Critical Care 1

Critical care and the global burden of critical illness in adults

Neill K J Adhikari, Robert A Fowler, Satish Bhagwanjee, Gordon D Rubenfeld

Critical care has evolved from treatment of poliomyelitis victims with respiratory failure in an intensive care unit to treatment of severely ill patients irrespective of location or specific technology. Population-based studies in the developed world suggest that the burden of critical illness is higher than generally appreciated and will increase as the population ages. Critical care capacity has long been needed in the developing world, and efforts to improve the care of the critically ill in these settings are starting to occur. Expansion of critical care to handle the consequences of an ageing population, natural disasters, conflict, inadequate primary care, and higher-risk medical therapies will be challenged by high costs at a time of economic constraint. To meet this challenge, investigators in this discipline will need to measure the global burden of critical illness and available critical-care resources, and develop both preventive and therapeutic interventions that are generalisable across countries.

Introduction

Critical care or intensive care medicine is often thought to have begun in 1953 when Danish patients with poliomyelitis received invasive mechanical ventilation,[1] although areas of some hospitals had been designated for patients recovering from anaesthesia or traumatic injuries a century earlier.[2] The high mortality associated with negative-pressure ventilation for the poliomyelitis epidemic in the 1950s prompted the development of hand-delivered positive-pressure ventilation via tracheostomy. These patients received care in a common location with intensified nursing support and manual ventilation provided by students, and mortality declined. Intensive care units (ICUs) subsequently became a crucial component of hospital care.

Expansion of ICUs has followed advances in understanding the pathophysiology of dysfunctional organs (including lungs, heart, kidney, liver, and brain) and concomitant innovations in supportive technology. Examples of monitoring devices are central venous, pulmonary artery, and intracranial pressure catheters. Examples of organ support are mechanical ventilation for respiratory dysfunction; inotropes, vasopressors, intra-aortic balloon counterpulsation for cardiac dysfunction; dialysis for renal dysfunction; and hypothermia for brain protection after cardiac arrest. The efficacy of some organ support technologies is generally accepted on physiological grounds. For example, we assume that patients with septic shock or acute respiratory failure who do not receive vasopressors or mechanical ventilation will die. However, the application of some technologies in specific clinical situations continues to be studied—for example, mechanical ventilation in acute lung injury[3] and pulmonary arterial catheterisation in critical illness.[4]

Unlike other specialties of medicine defined by organ system, disease process, or procedure, critical care has always been challenged to establish its identity.[5] New definitions have tried to broaden the focus of critical care to include the patient's complexity of illness, severity of organ dysfunction, and risk of imminent death, irrespective of physical location. Although patients with critical illness in this broad sense might be found throughout hospitals, many receive care in an ICU. Patients in an ICU generally fall into three main categories: those with acute organ dysfunction (including those whose ultimate outcome is unclear and thus receive long-term intensive organ support), those who have undergone a major procedure and are monitored in the peri-intervention period to prevent and detect acute organ dysfunction, and those whose trial of intensive care has failed and are receiving end-of-life care. Intensive care is delivered by an interdisciplinary team that includes not only nurses and physicians, but also respiratory therapists, physical and occupational therapists, biotechnicians, pharmacists, nutritionists, social workers, and spiritual care providers. The daily practice of intensive care requires three related activities. First, clinicians have to simultaneously resuscitate, diagnose, and provide definitive care for acutely sick patients on a rapidly deteriorating but potentially reversible path towards organ dysfunction and death. Second, they have to prevent, recognise, and treat complications of treatments to support failing organs. Finally, clinicians' greatest challenge is to engage in decisions about the appropriate extent of life-supporting therapies for patients whose immediate death has been averted, but whose likelihood of returning to a meaningful survival is poor.

Intensive care medicine and nursing are young specialties, since ICUs were uncommon before the 1970s.

> ### Search strategy and selection criteria
>
> We searched for relevant studies published after 1999 in Medline using the MeSH terms "critical illness", "respiratory distress syndrome/adult", and "sepsis", limited to the subheading epidemiology and to adults. We supplemented the search with personal files.

Interdepartmental Division of Critical Care, University of Toronto and Department of Critical Care Medicine, Sunnybrook Health Sciences Centre, Toronto, ON, Canada (N K J Adhikari MD, R A Fowler MD, Prof G D Rubenfeld MD)**; and Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, WA, USA** (Prof S Bhagwanjee MB ChB)

Correspondence to:
Dr Gordon D Rubenfeld, Department of Critical Care Medicine, Sunnybrook Health Sciences Centre, 2075 Bayview Avenue,Toronto, ON, Canada M4N 3M5
gordon.rubenfeld@ sunnybrook.ca

	Population in 2004 (×10³)	Number of deaths in 2004 (×10³)†						Estimated potential burden of selected critical illnesses per year (×10³)‡		
		Total	Infection	Maternal conditions	Malignant neoplasms	Cardiovascular diseases	Injuries	Patients mechanically ventilated	Acute lung injury	Sepsis
High-income countries	949 818	8008	468 (6%)	1 (0%)	2146 (27%)	2978 (37%)	490 (6%)	2000–3000	170–820	2300–2800
East Asia and Pacific	1 892 113	14 000	1776 (13%)	44 (<1%)	2284 (16%)	4439 (32%)	1678 (12%)	3900–5900	340–1600	4500–5700
Europe and central Asia	476 096	5684	284 (5%)	3 (<1%)	820 (14%)	3248 (57%)	604 (11%)	990–1500	85–410	1100–1400
Latin America and Caribbean	549 187	3499	474 (14%)	16 (<1%)	543 (16%)	998 (29%)	407 (12%)	1100–1700	98–470	1300–1600
Middle East and north Africa	324 542	2114	299 (14%)	15 (<1%)	181 (9%)	732 (35%)	281 (13%)	680–1000	58–280	780–970
South Asia	1 493 430	13 778	3993 (29%)	179 (1%)	954 (7%)	3438 (25%)	1476 (11%)	3100–4700	270–1300	3600–4500
Sub-Saharan Africa	749 269	11 662	6475 (56%)	269 (2%)	493 (4%)	1232 (11%)	847 (7%)	1600–2400	130–650	1800–2200
World	6 436 826	58 772	13 777 (23%)	527 (1%)	7424 (13%)	17 073 (29%)	5784 (10%)	13 000–20 000	1150–5500	15 000–19 000

