crit Care Med. 2011; 39(4): 860–867. DOI: https://doi.org/10.1097/CCM.0b013e3182026dd65
35. Marshall JC. Global collaboration in acute care clinical research. Crit Care Med. 2017; 45(2): 311–320. DOI: https://doi.org/10.1097/CMM.0b013e31820d6d5
36. Prin M and Wunsch H. International comparisons of intensive care: Informing outcomes and improving standards. Curr Opin Crit Care. 2012; 18(6): 700–706. DOI: https://doi.org/10.1097/MCC.0b013e32835914d5
37. Murthy S and Wunsch H. Clinical review: International comparisons in critical care-lessons learned. Crit Care. 2012; 16(2): 218. DOI: https://doi.org/10.1186/cc1140
38. Adhikari NKJJ and Rubenfeld GD. Worldwide demand for critical care. *Curr Opin Crit Care*. 2011; 17(6): 620–625. DOI: https://doi.org/10.1097/MCC.0b013e3283d39c

39. Amin P, Fox-Robichaud A, Divatia JV, et al. The intensive care unit specialist: Report from the Task Force of World Federation of Societies of Intensive and Critical Care Medicine. *J Crit Care*. 2016; 35: 223–228. DOI: https://doi.org/10.1016/j.jcrc.2016.06.001

40. Karthikeyan B, Kadhiravan T, Deepanjali S and Swaminathan RP. Case-mix, care processes, and outcomes in medically ill patients receiving mechanical ventilation in a low-resource setting from southern India: A prospective clinical case series. *PloS One*. 2015; 10(8): e0135336. DOI: https://doi.org/10.1371/journal.pone.0135336

41. Nkurunziza T, Toma G, Odhiambo J, et al. Referral patterns and predictors of referral delays for patients with traumatic injuries in rural Rwanda. *Surgery*. 2016; 160(6): 1636–1644. DOI: https://doi.org/10.1016/j.surg.2016.08.006

42. Naidoo K, Singh J and Lalloo U. A critical analysis of ICU/HC beds in South Africa: 2008–2009. *S Afr Med J*. 2013; 103(10): 751–3. Sep 3. DOI: https://doi.org/10.7196/SAMJ.6415

43. Acharya SP. Critical care medicine in Nepal: Where are we? *Int Health*. 2013; 5(2): 92–95. DOI: https://doi.org/10.1093/inthealth/ith010

44. Mendsaikhan N, Begjjav T, Lundeg G, Brunauer A and Dünger MW. A nationwide census of ICU capacity and admissions in Mongolia. *PloS One*. 2016; 11(8): e0160921. DOI: https://doi.org/10.1371/journal.pone.0160921

45. Moran JL, Bristow P, Solomon PJ, George C and Hart GK. Mortality and length-of-stay outcomes, 1993–2003, in the binational Australian and New Zealand intensive care adult patient database. *Crit Care Med*. 2008; 36(1): 46–61. DOI: https://doi.org/10.1097/01.CCM.0000295313.08084.58

46. Maitland K, Kiguli S, Opoka RO, et al. Mortality after fluid bolus in African children with severe infection. *N Engl J Med*. 2011; 364(26): 2483–2495. DOI: https://doi.org/10.1056/NEJMoa1101549

47. Andrews B, Muchemwa L, Kelly P, Lakhi S, Heimburger DC and Bernard GR. Simplified severe sepsis protocol: A randomized controlled trial of modified early goal-directed therapy in Zambia. *Crit Care Med*. 2014; 42(11): 2315–2324. DOI: https://doi.org/10.1097/CCM.0000000000001541

48. Andrews B, Semler MW, Muchemwa L, et al. Effect of an early resuscitation protocol on in-hospital mortality among adults with sepsis and hypotension: A randomized clinical trial. *JAMA*. 2017; 318(13): 1233–1240. DOI: https://doi.org/10.1001/jama.2017.10913

49. Jordan J, Rose L, Dainty KN, Noyes J and Blackwood B. Factors that impact on the use of mechanical ventilation weaning protocols in critically ill adults and children: A qualitative evidence-synthesis. *Cochrane Database Syst Rev*. 2016; 10: CD011812. DOI: https://doi.org/10.1002/14651858.CD011812.pub2

