Factors to be considered in advancing pediatric critical care across the world

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Abstract

A narrative review of the many factors that have to be taken into account as we consider the advancement of pediatric critical care in multiple settings across the world. In this review we consider the extent of pediatric critical care (PCC), and the range of patients who are cared for in this environment. As we review the treatment and technology advances that are ongoing in the PCC setting, we also consider the structures and systems required to support these services.

As one takes into account the range of professional skills required for PCC we also consider the training and credentialling of personnel, and organisational structures required to facilitate patient care.

Finally we address the question of how pediatric critical care can be made sustainable in a volatile world with the impacts of global crises such as climate change.

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Introduction

Pediatric intensive care is a relatively new discipline, as outlined in several publications [1-3]. With the development of pediatric intensive care has come the conceptualization of pediatric critical care (PCC). One perspective is that PCC encompasses the care of children with a life-threatening illness or injury, or who require major elective surgery; that care includes everything from the first point of contact with healthcare services through to full rehabilitation at home [4]. The Pediatric Acute Lung Injury & Sepsis Initiative (PALISI) group have recently been addressing this issue via a systematic review and a Delphi study, while the World Health Organisation (WHO) has been focussing on what constitutes essential emergency and critical care medicine[5]. These initiatives underline the need for a lexicon of terms relating to the management of critically ill or injured children and an understanding of the interventions and standards of care that can and should be expected at each level of a healthcare system.

Across the world, there is a constant tension between the realities and aspirations of critical care in high-income countries (HIC), vs those of the low and middle-income countries (LMICs). To add to the complexity, there are communities in HIC that have very limited access to PCC and communities in LICs that have access to highly-resourced advanced care. Regardless of resource limitations, ensuring that resources are used to achieve the most good is important. However, an overarching principle should be that critical care involves many other disciplines and segments of society and should not be practised in isolation but in the context of overall care in society. (Figure 1)

Where does PCC begin and end?

There is increasing recognition that critical care should not be limited within the walls of an institution but should include care delivered in the community, the "pre-intensive care setting", as well as the care of children following discharge from paediatric intensive care units. There has thus been a proliferation of triage tools (for use in emergency departments or in mass casualty events [6]), early warning systems (to identify sick children in wards and healthcare systems [7]) and criticality indices [8] (to identify critically ill children within healthcare systems). Not all systems have been successfully implemented, and substantial change may be required within systems to ensure that critically ill children are identified and treated expeditiously (Figure 2).

There is a growing realization that patients (and families) that survive intensive care (and PCC) admission and treatment may develop long-term challenges related specifically to that experience. That is leading to increased research into the post-PCC discharge outcomes and quality of life. That has included a refocus of outcomes assessment (from PICU survival to hospital survival and on towards outcomes years later); from survival through to quality of life outcomes [9], and impact of pediatric critical illness on the family [10, 11] (and possibly the extended community). Adult and paediatric intensive care services are increasingly recognising the "post intensive care syndrome"[12] and are developing long-term follow up clinics to provide support and specialist care to "graduates" of those services.

There is recognition of the post-discharge mortality of critically ill children, particularly in LMICs [13-15]. The causes of the mortality may relate to what has happened within the hospital and the PICU, but may also relate to multiple factors that increase risk of severe illness including the child [16, 17], the home environment, social structures and the interactions of all these. There is increasing interest, but limited data, on the contribution of the "child context" to ongoing morbidity and mortality. Indeed, in some settings, PICU has also played the role of the "canary in the coalmine" in alerting healthcare systems about problems that are developing within communities.[18, 19]

Who is cared for in the PCC environment?

