



OPEN LETTER

REVISED **New technologies to improve healthcare in low- and middle-income countries: Global Grand Challenges satellite event, Oxford University Clinical Research Unit, Ho Chi Minh City, 17th-18th September 2019 [version 2; peer review: 2 approved]**

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Abstract




We report the outputs of a satellite event in Ho Chi Minh City, Vietnam, organized as part of the “2nd Global Grand Challenges of Engineering Summit”. The event considered challenges and potential solutions for improving low- and middle-income country (LMIC) healthcare systems, with particular reference to critical care. Participants from key regional and local stakeholders in healthcare and engineering discussed how new advances in technology, especially in the field of Artificial Intelligence, could be of potential benefit. This article summarizes the perspectives and conclusions of a group of key stakeholders from LMICs across South and South East Asia.



Keywords

LMIC, healthcare, machine learning, artificial intelligence, technology, engineering

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REVISED Amendments from Version 1

The updates for the text and addition of a table (new [Table 1](#)) were following reviewer comments. They asked specifically for a table and for extra examples related to critical care which have both been added. The (new) [Figure 4](#) was submitted in the original version but held back from publication whilst we confirmed permissions to use this. These have now been given.

Any further responses from the reviewers can be found at the end of the article

Introduction

In September 2019, The UK, US and Chinese academies of engineering co-hosted the 2nd Global Grand Challenges Summit in London. This event, inspired by the '14 Grand Challenges of Engineering' involved engineers, researchers, innovators, entrepreneurs, and policymakers from around the world to discuss the theme 'Engineering in an Unpredictable World'. As part of the summit, satellite events were held in India, Kenya, Mexico, Thailand, Uganda and Vietnam to discuss globally relevant topics related to the principle theme. In this report, we summarize the outputs of the Vietnamese event, which brought together key regional and local stakeholders in healthcare and engineering to discuss challenges and potential benefits of introducing new technologies to improve healthcare in low- and middle-income countries (LMICs).

Care quality in low- and middle-income country healthcare systems

Healthcare systems in many LMICs have undoubtedly improved over the last few decades. Areas such as maternal health and preventative medicine have benefited from a sustained drive to implement universal standards of care. Nevertheless, a recent report by the Lancet Global Health Commission estimated that almost 9 million lives and \$1.6 trillion in productivity are lost each year as a result of poor quality medical care, the majority of which occurs in LMICs¹. Important limitations in diagnosis and treatment were identified as causes of this, in addition to systems-level problems with safety, integration and continuity of care. Overall quality of care was worst in vulnerable groups, such as the low-income groups, and those with stigmatized conditions¹.

The Lancet Commission argues that providing any health system that is not of high quality is unethical². However, in improving care quality, health systems face many challenges, particularly with regard to critical illness, where providing healthcare is most complex, requiring highly-trained staff and expensive equipment for diagnostics and treatment. These challenges are often common to all resource settings, however in LMICs where resources are already limited, overcoming them may be more difficult.

This satellite event focused on the provision of high-quality care to critically ill patients and enabled a wide variety of engineering and healthcare stakeholders from the region to share perspectives on the potential for new technologies to improve health care and particularly critical care in LMIC settings.

Challenges to providing high quality care of critically ill patients: perspectives from South and Southeast Asian LMICs**Access to care**

In many LMICs, there is wide variation in access to healthcare services, and particularly large differences between care available to urban and rural communities. Throughout the world, in critically ill patients, when rapid assessment and treatment are necessary, ensuring timely access to services for remote communities is a particular challenge. In high-income settings, dedicated retrieval services have been employed to transfer critically ill patients to specialized centres. These are expensive and rely on non-specialist medical staff to triage and stabilize patients. In LMICs, even if there are rural health stations, staff may often have little or no medical training at all, and there are even fewer options to safely transfer their patients.

Appropriate diagnosis and treatment

Timely identification of critical illness and prompt implementation of treatment are vital in improving outcome in seriously ill individuals. Indeed, delayed diagnosis and slow initiation of treatment were both identified as the main reasons for poor quality of care by the Lancet Care Quality Commission². However, there are important contextual differences between LMICs and high-income settings, which necessitate innovative solutions to these challenges. For example, the causes of critical illness themselves are often different. In low-income countries, more than half of all deaths are due to maternal causes, nutritional deficiencies or communicable diseases compared to just 7% in high-income settings³. This means diagnosis may require different laboratory infrastructure and equipment in LMICs. In almost all critical illness, once a diagnosis has been reached, treatment requires expensive equipment and careful monitoring to assess response to treatment and anticipate complications early. Whilst these may be available in LMICs, usually this is only in a limited number of specialist centres⁴.

Health systems

LMIC health systems vary widely between countries making quality improvement measures and benchmarks difficult to compare. Increasingly, private providers provide critical illness care, but standards are variable, and lack of comprehensive regulatory systems are a further challenge to implementation of high-quality care. Corruption within some healthcare systems has been cited as a major barrier to advancement and sustainability of quality care, taking forms such as favouritism, informal payments, absenteeism or data manipulation⁵. An estimated 10–25% of global health spending is lost to corruption with unquantifiable impact on lives, communicable disease control or antimicrobial resistance⁵. In most healthcare systems, about 70% of recurrent healthcare resources are spent on people. In many LMICs, there are particular deficiencies in numbers and distribution of appropriately trained staff, thus improving management, distribution and training can have a huge impact on healthcare quality and outcomes⁶. As lack of knowledge amongst healthcare providers has been identified as a factor in itself preventing further development, WHO have stated that improving training and knowledge should be a priority⁶.

