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Abstract

Pediatric critical care aims on saving the lives of sick and injured children, however, most children die without access to pediatric critical care. With progress towards attainment of the Millennium Development Goals across the world, there has been a significant drop in child mortality in most countries. As issues such as nutrition, immunization, access to clean water and sanitation, and access to healthcare are addressed, pediatric critical care will become an increasingly important part of any strategy to reduce childhood deaths. Critical care can only be beneficial in an integrated health system, but the time-sensitive nature of the care required by sick children poses specific challenges. As processes to recognize and treat sick children improve, the role of and need for intensive care services will increase. It is important that these services should be efficient as possible and should not develop de novo but within an integrated network for the provision of care for critically ill children.

Keywords

Critical care • Children • Developing world • Resource-limited settings • Mortality

Introduction

The ultimate aim of critical care services is to save lives and limit morbidity in the critically ill. However, globally the majority of children live in poorer countries and most childhood deaths occur in a few poor countries. Most children,

who die, live in circumstances where they have extremely limited access to any medical services and no intensive care facilities. Indeed, there is a link between mortality among children <5 years of age and the country per capita income, as can be clearly seen in Fig. 1.1, with most childhood deaths occurring in the poorest countries of the world. However, Fig. 1.1 also demonstrates that countries with similar incomes may have widely different mortality among children <5 years (consider South Africa, Brazil, and Chile), and countries with widely divergent incomes, may have similar mortality among children <5 years (consider Cuba and the United States of America). It is thus important to focus not only the resources that are available for the care of sick children, but among a myriad of factors, also on the way in which those resources are deployed and utilized.

Frustratingly we already know how to save most of the 23,000 children who die every day [1] although the implementation of those measures are complex and vary among different locations [2]. The interventions required to save those lives have been clearly outlined by several authors in the last decade [3–7]. The financial requirements of

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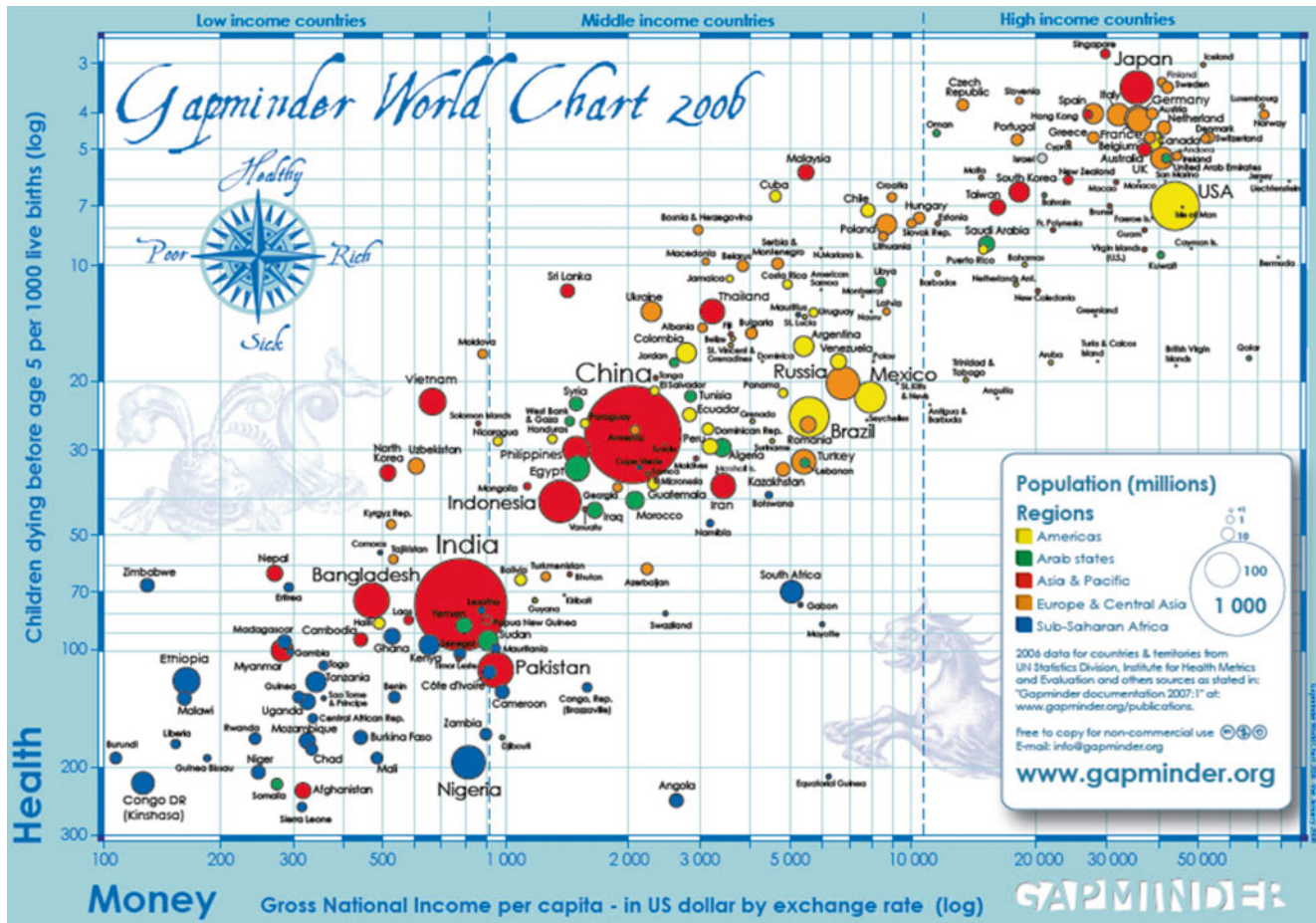