Data are number (percentage of total in region). Percentages do not add up because other causes of death are not listed. Data for population and deaths are from the Global Burden of Disease project, available at http://www.who.int/healthinfo/global_burden_disease/en/index.html. *Classification was done according to the World Bank income and geographical categories used in the disease control priorities project (details available at http://www.dcp2.org/pubs/GBD). World totals include some countries and territories that are not part of the World Bank regions. †Infection includes categories of infectious or parasitic diseases and respiratory infections; maternal conditions include sepsis, haemorrhage, hypertensive disorders, obstructed labour, and abortions; cardiovascular diseases include rheumatic, ischaemic, hypertensive, inflammatory, and cerebrovascular diseases; injuries include both unintentional and intentional causes. ‡Data are estimates based on estimates of North American population yearly incidence of mechanical ventilation,[32,33] acute lung injury,[28,30] and sepsis[25] and severe sepsis,[24] extrapolated to other regions based on population. These estimates are for illustration purposes only and assume that those other regions have similar intensive care capacity, underlying risk factors for the outcomes listed, and age-distributions and sex-distributions to North America. These numbers can best be interpreted as the burden of critical illness given capacity and population similar to North America.

Table 1: Estimates of global burden of critical illness by World Bank region*

Organisational details of ICUs continue to be debated. For example, some jurisdictions subdivide ICUs into those that provide full organ support, and intermediate units, which provide some support and monitoring to patients at risk of further deterioration. In another example, ICUs were initially separated into surgical units treating postoperative patients and medical units treating non-operative patients. Subsequently, specialty-specific units were developed for patients with traumatic injuries or burns, or who had undergone neurosurgery, cardiac surgery, or solid organ transplantation. Although specialty ICUs might improve outcomes by reduction of practice variability and use of specialist nursing skills, US observational data suggest that risk-adjusted mortality is similar for patients treated in general ICUs and specialty ICUs, but might be worse when patients are looked after in specialty ICUs with less experience in their illness.[6]

Intensive care physician training has developed, with substantial general variation in the duration, content, assessment, and official recognition of training.[7,8] Although some regions are developing competency-based assessment models, the optimum model for training and assessment of intensivists is not clear.[9] From an academic perspective, the first issue of the journal *Critical Care Medicine* was published in 1973 and *Intensive Care Medicine* in 1975; nowadays, many journals and yearly scientific meetings report and present advances in the care of critically ill patients.

Defining the global burden of critical illness

A detailed picture of the global burden of various diseases, including cancer, cardiovascular disease, tuberculosis and HIV/AIDS, is available from web-based resources such as WHO's Global Health Observatory. However, no reliable international comparative epidemiological data

of critical illness syndromes such as acute lung injury, sepsis, and multiple-organ dysfunction are available because of several fundamental challenges. First, critical illness syndromes cannot be diagnosed with one test, unlike HIV with serology or malaria with blood smears. Definitions for sepsis,[10] nosocomial infections,[11] and acute lung injury[12] are based on clinical, laboratory, radiological, and physiological criteria, derived by consensus panels, and under continual debate and revision. Independent of the definitions' validity is their absence of reliability,[13,14] which makes comparative epidemiology challenging. Second, compared with chronic diseases like cancer, asthma, and tuberculosis, critical illness syndromes have a brief prodrome and high short-term mortality, which could be especially high in countries with few ICU resources. Such short time spans reduce the number of prevalent cases available for study at any given time, relative to chronic diseases. Third, critical illness is harder to study with existing administrative databases[15] than are trauma or cardiovascular disease because it is not defined by a procedure or accurately captured by hospital coding. Finally, the epidemiology of critical illness and ICU resources is dependent on the availability and intensity of other health services. Even mortality after critical illness is related to a complex interplay between a clinical decision to limit intensive care and the consequences of the disease.[16]

Countries with the resources to provide organ transplantation, intensive chemotherapy for cancer, and surgery for cardiovascular disease in elderly patients with comorbid illness will have a higher burden of critical illness associated with these disorders and treatments than will those that do not have these resources. Although there is agreement that critical illness occurs outside the ICU, research on critical illness, particularly

For more on **WHO's Global Health Observatory** see http://www.who.int/gho/en/

internationally comparative epidemiology, generally occurs inside the ICU. Observational studies of international practice have been done for sepsis,[17] nosocomial infection,[18] mechanical ventilation,[19] and end-of-life care,[20] and have been used to generate illness severity scores.[21] These studies were done in ICUs by use of period prevalence data collection over short periods (snapshot data). Although the studies' results show process and outcome differences within and between countries, they do not provide accurate population-based incidence data, because there is no population denominator or complete case ascertainment within geographical regions. With a few exceptions,[22] these studies have not included data from the developing world.

As a prototype critical illness syndrome, observational studies of sepsis show these epidemiological challenges. Incidence, prevalence, and prognosis are dependent on whether the study design considers measurement of population-based incidence, or incidence in those treated in ICUs. Other important sources of bias are the duration of follow-up for patients admitted (for one day vs the entire hospital stay), case definition, type of institution, study site (restricted to ICU or not), seasonal variability, and casemix.[23] Results from US-based population studies from administrative data suggest a population-based incidence of 300 cases per 100 000 person-years for severe sepsis[24] and 240 cases per 100 000 person-years for sepsis.[25] When the setting is the ICU, most results show treated incidence of about ten cases per 100 ICU admissions.[26] Others have reported a much higher incidence in settings with fewer ICU beds,[27] probably indicating admission of very sick patients or exclusion of low-risk patients for postoperative monitoring from the denominator.[17] Similarly, in population-based studies of acute lung injury, results show an incidence of 18,[28] 34,[29] and 79 cases[30] per 100 000 person-years in Scandinavia, Australia, and USA, respectively, with an estimated 74 500 deaths every year in the USA.[30] This number exceeds the yearly number of deaths from breast cancer, HIV/AIDS, and asthma,[31] and shows the underappreciated burden of critical illness to population health, at least in developed nations.