Cost of care

Critical care is costly due to the expensive treatments, sophisticated equipment and labour-intensive care required. Although healthcare coverage is increasing, in LMICs, many of these expenses are still passed directly as out-of-pocket costs to patients and their families⁷. Currently about 100 million people are pushed into extreme poverty every year as a result of out-of-pocket medical costs⁸. Additionally, many survivors are left with long-term disability which, in addition to costs of hospitalization, puts huge economic strain on families and communities.

Until now, intensive care units (ICUs) in LMICs have adopted similar models of care to those used in high income settings. However, the associated requirement for staff, equipment and training is limiting if not prohibitive in most LMICs (Table 1). Recent advances in engineering and technology may negate this need for costly staff and equipment, offering disruptive and novel alternatives to conventional care approaches.

Recent advances in engineering and technology in the healthcare context

Artificial Intelligence and Machine Learning: definitions and applications in healthcare

“Artificial Intelligence” (AI) refers to a field of computer science that accentuates the creation of intelligent machines that operate and react like humans. However, the general goal of AI is not well-defined because there is no general consensus on what specifically constitutes intelligence. Alan Turing, via his famous Turing Test, defined the goal of AI is to produce responses that are indistinguishable from those of a human (Figure 1)⁹. Early applications of AI in healthcare included expert systems, such as MYCIN¹⁰, which assisted physicians in diagnosing blood infections, and DENDRAL¹¹, which aided chemists in determining the structure of organic molecules. Unfortunately, these expert systems, which relied on static sets of predefined rules, failed to address the dynamic and the probabilistic nature of medical phenomenon and human activities.

Recently, Machine Learning (ML) and Deep Learning (DL) have gained more attention as principled frameworks to implement AI in the age of Big Data^{12,13}. ML focuses more on improving

the learning and the adaptation capability of machines and computer systems, given the continuing changes in its operational context, while DL introduces the neural network-based methodology where the learning process loosely emulates the information processing and distributed communication nodes in biological systems. Figure 2 puts AI, ML and DL into perspective, in which ML is a subfield of AI and DL is a specific methodology to improve the machine’s capacity to learn. ML is seeing gradual acceptance in the healthcare industry thanks to the capacity to analyze large sets of medical data in order to provide timely risk scores, precise resource allocation, and illness diagnosis. We review some major applications of AI and ML in improving the state-of-the-art in healthcare.

Enhanced diagnosis. WHO estimate that up to two third’s of the world’s population lack access to chest X-rays and diagnostics¹⁴. Whilst in many LMIC ICU settings, chest X-rays are available, there are limited number of experts able to interpret these images. AI, and DL in particular may provide a potential solution to this problem as they are well-suited to pattern recognition. Increasing numbers of publications show DL applications to chest radiography where a wealth of high volume datasets allow algorithms to be constructed¹⁵. Whilst to date, there are few examples specific to ICU or critical care, algorithms are able to distinguish common ICU-related X-ray findings, for example Chexnet, a deep learning algorithm detected pneumonia better than radiologists with up to 25 years of experience¹⁶. Whilst most studies pertain from high income settings, a recent study demonstrates that a DNN used to analyse chest X-rays from Indian hospitals perform similarly to four experienced radiologists¹⁷. AI has also been applied to MRI or CT. For example, DL systems improved accuracy of lung cancer detection from low-dose CT and a ML system for MR breast cancer detection has received FDA approval^{18–20}. Many LMIC ICUs lack access to CT and MRI, thus currently AI systems related to X-ray interpretation are potentially of greatest value. Here the ability to detect changes over time and with often sub-optimal images is a particular challenge to AI systems. AI and ML methods can also be applied to other modalities to aid diagnosis. With particular interest to critical care are AI methods of interpreting vital sign waveforms. Algorithms

Table 1. Barriers to providing high quality ICU care as identified by event participants.

Access	Limited number of critical care beds. Often highly centralized and difficult to access from remote areas
Cost	Lack of universal healthcare coverage High out-of-pocket costs to families and patients
Staff: numbers, training, accessibility	Low numbers of staff Less highly-trained staff Better trained staff concentrated in a few urban centres
Equipment and infrastructure	Lack of equipment (expensive) Difficulty maintain equipment Harsh operational environments (heat, humidity, power cuts etc) Lack of supportive infrastructure (imaging, laboratory etc)
Health systems	Lack of community services Lack of health system integration Limited health system data available

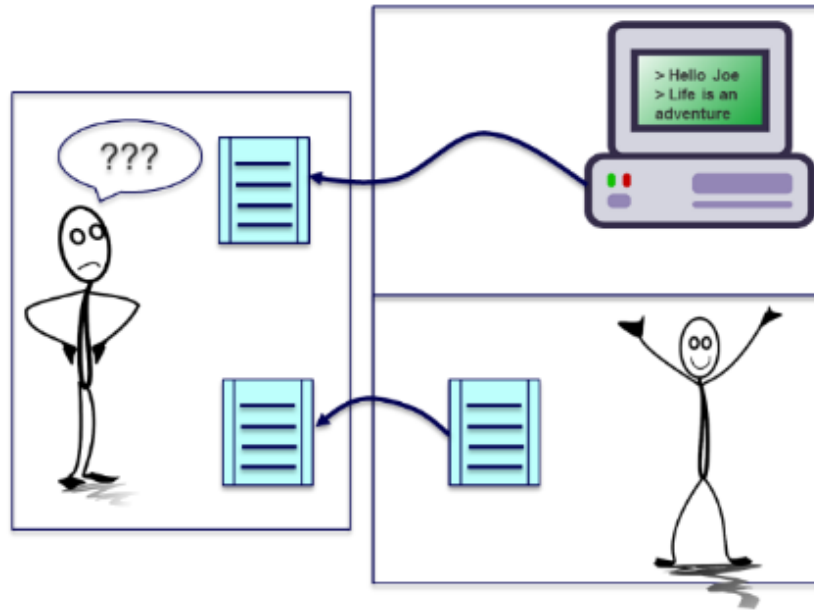


Figure 1. The Turing Test.