Fig. 1.1 The relationship between per capita income and under-5 mortality (Reprinted with permission from <http://www.worldmapper.org> © Copyright 2006 SASI Group (University of Sheffield) and Mark Newman (University of Michigan))

implementing those interventions have also been calculated, posing huge ethical challenges and dilemmas for policy makers and citizens in the small proportion of the world who control most of the international financial resources [5, 8, 9]. There can be little doubt, in countries where mortality for children <5 years exceeds 50/1,000 live births that the focus of child death prevention should be on immunization, maternal education and health, provision of clean water and adequate sanitation (together with programs to ensure personal hygiene and hand washing throughout communities), and access to basic healthcare resources [10]. There have been dramatic improvements in child survival wherever these services are implemented [3, 11].

Although the term “pediatric critical care” is often applied specifically to the care of children in the pediatric intensive care unit (PICU), the term more appropriately applies to “the treatment of any child with a life threatening illness or injury (or who requires major elective surgery) from the time of first presentation to health care services until discharge home and completion of rehabilitation” [12]. In this context, critical care services are not confined to any special unit or location

and includes interventions in a wide range of situations throughout healthcare systems, including training of villagers in basic first aid and resuscitation [13], provision of low-cost antibiotics to village healthcare workers [14], appropriate modification of the World Health Organization’s (WHO) Integrated Management of Childhood Illness (IMCI) protocols (see below), development of district hospital services [15, 16] and development of other aspects of hospital services [17], reorganization of emergency services at referral hospitals [18], provision of oxygen therapy for hypoxemic children [19–21], and development of emergency medicine services.

What Is Required to Provide Critical Care?

The underlying principles intrinsic to the development of critical care services for children are outlined in Table 1.1 and highlight the need for integrated systems that provide consistent and effective therapy for sick or injured children from presentation through discharge home (Fig. 1.2) [22]. In resource poor environments, many system changes