Application of these data to the world's population provides very rough estimates of the global burden of critical illness syndromes (table 1). Of note, these values might underestimate the burden in developing countries, where a higher proportion of deaths is caused by infection and injury. In addition, they assume that the age, sex, risk factor distributions, and critical care capacity are similar to those of the North American populations that generated the epidemiological data. Even in the developed world, epidemiological data for availability of ICU beds are sparse (table 2).

These challenges imply that the global burden of critical illness might never be possible to define. Even the less ambitious goal of defining the global capacity to deliver critical care is difficult, in view of the absence of uniform definitions for an ICU bed, as noted in a study

	Number of ICUs	Number of ICU beds per 100 hospital beds	Number of ICU beds per 100 000 population
North America			
Canada (excluding Quebec)*	319	3·4	13·5
USA*	5980	9·0	20·0
Carribean and South America			
Colombia†	89	3·5	..
Trinidad and Tobago‡	6	..	2·1
Europe			
Belgium*	135	4·4	21·9
Croatia§	123	3·3	20·3
France*	550	2·5	9·3
Germany*	..	4·1	24·6
Netherlands*	115	2·8	8·4
Spain*	258	2·5	8·2
Sweden¶	89	..	8·7
UK*	268	1·2	3·5
Africa			
South Africa‖	308		8·9
Public sector	..	1·7	3·8
Private sector	..	8·9	5·1
Zambia**	29	0·2	..
Australasia			
Australia††	160	..	8·0
Public sector	104	..	5·6
Private sector	56	..	2·4
New Zealand††	26	0·9	4·8
Public sector	24	1·5	4·6
Private sector	2	0·097	0·3
China‡‡ (median, IQR)	..	1·8, 1·3–2·1	3·9, 2·8–4·6
Sri Lanka§§ (public sector)	52	..	1·6

Data are estimates. Data were obtained at different times and are based on different definitions of intensive care unit (ICU) and hospital beds. IQR=interquartile range. *From reference 34; data include adult ICUs and acute care hospital beds. †From reference 35; the type of ICU is not reported. The estimate of ICU beds per 100 hospital beds is based on data from 63 ICUs. ‡From reference 36; data include adult and paediatric ICUs. The estimate of ICU beds per 100 000 population includes data from five of six ICUs; the sixth ICU "was not fully developed"[36]. §From reference 37; data include adult, paediatric, and neonatal ICUs. Estimates of ICU beds per 100 hospital beds and per 100 000 population are based on 117 of 123 ICUs (including six psychiatric ICUs). ¶From reference 38; refers to staffed beds and the estimate of ICU beds per 100 000 population includes data from at least 80 of 89 ICUs. ‖From reference 39; data include adult, paediatric, and neonatal ICUs. Number of ICUs refers to number of hospitals with an ICU, and the denominator of number of ICU beds per 100 hospital beds includes all hospitals. If hospitals with ICUs are used to calculate ICU beds per 100 hospital beds, the figures are 3·9 (public sector) and 9·3 (private sector). **From reference 40; data from 69 of 87 hospitals in the country. ††From reference 41; data on number of ICU beds include 93% and 96% of both adult and paediatric ICUs in Australia and New Zealand, respectively. ‡‡From reference 42; which reviewed eight papers and a national professional society survey. §§From reference 43; data include adult, paediatric, and neonatal ICUs. The number of beds per 100 000 population is based on 49 ICUs and assumes that each has six beds (the number of beds per ICU varied from four to eight).

Table 2: Availability of intensive care resources by country

in which the results showed a five or more fold variation in ICU bed availability in eight developed countries.[34] Nevertheless, meeting this goal is necessary to allocate health-system resources, improve the quality of care for critically ill patients, and plan for unexpected surges, such as during a pandemic. Definition of the global burden of critical illness would also provide impetus for initiatives to improve the outcomes of acutely ill adults in low-resource settings, such as the WHO's integrated management of adolescent and adult acute illness

Panel: Long-term sequelae of critical illness

- Physical morbidity
  - Neuromuscular dysfunction (neuropathy, myopathy)
  - Heterotopic ossification
  - Frozen joints
  - Compression neuropathies
  - Pulmonary dysfunction
  - Tracheostomy problems (excess scar tissue at skin site; subglottic stenosis)
- Neurocognitive and psychiatric morbidity
  - Abnormalities in memory, attention, concentration and executive function
  - Depression
  - Post-traumatic stress disorder
  - Anxiety
- Financial burdens and carer burnout

guidelines (IMAI). A model for this approach is a recent initiative to improve global surgical care that started with a study of the global burden of surgery.[44,45]

What is the mortality and morbidity of critical illness?

