


WHAT'S NEW IN INTENSIVE CARE



Intensive care for COVID-19 in low- and middle-income countries: research opportunities and challenges

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The impact of the coronavirus disease 2019 (COVID-19) pandemic has been felt worldwide. However, of the 10 countries with the highest number of COVID-19 patients and deaths, seven are low- and middle-income countries (LMICs) [1]. As of the end of August 2020, more than 9 million cases had been reported in just two LMICs: Brazil and India. In these 2 countries, more than 200,000 deaths have been recorded to date. Current data show that in Brazil and South Asia, mortality rates among ventilated intensive care unit (ICU) patients are high: up to 66% [2]. At the same time, there remain large global variations in the incidence, severity and outcomes of this illness. The basic epidemiology of the pandemic, including in LMICs, has already been well described [2–4]. However, given that over 75% of the global population resides in LMICs, and agencies such as the WHO have warned that the worst of the pandemic may be yet to come, its potential impact in LMICs, both on patients and on healthcare workers, is difficult to overstate. This editorial summarises the present situation from the perspective LMIC critical care research, highlighting possible opportunities, responses and challenges.

Critical care provision in LMICs is challenging in non-pandemic times with the quality of care and outcomes in these settings lagging behind what is observed in

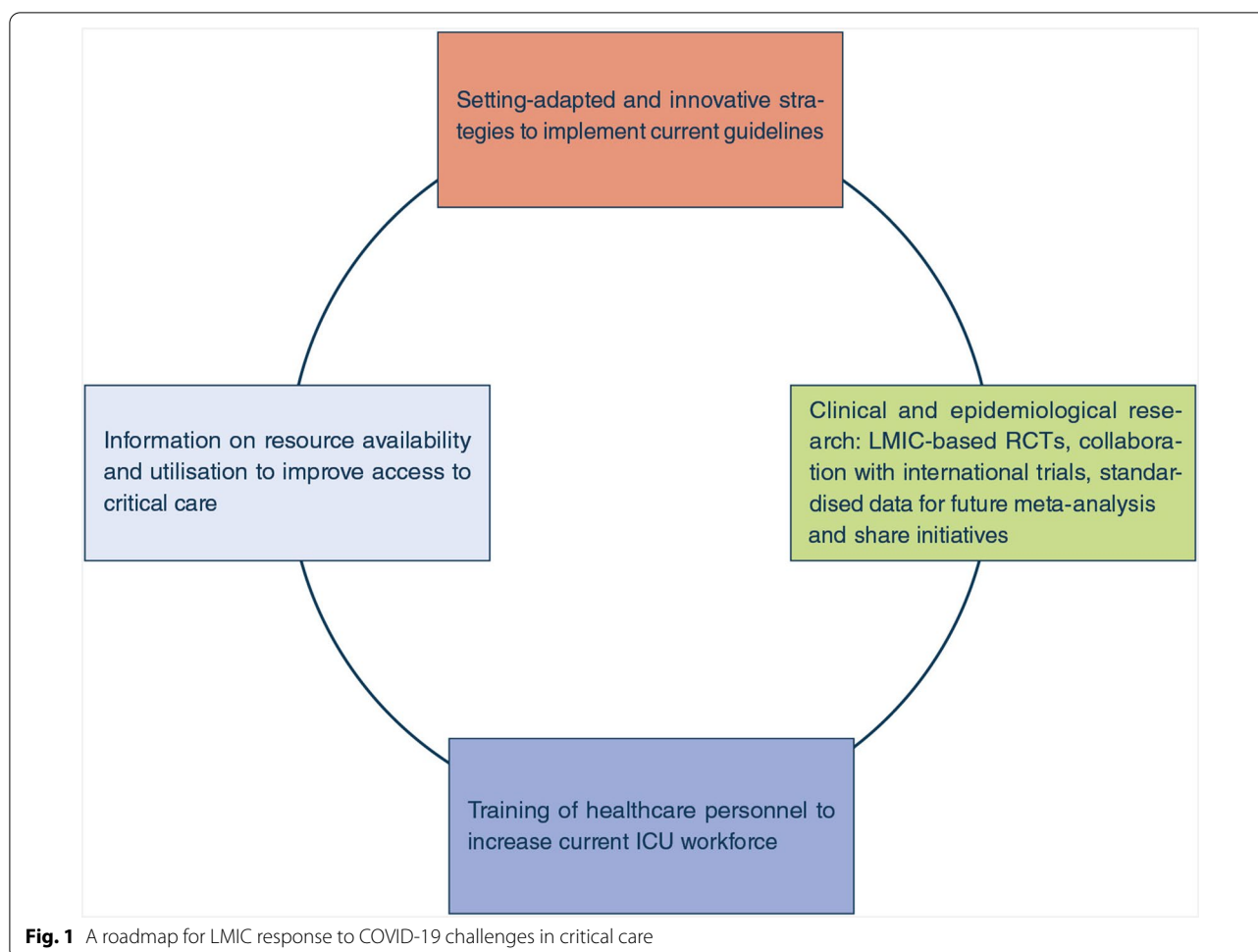
high-income country (HIC) settings [5, 6]. The pandemic has disrupted health system structure and organisation, resulting in a de-prioritisation of healthcare evaluation, improvement and research.