50. Papali A, McCurdy MT and Calvello EJB. A “three delays” model for severe sepsis in resource-limited countries. *J Crit Care*. 2015; 30(4): 861.e9–14. DOI: https://doi.org/10.1016/j.jcrc.2015.04.003

51. Baelani I, Jochberger S, Laimer T, et al. Availability of critical care resources to treat patients with severe sepsis or septic shock in Africa: A self-reported, continent-wide survey of anaesthesia providers. *Crit Care*. 2011; 15(1): R10. DOI: https://doi.org/10.1186/cc9410

52. Rhodes A, Evans LE, Alhazzani W, et al. Surviving sepsis campaign: International guidelines for management of sepsis and septic shock: 2016. *Crit Care Med*. 2017; 45(3): 486–552. DOI: https://doi.org/10.1097/CCM.0000000000002255

53. Phua J, Koh Y, Du B, et al. Management of severe sepsis in patients admitted to Asian intensive care units: Prospective cohort study. *BMJ*. 2011; 342: d3245. DOI: https://doi.org/10.1136/bmj.d3245

54. Kruiswinkel R, Kwizera A, Crowther M, et al. Modified Early Warning Score (MEWS) identifies critical illness among ward patients in a resource restricted setting in Kampala, Uganda: A prospective observational study. *PloS One*. 2016; 11(3): e0151408. DOI: https://doi.org/10.1371/journal.pone.0151408

55. Riviello ED, Kiviri W, Fowler RA, et al. Predicting mortality in low-income country ICUs: The Rwanda Mortality Probability Model (R-MPM). *PloS One*. 2016; 11(5): e0155858. DOI: https://doi.org/10.1371/journal.pone.0155858

56. Olson D, Davis NL, Milazi R, et al. Development of a severity of illness scoring system (inpatient triage, assessment and treatment) for resource-constrained hospitals in developing countries. *Trop Med Int Health*. 2013; 18(7): 871–878. DOI: https://doi.org/10.1111/tmi.12137

57. Mpimbaza A, Sears D, Sserwanga A, et al. Admission risk score to predict inpatient pediatric mortality at four public hospitals in Uganda. *PloS One*. 2015; 10(7): e0133950. DOI: https://doi.org/10.1371/journal.pone.0133950

58. Soares M and Salluh JIF. Validation of the SAPS 3 admission prognostic model in patients with cancer in need of intensive care. *Intensive Care Med*. 2006; 32(11): 1839–1844. DOI: https://doi.org/10.1007/s00134-006-0374-4

59. Moreno RP, Metnitz PGH, Almeida E, et al. SAPS 3—From evaluation of the patient to evaluation of the intensive care unit. Part 2: Development of a prognostic model for hospital mortality at ICU admission. *Intensive Care Med*. 2005; 31(10): 1345–1355. DOI: https://doi.org/10.1007/s00134-005-2763-5

60. Ho LO, Li H, Shahidah N, Koh ZX, Sultana P and Hock Ong ME. Poor performance of the modified early warning score for predicting mortality in critically ill patients presenting to an emergency department. *World J Emerg Med*. 2013; 4(4): 273–278. DOI: https://doi.org/10.5847/wjem.jissn.1920-8642.2013.04.005
61. Wheeler I, Price C, Sitch A, et al. Early warning scores generated in developed healthcare settings are not sufficient at predicting early mortality in Blantyre, Malawi: A prospective cohort study. *PLoS One*. 2013; 8(3): e59830. DOI: https://doi.org/10.1371/journal.pone.0059830

62. Blanch L, Abillama FF, Amin P, et al. Triage decisions for ICU admission: Report from the Task Force of the World Federation of Societies of Intensive and Critical Care Medicine. *J Crit Care*. 2016; 36: 301–305. DOI: https://doi.org/10.1016/j.jcrc.2016.06.014

63. Christian MD, Devereaux AV, Dichter JR, Rubinson L and Kissoon N. Introduction and executive summary: Care of the critically ill and injured during pandemics and disasters: CHEST consensus statement. *Chest*. 2014; 146(4 Suppl): 8S–34S. DOI: https://doi.org/10.1378/chest.14-0732