In the early years of pediatric critical care, there was a heavy preponderance of patients with acute infections and trauma. Across the world, the incidence of infections in previously well children has decreased dramatically as a result of improved living conditions, and immunization against many common childhood illnesses.[20]. In poorer countries, the impact of these measures has been substantial, but there are still areas of the world where previously well children suffer critical illness as a result of infections such as pneumonia, malaria, dengue, tuberculosis and diseases due to zoonotic pathogens (including cysticercosis and a range of bacterial pathogens). While the use of antibody preparations has reduced the impact of infections such as RSV in preterm infants in richer countries, the global burden of RSV remains substantial (particularly in LMICs) and the development of effective maternal and/or paediatric vaccines would have significant impact [21].

The development of disciplines such as pediatric oncology and transplant services have led to increasing numbers of children who develop complications related to their underlying disease processes and management, and are admitted to PICU with complex medical conditions and associated infections. In addition disciplines such as paediatric cardiac surgery are undertaking ever more complex procedures (often in neonates or very young infants) resulting in patient populations where appropriate therapy can only be provided by teams with detailed knowledge of those conditions and the associated physiology, and with access to sophisticated imaging and monitoring technologies. That is in contrast to poorer countries where the majority of PICU admissions are related to either infection and/or trauma in previously well children (despite the increasingly recognised burden of paediatric congenital heart disease in these regions [22]).

Medical advances in the recognition of "rare diseases"[23] especially in richer parts of the world have led to an increasing proportion of patients admitted to the PICU – often for long stays - suffering from these conditions. These conditions pose substantial challenges to the PCC team because of limited experience of treating patients with those conditions. Inevitably adequate clinical management relies on the development and experience of multidisciplinary teams [24] working in innovative ways. Related to the diagnosis and management of rare diseases, is the increasing utilization of genomic studies to provide potential diagnoses in these children [25-27] (particularly in critically ill infants). The use of these technologies raises new ethical dilemmas [28] regarding issues such as consent for these studies; dealing with unexpected results; dealing with results where the significance of the abnormalities detected is not known or understood. Currently, access to and utilization of many of these tests are limited to high-income countries.

An ongoing challenge in the PCC environment relates to the availability / non-availability of PCC bed spaces, particularly in LMICs. Processes to prioritize admission to the limited beds available are an ongoing consideration.[29, 30] Long-stay patients raise challenging issues in the PCC. While some of the long-stay patients may have good long-term outcomes, in general, they have worse outcomes than those admitted for short periods of time [31-34]. The underlying reality is that access to PCC beds requires the allocation of substantial resources.

The COVID-19 pandemic has overwhelmed adult critical care resources leading to PCC communities caring for adolescents and young adults. At the other end of the age spectrum, neonatal care has frequently overlapped with PCC, particularly in the management of infants requiring surgical intervention (for many years most neonatal cardiac intensive care, has taken place under the ambit of pediatric intensivists). There is a growing need to provide advanced neonatal services including respiratory support [35], and particularly to provide neonatal surgical and anaesthetic support in LIMCs [36]. This creates an opportunity to integrate the neonatal and pediatric peri-surgical services and PCC.

Generally, adolescents in LMICs are cared for in adult intensive care units. This is problematic because their specific needs are not being met. A particular concern is that the adult units may not be attuned to the physiology of congenital heart disease. That becomes increasingly relevant as the global population of "grown-up patients with congenital heart disease" now exceeds the population of children with congenital heart disease

The treatment and technology advances in PCC

Over time, the technology available for diagnostic and therapeutic purposes in the PICU has become increasingly sophisticated. That provides wonderful opportunities to optimize therapy, but also carries inevitable associated costs to provide maintenance; supply ongoing consumables (usually disposable and not for repeat use) and train all the PICU staff to the appropriate levels of competence and expertise with that equipment.

There is growing realisation that interventions to provide organ systems can cause injury to patients. This might be a direct injury, for example from excessive airway pressures or tidal volume [37], or indirect from medication (sedative drugs).[38] and procedures (vascular access) [39] that facilitate these therapies.