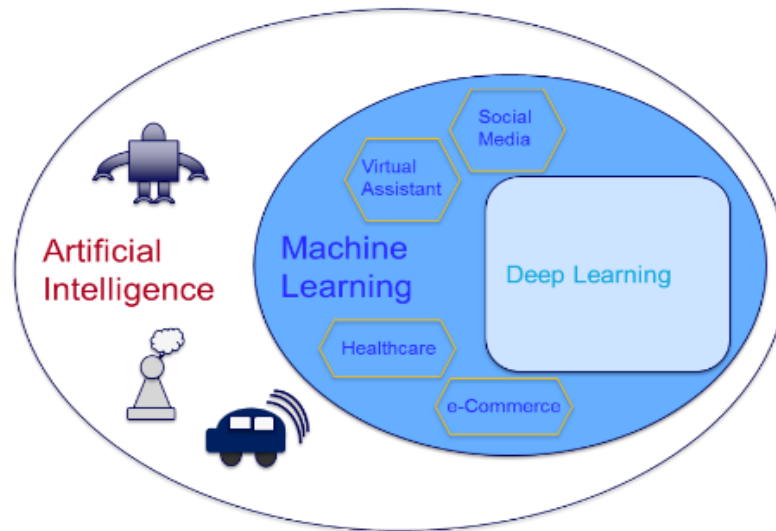


Figure 2. From Artificial Intelligence to Deep Learning.

applied to arterial blood pressure waveforms have been used to predict intra-operative hypotension and similarly to intracranial pressure waveforms predict the onset of raised intracranial pressure^{21,22}. Whilst these are clearly of utility in high income settings, in LMICs with little access to invasive monitoring, such systems may be of less value.

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Decision support. ML offers a framework for analysis of high-dimensional multimodal data, which is of particular advantage

in examining complex biomedical data, and shows promise in improving detection, diagnosis, and monitoring of disease. For critical care where there are often huge volumes of data, ML approaches are particularly attractive. In high income settings ML systems for early warning scores prognosis or sepsis prediction have been developed^{23–26}. Examples include recurrent neural networks to provide real-time prediction of post-cardiovascular complications such as mortality, renal failure, and postoperative bleeding²⁶, and prediction of optimal treatment sepsis using reinforcement learning²⁴. In this latter example, reinforcement learning methods were employed on a large multimodal critical care dataset to identify optimal treatment strategies for patients in sepsis. These were then tested using a different dataset, showing that patients who received treatments

closest to those suggested by the AI algorithm had improved outcome. There are limited data from LMICs and it is not clear whether HIC algorithms can be applied, especially as monitoring data in LMIC ICUs is much more limited in both frequency and type. Tanner *et al.*²⁷ develop decision tree algorithms that are capable of separating dengue from other febrile illnesses in the primary care setting (Figure 3).

Healthcare systems. To aid healthcare management, ML applications can be developed to better identify and track chronic disease states and high-risk patients, design appropriate interventions, and reduce the number of hospital (re)admissions and claims. For example, BERG’s Interrogative Biology platform uses ML to identify the molecular basis of efficacy and adverse events in order to map disease and treatments in oncology, neurology and other rare conditions²⁸. Such technology allows healthcare providers to take a more predictive approach rather than relying on trial-and-error. With growing use of electronic healthcare records in LMICs, these technologies are increasingly relevant to resource-limited health systems, particularly as many systems are designed around costing and billing. As already discussed, costs of ICU in many in LMICs results in huge out-of-pocket expenses. Better understanding of costs of ICU care may be able to allow appropriate interventions, use of resources and protect these vulnerable populations against excessive or disproportionate costs.

AI healthcare potential for critical care in LMICs. The above mentioned AI systems have potential for significant impact in LMICs and address many of the barriers to providing high quality ICU care as identified by the event participants. Reducing the cost and expertise needed to monitor and treat critically ill patients is an important step not only in improving patient outcomes *per se*, but also in reducing inequalities in service provision. For example, the requirement for highly trained radiology staff can be reduced with DL systems. Busy and less well-trained staff can be supported by ML clinical decision support systems trained or optimized on relevant contextualized data. Furthermore, as more countries embrace electronic health records, data from these could be used either for clinical decision support or healthcare service optimization.

There are already examples from event participants of initiatives towards using these technologies in LMICs. In Vietnam, ML-based clinical decision support tools for tetanus and dengue are being developed as well as DL image-analysis in tuberculous meningitis and dengue as part of the **VITAL (Vietnam ICU Technology Applications Laboratory) project**.

Nevertheless, despite these potential advantages there remain several challenges and limitations to the adoption of AI technologies.