64. Papali A, Schultz MJ and Dünser MW. European Society of Intensive Care Medicine (ESICM) Global Intensive Care working group and The Mahidol–Oxford Research Unit (MORU) in Bangkok, Thailand. *Intensive Care Med*. 2018; 44(7): 1133–1137. July. Epub 2017 Nov 20. DOI: https://doi.org/10.1007/s00134-017-4972-0

65. Oliveira CF, Nogueira de Sa FR, Oliveira DSF, et al. Time- and fluid-sensitive resuscitation for hemodynamic support of children with septic shock: Barriers to the implementation of the American College of Critical Care Medicine/Pediatric Advanced Life Support Guidelines in a pediatric intensive care unit. *Pediatr Emerg Care*. 2008; 24(12): 810–815. DOI: https://doi.org/10.1097/PEC.0b013e3181e9f3a

66. Joynt GM, Zimmerman J, Li TST and Gomersall CD. A systematic review of short courses for nonspecialist education in intensive care. *J Crit Care*. 2011; 26(5): 533.e1–533.e10. DOI: https://doi.org/10.1016/j.jcrc.2011.01.007

67. Turner EL, Nielsen KR, Jamal SM, von Saint André-von Armim A and Musa NL. A review of pediatric critical care in resource-limited settings: A look at past, present, and future directions. *Front Pediatr*. 2016; 4: 5. February. DOI: https://doi.org/10.3389/fped.2016.00005

68. Alem A, Pain C, Araya M and Hodges BD. Co-creating a psychiatric resident program with Ethiopians, for Ethiopians, in Ethiopia: The Toronto Addis Ababa Psychiatry Project (TAAPP). *Acad Psychiatry*. 2010; 34(6): 424–432. DOI: https://doi.org/10.1176/appi.ap.34.6.424

69. Sherman CB, Carter EJ, Braendli O, Getaneh A and Schluger NW. The East African Training Initiative (EATI): A model training program in pulmonary and critical care medicine for low-income countries. *Ann Am Thorac Soc*. 2016; 13(4): 451–455. DOI: https://doi.org/10.1513/AnnalsATS.201510-6730C

70. Basic Assessment & Support in Intensive Care. https://www.aic.cuhk.edu.hk/web8/BASIC.htm

71. Diaz JV, Ortiz JR, Lister P, Shindo N, Adhikari NKJ and WHO Critical Care Training Short Course collaborators. Development of a short course on management of critically ill patients with acute respiratory infection and impact on clinician knowledge in resource-limited intensive care units. *Influenza Other Respir Viruses*. 2018; May 4. DOI: https://doi.org/10.1111/irv.12569. [Epub ahead of print] PubMed PMID: 29727522; PubMed Central PMCID: PMC6086848.

72. The Network for Intensive Care Skills Training (NICST). http://www.nics-training.com.

73. Beane A, Stephens T, De Silva AP, et al. A sustainable approach to training nurses in acute care skills in a resource limited setting (Network for Intensive Care Skills Training, NICST). *Resuscitation*. 2016; 101: e1–e2. DOI: https://doi.org/10.1016/j.resuscitation.2016.01.017

74. De Silva AP, Stephens T, Welch J, et al. Nursing intensive care skills training: A nurse led, short, structured, and practical training program, developed and tested in a resource-limited setting. *J Crit Care*. 2015; 30(2): 438.e7–438.e11. DOI: https://doi.org/10.1016/j.jcrc.2014.10.024

75. Buist AS and Parry V. The American Thoracic Society methods in epidemiologic, clinical, and operations research program. A research capacity-building program in low- and middle-income countries. *Ann Am Thorac Soc*. 2013; 10(4): 281–289. DOI: https://doi.org/10.1513/AnnalsATS.201304-0810T

76. Binagwaho A, Kyamanywa P, Farmer PE, et al. The human resources for health program in Rwanda – New partnership. *N Engl J Med*. 2013; 369(21): 2054–2059. DOI: https://doi.org/10.1056/NEJMsr1302176

77. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2015; 385(9963): 117–171. DOI: https://doi.org/10.1016/s0140-6736(14)61682-2

