# Leveraging Opportunities for Critical Care in Resource-Limited Settings

Vanessa B. Kerry<sup>\*,†,‡,§</sup>, Sadath Sayeed<sup>‡,§,||</sup> *Boston, MA, USA* 

Critical or intensive care is, in its simplest rendition, the provision of medical care for the severely ill patient. In its more advanced forms, critical care can provide needed support to temporarily do the work of almost any vital end organ, such as dialysis to mimic the actions of the native renal system, or ventilation and oxygenation to mimic the native actions of the respiratory system. In advanced health systems, a critical care unit is often relied on to provide escalated care for patients at risk of imminent death in order to prevent an untimely demise. Critical care as a clinical discipline in resource-rich settings is associated with highresource (financial, human, technological) intensity. For this reason, among others, critical care has received far less investment in resource-poor countries suffering from huge epidemics of communicable diseases such as human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome, tuberculosis, and malaria. However, with improved strategies and increased access to medications to treat the major infectious disease killers in many if not most countries, the need to turn attention to address the critical care gap between rich and poor is clearer than before. Although numerous challenges to scaling up high-quality intensive care services present themselves, even more opportunities to creatively innovate in this field exist that hold promise to move us closer to equity in global health care.

## THE NEED

At the individual patient level, the need for critical care is often unpredictable and can occur unexpectedly with any number of initially discrete disease processes that lead to acute end organ compromise or failure. Because death is often attributed to antecedent pathologies, and because data on the actual need for critical care services in resource-limited settings is extremely difficult to collect, the exact contribution of critical care to the global morbidity and mortality is not well characterized. A Lancet study in 2010 aimed to provide epidemiological estimates of the global burden of critical care morbidity and mortality [1]. The investigators argued that existing data on critical illness prevalence to date was incomplete because the data failed to provide accurate population-based incidence of critical illness and overwhelmingly did not include data from resource-limited settings. To attempt to provide a more comprehensive picture of the global burden of critical illness using "prototypical" illnesses of sepsis, acute lung injury, and mechanical ventilation, the investigators drew incidence and prevalence rates from observational population-based studies in several countries [2-8] and applied them to data on population and deaths from the Global Burden of Disease project by World Bank regions [9]. The results demonstrated significant burden across all regions, but especially in East and South Asia and Sub-Saharan Africa (Table 1) [1].

Prevention and/or early treatment of common infectious diseases remains the mainstay strategy to reduce the burden of mortality in resource-limited countries; many recent efforts have focused on piloting or scaling innovative "delivery" strategies to large at-risk populations. However, 97% of all deaths from infectious diseases including from HIV, diarrhea, meningitis, and pneumonia; 90% of all deaths from trauma; and 81% of deaths from cardiovascular causes occur in resource-limited countries because cases present or advance beyond stages at which early treatment is effective [10]. A South African survey of admissions to a secondary-level hospital in South Africa found that 25% of admitted patients were sufficiently ill to merit intensive care unit (ICU)-level care [11,12]. It is plausible that large proportions of hospital deaths could be prevented with access to adequate but not necessarily highly costly critical care services. Current quality of critical care is often informal and absent [13], and, in many cases, basic triage systems do not exist [14-16].

## **COST: A FALSE DEBATE**

A decision to invest in critical care services in resourcelimited settings is often simplistically criticized as an ineffective use of scarce resources. Simultaneously, agendasetting donors often insist that investments exclusively follow a macroscopic public health model where community health and primary care are seen as the only sustainable means to reduce disease burden. Putting aside larger social justice questions about the geo-political-socialeconomic-historical circumstances that have led some "Northern" countries to have significantly more power and resources than their "Southern" counterparts, these stereotypical responses miss the point that caring for critically ill patients need not be prohibitively expensive. They also miss the target in failing to acknowledge that some disease conditions are not preventable or present beyond the point of simple pill taking. As Riviello et al. [17] note in their review,

[Care for critically ill patients] may include oxygen administration or frequent nurse monitoring. Although these interventions may not be considered critical care in resource-rich settings, they are nonetheless important aspects of caring for critically ill patients and not universally available. The authors report no relationships that could be construed as a conflict of interest

From the \*Division of Pulmonary and Critical Care, Department of Medicine. Massachusetts General Hospital, Boston, MA, USA; †Center for Global Health Massachusetts General Hospital, Boston, MA, USA; <sup>‡</sup>Department of Global Health and Social Medicine Harvard Medical School, Boston, MA, USA; §Seed Global Health, Boston. MA. USA: and the Division of Newborn Medicine. Department of Medicine, Boston Children's Hospital, Boston, MA. USA. Correspondence: V. B. Kerry (vbk@ seedglobalhealth.org).