ICU mortality in unselected patients in North America, Europe, Australia, and New Zealand, studied for development of scoring systems, is 8–18%, and serial assessments of similar scoring systems suggest that overall ICU mortality over time might be falling.[21,46,47] However, these summary measures incorporate the generally excellent outcomes of patients admitted for routine monitoring and conceal the high mortality of the most acutely ill patients. For example, mortality is 35–45%[48] in heterogeneous cohorts of patients with acute lung injury and 50–60%[49] in patients with septic shock, for whom temporal improvements in mortality are slight at best.[24,27,48,49] By contrast, mortality after myocardial infarction with ST-elevation is about 7% in developed world hospitals[50] and continues to decline.[51]

Investigations have broadened consideration of ICU outcomes from short-term mortality to long-term mortality, morbidity, and quality of life (panel).[52] ICU survivors have to face challenges related to physical morbidity (muscle loss and weakness, contractures, pain)[53] and non-physical morbidity (depression, anxiety, post-traumatic stress disorder, long-lasting delirium, and cognitive impairment).[54] Despite this growing recognition, clinicians do not have measures to prevent post-ICU morbidity while patients remain critically ill. The results of one prominent randomised trial suggested that the combination of daily interruption of sedation and early exercise and mobilisation improved functional outcomes at hospital discharge.[55] Whether this treatment is generalisable and feasible, and whether the effect is mainly driven by early exercise or by reduced sedation and delirium, remain to be seen. Similarly, strategies implemented after ICU discharge to decrease delayed morbidity remain elusive,[56] as shown by a recent randomised trial that identified no benefit of a manual-based, self-directed physical rehabilitation programme, including nurse-led clinic follow-up and screening for psychological morbidity.[56]

Why does critical illness have a poor prognosis?

Several reasons explain why the improvement of survival of critically ill patients has been harder to achieve than for those with single homogeneous diagnoses such as myocardial infarction. First, clinicians might not recognise critical illness until organ dysfunction is already advanced.[57] Attempts to augment clinicians' judgment of the severity of illness in hospital patients has led to the development of early warning scores, but these do not have enough sensitivity, reliability, and validity.[58] Second, there are few effective specific treatments for heterogeneous critical illness syndromes. For example, in many statistically negative randomised trials of treatments for acute lung injury, only avoidance of injurious tidal volume ventilation reduces mortality.[3] Even when an effective treatment exists, universal implementation has been difficult to achieve,[59] indicating the challenges of translating complex care protocols delivered by interdisciplinary teams to the patient's bedside.[60] This theme persists in examples of other effective supportive treatments, such as early aggressive resuscitation[61] and early appropriate antibiotics[62] in severe sepsis, enteral nutrition,[63] and weaning from mechanical ventilation.[64] Third, patients with critical-illness syndromes have variable severity of illness, burden of comorbidities, and baseline risk of mortality, all of which are broader than the narrow subset enrolled in randomised trials.[65] The evidence base for critical care therapeutics, derived from few positive randomised trials, thus might not be generalisable to many patients cared for in ICUs.[66]

What global trends will affect the burden of critical illness?

Several emerging trends almost guarantee that the demand for critical care services will increase while the ability to pay for them will decrease.

With respect to patient demographics, the frequency of diseases and comorbid disorders that cause critical illness increases with age. As the rest of medicine advances, care has intensified for high-risk patients with many comorbidities (such as diabetes mellitus, chronic kidney disease, congestive heart failure, chronic obstructive pulmonary disease, and cancer), compromised immune systems, and extreme old age. As these treatment boundaries are pushed, complications can be expected to increase. On the assumption of no effective prevention strategies for acute lung injury, extrapolation of present US epidemiology predicts over 330 000 cases per year by 2030, a 50% increase over present numbers.[30] Parallel increases can be expected for sepsis[24] and mechanical ventilation.[67,68] Driven by this demographic reality, such

demand might be especially acute in the USA, in which use of ICU by hospital patients who die is very high (47% *vs* 10% in England), especially for elderly people.[69]

The combination of an ageing population and fewer young wage earners in developed countries will create a demand for critical care that cannot be fulfilled as it is presently delivered, even if shrinking economies recover. The inverted demographic pyramid in developed nations will be mirrored by a predominantly youthful population in many developing nations, with high fertility rates and restricted public health and critical care infrastructure. In addition to the medical implications of an ageing population, the geopolitical consequences are expected to be profound and might include civic unrest and shifts in power from traditional economies.[70] With these inevitable demographic changes it seems that the burden of untreated critical illness in the developing world will increase, with poor outcomes, unless the present minimum ICU capacity grows.

Demand for intensivists' services will not only be driven by demographics, but also by their expanding role in inpatient care. In the USA, the number of ICU beds in hospitals increased by 26% from 1985 to 2000, whereas other inpatient beds decreased by 31%, with care shifted to other settings, indicating prioritisation of intensive care services.[71] Some have advocated for an increased role for intensivists outside the ICU by directing rapid-response teams consisting of physicians, nurses, and respiratory therapists, whose mandate is to assess acutely ill patients on general wards and prevent critical illness by early intervention.[72] Like many treatments for critical illness, rapid-response teams have substantial patho-physiological rationale and supporting observational data. Although present evidence from clinical trials supporting this strategy is mixed, some health authorities and quality agencies are recommending it.[73]

Data from a study of the outcomes of mechanical ventilation suggested that mortality associated with this intervention was lower at higher volume centres,[74] raising the hypothesis that population outcomes might be improved by regionalisation of intensive-care services. However, these observational data do not prove that patients would benefit from regionalisation, and important barriers to the transfer of critically ill patients from low-volume to high-volume centres exist.[75] Regionalisation of critical care services, like regionalisation of trauma services, will increase requirements for critical care services at high-volume centres. Most critical care services are organised with a trained intensivist managing the ICU, a model known as intensivist staffing, although this model is not universal. Most studies exploring the effects of this model come from the USA, the country with the most variation in intensive care delivery models. Data generally suggest that intensivists improve patient outcomes,[76] possibly because they have the training and time commitment to provide complete care to very sick patients and their families, or because they are able to manage the critical care team most effectively. But this hypothesis does not lend itself to randomised trials, and the evidence is not uniform.[77] Hospital physicians and surgeons, who are playing an increasing role in the management of patients in US acute-care hospitals, might share responsibility for critically ill patients in settings in which intensivist staffing is not possible.