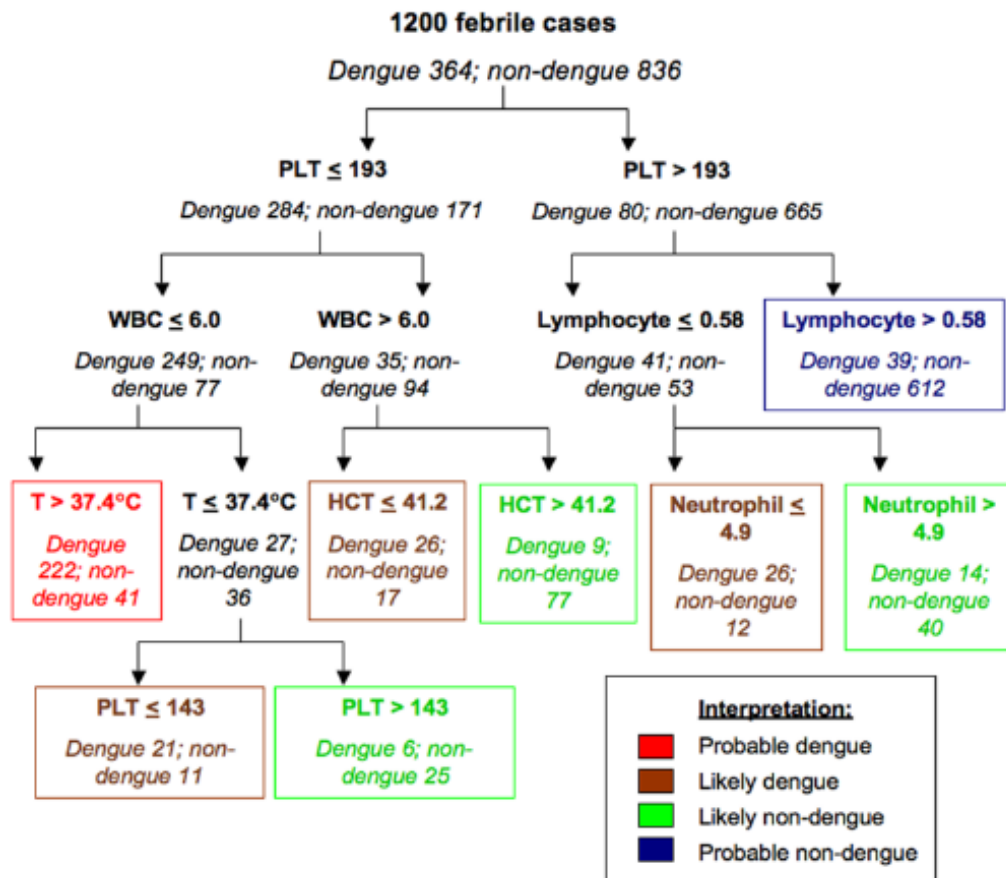


Figure 3. A decision tree for dengue diagnostics²⁷.

Other emerging technologies in healthcare

A new generation of information technologies including internet of things (IoT), big data, cloud computing, and crowdsourcing, has transformed healthcare to become not only more efficient and more convenient, but also more personalized, yet deliverable at low-costs. For example, patients can be equipped with wearable devices to monitor their health constantly. Another example is that of low-cost mobile devices can be used as live source of data for monitoring spread of diseases. We identify several trends in which healthcare systems, and in particular critical care, in LMICs can benefit.

Smart healthcare. The smart healthcare model focuses on enabling real-time monitoring and immediate feedback of health data in order to deliver timely medical interventions. This model drives on the emergence of implantable/wearable devices, and smart health information platforms, which are connected by IoT technology. In particular, by integrating advanced sensors with high-performance microprocessors, wearable/implantable devices can continuously sense and monitor various physiological indicators of patients in an intelligent manner. Another system developed by RMIT researchers detects human respiration using WiFi devices²⁹. The system does not require subjects to wear a device at all. Such technologies are particularly attractive in LMIC settings where wearable devices and monitoring systems (e.g. commodity WiFi devices) may be much cheaper (often <10% cost) and allow remote monitoring. Thus, solutions like this can support clinical care for isolated communities, requiring little equipment or significant on-site medical expertise. The primary challenges for such systems are the limited

battery life and maintaining a wireless network connection. Nevertheless, these technologies have shown to be improving comfort, while allowing sensed data to be combined with health information for better and more timely medical intervention.

There are many other uses beyond the ICU or for patients undergoing post-ICU rehabilitation. For example, the HCMC University of Technology and Education, Vietnam, demonstrated IoTs-based fall detection system, in which data collected from tri-axial accelerometer sensors and/or Kinect camera systems are transferred continuously to a cloud server for processing and detecting fall states³⁰. Fall detection and alerts can be sent to relatives or healthcare personnel for immediate medical assistance. Data could similarly be used to monitor recovery and rehabilitation as post-discharge medical services rarely exist in LMICs.

Crowdsourcing and Big Data. The concept of Crowdsourcing is to utilize the vast wealth of the public data to address social challenges including healthcare. For example, collecting and analyzing geolocation data from sensor-based and mobiles devices allows monitoring the spread of diseases or levels of air pollution. Such capacity provides data to better understand causes of disease or can enable prevention and control. Other uses of crowdsourcing data with geolocation technologies include measuring and predicting network performance and coverage, monitoring emergency responders' locations, tracking and backtracking disease carriers, and determining the effectiveness of quarantine and isolation (Figure 4).

