patients with and without preadmission metformin treatment: a Danish registry-based cohort study. *Ann Intensive Care* 2020; **10**: 36
9. Reitz KM, Marroquin OC, Zenati MS, et al. Association between preoperative metformin exposure and postoperative outcomes in adults with type 2 diabetes. *JAMA Surg* 2020; **155:** e200416
10. Cameron AR, Morrison VL, Levin D, et al. Anti-inflammatory effects of metformin irrespective of diabetes status. *Circ Res* 2016; **119**: 652–65

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Mechanical ventilators for low- and middle-income countries: informing a context-specific and sustainable design

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Editor—The COVID-19 pandemic transiently raised the need for greater intensive care mechanical-ventilation capacity around the world. Whilst ICUs were under immense pressure globally, several high-income countries (HICs) did not ultimately require novel prototype ventilators, as standard ventilator supplies were sufficient to meet demand. In contrast, mechanical-ventilation capacity was, and largely remains, insufficient in the vast majority of low- and middle-income countries (LMICs), limiting access to critical care and surgery.[1]

Standard ventilators used in HIC hospitals are unaffordable and unsustainable for hospitals with limited resources in LMICs. In response to the COVID-19 pandemic, some non-governmental organisations specifically began work on designing ventilators for LMICs. However, to our knowledge, no one has systematically surveyed a variety of LMIC sites to understand the contexts and challenges that need to be addressed in ventilator design.

Here, we identify the key technical requirements for the design of a context-specific and sustainable mechanical ventilator for use across LMICs.

We performed a cross-sectional survey aimed at providing an overview of mechanical-ventilation capacity and infrastructure in LMICs. The information was requested with reference to typical working patterns, not specifically to any surge in service demand, like that associated with the COVID-19 pandemic waves. Results from this survey and those available in the literature were critically considered to identify key technical parameters to support the design of a context-specific and sustainable mechanical ventilator. Ethical approval was not required for this survey because it did not require patient data. The study followed the Enhancing the Quality and Transparency of Health Research Network guidelines and standards for reporting qualitative research.

The survey (Supplementary Appendix) consisted of 63 questions used to define respondents' profiles, their hospitals' characteristics, current mechanical-ventilation infrastructure and environment, and the estimated need for mechanical ventilation, associated maintenance and monitoring equipment. The survey was shared *via* e-mail to 16 anaesthesia and critical care national and international societies and healthcare institutions, and *via* social media, directly reaching out to a convenience sample of 81 LMICs as defined by the World Bank.

Fifty respondents, mostly anaesthetists (45%) and intensivists (44%), with >6 yr experience (72%), from different large teaching and public hospitals (76%) contributed from 23 LMICs in Africa, Asia, and Central and South America. Characteristics of respondents and their institutions are presented in Supplementary Table S1, country-by-country details are listed in Supplementary Table S2, and the geographical distribution of responses is illustrated in Supplementary Figure S1.

Supplementary Table S3 summarises the availability of power and gases. Loss of electricity was found to occur daily 19% (9/48), weekly 25% (12/48), less frequently 48% (23/48), or did not occur 8% (four/48). The majority of these outages (72% [31/44]) were reported to last <2 h, with back-up power from external fossil fuel generators and batteries reported to be supplied within 1 h in 91% (40/44). This electricity availability was similar to that reported in a survey of 10 hospitals in Tanzania.[2] As access to electricity varies within most LMICs, where larger hospitals typically have more reliable supply,[3] the design of a context-specific mechanical ventilator needs to include an emergency battery to supply electricity, but our results suggest that the battery power may only be needed for a few hours (Table 1), limiting the cost for this relatively expensive component.