Table 1.1 The essential components of pediatric critical care

Focus	Recognition of life-threatening injury or illness Rapid response (in structured format) to issues that are likely to threaten life (ABC approach) Rapid intervention (surgery or medical therapy or both) to try and stop the development of further problems Ongoing attention to basic care (Airway, Breathing, Circulation, Disability/Drug therapy, Fluids, Glucose levels, Nutrition etc.) Search for underlying diseases processes that are amenable to therapy and then timely provision of that therapy
Team approach	Need for continuous care that is consistent and delivery by a multidisciplinary team with complementary skills Concern for the overall context of the child including the family and the community Care that crosses the conventional boundaries of medical disciplines
Structured organization	Need for a stable organizational structure and function that ensures that all the services, consumables, staff etc. are available as and when required Use of evidence based protocols (preferably ones that have been developed for local conditions and implemented using the team approach) Development structured protocols on issues such as discharge and admission policies (preferably ones that have been developed and agreed up by the health structures) Integration within the health care services of the region
Accountability	Monitoring of outcomes (and ideally resource utilization) Accountability to all interested parties
Sustainability	An underlying premise of the development of a critical care service must be that the resources are available to maintain and sustain that service over a reasonable period of time, without undermining other services within the health care services
Equipment	The equipment required for critical care can range from very basic (provision of oxygen and intravenous fluids) through to highly complex machines that are expensive and have very high operating costs