The overall effect of these and other decisions about hospital organisation on the demand for critical care services is unclear. Most seem to increase demand on a specialty that might have insufficient numbers and trainees.[78–80] Potential solutions to this shortfall are increased development and dissemination of guidelines and protocols, training of non-physician clinicians to substitute for intensivists, and telemedicine to allow experienced physicians and nurses to expand the geographical scope of their care.[81] The training and telemedicine approaches would need additional human and technological resources, which might be feasible in middle-income or high-income settings, but would challenge the capacity of health systems in the developing world. The evidence that either approach is a safe and effective substitute for intensivist staffing is slight.

Natural and human-generated events such as disasters and wars generate acute and unpredictably large numbers of critically ill patients. Examples in the modern medical era have been rare; however, this situation could change if a pandemic of influenza or another virulent infection emerges to cause respiratory or other organ dysfunction. The 2003 outbreak of severe acute respiratory syndrome (SARS), mostly localised to east Asia[82] and Toronto, Canada,[83] highlighted challenges that would be amplified by a much broader pandemic: high illness severity of affected patients, stretched critical care resources diverted from general medicine and high-risk elective surgery to look after SARS patients, transmission to health-care workers, and high workload for remaining clinical staff.[84] Data from the present pandemic of H1N1 influenza show that in certain geographical areas the virus causes serious illness and death in young, previously healthy people, with a high burden of mechanically ventilated patients and deaths.[85,86]

Continuing wars, acts of terrorism, the 2004 tsunami in Asia, and the 2010 Haitian earthquake remind us that both human-generated and natural disasters can quickly overwhelm local health-care infrastructure in both developed and developing countries, even with mild to moderate numbers of casualties. Only recently has disaster management, including advance planning for surge capacity, mobile critical care, triage and rationing, hospital resource management, and staffing, become an integrated part of critical care academic activity.[87] However, during times of war, we should remember that evidence from systematic household cluster sampling suggests that most excess deaths, and, by extension, most demands for intensive care, do not arise from violence but from medical disorders resulting from the breakdown of public health

infrastructure (eg, cholera), or from the discontinuation of treatment of chronic diseases caused by interruption of pharmaceutical supplies.[88,89] In developing countries, these realities are aggravated by the presence of endemic diseases, such as HIV and trauma, that represent a substantial burden to health-care systems.

In terms of economics, the present financial crisis will probably harm health-care delivery in both developed and developing countries by decreasing government and donor expenditures, diverting household funds for health care to other essential expenditures, and increasing competition for government services as private insurance becomes less affordable.[90] Critically ill patients will not be spared since their care consumes between 0·5% and 1% of gross domestic product, at least in North America.[71,91] As the gross world product falls, the proportion consumed by health care in developed countries, and critical care specifically, will rise greatly, unless the demand for these services falls or their delivery becomes cheaper. Health-care funders facing these facts might focus spending on primary and preventive care. The present global recession and heightened disparities are drawing attention to decades-old questions. How effective is critical care? How cost effective is critical care? How can we ration a service perceived to rescue lives at imminent risk of death?[92] Despite these realities, US clinicians perceive little or no resource restraints on their ability to deliver intensive care.[93]

Data for structure, casemix, care processes, and outcomes of critical care in least developed countries (as by the UN definition based on low income, human resource weakness, and economic vulnerability) are restricted to descriptive studies suggesting few beds in intensive care, infrastructure, personnel, and equipment. Patients are thus admitted to ICUs with very high illness severity, and, not surprisingly, narrative reviews suggest that clinical outcomes are poor.[94] Maximising use of this scarce resource (table 2) implies attention to regionalisation and integration, based on prevailing local realities.[39]

Some have argued that financial inequities and cultural expectations make the notion of considering intensive care in developing countries misguided, and a universally applicable critical care ethic impossible.[95] Mitigating arguments emphasise philosophical principles of universal justice and harm to national economies[96] of untreated critical illness. Extrapolating from disease-specific data from the WHO's Global Health Observatory, infection and perinatal complications are much more common causes of admission to an ICU in the developing world than complications of chronic cardiac, vascular, and pulmonary disease, which predominate in the developed world. Before, little attention was focused on translation of intensive care techniques to low-resource settings, but more workers have now argued that safe emergency medical care is a worthwhile component of public health;[97] others have published practical proposals to extend evidence-based sepsis care to low-resource settings.[98] Any

improvements to the delivery of critical care will need adequate numbers of trained health-care workers,[99] feasible care guidelines and protocols that can be scaled across low-resource settings, and reversal of the so-called brain drain to developed world health-care systems.[100]

Conclusions

The young specialty of intensive care has evolved from its origins in treatment of poliomyelitis victims with respiratory failure, to an interdisciplinary team that cares for patients in an ICU, and to a broader mandate to treat critically ill patients irrespective of geographical location or use of specific technology. Determination of the global burden of critical-illness syndromes poses epidemiological challenges to separate the care for critically ill patients from the available intensive-care resources to treat them. Results from population-based studies in the developed world suggest that the burden of critical-illness syndromes is higher than generally appreciated and will increase as the population ages. Although intensive care capacity is scarce in the developing world, efforts to improve the care of the critically ill in these settings are emerging. Unlimited expansion of intensive care to meet the needs of an ageing population and handle the consequences of natural disasters, conflict, inadequate primary care, and high-risk treatments for very sick patients, will be challenged by high costs at a time of economic constraint. To meet this challenge, the specialty of intensive care will need to measure better the global burden of critical illness and develop both preventive and therapeutic interventions for the sickest patient. These interventions will need to be scalable across health-care systems at all the world's latitudes.