Compressed air was always available in 35% of hospitals, either piped 68% (19/28) or *via* cylinders 29% (eight/28) (Supplementary Fig. S2). Oxygen was reported as always available in 74% of hospitals, at high pressure either piped 44% (20/46) or *via* cylinders 46% (21/46), or at low pressure *via* concentrators 11% (five/46). This oxygen availability was lower than observed in 99 Sri Lankan ICUs, where piped oxygen was available,[6] and lower than in 10 hospitals in Tanzania.[2] Our result on oxygen availability matches a survey of 97 clinicians from public district and provincial hospitals in urban and rural areas in 19 countries throughout Africa, Asia, and South America, where 75% reported that oxygen was available most or all of the time[7] and is similar to that reported from 97 Ugandan anaesthetists, where 63% always had access to oxygen.[8] Overall, our results were more conservative than or comparable with those obtained from a total of 293 respondents plus 10 hospitals across 22 LMICs, supporting that our findings are representative of a broader scenario. Considered together with evidence from the literature,[2,6,8] our results on compressed air and oxygen availability suggest that the design of a mechanical ventilator for hospitals with limited resources may need to include an air compressor and either a gas cylinder or an oxygen concentrator (Table 1), where modular designs would allow integration of features as necessary.

Most institutions (96%; 48/50) reported having emergency departments, operating theatres, and ICUs, and 4% (two/50) reported having only two of these three resources. Supplementary Figure S3 displays the number of ventilators that were functioning, non-functioning, and perceived to be required for each of these three departments. More than half of respondents (25/48) reported that ventilators were used 7 days a week, and 15 of these reported they were in use 24 h per day. ICUs had the greatest estimated requirement for ventilators with 28% (13/47) requiring more than 15, 40% (19/47) requiring from six to 15, and 32% (15/47) requiring from zero to five ventilators per Unit. Emergency departments and operating theatres required a relatively smaller number of ventilators, with 76% (35/46) and 50% (23/46) requiring

Table 1 Overview of key requirements for the design of a mechanical ventilator usable and sustainable in low- and middle-income countries. Bold text, requirements identified by this survey; italic text, requirements based on prior work,[4] expert opinion, and on the authors' baseline experience of known needs. *For electricity international standards, see International Electrotechnical Commission guidelines: https://www.iec.ch/world-plugs; †98% (135/137) LMICs have either 220 or 230 V, AC, and 84% (115/137) LMICs have a frequency of 50 Hz; ‡listed in order from highest perceived importance from our survey (see Supplementary Fig. S6 for details); ¶apart from suction, all these monitoring priorities match the recent recommended standards of monitoring during anaesthesia and recovery;[5] §calibration and testing systems need to consider environmental conversion factors (e. g. high altitude); ||tolerance error <10%; #30 ml for ventilation in neonates. AC, alternating current; CE, Conformité Européenne; DC, direct current; FDA, US Food and Drug Administration; LMICs, low- and middle-income countries; PEEP, positive end-expiratory pressure.

Parameter	Requirement
Electricity supply	**AC: 100–240 V; 50/60 Hz; DC: 12–30 V; battery operation >2 h*†**
Compressed air	**Air compressor***
Oxygen supply	**Oxygen concentrator to deliver >10 L min^{-1}* or green-labelled gas cylinder to support 2 h of operation**
Electricity and gas supply	**Match the national infrastructure (e. g. gas connectors, compatible gas pressures, electricity voltage and frequency, plugs, and sockets*)**
Operating temperature	**15–35°C**
Operating humidity	**20–70%**
Patient monitoring‡¶	**Pulse oximetry, noninvasive BP, electrocardiography, airway oxygen, pressure and flow, end-tidal carbon dioxide, and suction**
Internet connectivity	**Network access for remote device monitoring (location, usage, self-calibration,§ and self-testing reports) and firmware updates**
Consumables costs	**<US$ 50 per patient per day**
Support: technical and training	*Local or in country as a priority, long-term contract for remote support, built-in self-calibration system, product life cycle*
Manufacture, assembly, and testing	*In country as a priority, bench testing to meet regulatory standards; continuous operation >14 days for critical care applications; built-in self-testing system§*
Regulatory standards	*CE marked or FDA approved (or similar)*
Modes of ventilation	*Pressure and/or volume control; spontaneous breathing support if ventilation is required for >1 day*
Fraction of inspired oxygen	*Up to at least 80%*
Ventilatory frequency	*10–50 bpm; increments of 1 or 2||*
PEEP	*5–20 cm H_2O, in 5 cm H_2O steps or less||*
Inspired-to-expired ratio	*1:1 to 1:3*
Tidal volume	*50#–700 mL, in steps of 50 mL or less||*
Inspiratory pressure limits	*15–40 cm H_2O, in 5 cm H_2O steps or less||*
Alarms	*Gas or electricity supply failure, switched off, tidal volumes and pressures exceeded or not reached*
Filtering and humidification	*Bacterial/viral filter; heat and moisture exchanger*
Display and ventilation monitoring	Set and delivered *inspiratory pressure, tidal volume, ventilatory frequency, PEEP, fraction of inspired oxygen, and ventilation mode*