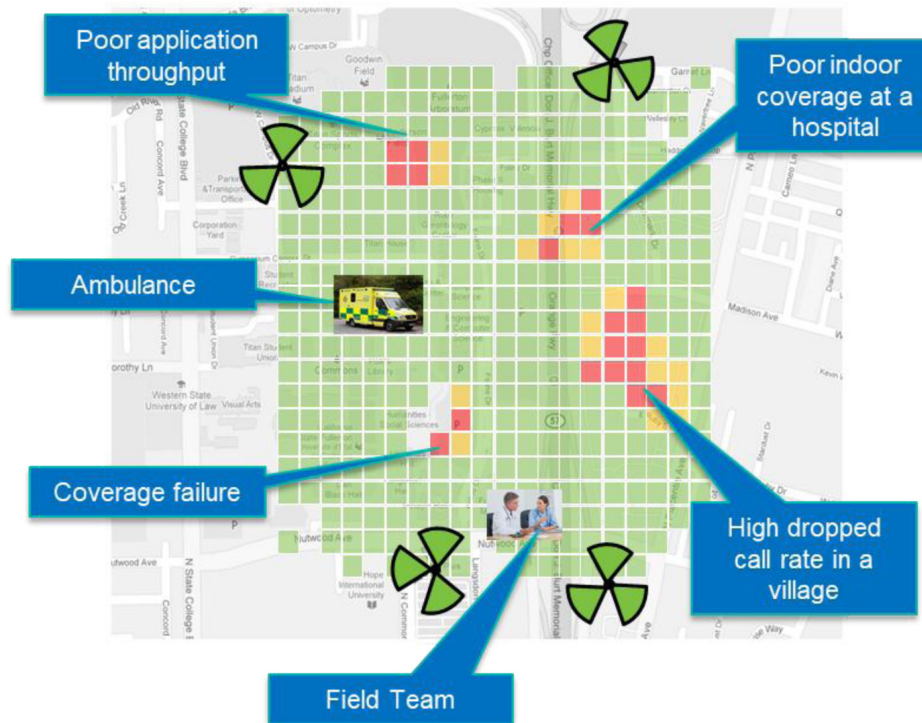


Figure 4. Monitoring emergency responders' locations. Figure adapted from "Applying Machine Learning in Managing Deployable Systems," 2018 IEEE International Symposium on Technologies for Homeland Security (HST)³¹.

In the critical care setting, large amounts of data are already routinely collected. In high income countries, national-level datasets are routinely gathered and are an invaluable resource for improving care quality and patient outcomes³². Improving the quality of these data in LMICs would facilitate similar improvements in these countries. One example of a successful platform is in Sri Lanka where an ICU registry provides accurate real-time data for network partners using a cloud-based platform³³. This platform has been expanded and adopted by 9 countries as part of the CRIT CARE Asia network and adopted in over 44 sites across the region³⁴. Data from the registry allows quality improvement initiatives and audit, with demonstrable benefits in ICU patient outcomes⁴.

mHealth and telemedicine. To date, smartphone ownership worldwide surpasses three billion and continues to grow in the next few years. In 2018, 48% of the global population were connected to the internet, and in LMICs mobile phones were the primary medium for this³⁵. South and Southeast Asia notably have amongst the world's most affordable mobile internet making these countries ideal sites for telemedicine services. In Vietnam 40% of the population are expected to have a smartphone by 2021. Such uptakes introduce the opportunity for mHealth, which focuses on improving the quality, efficiency and cost of healthcare via mobile platforms (see Figure 5). For example, a Cloud Telemedicine Information system, which consists of 100 devices to measure blood pressures and heart rate, can obtain live patient data to enable physicians to monitor patient's blood pressures online³⁶. This pilot cyber medical system, developed by the School of Biomedical Engineering of International University - Vietnam National Universities in Ho Chi Minh City, was successfully implemented in Binh Duong province (Vietnam) to test its efficacy. At the University of Medicine and

Pharmacy Ho Chi Minh City, the Department of Family Medicine leads a project connecting family doctors and patients through telemedicine. Whilst currently these projects mainly focus on non-acute care, there is potential for similar technologies to be used to support ICU care in remote sites, or for patients after discharge from hospital. The main focus of telemedicine in acute ICU care would be support of clinicians remotely. Such initiatives are being explored in Vietnam to support clinicians caring for patients with tetanus outside of specialist centres.

Issues of adopting emerging technologies in healthcare Despite much interest and enthusiasm in the technologies described above, the application in patient care has some limitations. Compared to traditional statistical analysis tools, many AI solutions (particularly DL) are considered 'black boxes' because outputs from AI models lack transparency and their rationale cannot be clearly explained. Using systems without clear biologically-plausible reasoning concerns many clinicians and regulators, especially if results have direct impact on patient care. There are critical questions around ethics, such as who is responsible for biases produced by AI. Finally, some practitioners consider AI a 'hype' because its recent success in other disciplines mainly due to the advent of brute-force computing power and the availability of more data. This sentiment generates caution in adopting AI and ML solutions in patient care and clinical practices. For mHealth and Big Data technologies there are concerns about data privacy and ownership. These issues may be particularly pertinent in LMIC settings where regulation and control may be lacking (Table 2). Additionally, concepts of data privacy and sharing are often very different in LMICs in our region and principals applied from HIC are not always acceptable. Establishing clear regulations in this area is, however a priority to allow appropriate development and application of these technologies.



Figure 5. mHealth infrastructure to support online monitoring of patient's condition.

Table 2. Barriers to adoption of Artificial Intelligence (AI) in low- and middle-income country healthcare settings.

Poor quality of data or insufficient volume due to data, especially health care data, is often in inconsistent formats and consists of a lot of noise and bias; limited infrastructure to collect data
Integration into existing clinical workflows
Lack of skilled staff to lead and use AI because it is challenging to find and employ staffs with both healthcare background and Machine Learning skills
No clear benefits from using AI because medical doctors often found AI outputs lack transparency to support medical decisions
Regulatory and legal requirements

Summaries and next steps

Improving the provision and quality of critical care in South and Southeast Asia is a significant step towards achieving sustainable development goals and improving quality of life in the region. Heterogeneity of health systems, remote rural populations and cost of providing critical care are significant barriers to achieving this.