GLOBAL HEART © 2014 World Heart Federation (Geneva). Published by Elsevier Ltd. All rights reserved. VOL. 9, NO. 3, 2014 ISSN 2211-8160/\$36.00. http://dx.doi.org/10.1016/ j.gheart.2014.09.002

		Number of Deaths in 2004 ( $\times 10^3$ )						Estimated Potential Burden of Selected Critical Illnesses per Year $(\times 10^3)$		
	Population in 2004 (×10 <sup>3</sup> )	Total	Infection	Maternal Conditions	Malignant Neoplasms	Cardiovascular Diseases	Injuries	Patients Mechanically Ventilated	Acute Lung Injury	Sepsis
High-income countries	949,818	8,008	468 (6)	1 (0)	2,146 (27)	2,978 (37)	490 (6)	2,000—3,000	170-820	2,300—2,800
East Asia and Pacific	1,892,113	14,000	1,776 (13)	44 (<1)	2,284 (16)	4,439 (32)	1,678 (12)	3,900—5,900	340—1,600	4,500—5,700
Europe and Central Asia	476,096	5,684	284 (5)	3 (<1)	820 (14)	3,248 (57)	604 (11)	990—1,500	85-410	1,100—1,400
Latin America and Caribbean	549,187	3,499	474 (14)	16 (<1)	543 (16)	998 (29)	407 (12)	1,100—1,700	98-470	1,300—1,600
Middle-East and North Africa	324,542	2,114	299 (14)	15 (<1)	181 (9)	732 (35)	281 (13)	680—1,000	58-280	780—970
South Asia	1,493,430	13,778	3,993 (29)	179 (1)	954 (7)	3,438 (25)	1,476 (11)	3,100-4,700	270-1,300	3,600-4,500
Sub-Saharan Africa	749,269	11,662	6,475 (56)	269 (2)	493 (4)	1,232 (11)	847 (7)	1,600—2,400	130—650	1,800—2,200
World	6,436,826	59,772	13,777 (23)	527 (1)	7,424 (13)	17,073 (29)	5,784 (10)	13,000-20,000	1,150-5,500	15,000-19,000

TABLE 1. Estimates of global burden of critical illness by World Bank region

Further, critical care could strengthen hospitals' overall ability to provide better care, which is essential to both improving outcomes [13,18–20] and to increasing public opinion to seek care in facilities. Currently, populations often perceive hospitals in resource-limited settings as a place where one goes to die.

The debate and scale-up of critical care should thus center not on whether it is worth the investment writ large, but instead on determining those aspects of critical care that can be easily implemented in order to build a foundation to grow more advanced capabilities over time. Oxygen, a lifesaving therapy, for example, can cost little [21], and studies have shown that the introduction of oxygen and pulse oximetry can reduce fatalities from pneumonia [22]. Adequate patient-to-nursing ratios are an important prerequisite to close monitoring and timely intervention. These inexpensive interventions do not depend on advanced technology. Measured against the World Health Organization definition of cost-effectiveness [23], a number of studies have helped demonstrate that critical care interventions are meritable and cost-effective [17,24-27].

### **OPPORTUNITIES**

There is an increasing amount of literature describing critical care in resource-limited settings [15,17,28], the demographics in particular ICUs [15,29–31], the challenges to scaling up ICU care [32,33], and recommendations [17,34,35]. Despite the challenges, there are many readily available opportunities to change the quantity, quality, and distribution of critical care in many resource-

limited settings. These opportunities can be broadly categorized as effective triage; equipment and resources; training and human resources; task shifting and protocolized care; and affordable technology and research and information dissemination.