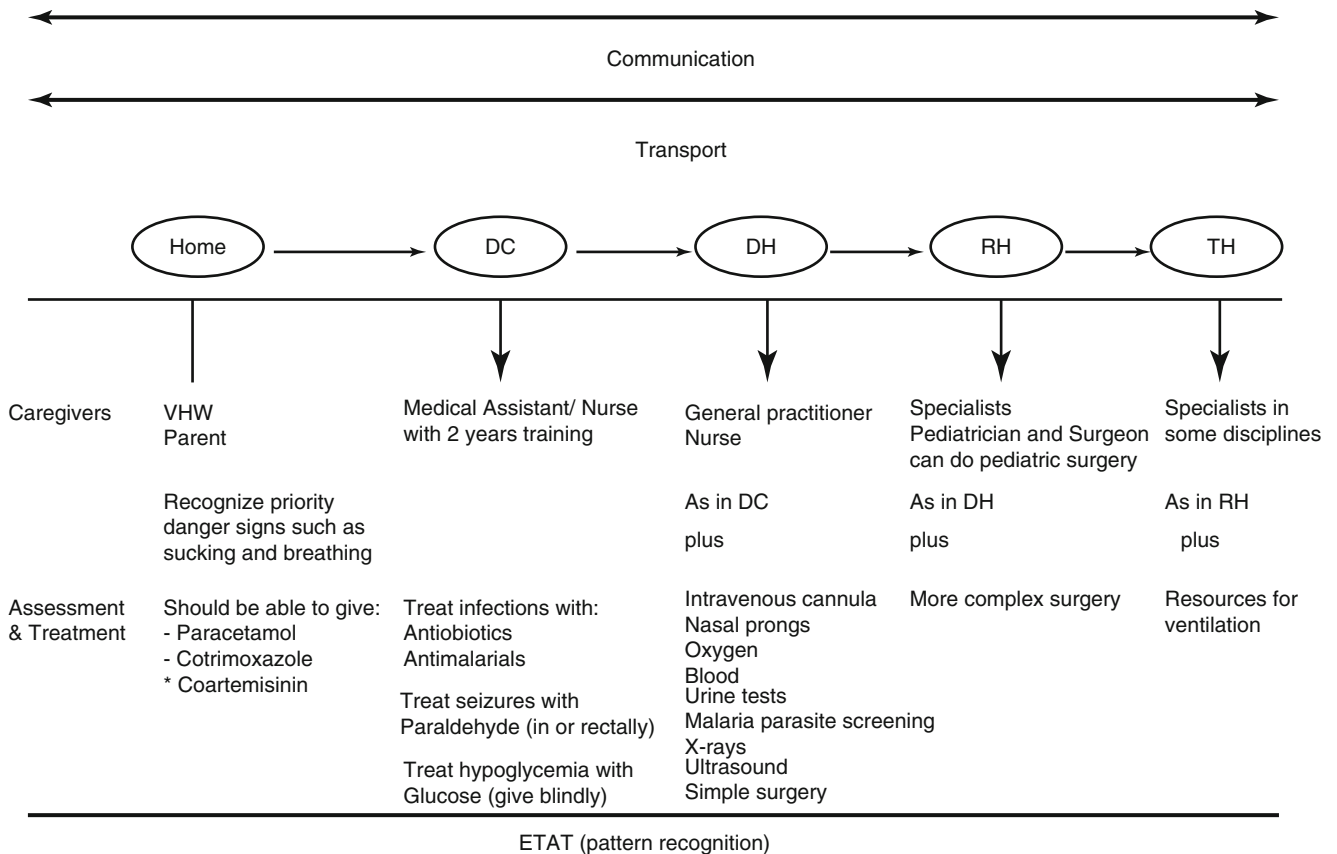


Fig. 1.2 The journey in seeking healthcare for the critically ill child. DC district clinic, DH district hospital, RH regional hospital, TH tertiary hospital, VHW village health worker, IMCI integrated management of childhood illnesses, ETAT emergency triage assessment and treatment

Table 1.2 Resources available for healthcare

Country	Income per capita (GDP per capita in US\$)	Government health expenditure per person per annum (current US\$)	Doctors per 1,000 population	Nurses per 1,000 population
USA	\$39,710	\$2,548	2.56	9.37
South Africa	\$10,960	\$114	0.77	4.08
Chile	\$10,500	\$137	1.09	0.63
Brazil	\$8,020	\$96	1.15	3.84
India	\$3,100	\$7	0.6	0.8
Nigeria	\$930	\$6	0.28	1.7

Based on data obtained from World Health Statistics 2006. World Health Organization (WHO). France; 2006

that can improve care and outcomes for the critically ill do not require major capital investments or substantial increases in resources. For example, a number of authors have described how reorganization of trauma and emergency services can significantly lower pediatric mortality from acute illness or injury [23]. In settings such as Northern Cambodia and Iraq, substantial reductions in trauma mortality were achieved by providing training to prehospital personnel [24, 25], while in Ghana innovative training programs for professional drivers reduced trauma mortality [26]. In Malawi, reorganization of pediatric emergency services at a large urban hospital substantially reduced pediatric mortality at minimal expense [18]. An important component of this particular reorganization was that pediatric trauma patients were channeled through a pediatric service, and not through an adult trauma service. Even within the developed world, there is evidence that children have better outcomes following severe trauma when managed in centers and by services that are focused on the needs of children [27–29]! At an international level, the WHO sponsored program for IMCI was developed in an attempt to standardize and improve the care quality of sick children across the world, with at least some evidence of success [2, 30–33]. The WHO program appropriately focuses on improvement in hospital care of sick children [17, 34].

Thus critical care principles can and should be applied to the provision of healthcare services for severely ill or injured children throughout the world and are not limited to intensive care units. However one of the specific requirements of critical care is the time dependency of effective therapy. In a range of settings, it has clearly been shown that early and effective therapy may substantially improve outcomes for critically ill patients. Time sensitive treatment is important in both adults [35, 36] and children [37, 38]. This may provide substantial challenges in resource limited settings, where transport services and access to surgical and anesthetic services (particularly for children) may be severely limited.

What Is Required to Provide Intensive Care?

Recently, a number of authors have suggested that intensive care services should be available to both adults and children throughout the world [39–42]. There is hardly any ethical justification for children in different parts of the world having different access to intensive care [10]. Ideally every child in the world should have ready access to appropriate medical care, however the simple reality is that in many parts of the world intensive care is unaffordable to children, as shown in Table 1.2 which highlights some of the resources available for healthcare in various parts of the world. When <\$10 is available per capita per annum for healthcare expenditure, it is simply not possible to spend \$100 per day on basic ventilatory facilities [40] let alone the \$1,000 per day as is commonly spent in modern intensive care facilities in the rich countries. However it is perhaps possible to spend the \$51 per patient required to provide oxygen therapy to children with pneumonia [20], and it is certainly possible to spend the \$6 per annum required to implement most of the measures required to substantially reduce child mortality, and the very low expenditure required to provide early antibiotic therapy to sick neonates in rural communities [14, 43, 44].