References
1   Ibsen B. The anaesthetist's viewpoint on the treatment of respiratory complications in poliomyelitis during the epidemic in Copenhagen, 1952. *Proc R Soc Med* 1954; **47:** 72–74.
2   Grenvik A, Pinsky MR. Evolution of the intensive care unit as a clinical center and critical care medicine as a discipline. *Crit Care Clin* 2009; **25:** 239–50.
3   The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000; **342:** 1301–08.
4   Harvey S, Young D, Brampton W, et al. Pulmonary artery catheters for adult patients in intensive care. *Cochrane Database Syst Rev* 2006; **3:** CD003408.
5   Kelley MA. Critical care medicine—a new specialty? *N Engl J Med* 1988; **318:** 1613–17.
6   Lott JP, Iwashyna TJ, Christie JD, Asch DA, Kramer AA, Kahn JM. Critical illness outcomes in specialty versus general intensive care units. *Am J Respir Crit Care Med* 2009; **179:** 676–83.
7   Barrett H, Bion JF. An international survey of training in adult intensive care medicine. *Intensive Care Med* 2005; **31:** 553–61.

8   The CoBaTrICE Collaboration. The educational environment for training in intensive care medicine: structures, processes, outcomes and challenges in the European region. *Intensive Care Med* 2009; DOI:10.1007/s00134-009-1514-4.

9   Bion JF, Barrett H. Development of core competencies for an international training programme in intensive care medicine. *Intensive Care Med* 2006; **32:** 1371–83.

10 Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. *Chest* 1992; **101:** 1644–55.

11 Calandra T, Cohen J. The international sepsis forum consensus conference on definitions of infection in the intensive care unit. *Crit Care Med* 2005; **33:** 1538–48.

12 Bernard GR, Artigas A, Brigham KL, et al. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med* 1994; **149:** 819–24.

13 Villar J, Perez-Mendez L, Lopez J, et al. An early PEEP/F$_i$O$_2$ trial identifies different degrees of lung injury in patients with acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2007; **176:** 795–804.

14 Rubenfeld GD, Caldwell E, Granton J, Hudson LD, Matthay MA. Interobserver variability in applying a radiographic definition for ARDS. *Chest* 1999; **116:** 1347–53.

15 Wunsch H, Harrison DA, Rowan K. Health services research in critical care using administrative data. *J Crit Care* 2005; **20:** 264–69.

16 Cook D, Rocker G, Marshall J, et al. Withdrawal of mechanical ventilation in anticipation of death in the intensive care unit. *N Engl J Med* 2003; **349:** 1123–32.

17 Vincent JL, Sakr Y, Sprung CL, et al. Sepsis in European intensive care units: results of the SOAP study. *Crit Care Med* 2006; **34:** 344–53.

18 Vincent JL, Bihari DJ, Suter PM, et al. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) Study. EPIC International Advisory Committee. *JAMA* 1995; **274:** 639–44.

19 Esteban A, Anzueto A, Frutos F, et al. Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. *JAMA* 2002; **287:** 345–55.

20 Sprung CL, Cohen SL, Sjokvist P, et al. End-of-life practices in European intensive care units: the Ethicus Study. *JAMA* 2003; **290:** 790–07.

21 Metnitz PG, Moreno RP, Almeida E, et al. SAPS 3—From evaluation of the patient to evaluation of the intensive care unit. Part 1: Objectives, methods and cohort description. *Intensive Care Med* 2005; **31:** 1336–44.

22 Rosenthal VD, Maki DG, Graves N. The International Nosocomial Infection Control Consortium (INICC): goals and objectives, description of surveillance methods, and operational activities. *Am J Infect Control* 2008; **36:** e1–12.

23 Angus DC, Pereira CA, Silva E. Epidemiology of severe sepsis around the world. *Endocr Metab Immune Disord Drug Targets* 2006; **6:** 207–12.

24 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.

25 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.

26 Linde-Zwirble WT, Angus DC. Severe sepsis epidemiology: sampling, selection, and society. *Crit Care* 2004; **8:** 222–26.

27 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.

28 Luhr OR, Antonsen K, Karlsson M, et al. Incidence and mortality after acute respiratory failure and acute respiratory distress syndrome in Sweden, Denmark, and Iceland. The ARF Study Group. *Am J Respir Crit Care Med* 1999; **159:** 1849–61.

29 Bersten AD, Edibam C, Hunt T, Moran J, 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:** 443–48.

30 Rubenfeld GD, Caldwell E, Peabody E, et al. Incidence and outcomes of acute lung injury. *N Engl J Med* 2005; **353** (4 suppl): 1685–93.

31 Rubenfeld GD. Epidemiology of acute lung injury. *Crit Care Med* 2003; **31** (4 suppl): S276–84.

32 Carson SS, Cox CE, Holmes GM, Howard A, Carey TS. The changing epidemiology of mechanical ventilation: a population-based study. *J Intensive Care Med* 2006; **2:** 173–82.

33 Needham DM, Bronskill SE, Sibbald WJ, Pronovost PJ, Laupacis A. Mechanical ventilation in Ontario, 1992–2000: incidence, survival, and hospital bed utilization of noncardiac surgery adult patients. *Crit Care Med* 2004; **32:** 1504–09.

34 Wunsch H, Angus DC, Harrison DA, et al. Variation in critical care services across North America and Western Europe. *Crit Care Med* 2008; **36:** 2787–89.

35 Celis E. ICUs worldwide: results of a nationwide survey of Colombian intensive care units. *Crit Care* 2002; **6:** 405–06.

36 Hariharan S, Chen D, Merritt-Charles L, et al. An evaluation of the intensive care unit resources and utilization in Trinidad. *West Indian Med J* 2007; **56:** 144–51.

37 Degoricija V, Sefer S, Kujundzic-Tiljak M, Gjurasin M. Intensive care units in Croatia: 2001 survey. *Croat Med J* 2002; **43:** 713–21.

38 Walther SM, Wickerts CJ. Large regional differences in Swedish intensive care. A nation-wide inquiry shows that the lowest number of beds is in big cities [Swedish]. *Lakartidningen* 2004; **101:** 3768, 3771–73.

39 Bhagwanjee S, Scribante J. National audit of critical care resources in South Africa—unit and bed distribution. *S Afr Med J* 2007; **97:** 1311–14.