Effective triage systems can help improve patient care and mortality for admissions from ambulance and emergency and outpatient units [16,36] and for management of patients on the inpatient ward [13]. Yet, many sites lack effective triage systems for either [13-16]. This can result in delays in treatment, which can be the difference between life and death. Appropriate triage systems can be instituted to be nurse- or medical-trainee-led to optimize available human resources. Further, certain emergency treatments can be administered before a specific diagnosis is made [37]. Finally, movement of critically ill patients to a dedicated unit can achieve 2 goals. First, it can ensure more monitored care for a critically ill patient. Second, clustering of critically ill patients together can help pool available resources and ensure their more efficient use [13,38].

The most severely ill patients need close monitoring to assess cardiopulmonary function, including heart rate and rhythm, blood pressure, and oxygen saturation. This can be achieved by continuous electronic monitoring with purchased or donated equipment. Frequent vital signs supported by spot echocardiograms can help yield important information in the absence of electronic monitoring. Laboratory monitoring is also essential with special attention to electrolytes; hemoglobin; glucose; blood urea nitrogen; creatinine; and, ideally, arterial blood gases, coagulation, and lactate. Even though central labs are often rare or poorly equipped, there is a growing use of portable blood analyzers, which provide point-of-care information [39–41]. Point-of-care testing can provide bedside analysis with the fidelity of most major laboratories, for example [42].

Most resource-limited settings are challenged by severe staffing needs. The World Health Organization has identified more than 57 countries with critical health professional shortages [43]. These shortages are perpetuated by loss of trained personnel to more resource-rich settings [44], as well as poor training opportunities [45-48]. Trained intensivists are rare in resource-limited settings where critical care is often managed by internal medicine, anesthesia, or general surgery-trained physicians [32]. In a recent survey of 13 hospitals on ICU resources, included in this issue of Global Heart, 10 of the 13 responding hospitals cited trained staff as a central, needed input for better ICUlevel care at their facility [49]. Appropriately trained physicians, nurses, and support staff are essential to scaling up even the most modest critical-care services. There are growing partnerships across institutions in resource-rich countries that partner with institutions in resourcelimited countries, which can help expand training [48]. Ongoing professional development opportunities for local staff can occur through dedicated mentorship, didactics and focused courses, and teaching on new modalities.

Training needs to encompass both clinical education and increased research and knowledge generation. It should prioritize competencies over just knowledge. Yet, many training programs are currently dominated by lectures and didactics that fail to offer bedside clinical management of patients [50–52]. Increased faculty and staff will be needed to provide the supervision and sustained mentorship needed. Several training programs, academic partnerships, and consortia are adopting this model both broadly and in other clinical specialties [17,53–55].

Task shifting and empowering staff such as nurses to initiate certain treatments before diagnosis or physician evaluation can have an impact. Though both doctors and nurses are in short supply, the vast majority of health care is provided by nonphysicians in resource-limited settings. The increase in protocols [56], checklists [57], and bundled care [58-62] help facilitate both direct care and task shifting by creating processes that rely less on advanced knowledge than on adherence. They will reduce variability of care across providers and institutions and can help promote a culture of safety and accountability. Protocols have been implemented for sepsis [35], weaning of ventilation [63-67], glucose control [68-70], and sedation [71,72]. Recently, checklists have been implemented effectively to help improve mortality and reduce complications in surgery in settings of both high and low resources. This is promising for similar interventions in critical care because both fields are complex, technical, and multidisciplinary [57,73,74]. Care will be needed to adapt these guidelines appropriately to resource-limited settings. For example, blood gases or central venous oxygen saturations may not readily be available. However, there are opportunities. Sepsis guidelines have been adapted to help provide definition and recommendations on management including fluid resuscitation, timely antibiotics, airway protection, and source control [35,75].

Affordable technology is an underdeveloped opportunity to transform critical care as well as global health broadly [76]. Technology advancements can include pharmaceuticals, vaccines, diagnostics, devices, and communications. Examples include a negative pressure wound therapy device that decreases the cost and energy reliance of traditional wound pumps, increasing its applicability in resourcelimited settings. The new device costs approximately \$2 to manufacture [77]. Another example is an add-on device to ventilation equipment to monitor and record resuscitation performance, to provide real-time feedback on technique, and to improve training and care [77]. The device measures the rate and pressure of air entering an infant's lungs and can signal correct mask seal, need to augment or slow rate of breath delivery, and other parameters. Such technologies designed in resource-limited contexts can lead to reverse innovation to help improve care and reduce costs in more developed healthcare contexts. Further, adaptation and leveraging of existing technology can have an impact. Smart phones have been used with enough fidelity to reproduce a detailed neurological exam [78]. Low-cost mobile devices have been adapted in resource-limited settings to provide diagnostic testing for HIV and then to synchronize results in real time with electronic medical health records to expand both care and epidemiological data collection [79].