During the satellite event in Vietnam, we identified a range of technology advances that are beneficial to healthcare systems in LMICs. However, these may have significant disruptive potential to conventional models of care provision, but ultimately offers cost-effective solutions for LMICs in the region. Nevertheless, significant barriers exist before such technologies can be widely employed, including technical, regulatory and behavioural challenges. This multidisciplinary meeting enabled professionals from relevant backgrounds to discuss key elements of this. Attendees made a firm commitment to maintaining working together in the future. This includes activities such as an international meeting in 2020, shared student projects and new research initiatives.

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Data availability

No data is associated with this article.

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Reviewer Report 21 August 2020

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 **James Malycha** 

Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK

This revision is excellent and addresses all the issues raised. There are some very small typo's so just do a final edit before final indexing.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: The deteriorating ward patient

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 13 August 2020

<https://doi.org/10.21956/wellcomeopenres.17778.r39969>

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 **Alejandra Aranceta Garza** 

Department of Biomedical Engineering, University of Strathclyde, Glasgow, UK

Authors have clarified all my comments.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Development of medical technology.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 30 June 2020

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James Malycha 

Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK

Reason for conference: focus on the provision of high-quality care to critically ill patients, enable various interested parties to provide input on potential for new technologies to improve health care (critical care specifically).

Challenges:

Access to care:

- *Rapid assessment and treatment are necessary*
In most developed countries, roughly 30% of critical care involves the management of non-acute patients requiring peri-operative care or patients with multiple comorbidities who are at higher risk of complications than other cohorts. I am unsure of the percentage in LMIC but it is probably reasonable to note that not all critical care patients are those that require rapid assessment and management plans.
- *...for remote communities, it is a particular challenge*
This is also the case for developed countries, and we get around this issue by funding expensive and skill dense retrieval services. The point being that I don't think this is an issue that is unique to LMIC. What may be worth commenting on is that these countries (may?) have a higher proportion of their populations in rural settings, making the logistics of servicing the population more onerous. A retrieval logistics are very expensive!
- *Even if there are rural health stations, staff may often have limited medical training and few options to safely transfer their patients to larger centres*
Retrieval services are very expensive (as mentioned above) and they have a very specific process of acquiring and maintaining skills (the details of which I am not knowledgeable). In Australia, the process of stabilising a critical patient in a remote location is often left to a non-critical care trained person until the retrieval service arrives. This is a hypothesis, but for this small aspect of critical care service provision perhaps LMIC countries are not as challenged as in other aspects?

Appropriate diagnosis and treatment:

- *In low-income countries, more than half of all deaths are due to maternal causes, nutritional deficiencies or communicable diseases compared to just 7% in high-income settings. This means diagnosis may often require more highly developed laboratory infrastructure and equipment in LMICs.*

I am concerned about this statement. I don't understand how maternal, nutritional and communicable disease critical care presentations require more developed lab infrastructure than, for example, trauma or cardiothoracic presentations which are very prevalent in developed countries? I'm not sure how this is distinctive for LMIC. They probably require different lab infrastructure. It may be worth emphasising this point. Or it may be worth emphasising that lab infrastructure is not as widely available (if that is the case, which I assume it might be).

Likewise, diagnostic tests being time-consuming doesn't seem a key issue in LMIC where the cost and availability of labour may be less of an issue than it is in developed countries. I don't think that is a major barrier to good care being provided. It certainly requires further expertise. Overall, my best guess (having had no experience in such a setting I must emphasise this it is a guess) is that a significant challenge is the provision and maintenance of highly trained clinicians and laboratory scientists/technicians working in concert in a timely manner for critical unwell patients. That is expensive both materially and in terms of human capital and is difficult to achieve when the social structures within which hospitals exist are not sufficiently developed. This involves extremely complex manufacturing, engineering and educational supply chains (about which I know very little) but may warrant mentioning and/or exploring. I'd certainly be interested to learn more.

Health systems:

- *Private health care provision is growing in LMIC, which is unregulated and standards vary. Additionally, they are prone to corruption (paraphrased).*

That seems very important but a broad description of the health systems as they currently exist in both settings and setting out a clear and concise description of the main differences and why that matter clinically in the critical care setting. A table would be intuitive and would help the reader. And there is no description of how/when/why corruption is more damaging to health systems in LMIC than in developed countries. I'd be very interested to know more.

- *Recognising the need to invest in the development, training and knowledge of clinical staff (paraphrased).*

This seems logical and important, but this statement is true of all health systems, developed or otherwise. How are their distinctions in the LMIC setting? How can these be targeted? With specific discussion around emerging technologies?

Costs of care:

- *Currently about 100 million people are pushed into extreme poverty every year as a result of out-of-pocket medical costs. Additionally, many survivors are left with long-term disability which, in addition to costs of hospitalization, puts huge economic strain on families and communities...*

This statement is startling and is of huge importance. One hypothesis might be that private health care provision (as mentioned above) is filling the gaps left by struggling publicly

funded health systems – which is possibly a ‘double edged sword’? I.e. because these private health systems are financially motivated, insufficient consideration and regulation is being adopted to prevent serious financial hardship post critical care. This raises important ethical/moral questions that might be useful to touch on briefly. It would seem logical to think such families in need of critical care support (which is usually life threatening) are vulnerable to predatory providers whose primary motivation is making money. How can we quantify this? Use technology to defend against this? Perhaps this opens an interesting line of thought around financial/tax data being used to indirectly improve critical care provision in LMIC? I.e. Maybe we need to think outside the box a bit?

- *...Recent advances in engineering and technology, however, offer disruptive and novel alternatives to conventional care approaches.*

This is encouraging but the author has provided no further detail on the matter. What disruptive and novel alternatives? Having been informed on the above issue, this would be useful to know. Little of what follows in the paragraphs below explores that in great detail.