In contrast to critical care, intensive care can only be provided where there is substantial infrastructure in place. Recommendations for the facilities required for intensive care in countries such as the United States of America [45, 46] and the United Kingdom include substantial requirements for services such as trained staff (in PICU, in operating rooms, surgical staff, anesthesia), laboratory services, blood bank supplies, imaging equipment, etc. For many of the poorer countries in the world such facilities are either simply not available, or access and availability is extremely limited. However, the WHO recommends that intensive care facilities should be available in all hospitals that provide for major surgery [47]. In this context, they are referring to the provision of facilities with increased capacity for monitoring and intervention, not necessarily “intensive care” as would be expected in the richer countries. This recommendation highlights the

significant role that intensive care services may play in facilitating the development of surgical programs, with the capacity to perform major surgery on children.

It is also important to note that within the last decade there has been a substantial increase in the number of countries that have lowered the mortality rate among children <5 years to <20–30 per 1,000 live births, and where there has been an improvement in per capita income, and in the amount of resources available for the provision of healthcare services. In this context there is an appropriate growth in the availability of intensive care services for children. It is difficult to establish the growth in the number of PICUs across the world, but in countries such as China there have been substantial increases in the number of PICUs established and functional, as is illustrated by a recent report from 26 intensive care units with 11,521 patients over a 12 month period [48]. There is considerable variation in the reported outcomes for children from intensive care units in developing countries, with many units reporting very high mortality rates. Many reasons may contribute to the high mortality, including a high incidence of infectious disease [49] and trauma (compared to the high proportion of elective surgical patients seen in the PICUs of rich countries), late referral of patients due to difficulties in the overall delivery of critical care, inadequate PICU numbers for the patient load, poor selection of patients for PICU admission and management, high rates of nosocomial infection, low staffing ratios and infrequent presence of pediatric intensivists, and poor education of staff among others. To this end, a number of studies demonstrated that the presence of a pediatric intensivist lowers mortality in a developing world context [50, 51] with similar effects related to centralization of pediatric intensive care facilities [52].

There are considerable challenges in the provision of training programs for pediatric intensive care in the developing world, and a number of organizations such as the World Federation of Pediatric Intensive and Critical Care Societies (WFPICCS) have recently focused on programmes to provide educational materials [12]. There is also considerable debate around issues such as whether intensivists (or anesthetists) from the developing world should travel to rich countries for training, or whether it is preferable for rich countries to provide training support to developing countries [53, 54] – both options may be appropriate depending upon local circumstances.

Critical Care in Mass Disaster Situations

Complex emergencies include crisis, wars and natural disasters that adversely and acutely impact public health systems and its protective infrastructure (water, sanitation, shelter, food, health). Under these circumstances there is excess

mortality, usually greater than one death per 10,000 of the population per day. These complex emergencies seem to be more common in poorer regions of the world and their adverse impact greater because of inadequate resources even under stable conditions. Complex emergencies are dynamic with variable duration of impact, need for emergency services, recovery, rehabilitation and developmental processes. Critical care has a major role to play in these emergencies. While in the developed world there are networks of care and transport systems, robust infrastructure in many cases to combat these emergencies, in many parts of the world they are sorely lacking. The challenge in these settings may well be to improve existing critical care facilities (which will improve day to day care of patients) and hence increase the capacity to cope with disaster situations. Critical care during mass disaster situations and in austere environments are covered separately elsewhere in this textbook.

Ethical Considerations

While there are no ethical grounds for limiting the access of children in poor countries to intensive care [10], the reality is that children in poorer settings have access to fewer intensive care resources. In this situation there is a significant need to focus on the appropriate allocation of limited resources. When resources are limited ethical decisions around access to intensive care are related not only to the needs of the individual child, but also to the needs of the healthcare system and the implications of access to intensive care for the development of other important health programs. Thus there is increased focus on the ethical grounds underpinning the allocation of scarce critical care resources in developing countries [55, 56], with programs such as the accountability for reasonableness showing potential as a framework for decision making [11, 57, 58]. This stands in contrast to some of the ethical issues that seem to be in the forefront in richer countries [59].