Research and its dissemination are essential to broadening the understanding of specific disease pathophysiology and management. Knowledge gaps stem from differences in acute disease burden depending on geography, such as with Ebola, severe acute respiratory syndrome, or Middle East respiratory syndrome, as well as from management in resource-limited areas where diagnostics and treatment modalities may not be readily available or patients present in the community and not at more centralized health facilities. Important areas for mutual collaboration and scale-up include developing research priorities, technical capacity building, mentorship, and dissemination where local investigators should take the lead with support from partners [48]. Research should center on needs assessment, prognostic scoring, implementation and outcomes of appropriate management, costeffectiveness, and affordable technology solutions [17,80].

#### SUMMARY

Perhaps the most compelling rationale for building critical care capacity in resource-limited settings is its power to save younger lives. Whereas much of critical care in resource-rich countries is in older populations who spend longer periods in ICUs supported by complex technology, in resource-limited settings, the majority of critically ill patients are children and young adults [29,81]. In this population, short-term interventions can be transformative

and have a significant impact on not only the individual, but also the community. For example, saving a young woman's life from peripleural sepsis will ensure her children are more likely to live to the age of 2 years and less likely to be socially or economically disadvantaged over their lifetime [82]. Avoiding preventable death will not only reduce mortality and disease burden, but it will help improve life expectancy, decrease birth rates, increase household productivity, and even have an impact on gross domestic product [83]. Investments in critical care need not be technology or cost intensive, but they should be appropriate and effective. Such investments, though, will have dividends across many clinical specialties as well as have an impact on the health outcomes of a population.

#### REFERENCES

- Adhikari NK, Fowler RA, Bhagwanjee S, Rubenfeld G. Critical care and the global burden of critical illness in adults. Lancet 2010;376:1339–46.
- Luhr OR, Antonsen K, Karlsson M, et al., for the ARF Study Group. Incidence and mortality after acute respiratory failure and acute respiratory distress syndrome in Sweden, Denmark, and Iceland. Am J Respir Crit Care Med 1999;159:1849–61.
- Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med 2003;348:1546–54.
- Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Crit Care Med 2001;29:1303–10.
- Bersten AD, Edibam C, Hunt T, et al., for the Australian and New Zealand Intensive Care Society Clinical Trials Group. Incidence and mortality of acute lung injury and the acute respiratory distress syndrome in three Australian States. Am J Respir Crit Care Med 2002; 165:443–8.
- Linde-Zwirble WT, Angus DC. Severe sepsis epidemiology: sampling, selection, and society. Crit Care 2004;8:222–6.
- Rubenfeld GD, Caldwell E, Peabody E, et al. Incidence and outcomes of acute lung injury. N Engl J Med 2005;353:1685–93.
- Harrison DA, Welch CA, Eddleston JM. The epidemiology of severe sepsis in England, Wales and Northern Ireland, 1996 to 2004: secondary analysis of a high quality clinical database, the ICNARC Case Mix Programme Database. Crit Care 2006;10:R42.
- World Health Organization. Health Statistics and Information Systems: Global Health Estimates. Geneva, 2014. Available at: http:// www.who.int/healthinfo/global\_burden\_disease/en/. Accessed July 31, 2014.
- Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2095–128.
- **11.** Burch VC, Benatar SR. Rational planning for health care based on observed needs. S Afr Med J 2006;96:796,800,802.
- Van Zyl-Smit R, Burch V, Willcox P. The need for appropriate critical care service provision at non-tertiary hospitals in South Africa. S Afr Med J 2007;97:268,270,270.
- 13. Baker T. Critical care in low-income countries. Trop Med Int Health 2009;14:143–8.
- Nolan T, Angos P, Cunha AJ, et al. Quality of hospital care for seriously ill children in less-developed countries. Lancet 2001;357:106–10.
- Dünser M, Baelani I, Ganbold L. A review and analysis of intensive care medicine in the least developed countries. Crit Care Med 2006; 34:1234–42.
- Wallis PA, Gottschalk SB, Wood D, et al., for the Cape Triage Group. The Cape triage score— a triage system for South Africa. S Afr Med J 2006;96:53–6.