Recent advances in engineering/tech in Healthcare:

AI/ML definitions:

- The descriptions of AI/ML are slightly confusing. These paragraphs are lacking a clear focus.

Enhanced Diagnosis:

- The author makes the point that AI/DL are particularly well adapted to pattern matching in radiology (although the 2 examples are for cancer detection, which has little or no relevance to most critical care imaging requirements). They then go on to mention that this might be helpful in terms of negating fatigue. That does seem useful but wouldn't a major challenge in LMIC be accessing highly trained medical staff? As such, a more obvious advantage might be the use of AI systems that quickly and reliably interpret radiological images in place of a doctor/under the remote supervision of a doctor (if indeed that AI can function at a similar level of accuracy). There are many caveats to that statement because the interpretation of an image also requires an understanding of the clinical context. This is particularly true in critical care, where the rapid evolution of pathologies need to be regularly reviewed, and forward and backward comparisons made to enable decision making. I would also guess that remote radiology might be highly applicable to LMIC where the availability of expertise might be limited? Figure 1 is also somewhat confusing.

Decision support:

- As above, these two examples have little or no relevance to helping decision making in critical care. The example provided (Komorowski) is highly relevant and it might be helpful to expand on exactly what they did, which was extremely interesting, innovative and exciting. It was slightly limited in certain ways and expanding on the positives and negatives of this example might be useful.

Healthcare systems:

- As above, examples not highly relevant to critical care. There are many applications of ML being used for the deteriorating patient (Churpek in particular). It might be worth mentioning those.

AI healthcare potential for critical care in LMICs:

The above-mentioned AI systems have potential for significant impact in LMICs and address many of the barriers to providing high quality ICU care as identified by the event participants

In light of what has been mentioned above, this statement needs to be better reinforced. I don't think the examples mentioned above demonstrably show potential to address the barriers to providing good critical care. Although I concede this might be open to interpretation. Regardless, I would also add that those barriers (described in the first section) have not been described sufficiently clearly and that would make a nice addition to the paper. Perhaps a table? E.g. Barriers to the provision of critical care in LMIC:

1. It's very expensive – how expensive? What is the comparison? Where might savings be made? What are the potential advantages of LMIC?
2. It's reliant on complex supply chains? Perhaps describe one or two as examples? Like a blood gas machine, a CT machine and an Infectious Diseases lab?
3. It's reliant on highly trained personnel – what are the barriers here?
4. Retrieval is challenging.
5. Public Health Service provision is limited.
6. Private Health Service provision is patchy and ethically ambiguous – this seems very important. Are there data to further inform this point in the paper?

Other emerging technologies:**Smart healthcare:**

- *Timely intervention of medical behaviour*
This sentence is confusing. Perhaps try it another way.
Wearables are still in the early stages but are evolving fast. Perhaps some critical care relevant examples in this paragraph. There is considerable work being done in Oxford on this. You mention trends where LMIC might benefit. Please describe them.
- *Such technologies are particularly attractive in LMIC critical care settings where wearable monitoring systems may be much cheaper.*
Can you provide examples of the cost comparison? This would be informative and relevant.
- *....and even allow remote monitoring and clinical decision tools to support patient care in isolated communities.*
This is an interesting point. The logistics of such an exercise would be very interesting to learn about. Perhaps consider expanding on this briefly.
You then expand on non-critical care related research – this is not relevant to the remit of this paper.

Crows sourcing and Big Data:

- Good points.

mHealth and telemedicine:

- Good points. However, critical care medicine is a particularly 'hands on' specialty making it difficult to extract benefit from telemedicine without careful planning. Was there anything in the conference discussion around this point?

Issues of adapting emerging tech into health care:

- You have mentioned: 1. Black box issues 2. Lack of clinician 'buy in' 3. Ethics 4. Data privacy – each of these seem to have merit but my best guess is that these four issues are not the key rate-limiting-steps when it comes to adapting tech into the LMIC critical care setting.
- I hypothesise the following are at least as or more important: ongoing technical limitations, the real difficulties around merging data-driven algorithmic outputs with health care systems that are (essentially) run by people, data inaccuracy, data delay, software/hardware maintenance, lack of data science expertise. I hasten to add I am not an expert in the LMIC domain so these are just guesses.

Conclusions:

- The barriers you mention were not really mentioned above. I think the conclusion should be a brief synopsis of the above points followed by your subjective interpretation of what this means.

Summary statement by the Reviewer:

- Thanks for the opportunity to review this interesting and important paper. It is an important topic that requires the attention and resources of the international critical care community. I have made suggestions which may help the author but I hasten to add I am not an expert on LMIC critical care provision so please interpret these comments with that in mind. There are some grammatical issues that need to be addressed. The headings are helpful but I'd argue that the examples provided are often not relevant to critical care, and those that are not sufficiently explored. The overall format of the paper might be worth simplifying and the author may consider adding in a table or two to summarise the key points. It also gives the impression that the discussions were very broad but not specific. This seems reasonable, but it might be helpful to mention that in the paper.

Is the rationale for the Open Letter provided in sufficient detail?

Partly

Does the article adequately reference differing views and opinions?

Partly

Are all factual statements correct, and are statements and arguments made adequately supported by citations?

Yes

Is the Open Letter written in accessible language?