78. Dare AJ, FuSH, Patra J, et al. Renal failure deaths and their risk factors in India 2001–13: Nationally representative estimates from the Million Death Study. *Lancet Glob Heal*. 2017; 5(1): e89–e95. DOI: https://doi.org/10.1016/s2214-109x(16)30308-4

79. Dare AJ, Ng-Kamstra JS, Patra J, et al. Deaths from acute abdominal conditions and geographical access to surgical care in India: A nationally representative spatial analysis. *Lancet Glob Heal*. 2015; 3(10): e646–53. DOI: https://doi.org/10.1016/s2214-109x(15)00079-0

80. Schell CO, Castejegn M, Lugazia E, et al. Severely deranged vital signs as triggers for acute treatment modifications on an intensive care unit in a low-income country. *BMC Res Notes*. 2015; 8: 313. DOI: https://doi.org/10.1186/s13104-015-1275-9

81. Bellani G, Laffey JG, Pham T, et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care
units in 50 countries. *JAMA*. 2016; 315(8): 788–800. DOI: https://doi.org/10.1001/jama.2016.0291

82. **Weiss SL, Fitzgerald JC, Pappachan J**, et al. Global epidemiology of pediatric severe sepsis: The sepsis prevalence, outcomes, and therapies study. *Am J Respir Crit Care Med*. 2015; 191(10): 1147–1157. DOI: https://doi.org/10.1164/rccm.201412-2323OC

83. **Levy MM, Rhodes A, Phillips GS**, et al. Surviving sepsis campaign: Association between performance metrics and outcomes in a 7.5-year study. *Intensive Care Med*. 2014; 40(11): 1623–1633. DOI: https://doi.org/10.1007/s00134-014-3496-0

84. **Reinhart K, Daniels R, Kissong N, O’Brien J, Machado FR and Jimenez E**. The burden of sepsis – A call to action in support of World Sepsis Day 2013. *J Crit Care*. 2013; 28(4): 526–528. DOI: https://doi.org/10.1016/j.jcrc.2013.04.012

85. World Health Assembly Resolution – Improving the Prevention, Diagnosis and Management of Sepsis. https://apps.who.int/gb/ebwha/pdf_files/EB140/B140_R5-en.pdf Published 2017.

86. **Schultz MJ, Dunser MW, Dondorp AM**, et al. Current challenges in the management of sepsis in ICUs in resource-poor settings and suggestions for the future. *Intensive Care Med*. 2017; 43(5): 612–624. DOI: https://doi.org/10.1007/s00134-017-4750-z

87. **Noritomi DT, Ranzani OT, Monteiro MB**, et al. Implementation of a multifaceted sepsis education program in an emerging country setting: Clinical outcomes and cost-effectiveness in a long-term follow-up study. *Intensive Care Med*. 2014; 40(2): 182–191. DOI: https://doi.org/10.1007/s00134-013-3131-5

88. **Writing Group for the CHECKLIST-ICU Investigators and the Brazilian Research in Intensive Care Network (BRICNet), Cavalcanti AB, Bozza FA**, et al. Effect of a quality improvement intervention with daily round checklists, goal setting, and clinician prompting on mortality of critically ill patients: A randomized clinical trial. *JAMA*. 2016; 315(14): 1480–1490. DOI: https://doi.org/10.1001/jama.2016.0291

89. **Vukoja M, Kashyap R, Gavrilovic S**, et al. Checklist for early recognition and treatment of acute illness: International collaboration to improve critical care practice. *World J Crit Care Med*. 2015; 4(1): 55–61. DOI: https://doi.org/10.5492/wjccm.v4i1.55

90. **Folayan MO, Brown B, Haire B, Yakubu A, Peterson K and Teegi J**, Stakeholders’ engagement with Ebola therapy research in resource limited settings. *BMC Infect Dis*. 2015; 15: 242. DOI: https://doi.org/10.1186/s12879-015-0950-8

91. **Dunning JW, Merson L, Rohde GGU**, et al. Open source clinical science for emerging infections. *Lancet Infect Dis*. 2014; 14(1): 8–9. DOI: https://doi.org/10.1016/S1473-3099(13)70327-X