- Riviello E, Letchford S, Achieng L, Newton M. Critical care in resourcepoor settings: lessons learned and future directions. Crit Care Med 2011;39:860–7.
- **18.** Watters D, Wilson I, Leaver R, et al. Care of the Critically III Patient in the Tropics and Subtropics. 1st ed. Oxford, UK: Macmillan; 1991.
- 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;363:1948–53.
- **20.** Veirum JE, Biai S, Jakobsen M, et al. Persisting high hospital and community childhood mortality in an urban setting in Guinea-Bissau. Acta Paediatr 2007;96:1526–30.
- **21.** Howie SR, Hill S, Ebonyi A, et al. Meeting oxygen needs in Africa: an options analysis from the Gambia. Bull World Health Organ 2009;87: 763–71.
- Duke T, Walsh F, Jonathan M, et al. Improved oxygen systems for childhood pneumonia, a multihospital effectiveness study in Papua New Guinea. Lancet 2008;372:1328–33.
- World Health Organization. World Health Organization: CHOosing Interventions that are Cost Effective (WHOCHOICE). Geneva, Switzerland: World Health Organization; 2010.
- McCord C, Chowdhury Q. A cost effective small hospital in Bangladesh: what it can mean for emergency obstetric care. Int J Gynaecol Obstet 2003;81:83–92.
- 25. Gosselin RA, Thind A, Bellardinelli A. Cost/ DALY averted in a small hospital in Sierra Leone: what is the relative contribution of different services? World J Surg 2006;30:505–11.
- **26.** Gosselin RA, Heitto M. Cost-effectiveness of a district trauma hospital in Battambang, Cambodia. World J Surg 2008;32:2450–3.
- Gosselin RA, Maldonado A, Elder G. Comparative cost-effectiveness analysis of two MSF surgical trauma centers. World J Surg 2010;34: 415–9.
- Alberto L. Critical care practice—Latin American perspective. Nurs Crit Care 2010;15:10–1.
- 29. Jochberger S, Ismailova F, Lederer W, et al., for the Helfen Berührt Study Team. Anesthesia and its allied disciplines in the developing world: a nationwide survey of the Republic of Zambia. Anesth Analg 2008;106:942–8.
- **30.** Towey RM, Ojar S. Practice of intensive care in rural Africa: an assessment of data from Northern Uganda. Afr Health Sci 2008;8: 61–4.
- Kwizera A, Dünser M, Nakibuuka J. National intensive care unit bed capacity and ICU patient characteristics in a low income country. BMC Res Notes 2012;5:475.
- 32. Bhagwanjee S. Critical care in Africa. Crit Care Clin 2006;22:433-8.
- 33. 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;12:225.
- 34. World Health Organization. Integrated management of adolescent and adult illness: interim guidelines for first-level facility health workers at health centre and district outpatient clinic: acute care. Geneva: WHO. 2009. Available at: http://www.who.int/hiv/pub/imai/ acute\_care.pdf. Accessed July 31, 2014.
- 35. Dünser MW, Festic E, Dondorp A, et al., for the Global Intensive Care Working Group of European Society of Intensive Care Medicine. Recommendations for sepsis management in resource-limited settings. Intensive Care Med 2012;38:557–74.
- Wallis LA, Balfour CH. Triage in emergency departments. S Afr Med J 2007;97:13.
- 37. Gove S, Tamburlini G, Molyneux E, Whitesell P, Campbell H. 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;81:473–7.
- **38.** Watters D, Wilson I, Leaver R, Bagshawe A. Care of Critically III Patient in the Tropics. Oxford, UK: MacMillan; 2004.
- Bailey TM, Topham TM, Wantz S, et al. Laboratory process improvement through point-of-care testing. Jt Comm J Qual Improv 1997;23:362–80.
- 40. Price C. Point of care testing. BMJ 2001;322:1285-8.