Conclusions

While pediatric critical care is focused on saving the lives of sick and injured children, most children world wide die without access to paediatric critical care. With progress towards attainment of the Millenium development goals across the world, there has been a significant drop in child mortality in most countries. As issues such as nutrition, immunization, access to clean water and sanitation, access to healthcare are addressed, pediatric critical care will become an increasingly important part of any strategy to further reduce childhood deaths. Critical care can only function in the context of an integrated health system, but

the time –sensitive nature of the care required by sick children poses specific challenges to the development of these systems. As processes to recognize and treat sick children improve the role of and need for intensive care services will increase. It is fundamentally important that these services be as efficient as possible and should not develop *de novo* but within an integrated network for the provision of care for critically ill children.

References

- Shann F, Duke T. Twenty-three thousand unnecessary deaths every day: what are you doing about it? *Pediatr Crit Care Med.* 2009;10(5):608–9.
- Anand K, Patro BK, Paul E, et al. Management of sick children by health workers in Ballabgarh: lessons for implementation of IMCI in India. *J Trop Pediatr.* 2004;50(1):41–7.
- Bhutta ZA, Ahmed T, Black RE, et al. What works? Interventions for maternal and child undernutrition and survival. *Lancet.* 2008;371(9610):417–40.
- Victora CG, Black RE, Bryce J. Learning from new initiatives in maternal and child health. *Lancet.* 2007;370(9593):1113–4.
- Bryce J, Black RE, Walker N, et al. Can the world afford to save the lives of 6 million children each year? *Lancet.* 2005;365(9478):2193–200.
- Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? *Lancet.* 2003;361(9376):2226–34.
- Jones G, Steketee RW, Black RE, et al. How many child deaths can we prevent this year? *Lancet.* 2003;362(9377):65–71.
- Knippenberg R, Lawn JE, Darmstadt GL, et al. Systematic scaling up of neonatal care in countries. *Lancet.* 2005;365(9464):1087–98.
- Lawn JE, Cousens SN, Darmstadt GL, et al. 1 year after the Lancet Neonatal Survival Series – was the call for action heard? *Lancet.* 2006;367(9521):1541–7.
- Shann F, Argent AC. In: Fuhrman BP, Zimmerman JJ, editors. *Pediatric intensive care in developing countries.* 3rd ed. Philadelphia: Mosby/Elsevier; 2006.
- Kapiriri L, Martin DK. Successful priority setting in low and middle income countries: a framework for evaluation. *Health Care Anal.* 2009;18(2):129–47. Epub 2009 Mar 14.
- Kissoon N, Argent A, Devictor D, et al. World Federation of Pediatric Intensive and Critical Care Societies (WFPICCS) – its global agenda. *Pediatr Crit Care Med.* 2009;10(5):597–600.
- Tiska MA, Adu-Ampofo M, Boakye G, et al. A model of prehospital trauma training for lay persons devised in Africa. *Emerg Med.* 2004;21(2):237–9.
- Bhutta ZA, Zaidi AK, Thaver D, et al. Management of newborn infections in primary care settings: a review of the evidence and implications for policy? *Pediatr Infect Dis J.* 2009;28(1 Suppl): S22–30.
- English M, Esamai F, Wasunna A, et al. Delivery of paediatric care at the first-referral level in Kenya. *Lancet.* 2004;364(9445):1622–9.
- English M, Esamai F, Wasunna A, et al. Assessment of inpatient paediatric care in first referral level hospitals in 13 districts in Kenya. *Lancet.* 2004;363(9425):1948–53.
- Duke T, Kelly J, Weber M, et al. Hospital care for children in developing countries: clinical guidelines and the need for evidence. *J Trop Pediatr.* 2006;52(1):1–2. Epub 2006 Jan 16.