92. **U.S. Critical Illness and Injury Trials Group Program for Emergency Preparedness ISAR and EIC**. Short-period incidence study for severe acute respiratory infections: USA experience. *Crit Care Med*. 2016; 44(12): 236. DOI: https://doi.org/10.1097/01.ccm.0000509318.34169.a4

93. **Barr J, Fraser GI, Puntillo K**, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med*. 2013; 41(1): 263–306. DOI: https://doi.org/10.1097/CCM.0b013e3182783b72

94. Pediatric acute respiratory distress syndrome. *Pediatr Crit Care Med*. 2015; 16(5): 428–439. DOI: https://doi.org/10.1097/PCC.0000000000000350

95. **Serpa Neto A, Schultz MJ and Festic E**. Ventilatory support of patients with sepsis or septic shock in resource-limited settings. *Intensive Care Med*. 2016; 42(1): 100–103. DOI: https://doi.org/10.1007/s00134-015-4070-0

96. **Kwizera A, Festic E and Dünser MW**. What’s new in sepsis recognition in resource-limited settings? *Intensive Care Med*. 2016; 42(12): 2030–2033. DOI: https://doi.org/10.1007/s00134-016-4222-x

97. **World Health Organization (WHO)**. Pocket Book of Hospital Care for Children: Guidelines for the Management of Common Childhood Illnesses; 2013. http://www.who.int/maternal_child_adolescent/documents/9241546700/en/.

98. **World Health Organization (WHO)**. Oxygen Therapy for Children: A Manual for Health Workers; 2016. http://www.who.int/maternal_child_adolescent/documents/child-oxygen-therapy/en/.

99. **World Health Organization (WHO)**. Paediatric Emergency Triage, Assessment and Treatment: Care of Critically-Ill Children Updated Guideline; 2016. http://www.who.int/maternal_child_adolescent/documents/ paediatric-emergency-triage-update/en/.

100. **World Health Organization (WHO)**. IMAI District Clinician Manual: Hospital Care for Adolescents and Adults. 2011. http://www.who.int/hiv/pub/imai/imai2011/en/.

101. **World Health Organization (WHO)**. Handbook for Clinical Management of Dengue WHO and Special Programme for Research and Training in Tropical Diseases (TDR) Report; 2012. http://www.who.int/denguecontrol/9789241504713/en/.

102. **World Health Organization (WHO)**. Guidelines for the Treatment of Malaria; 2015. https://www.who.int/malaria/publications/atoz/ 9789241549127/en/.

103. **World Health Organization (WHO)**. Clinical management of patients with viral haemorrhagic fever. A pocket guide for the front-line health worker; 2016. http://www.who.int/csr/resources/publications/clinical-management-patients/en/.

104. **Clark M, Spry E, Daoh K, Baion D and Skordis-Worrall J**. Reductions in inpatient mortality following interventions to improve emergency hospital care in Freetown, Sierra Leone. *PLoS One*. 2012; 7(9): e41458. DOI: https://doi.org/10.1371/journal.pone.0041458
105. Papali A, Eoin West T, Verceles AC, et al. Treatment outcomes after implementation of an adapted WHO protocol for severe sepsis and septic shock in Haiti. J Crit Care. 2017; 41: 222–228. DOI: https://doi.org/10.1016/j.jcrc.2017.05.024

106. Cubro H, Somun-Kapetanovic R, Thiery G, Talmor D and Gajic O. Cost-effectiveness of intensive care in a low-resource setting: A prospective cohort of medical critically ill patients. World J Crit Care Med. 2016; 5(2): 150–164. DOI: https://doi.org/10.5492/wjccm.v5.i2.150

107. Sutherland T, Musafiri S, Twagirumugabe T, Talmor D and Riviello ED. Oxygen as an essential medicine: Under- and over-treatment of hypoxemia in low- and high-income nations. Crit Care Med. 2016; 44(10): e1015–6. DOI: https://doi.org/10.1097/CCM.0000000000001912

108. Risko N, Calvello EJ, de Ramirez SS, Narayan M and Hirshon JM. Including emergency and acute care as a global health priority. Int J Emerg Med. 2011; 4: 75. DOI: https://doi.org/10.1186/1865-1380-4-75