40 Jochberger S, Ismailova F, Lederer W, et al. Anesthesia and its allied disciplines in the developing world: a nationwide survey of the Republic of Zambia. *Anesth Analg* 2008; **106:** 942–48.

41 Drennan K, Hart GK, Hicks P. Intensive Care Resources & Activity: Australia and New Zealand 2006/2007. Australian and New Zealand Intensive Care Society, 2008. http://www.anzics.com.au/downloads/doc_view/167-ccr-activities-report-2008?tmpl=component&format=raw (accessed June 25, 2010).

42 Du B, Xi X, Chen D, Peng J, China Critical Care Clinical Trial Group (CCCCTG). Critical care medicine in mainland China. *Crit Care* 2010; **14:** 206.

43 Yatawatte AB, Wanniarachchi CR, Goonasekera CD. An audit of state sector intensive care services in Sri Lanka. *Ceylon Med J* 2004; **49:** 51–54.

44 Haynes AB, Weiser TG, Berry WR, et al. A surgical safety checklist to reduce morbidity and mortality in a global population. *N Engl J Med* 2009; **360:** 491–99.

45 Weiser TG, Regenbogen SE, Thompson KD, et al. An estimation of the global volume of surgery: a modelling strategy based on available data. *Lancet* 2008; **372:** 139–44.

46 Harrison DA, Parry GJ, Carpenter JR, Short A, Rowan K. A new risk prediction model for critical care: the Intensive Care National Audit & Research Centre (ICNARC) model. *Crit Care Med* 2007; **35:** 1091–98.

47 Moran JL, Bristow P, Solomon PJ, George C, Hart GK. Mortality and length-of-stay outcomes, 1993-2003, in the binational Australian and New Zealand intensive care adult patient database. *Crit Care Med* 2008; **36:** 46–61.

48 Phua J, Badia JR, Adhikari NK, et al. Has mortality from acute respiratory distress syndrome decreased over time?: a systematic review. *Am J Respir Crit Care Med* 2009; **179:** 220–07.

49 Annane D, Aegerter P, Jars-Guincestre MC, Guidet B. Current epidemiology of septic shock: the CUB-Rea Network. *Am J Respir Crit Care Med* 2003; **168:** 165–72.

50 Granger CB, Goldberg RJ, Dabbous O, et al. Predictors of hospital mortality in the global registry of acute coronary events. *Arch Intern Med* 2003; **163:** 2345–53.

51 Tu JV, Nardi L, Fang J, Liu J, Khalid L, Johansen H. National trends in rates of death and hospital admissions related to acute myocardial infarction, heart failure and stroke, 1994-2004. *CMAJ* 2009; **180:** E118–25.

52 Dowdy DW, Eid MP, Sedrakyan A, et al. Quality of life in adult survivors of critical illness: a systematic review of the literature. *Intensive Care Med* 2005; **31:** 611–20.

53 Herridge MS, Cheung AM, Tansey CM, et al. One-year outcomes in survivors of the acute respiratory distress syndrome. *NEJM* 2003; **348:** 683–93.

54 Davydow DS, Desai SV, Needham DM, Bienvenu OJ. Psychiatric morbidity in survivors of the acute respiratory distress syndrome: a systematic review. *Psychosom Med* 2008; **70:** 512–19.

55 Schweickert WD, Pohlman MC, Pohlman AS, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet* 2009; **373:** 1874–82.

56 Cuthbertson BH, Rattray J, Campbell MK, et al. The PRaCTICaL study of nurse led, intensive care follow-up programmes for improving long term outcomes from critical illness: a pragmatic randomised controlled trial. *BMJ* 2009; **339:** b3723.

57 Garrard C, Young D. Suboptimal care of patients before admission to intensive care. Is caused by a failure to appreciate or apply the ABCs of life support. *BMJ* 1998; **316:** 1841–42.

58 Gao H, McDonnell A, Harrison DA, et al. Systematic review and evaluation of physiological track and trigger warning systems for identifying at-risk patients on the ward. *Intensive Care Med* 2007; **33:** 667–79.

59 Weinert CR, Gross CR, Marinelli WA. Impact of randomized trial results on acute lung injury ventilator therapy in teaching hospitals. *Am J Respir Crit Care Med* 2003; **167:** 1304–09.

60 Rubenfeld GD, Cooper C, Carter G, Thompson BT, Hudson LD. Barriers to providing lung-protective ventilation to patients with acute lung injury. *Crit Care Med* 2004; **32:** 1289–93.

61 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:** 1368–77.

62 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.

63 Heyland DK, Dhaliwal R, Drover JW, Gramlich L, Dodek P. Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients. *JPEN J Parenter Enteral Nutr* 2003; **27:** 355–73.

64 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:** 1864–69.

65 Van Spall HG, Toren A, Kiss A, Fowler RA. Eligibility criteria of randomized controlled trials published in high-impact general medical journals: a systematic sampling review. *JAMA* 2007; **297:** 1233–40.

66 Lazongas C, Pinto RL, Ferguson ND, Fowler RA. Eligibility criteria in randomized clinical trials in the critical care literature [abstract]. *Am J Respir Crit Care Med* 2008; **177:** A41.

67 Angus DC, Barnato AE, Linde-Zwirble WT, et al. Use of intensive care at the end of life in the United States: an epidemiologic study. *Crit Care Med* 2004; **32:** 638–43.

68 Needham DM, Bronskill SE, Calinawan JR, Sibbald WJ, Pronovost PJ, Laupacis A. Projected incidence of mechanical ventilation in Ontario to 2026: preparing for the aging baby boomers. *Crit Care Med* 2005; **33:** 574–79.

69 Wunsch H, Linde-Zwirble WT, Harrison DA, Barnato AE, Rowan KM, Angus DC. Use of intensive care services during terminal hospitalizations in England and the United States. *Am J Respir Crit Care Med* 2009; **180:** 875–80.