between 0 and 5 per Unit, and only 9% (four/46) emergency departments and 22% (10/46) operating theatres requiring >10 ventilators. A lack of funds and technical maintenance support combined was the most frequent reason for non-functioning or not using ventilators, where a lack of funding was cited in 74% (34/46) of responses (Supplementary Fig. S4).

The median reported minimum/maximum operating temperatures were 20/30°C, and humidity was 30/60%. The design needs to consider the different environmental working conditions, where temperature and humidity reported here were typically higher in LMICs than in HICs. Testing must be performed in a relevant range of temperature, humidity, and atmospheric pressure, depending on flow and pressure sensors used (Table 1).

Detailed information on the frequency of anaesthesia mode is presented in Supplementary Figure S5, the perceived importance of monitoring techniques in Supplementary Figure S6, and the proposed sustainable costs of consumables/patient/day in Supplementary Figure S7. Further results are presented and discussed in the Supplementary Appendix.

Table 1 summarises the key features to be considered when designing a mechanical ventilator to be useful and usable in LMICs, based on this survey's new and confirmatory findings, on evidence available from the literature,[1–10] on the authors' baseline experience of known needs, and on collaborators' expert opinion. The requirements listed in this table will not be fully applicable to the very wide variety of all LMIC sites. However, there will be similarities in resource-poor settings that are applicable to many sites. In this sense, the table considers the lower end of the resource spectrum and provides the 'lowest common denominator', which we think will capture some common issues of many sites. The trade-off between cost and sophistication is obvious, where in-country manufacture (or at least assembly) is needed for the design to be sustainable.

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Declarations of interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2022.01.007.

References

1. Baker T. Critical care in low-income countries. *Trop Med Int Health* 2009; **14**: 143–8
2. Baker T, Lugazia E, Eriksen J, Mwafongo V, Irestedt L, Konrad D. Emergency and critical care services in Tanzania: a survey of ten hospitals. *BMC Health Serv Res* 2013; **13**: 1–9
3. Adair TH, Gay WJ, Montani JP. Growth regulation of the vascular system: evidence for a metabolic hypothesis. *Am J Physiol* 1990; **259**: R393–404
4. US Food and Drug Administration. *Coronavirus disease 2019 (COVID-19) emergency use authorizations for medical devices* 2020. Available from: https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices. [Accessed 19 January 2022]
5. Klein AA, Meek T, Allcock E, et al. Recommendations for standards of monitoring during anaesthesia and recovery 2021. *Anaesthesia* 2021; **76**: 1212–23
6. Haniffa R, De Silva AP, Iddagoda S, et al. A cross-sectional survey of critical care services in Sri Lanka: a lower middle-income country. *J Crit Care* 2014; **29**: 764–8
7. Ginsburg AS, Van Cleve WC, Thompson MIW, English M. Oxygen and pulse oximetry in childhood pneumonia: a survey of healthcare providers in resource-limited settings. *J Trop Pediatr* 2012; **58**: 389–93
8. Hodges SC, Mijumbi C, Okello M, McCormick BA, Walker IA, Wilson IH. Anaesthesia services in developing countries: defining the problems. *Anaesthesia* 2007; **62**: 4–11
9. US Food and Drug Administration. *Appendix B: authorized ventilators, ventilator tubing connectors, and ventilator accessories* 2021. Available from: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/ventilators-and-ventilator-accessories-euas#appendixb. [Accessed 19 January 2022]
10. Ginsburg AS, Gerth-Guyette E, Mollis B, Gardner M, Chham S. Oxygen and pulse oximetry in childhood pneumonia: surveys of clinicians and student clinicians in Cambodia. *Trop Med Int Health* 2014; **19**: 537–44

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