We are starting to understand the complexity of the risks and benefits of even basic interventions for critical illness. Formal, larger-scale clinical trials in acutely unwell children are refining our practice. We now understand that less aggressive blood transfusion [40] or glycaemic control [41] and conservative use of parenteral nutrition [42] are not associated with worse outcomes. More conservative use of oxygen therapy [43-48], fluid administration [49-53], vascular access, antibiotic therapies [54] all have evidence to support them. There is growing awareness to titrate all of these therapies to the needs of specific patients; to specific and appropriate endpoints and goals; and with awareness of the associated adverse effects of all these interventions.

Across the board there has been a move towards the "minimum safe intervention" with the wider use of less invasive therapies, particularly respiratory support, where technologies such as high flow humidified nasal oxygen, nCPAP and non-invasive ventilation strategies with physician supervised monitoring [55-58] appear to have been effective in some groups of patients (e.g. bronchiolitis, WHO defined severe pneumonia with hypoxaemia, undifferentiated respiratory distress) and associated with reduced complications. Several major collaborative research networks are investigating options for less aggressive therapies in formal trials [58]. However there is substantial work required to determine how these therapies should be implemented.

The development of collaborative research networks (e.g. the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) across the world has increased research output significantly with developing focus on randomized controlled trials. A recurrent theme in multiple structured literature reviews on a wide range of topics has been the lack of robust evidence on which to base treatment recommendations for PCC. Unfortunately there remain concerns about the relationship between regions of high PCC mortality and those of high research interest and output. There are concerns about the very high rate of negative results from costly randomized control studies [59], and there are ongoing concerns about the processes and priorities in research in LMICs [60].

Over the last decades, there has been huge focus on the development of definitions and guidelines for conditions such as "Sepsis" [61, 62], "paediatric ARDS" [63]. This approach has been associated with substantial improvements in outcomes for patients with these clinical syndromes in some parts of the world. However, there is increasing realisation that these syndromes may have considerable heterogeneity, and may include a number of different phenotypes [64, 65] each of which requires different treatment, and may have different outcomes. We may need to consider moving away from

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the large categories of conditions to focus on the characteristics and needs of individual patients [66], or at least smaller groups of patients. With the development of new genomic, metabolomic and proteonomic technologies for the diagnosis of specific conditions and the identification of patients with particular responses (to the illness but also to the therapy), there is growing hope that we might be able to individualize care and deliver personalized medicine.

In many ways, this issue highlights the different challenges across the world. In many parts of the world, the focus (justifiably) has to be on getting things right most of the time for most of the patients (the 80:20 rule, see Table 1). In the absence of multiple highly trained professionals with sophisticated diagnostic and therapeutic resources, we have to find protocols and processes that can be implemented effectively by teams with less training and resources. That will have the most positive impact on the most patients (but inevitably compromise the care of some individuals). By contrast in HICs, the resources and skills are available to recognise relatively subtle differences between groups; to apply a wide range of contrasting therapies. PCC will serve fewer patients and save fewer lives in that setting but will do a better job for individuals.

What supporting structures and systems are required?

PCC cannot function in isolation. In many parts of the world infrastructure such as transport systems, stable power supplies, consistent clean water supplies, appropriate waste disposal systems and communication systems are taken for granted. Unfortunately, in many (if not most) LMICs many of these structures are not reliably in place, and that places great stress on the team to provide bridges to overcome these difficulties.

From a medical equipment perspective, reliable implementation of high technology services relies on well-established and functional supply chains (for both capital equipment and consumables) [67], support and maintenance infrastructure (particularly the presence of trained technologists), financial structures and controls. It is surprisingly difficult to introduce innovations in equipment and processes in an environment where there is little established infrastructure to validate and license the use of new equipment and systems.

From the medical consumable perspective, access to consumables and pharmaceuticals (such as essential antibiotics [68]) may be extremely limited in LMICs, and, to make financial pressures even worse, many medications are relatively expensive in these countries.