The pandemic is exacerbating endemic shortages in staffing and infrastructure, and has the potential to overwhelm services: access to emergency and critical care beds is limited, oxygen supplies inadequate, the scope for recruiting extra staff with acute care training scarce, and healthcare quality evaluations exceptional [7–9]. In Brazil, the provision of ICU care during the pandemic has been boosted through the creation of an additional 9000 ICU beds. Despite these efforts, Brazil is the country with the second highest number of deaths and is among the top ten when corrected for its population.

Although many of these challenges affect HICs, too, the scale of the pandemic, combined with the fact that critical care services in LMICs are already overburdened, means that specific setting-adapted and innovative strategies are needed (Fig. 1). When resuscitation guidelines for sepsis patients were directly adopted in LMICs, unexpected adverse outcomes became evident [7]. Similarly, even though guidelines on ICU organisation and preparedness during the COVID-19 pandemic exist, the adoption of such measures, primarily designed for HICs, are not straightforward in LMICs [10, 11]. Through examination of a series of aspects— isolation, quarantine and social distancing measures, information management strategies, healthcare system (including ICU) access, and diagnostic capacity—, a better understanding of the factors contributing to

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differences in infection and mortality rates between countries is needed.

Encouragingly, multidisciplinary LMIC-based networks are responding to the unprecedented challenge of this pandemic with collaborative initiatives in the fields of epidemiology, quality improvement, research and data sharing. Despite limited funding from local agencies, large randomised clinical trials have been initiated. In Latin America alone, there are currently 162 COVID-19 investigator-initiated clinical trials in progress [10]. Currently, Bricnet (the Brazilian Research in Intensive Care Network) and other Brazilian research groups are conducting several trials, including 7 simultaneous multicentre studies including ICU patients, to test interventions such as azithromycin, dexamethasone and hydroxychloroquine in patients with moderate-to-severe disease [10, 12]. The nine-country Wellcome-supported Crit Care Asia (CCA) network is operationalising the pandemic arm of REMAP-CAP [13] as a registry-embedded platform trial in South Asia, reducing the logistical, methodological and

financial barriers to interventional research participation by resource-limited settings.

Initiatives for public reporting of clinical characteristics and outcomes have been made available through LMIC networks such as CCA, the Brazilian intensive care registry, and the Argentinian society of critical care [14–16]. The Clinical Characterisation Protocol of WHO/ISARIC (a global federation of clinical research networks, providing a coordinated research response to outbreak-prone infectious diseases) is allowing these initiatives to be carried forward. These networks operate across a large number of LMIC hospitals, gathering and reporting daily information on all ICU patients. These LMIC initiatives have complemented more international efforts led by ISARIC and others, ensuring wider global representation. In parallel, data sharing among LMICs and HICs has been made possible through LOGIC, an international benchmarking initiative [2], and further secondary sharing of LMIC data with ISARIC and WHO is under way.

LMIC-based evaluations can be crucial both for the operational pandemic response and for research

purposes. Accurate daily updated data from LMIC ICU networks are providing essential information regarding resource utilisation, bed availability and staffing [12]. This information directly informs local and international stakeholders in the pandemic response, helping them to identify human resource gaps for reinforcement by additional staff, for example, or to manage the placement of new equipment such as ventilators. The networks are also supporting efforts to evaluate the impact of the pandemic and response measures, such as lockdown, on non-COVID patient services and staff.

Important COVID-19 respiratory research questions with a particular focus on LMICs remain unanswered. Some examples concern: the peripheral saturation threshold for the initiation of oxygen therapy, the optimal target saturation during oxygen therapy, the comparative effectiveness of different non-invasive ventilatory devices, the utility of awake proning, the optimal time for initiating mechanical ventilation, and the timing of tracheostomy. Also, the effectiveness of strategies that may prove effective in HICs (i.e. steroids and immunomodulating agents) should be tested in LMICs, since scenarios characterised by higher variability of care and with different rates of ICU-acquired complications (e.g. multiresistant bacteria infection) may blunt the effect of a given intervention. Given the ingrained scarcity of critical care beds, oxygen, ventilators and ICU staff, as well as the impracticality of manifold increases in these precious resources in LMICs, answers to these questions could also help with resource allocation, in addition to informing individual patient care [5]. Questions regarding the safety and optimal model for ward-based delivery of critical care, focusing particularly on nursing ratios and upskilling of staff in response to the pandemic, are particularly amenable to LMIC-based investigations. The disproportionate impact of the pandemic on ethnic minorities in HICs requires urgent, but fair, comparisons between these same groups internationally, in order to identify underlying risk factors and targets for intervention.

Finally, although no objective data on this issue are readily accessible, LMIC-based investigators are often under-represented in international non-governmental organisations responding to emergencies such as the present pandemic. The presumed inability of LMICs to implement improvement interventions and participate in observational and interventional research, a presumption reinforced by the chronic barriers highlighted previously, creates a vicious cycle leading to unrepresentative datasets, impractical guidelines and parachuted research projects. The increasing participation of LMIC-based networks in collaborative multi-centre observational and international research, quality improvement drives, and innovations, often alongside HICs, is generating

hope that LMIC critical care priorities, both pandemic and non-pandemic related, might now be effectively addressed. The improved capacity of LMIC actors to influence these conversations in a meaningful manner may prevent the disenfranchisement of large parts of the Global South and lead to further investment from funders. Such an outcome may at least mean that lessons from this pandemic have been learned.

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Compliance with ethical standards

Conflicts of interest

JIFS and RH are founding members of LOGIC (icubenchmarking.com)—an independent, non-profit collaborative of ICU registries.

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