Partly

Where applicable, are recommendations and next steps explained clearly for others to follow?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: The deteriorating ward patient

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 23 Jul 2020

C Louise Thwaites, Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam

The article is meant to reflect the proceedings of an event focused around LMICs rather than provide a comprehensive review of the field. Nevertheless, the comments have allowed us to include a high-income setting perspective into the article and many of the challenges faced by critical care services in LMICs are also present in resource-rich settings. We have reflected this in the second version of our article. Answering Specific points:

1. The reviewer raises an important point about the use of ICU beds for routine surgery or planned admissions. The participants however mainly wanted to discuss critically ill patients, not necessarily in ICU. We have clarified this by changing the sentence from critical illness to 'critically ill patients when rapid access and treatment are necessary'.
2. Ensuring access to care in rural communities is challenging in all communities and the text has been modified. However we feel in resource restricted settings challenges are more pronounced. Regarding rural health stations, our meaning here is that in LMICs, many rural health stations are staffed by non-health professionals with no or limited *medical* (certainly not critical care training) and transfers are done by foot, taxi or at best ambulances, usually accompanied by relatives only. Our participants felt that these were indeed different to HIC services.
3. Our section about differences in diagnosis was not a clear and the reviewer correctly queries this. The statement and has been revised in line with the comment and our original meaning. The group was trying to convey that the necessary infrastructure was different.
4. The section regarding private healthcare and corruption was also not clearly written and we have rephrased it to convey our meaning, i.e. that health care systems are variable and therefore difficult to compare and that the increased use of private healthcare makes it difficult to institute or evaluate quality improvement. Again the reviewer has correctly noted that this is not necessarily different in LMICs. The section on corruption has been expanded, but the article by Garcia (citation number 5) provides an excellent summary of the impact of corruption from the perspective of somebody directly involved in LMIC health service provision.
5. Concerning staff and training, these of course are problems in all healthcare settings, but our group felt that the difference in LMICs is that there are less resources to start with, therefore less staff, and that these staff are also much less equally distributed. This has been clarified in the text and readers can refer further to the WHO report specifically on this issue (citation number 6).

6. In many LMICs, private health providers are actively encouraged to develop to increase health system capacity. I am not aware of countries looking at the issues of financial hardship and many will rely on insurance companies to regulate cost of services. Generally private hospitals cater for more wealthy people with health insurance and it is not the private hospitals which are pushing people into poverty, sometimes the very poor will use them for convenience and speed. The approach in most countries is to aim for universal healthcare coverage. It is an interesting point that data may be useful to improve care and many countries are implementing electronic healthcare records which is very often driven by the need to provide medical insurance companies with accurate data. We have expanded the section on 'big data' to include this as a possibility.

7. We have expanded the sentence on potential roles of new technologies as an introduction to the latter sections.

8. The introductory paragraph on AI and ML have been altered. The first paragraph discusses AI as a field of study. The following paragraphs are on the application of AI in healthcare.

9. The enhanced diagnosis has been modified to include more ICU examples, but also note their limitations regarding LMIC application at present.

10. The decision support section has been expanded and further critical care examples included. Limitations regarding LMIC application are added.

11. Health systems in this section and our event, aimed to look at the larger scale health systems (mainly hospitals). Examples of critical care systems have been included in the above section. The value of ML applied to electronic health records and resource allocation/ costs of ICU care has been added.

12. A table of barriers to critical care provision has been added.

13. Examples of smart healthcare systems have been expanded, although as this section is meant to be more broad and less focused on critical care this has been reflected in the examples. As there are many different examples, an exact cost comparison is not possible but an approximate percentage estimate has been added.

14. We have expanded on the potential application of remote monitoring. We leave the more broad examples of local applications in this document but included why the examples, for example the fall-monitoring systems, are still relevant to ICU populations.

15. The section on telemedicine in ICU has been expanded and clarified with ICU examples added.

16. Regarding barriers to AI, this was not meant to be a comprehensive list but reflected views of participants. We have included infrastructure in the table. The other points are covered already in the table.

17. The conclusion represents the conclusion to the meeting. We have therefore expanded and re-titled this section to address the comments and be more clear.

Competing Interests: None

Reviewer Report 15 June 2020

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Alejandra Aranceta Garza 

Department of Biomedical Engineering, University of Strathclyde, Glasgow, UK

This open letter touches on very important issues in trying to improve healthcare provision and adoption of new technologies in LMIC. It reflects on an international event hosted at the Oxford University Clinical Research Unit in Ho Chi Minh City, Vietnam.

There are many important aspects that they discuss, from the complex (and almost impossible) task of a technology developed for HIC to be adopted by LMICs. The authors explained the different barriers and challenges in providing high-quality care in South and Southeast Asia, which is a complex, multivariate problem.

This letter comments on the importance and relevance of using machine learning and deep learning algorithms in order to help provide the best quality of care for LMICs, whilst not posing an excessive burden on an already tired healthcare system.

I believe, there are a couple of aspects that could be improved:

1. Figure 1 is a bit confusing, maybe the authors can add detail to Figure captions.
2. The authors could invite for further research/action by providing a list of recommendations from the satellite event.
3. The complexity of data protection in adopting cloud data systems was not discussed, this is a crucial aspect of telehealth and should be addressed from the beginning. If there was no discussion around the topic at the satellite event, the authors could perhaps make a note of it for future research on the topic.

Is the rationale for the Open Letter provided in sufficient detail?

Yes

Does the article adequately reference differing views and opinions?

Yes

Are all factual statements correct, and are statements and arguments made adequately supported by citations?

Yes

Is the Open Letter written in accessible language?

Yes

Where applicable, are recommendations and next steps explained clearly for others to follow?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Development of medical technology.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 23 Jul 2020

C Louise Thwaites, Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam

We have clarified Figure 1 to make it less confusing.

Unfortunately we did not as a group make any recommendations for future research. This would be a valuable component of any future meeting and is an excellent suggestion.

We have expanded the section about data security/ ethics in line with the comment.

Competing Interests: None