Provision of PCC may be challenging without optimal laboratory and medical imaging services together with blood transfusion services. Unfortunately, many of these services are substantially suboptimal in LMICs [69]. There is considerable opportunity developing in the current era with the development of point-of-care laboratory systems and particularly with the use of ultrasound systems (which have become portable, relatively robust and affordable). Unfortunately, there will be pressure on scarce staff to become competent in the utilization of this sort of technology.

One of the consequences of relatively easy access to antibiotics, extremely limited resources for microbiological services, and poor implementation of infection control is the looming menace of antibiotic resistance across the world [68]. This is a very real threat to PCC in the future.

The development of electronic healthcare records EHCR) for PCC has already had a huge impact in high-income countries (not always positive). EHCR has the potential to support PCC with data collection and optimization of multiple processes. Unfortunately, implementation has not always been successful, and inevitably requires a substantial infrastructure to support the system. However innovative use of computer records in areas such as East Africa has shown some remarkable benefits at very low cost [70].

How do we know that our staff are competent?
The issue of competence in PICU has become increasingly formalized in richer countries, whereas in poorer countries (but also often in the private sectors of rich countries) the level of surveillance over levels of staff competence is minimal. Defining and maintaining competence is potentially a very complex field. There is a need to ensure that new staff working in the PCC environment are given comprehensive training to utilize the equipment and the procedures that are available to them. This requires theoretical education, practical training and experience, and ongoing evaluation, both at the time of initial training and during ongoing clinical practice. Detailed licensing and credentialling processes have been developed in many areas e.g. point of care ultrasonography [71].

How are PCC services organized
PCC services have developed along multiple different pathways. In some centres PCC developed in close association with anaesthetic and perioperative services, and in those settings surgical patients (particularly related to disciplines such as neurosurgery and cardiothoracic surgery) have predominated in the patient population while the staff are predominantly from those disciplines. In other settings PCC has developed within the paediatric services, and many of these centres have focussed primarily on the care of patients with "medical" conditions, particularly infections. Over time these units have going through amalgamations and divisions into organ system-specific units.

There is substantial evidence to suggest that children are best cared for within paediatric CC services (vs mixed services with adults) [72], but there is also evidence that optimal patient outcomes may be achieved in specialist units (with the proviso that there is adequate allocation of staffing and resources) when there is adequate patient turnover to ensure appropriate training and experience for all cadres of staff.

One recent development has been the introduction of telemedicine as a tool to bring expertise and services to the children who are cared for in more remote areas of the world. [73].

Who works in PCC?
From initial units in HICs that were staffed with small numbers of nurses and doctors (relative to patients) PICUs have developed to include large multidisciplinary teams with high ratios of staff to patients. In the words of an editorial "it takes a well-educated village" [74] to staff and maintain the levels of care required in PCC.

Unfortunately poorer countries have not been able to emulate that growth, and so there is growing interest in the possibilities of incorporating the child caregivers (predominantly mothers) into the monitoring and caring team [75]. That particular process may be facilitated by the use of mobile devices to improve patient monitoring [76].

There has been substantial evidence over time (and in a variety of settings [77]) to show that the presence of pediatric intensivists in PCC is associated with improved patient outcomes. Some years ago there was evidence that (although training is essential), the presence of inexperienced residents in PCC was associated with worse outcomes [78]. More recently there has been increased emphasis in HIC on 24-hour intensivist presence in the PICU [79] which perhaps offsets that inexperience. On the other hand, in most LMICs, the presence of even a single trained intensivist is a luxury, and it may be impossible to ensure that there is 24-hour in-house subspecialist presence.. New developments in telemedicine are opening opportunities to "spread expertise", and make scarce, experienced intensivists virtually available to clinicians in less well staffed areas [73].

There is also substantial training required for nursing personnel, at all levels including advanced nurse practitioners [80] (who play a substantial role in management of the PCC environment in many HICs).

Apart from rigorous and ongoing training substantial clinical experience [81] makes a significant contribution to clinical care and patient outcomes. In addition there is evidence that limiting the resources available to train PCC nurses may be associated with worse outcomes. The development of training programmes for PCC nurses is a challenge in LMICs and one that is potentially a rate-limiting factor for the development of PCC services across the world. To that is added the complication of significant "brain drain" of trained nursing and medical personnel from LMICs to richer countries.