- **41.** Gruszecki A, Hortin G, Lam J, et al. Utilization, reliability, and clinical impact of point-of-care testing during critical care transport: six years of experience. Clin Chem 2003;49:1017–9.
- 42. National Academy of Clinical Biochemistry. Laboratory Medicine Guidelines: Evidence-Based Practice for Point-of-Care Testing. Washington, DC: American Association for Clinical Chemistry. 2006. Available at: www.aacc.org/SiteCollectionDocuments/NACB/LMPG/ POCTLMPG.pdf. Accessed July 31, 2014.
- **43.** World Health Organization. The World Health Report 2006—Working Together for Health. Geneva, Switzerland: World Health Organization; 2006.
- **44.** Mullan F. The metrics of the physician brain drain. N Engl J Med 2005;353:1810–8.
- **45.** Bundred P, Levitt C. Medical migration: who are the real losers? Lancet 2000;356:245–6.
- 46. Muula A. Is there any solution to the "brain drain" of health professionals and knowledge from Africa? Croat Med J 2005;46:21–9.
  47. Desuide heat M. Jaubert C. Jürgertra J. Struwig M. Desense for
- Bezuidenhout M, Joubert G, Hiemstra L, Struwig M. Reasons for doctor migration from South Africa. S Afr Fam Pract 2009;51:211–5.
- Kerry VB, Ndung'u T, Walensky RP, Lee PT, Kayanja F, Bangsberg DR. Managing the demand for global health education. PLoS Med 2011;8: e1001118.
- 49. Vukoja M, Riviello E, Gavrilovic S, et al. A survey on critical care resources and practices in low- and middle-income countries. Glob Heart 2014;9:337–42.
- Willis-Shattuck M, Bidwell P, Thomas S, Wyness L, Blaauw D, Ditlopo P. Motivation and retention of health workers in developing countries: a systematic review. BMC Health Serv Res 2008;8:247.
- Frenk J, Chen L, Bhutta Z, et al. Health professionals for a new century: transforming education to strengthen health systems in an interdependent world. Lancet 2010;376:1923–58.
- Kolars JC, Cahill K, Donkor P, et al. Perspective: partnering for medical education in Sub-Saharan Africa: seeking the evidence for effective collaborations. Acad Med 2012;87:216–20.
- **53.** Einterz R, Kimaiyo S, Mengech H, et al. Responding to the HIV pandemic: the power of an academic medical partnership. Acad Med 2007;82:812–8.
- **54.** Kerry VB, Mullan F. Global Health Service Partnership: building health professional leadership. Lancet 2014;383:1688–91.
- 55. Government of Rwanda. Human Resource for Health Rwanda: Program Overview. GOR, Kigali. Available at: http://www. hrhconsortium.moh.gov.rw/about-hrh/program-overview/. Accessed July 31, 2014.
- 56. Micek ST, Kollef MH. Using protocols to improve the outcomes of critically ill patients with infection: focus on ventilator-associated pneumonia and severe sepsis. In: Rello J, Kollef M, Diaz E, Rodriguez A, editors. Infectious Diseases in Critical Care. 2nd edition. Berlin, Heidelberg: Springer-Verlag; 2007. p. 78–84.
- Haynes AB, Weiser TG, Berry WR, et al., for the Safe Surgery Saves Lives Study Group. A surgical safety checklist to reduce morbidity and mortality in a global population. N Engl J Med 2009;360:491–9.
- Rivers E, Nguyen B, Havstad S, et al., for the Early Goal-Directed Therapy Collaborative Group. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345:1368–77.
- 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;34:1589–96.
- Dellinger RP, Levy MM, Carlet JM, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Intensive Care Med 2008;34:17–60.
- Pronovost PJ, Goeschel CA, Colantuoni E, et al. Sustaining reductions in catheter related bloodstream infections in Michigan intensive care units: observational study. Br Med J 2010;340:c309.
- **62.** Bouadma L, Mourvillier B, Deiler V, et al. A multifaceted program to prevent ventilator-associated pneumonia: impact on compliance with preventive measures. Crit Care Med 2010;38:789–96.
- Ely EW, Baker AM, Dunagan DP, et al. Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. N Engl J Med 1996;335:1864–9.