- Molyneux E, Ahmad S, Robertson A. Improved triage and emergency care for children reduces inpatient mortality in a resource-constrained setting. *Bull World Health Organ.* 2006;84(4):314–9. Epub 2006 Apr 13.
- Subhi R, Adamson M, Campbell H, et al. The prevalence of hypoxaemia among ill children in developing countries: a systematic review. *Lancet Infect Dis.* 2009;9(4):219–27.
- Duke T, Wandt F, Jonathan M, et al. Improved oxygen systems for childhood pneumonia: a multihospital effectiveness study in Papua New Guinea. *Lancet.* 2008;372(9646):1328–33. Epub 2008 Aug 15.
- Matai S, Peel D, Wandt F, et al. Implementing an oxygen programme in hospitals in Papua New Guinea. *Ann Trop Paediatr.* 2008;28(1):71–8.
- Kissoon N. Out of Africa – a mother’s journey. *Pediatr Crit Care Med.* 2011;12(1):73–9.
- Molyneux E. Emergency care for children in resource-constrained countries. *Trans R Soc Trop Med Hyg.* 2009;103(1):11–5. Epub 2008 Sep 2.
- Husum H, Gilbert M, Wisborg T, et al. Rural prehospital trauma systems improve trauma outcome in low-income countries: a prospective study from north Iraq and Cambodia. *J Trauma.* 2003;54(6):1188–96.
- Husum H, Gilbert M, Wisborg T. Training pre-hospital trauma care in low-income countries: the ‘Village University’ experience. *Med Teach.* 2003;25(2):142–8.
- Mock CN, Tiska M, Adu-Ampofo M, et al. Improvements in pre-hospital trauma care in an African country with no formal emergency medical services. *J Trauma.* 2002;53(1):90–7.
- Potoka DA, Schall LC, Ford HR. Improved functional outcome for severely injured children treated at pediatric trauma centers. *J Trauma.* 2001;51(5):824–32; discussion 832–4.
- Oyetunji TA, Haider AH, Downing SR, et al. Treatment outcomes of injured children at adult level 1 trauma centers: are there benefits from added specialized care? *Am J Surg.* 2011;201(4):445–9.
- Morrison W, Wright JL, Pidas CN. Pediatric trauma systems. *Crit Care Med.* 2002;30(11 Suppl):S448–56.
- Adam T, Edwards SJ, Amorim DG, et al. Cost implications of improving the quality of child care using integrated clinical algorithms: evidence from northeast Brazil. *Health Policy.* 2009;89(1):97–106. Epub 2008 Jun 25.
- Bryce J, Gouws E, Adam T, et al. Improving quality and efficiency of facility-based child health care through integrated management of childhood illness in Tanzania. *Health Policy Plan.* 2005;20 Suppl 1:i69–76.
- Bryce J, Victora CG, Habicht JP, et al. Programmatic pathways to child survival: results of a multi-country evaluation of integrated management of childhood illness. *Health Policy Plan.* 2005;20 Suppl 1:i5–17.
- Gove S, Tamburlini G, Molyneux E, et al. Development and technical basis of simplified guidelines for emergency triage assessment and treatment in developing countries. WHO Integrated Management of Childhood Illness (IMCI) referral care project. *Arch Dis Child.* 1999;81(6):473–7.
- Graham SM, English M, Hazir T, et al. Challenges to improving case management of childhood pneumonia at health facilities in resource-limited settings. *Bull World Health Organ.* 2008;86(5):349–55.
- Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med.* 2006;34(6):1589–96.
- Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med.* 2001;345(19):1368–77.
- Han YY, Carcillo JA, Dragotta MA, et al. Early reversal of pediatric-neonatal septic shock by community physicians is associated with improved outcome. *Pediatrics.* 2003;112(4):793–9.
- Dellinger RP, Levy MM, Carlet JM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2008. *Crit Care Med.* 2008;36(1):296–327.