A major concern relates to the sustainability of professional careers in the PCC environment. There are persistent reports of high levels of "stress", moral distress [82], burnout [83, 84], and poor mental health among nurses and doctors working in the PCC environment. Most of this information comes from high-income countries, but as PCC expands in LMICs (where there are much lower staff numbers) burnout is likely to become a greater problem.

Since its inception paediatric critical care has been associated with expectations that healthcare workers will work long shifts and extended hours on duty. There are cultural shifts in expectations from both healthcare workers and their families about what hours and conditions of work are acceptable. Inevitably it appears that for many reasons many healthcare workers will no longer be prepared to work extraordinarily long hours, and this will impact on the workforce requirements, as well as the time taken to complete clinical training. While there is evidence that shorter shifts from nursing staff may be associated with improved patient outcomes, there are parts of the world where changing to shorter shifts is limited by concerns about the safety of staff travelling to and from work at different times of day. Failure to address these matters will inevitably lead to ongoing concerns about PCC development and sustainability.

Is PCC sustainable?

The sustainability of PCC in LMICs is a considerable concern. In a financial environment where national annual per capita expenditure may be less than $30, it is extremely difficult to justify the high daily costs of PCC, particularly if the outcomes are poor. In poorer countries, individuals and their families bear a substantial part of the burden of healthcare costs, and in countries such as India and neighbouring Bangladesh, it is possible to reduce entire families to debt and extreme poverty with the bills related to PCC. Financial systems will need to be put in place to ensure that individuals and their families are protected, while at the same time providing financial resources to support the care of critically ill children.

Even in richer countries there are major concerns regarding the amount of waste that is produced by large intensive care units, with largely disposable consumable equipment (which may amount to a substantial burden of waste per patient per day[85]). In the light of current concerns about climate change and pollution, these issues will have to be addressed.

What are the implications of global climate change for paediatric critical care

Global climate change may adversely affect the resources needed and the delivery of PCC. We know that global climate change has been associated with increased weather instability with more frequent extreme weather events and disasters across the world [86], with increasing food insecurity, population displacement and considerable human costs (lives, morbidity, financial and social). Children especially in poorer parts of the world are deeply affected by these events, and the need for PCC will follow [87]. Changing weather patterns have also been associated with changes in

the geographical distribution of insect borne diseases such as Dengue [88] malaria, and Chikungunya, and this is likely to continue.

Conclusions

As we look to the future of PCC across the world, we are faced with multiple challenges, some that must be faced by all practitioners in PCC, others that are widely divergent in different settings. Hopefully, we will be able to learn from each other as a community and address these challenges in ways that benefit children in all settings.

Tables

Table 1: Examples of the 80/20 rules in prioritizing PCC delivery

1	**Identify the top conditions that pose acute life-threats in that region** e.g., in many poorer countries, the commonest diagnosis at PICU admission are previously healthy children with acute life-threats that can be treated with relatively low resources, infections, pneumonia, severe acute malnutrition, poisoning, seizures, head trauma.	Identify simultaneously the "resource-suckers": Where 80% of treatment options/ healthcare costs are attributed to and only help 20% of patients?
2	**Enable task-sharing between health professionals** to bridge the quality gap in settings with restricted human resources *(EECC concept)*	Identify the top 20% of basic life-saving actions that must be performed by 80% of health professions in the facility (irrespective of primary role)
3	**Manage equipment/technology wisely** Higher volume of low-tech and lower-volumes of high-tech may be preferred in LMIC. *Factor in service and support availability, consumables*	Identify the 20% of equipment / technology can aid in the management of 80% of patients admitted to the health facility
4	**Prevention** Depending on the region, create a plan of top 3 *actionables* that can be marketed/ displayed to educate public to do more that brings more impact (vaccination/ clean water/ helmets..)	Identify which 20% of public actions can decrease 80% of the region's preventable child illness