- Kollef MH, Shapiro SD, Silver P, et al. A randomized, controlled trial of protocol-directed versus physician-directed weaning from mechanical ventilation. Crit Care Med 1997;25:567–74.
- Horst HM, Mouro D, Hall-Henssens RA, Pamukov N. Decrease in ventilation time with a standardized weaning protocol. Arch Surg 1998;133:483–8. discussion 488–9.
- 66. Ely EW, Bennett PA, Bowton DL, Murphy SM, Florance AM, Haponik EF. Large scale implementation of a respiratory therapistdriven protocol for ventilator weaning. Am J Respir Crit Care Med 1999;159:439–46.
- Marelich GP, Murin S, Battistella F, Inciardi J, Vierra T, Roby M. Protocol weaning of mechanical ventilation in medical and surgical patients by respiratory care practitioners and nurses: effect on weaning time and incidence of ventilator-associated pneumonia. Chest 2000; 118:459–67.
- Van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. N Engl J Med 2001;345:1359–67.
- Preissig CM, Hansen I, Roerig PL, Rigby MR. A protocolized approach to identify and manage hyperglycemia in a pediatric critical care unit. Pediatr Crit Care Med 2008;9:581–8.
- 70. Lecomte P, Van Vlem B, Coddens J, et al. Tight perioperative glucose control is associated with a reduction in renal impairment and renal failure in non-diabetic cardiac surgical patients. Crit Care 2008;12: R154.
- Brook AD, Ahrens TS, Schaiff R, et al. Effect of a nursing-implemented sedation protocol on the duration of mechanical ventilation. Crit Care Med 1999;27:2609–15.
- Kress JP, Pohlman AS, O'Connor MF, Hall JB. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med 2000;342:1471–7.
- Revolus T, Tetrokalashvilli M. Implementation of evidence-based innovative bundle checklist for reduction of surgical site infection. Obstet Gynecol 2014;123(Suppl 1):32S.
- Gillespie BM, Chaboyer W, Thalib L, John M, Fairweather N, Slater K. Effect of using a safety checklist on patient complications after surgery. Anesthesiology 2014;120:1380–9.
- Becker JU, Theodosis C, Jacob ST, Wira CR, Groce NE. Surviving sepsis in low-income and middle-income countries: new directions for care and research. Lancet Infect Dis 2009;9:577–82.
- Howitt P, Darzi A, Yang GZ, et al. Technologies for global health. Lancet 2012;380:507–35.
- Massachusetts Institute of Technology, Department of Mechanical Engineering. Department News. MechEConnects 2013; 4. Available at: http://mecheconnects.mit.edu/?p=1863. Accessed July 31, 2014.
- Massachusetts Medical Society. New and Publications: Tele-Video-Medicine using Facetime via iPOD Touch Devices. 2011. Waltham, MA. Available at: http://www.massmed.org/News-and-Publications/ MMS-News-Releases/Boston-University-Medical-student-Mass%96 General-Hospital-Team-of-Residents-are-Winners-of-Information-Technology-Awards-from-Massachusetts-Medical-Society/#.U7IfjhbWLZ4. Accessed June 30, 2014.
- Chin CD, Cheung YK, Laksanasopin T, et al. Mobile device for disease diagnosis and data tracking in resource-limited settings. Clin Chem 2013;59:629–40.
- Walensky RP, Kuritzkes DR. The impact of the President's Emergency Plan for AIDS Relief (PEPFAR) beyond HIV and why it remains essential. Clin Infect Dis 2010;50:272–5.
- **81.** Firth P, Ttendo S. Intensive care in low-income countries—a critical need. N Engl J Med 2012;367:1974–6.
- 82. Stenberg K, Axelson H, Sheehan P, et al., for the Study Group for the Global Investment Framework for Women's and Children's Health. Advancing social and economic development by investing in women's and children's health: a new Global Investment Framework. Lancet 2014;383:1333–54.
- World Health Organization. Macroeconomics and Health: Investing in Health for Economic Development. Report of the Commission on Macroeconomics and Health. Geneva, Switzerland: WHO. 2001. Available at: http://whqlibdoc.who.int/publications/2001/92415455 0x.pdf. Accessed July 31, 2014.