39. Baker T. Pediatric emergency and critical care in low-income countries. *Paediatr Anaesth*. 2009;19(1):23–7.
40. Baker T. Critical care in low-income countries. *Trop Med Int Health*. 2009;14(2):143–8. Epub 2009 Jan 21.
41. Fowler RA, Adhikari NK, Bhagwanjee S. Clinical review: critical care in the global context - disparities in burden of illness, access, and economics. *Crit Care*. 2008;12(5):225. Epub 2008 Sep 9.
42. Walker IA, Morton NS. Pediatric healthcare – the role for anaesthesia and critical care services in the developing world. *Paediatr Anaesth*. 2009;19(1):1–4.
43. Bhutta ZA, Memon ZA, Soofi S, et al. Implementing community-based perinatal care: results from a pilot study in rural Pakistan. *Bull World Health Organ*. 2008;86(6):452–9.
44. Bhutta ZA, Darmstadt GL, Hasan BS, et al. Community-based interventions for improving perinatal and neonatal health outcomes in developing countries: a review of the evidence. *Pediatrics*. 2005;115(2 Suppl):519–617.
45. Haupt MT, Bekes CE, Brill R, et al. Guidelines on critical care services and personnel: recommendations based on a system of categorization of three levels of care. *Crit Care Med*. 2003;31(11):2677–83.
46. De Lange S, Van Aken H, Burchardi H, et al. European Society of Intensive Care Medicine Statement: intensive care medicine in Europe—structure, organisation and training guidelines of the Multidisciplinary Joint Committee of Intensive Care Medicine (MJCICM) of the European Union of Medical Specialists (UEMS). *Intensive Care Med*. 2002;28:1505–11.
47. Surgical care at the district hospital – the WHO manual. Geneva: World Health Organization; 2003. <http://whqlibdoc.who.int/publications/2003/9241545755.pdf>. Accessed 18 Feb 2014.
48. Hu X, Qian S, Xu F, et al. Incidence, management and mortality of acute hypoxemic respiratory failure and acute respiratory distress syndrome from a prospective study of Chinese paediatric intensive care network. *Acta Paediatr*. 2010;99(5):715–21. Epub 2010 Jan 21.
49. Isturiz RE, Torres J, Besso J. Global distribution of infectious diseases requiring intensive care. *Crit Care Clin*. 2006;22(3):469–88, ix.
50. Goh AY, Lum LC, Abdel-Latif ME. Impact of 24 hour critical care physician staffing on case-mix adjusted mortality in paediatric intensive care. *Lancet*. 2001;357(9254):445–6.
51. Goh AY, Abdel-Latif M, Lum LC, et al. Outcome of children with different accessibility to tertiary pediatric intensive care in a developing country – a prospective cohort study. *Intensive Care Med*. 2003;29(1):97–102. Epub 2002 Dec 4.
52. Goh AY, Mok Q. Centralization of paediatric intensive care: are critically ill children appropriately referred to a regional centre? *Intensive Care Med*. 2001;27(4):730–5.
53. Walker IA. Con: pediatric anesthesia training in developing countries is best achieved by out of country scholarships. *Paediatr Anaesth*. 2009;19(1):45–9.
54. Gathuya ZN. Pro: pediatric anesthesia training in developing countries is best achieved by selective out of country scholarships. *Paediatr Anaesth*. 2009;19(1):42–4.
55. Goh AY, Lum LC, Chan PW, et al. Withdrawal and limitation of life support in paediatric intensive care. *Arch Dis Child*. 1999;80(5):424–8.
56. Jeena PM, McNally LM, Stobie M, et al. Challenges in the provision of ICU services HIV infected children in resource poor settings: a South African case study. *J Med Ethics*. 2005;31(4):226–30.
57. Kapiriri L, Norheim OF, Martin DK. Fairness and accountability for reasonableness. Do the views of priority setting decision makers differ across health systems and levels of decision making? *Soc Sci Med*. 2009;68(4):766–73. Epub 2008 Dec 18.
58. Kapiriri L, Martin DK. A strategy to improve priority setting in developing countries. *Health Care Anal*. 2007;15(3):159–67.
59. Frey B. Overtreatment in threshold and developed countries. *Arch Dis Child*. 2008;93(3):260–3. Epub 2007 Sep 14.