70 Jackson R, Howe N. The graying of the great powers: demography and geopolitics in the 21st century. Washington, DC: Center for Strategic and International Studies, 2008.

71 Halpern NA, Pastores SM, Greenstein RJ. Critical care medicine in the United States 1985–2000: an analysis of bed numbers, use, and costs. *Crit Care Med* 2004; **32:** 1254–59.

72 Winters BD, Pham JC, Hunt EA, Guallar E, Berenholtz S, Pronovost PJ. Rapid response systems: a systematic review. *Crit Care Med* 2007; **35:** 1238–43.

73 Institute for Healthcare Improvement. Establish a Rapid Response Team. http://www.ihi.org/IHI/Topics/CriticalCare/IntensiveCare/Changes/EstablishaRapidResponseTeam.htm (accessed June 25, 2010).

74 Kahn JM, Goss CH, Heagerty PJ, Kramer AA, O'Brien CR, Rubenfeld GD. Hospital volume and the outcomes of mechanical ventilation. *N Engl J Med* 2006; **355:** 41–50.

75 Kahn JM, Asch RJ, Iwashyna TJ, et al. Physician attitudes toward regionalization of adult critical care: a national survey. *Crit Care Med* 2009; **37:** 2149–54.

76 Pronovost PJ, Angus DC, Dorman T, Robinson KA, Dremsizov TT, Young TL. Physician staffing patterns and clinical outcomes in critically ill patients: a systematic review. *JAMA* 2002; **288:** 2151–62.

77 Levy MM, Rapoport J, Lemeshow S, Chalfin DB, Phillips G, Danis M. Association between critical care physician management and patient mortality in the intensive care unit. *Ann Intern Med* 2008; **148:** 801–09.

78 Angus DC, Kelley MA, Schmitz RJ, White A, Popovich J Jr, Committee on Manpower for Pulmonary and Critical Care Societies (COMPACCS). Caring for the critically ill patient. Current and projected workforce requirements for care of the critically ill and patients with pulmonary disease: can we meet the requirements of an aging population? *JAMA* 2000; **284 (3 suppl):** 2762–70.

79 Robnett MK. Critical care nursing: workforce issues and potential solutions. *Crit Care Med* 2006; **34 (3 suppl):** S25–S31.

80 Scribante J, Bhagwanjee S. National audit of critical care resources in South Africa—nursing profile. *S Afr Med J* 2007; **97:** 1315–18.

81 Breslow MJ. Remote ICU care programs: current status. *J Crit Care* 2007; **22:** 66–76.

82 Tsang KW, Ho PL, Ooi GC, et al. A cluster of cases of severe acute respiratory syndrome in Hong Kong. *N Engl J Med* 2003; **348:** 1977–85.

83 Poutanen SM, Low DE, Henry B, et al. Identification of severe acute respiratory syndrome in Canada. *N Engl J Med* 2003; **348:** 1995–2005.

84 Fowler RA, Lapinsky SE, Hallett D, et al. Critically ill patients with severe acute respiratory syndrome. *JAMA* 2003; **290:** 367–73.

85 Dominguez-Cherit G, Lapinsky SE, Macias AE, et al. Critically ill patients with 2009 influenza A(H1N1) in Mexico. *JAMA* 2009; **302:** 1880–87.

86 Critical Care Services and 2009 H1N1 Influenza in Australia and New Zealand. *N Engl J Med* 2009; **361:** 1925–34.

87 Devereaux A, Christian MD, Dichter JR, Geiling JA, Rubinson L, Task Force for Mass Critical Care. Summary of suggestions from the Task Force for Mass Critical Care summit, January 26–27, 2007. *Chest* 2008; **133 (5 suppl):** 1S–7S.

88 Burnham G, Lafta R, Doocy S, Roberts L. Mortality after the 2003 invasion of Iraq: a cross-sectional cluster sample survey. *Lancet* 2006; **368:** 1421–28.

89 Coghlan B, Brennan RJ, Ngoy P, al. Mortality in the Democratic Republic of Congo: a nationwide survey. *Lancet* 2006; **367:** 44–51.

90 Horton R. The global financial crisis: an acute threat to health. *Lancet* 2009; **373:** 355–56.

91 Kelley MA, Angus D, Chalfin DB, et al. The critical care crisis in the United States: a report from the profession. *Chest* 2004; **125:** 1514–17.

92 Jonsen AR. Bentham in a box: technology assessment and health care allocation. *Law Med Health Care* 1986; **14:** 172–74.

93 Ward NS, Teno JM, Curtis JR, Rubenfeld GD, Levy MM. Perceptions of cost constraints, resource limitations, and rationing in United States intensive care units: results of a national survey. *Crit Care Med* 2008; **36:** 471–76.

94 Dunser MW, Baelani I, Ganbold L. A review and analysis of intensive care medicine in the least developed countries. *Crit Care Med* 2006; **34:** 1234–42.

95 Engelhardt HT Jr. Critical care: why there is no global bioethics. *J Med Philos* 1998; **23:** 643–51.

96 Kirigia JM, Oluwole D, Mwabu GM, Gatwiri D, Kainyu LH. Effects of maternal mortality on gross domestic product (GDP) in the WHO African region. *Afr J Health Sci* 2006; **13:** 86–95.

97 Razzak JA, Kellermann AL. Emergency medical care in developing countries: is it worthwhile? *Bull World Health Organ* 2002; **80:** 900–05.

98 Cheng AC, West TE, Limmathurotsakul D, Peacock SJ. Strategies to reduce mortality from bacterial sepsis in adults in developing countries. *PLoS Med* 2008; **5:** e175.

99 Anand S, Barnighausen T. Human resources and health outcomes: cross-country econometric study. *Lancet* 2004; **364:** 1603–09.

100 Mullan F. The metrics of the physician brain drain. *N Engl J Med* 2005; **353:** 1810–18.