Figures

Figure 1: A holistic approach to healthcare delivery

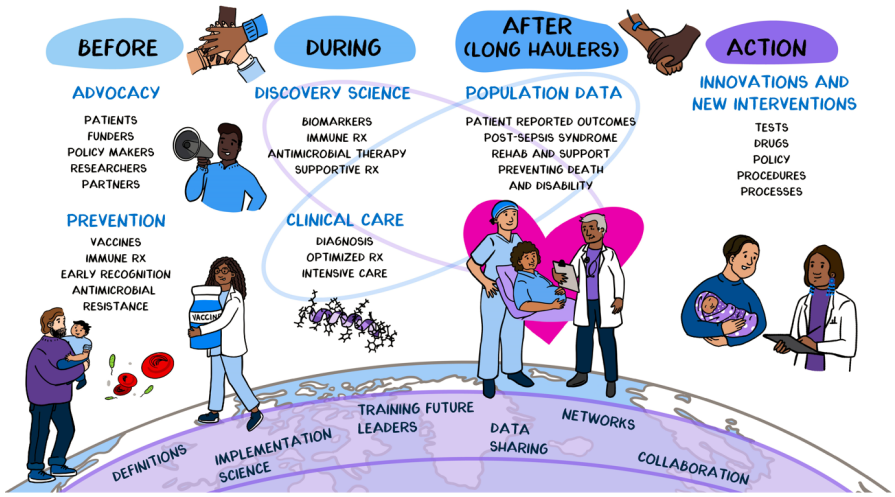
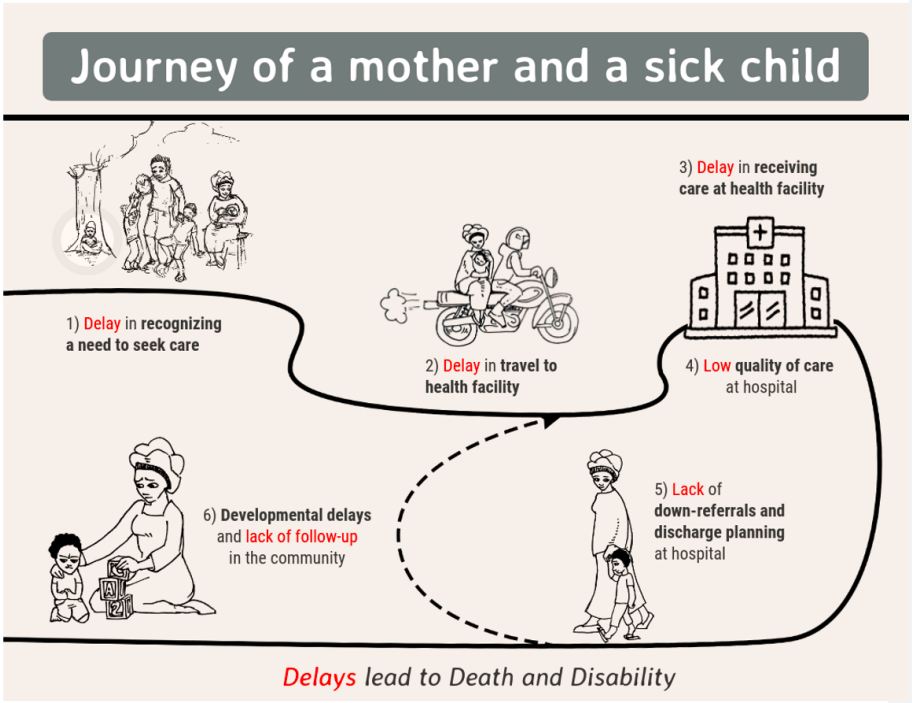


Figure 2: Journey of a mother and sick child: areas in need of intervention to improve pediatric critical care.



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