Intensive Care Med (2003) 29:368–377
DOI 10.1007/s00134-002-1624-8

EXPERT PANEL

Derek C. Angus
Jean Carlet
on behalf of the 2002 Brussels Roundtable Participants

Surviving Intensive Care: a report from the 2002 Brussels Roundtable

Received: 2 September 2002
Accepted: 29 November 2002
Published online: 21 January 2003

The Roundtable was sponsored by the European Society of Intensive Care Medicine, the American Thoracic Society, and the Society of Critical Care Medicine. See Appendix for full list of participants.

D. C. Angus (✉)
CRISMA (Clinical Research, Investigation, and Systems Modeling of Acute Illness) Laboratory,
Department of Critical Care Medicine,
School of Medicine,
University of Pittsburgh,
3550 Terrace Street, Pittsburgh, PA,
15261 USA
e-mail: angusdc@ccm.upmc.edu
Tel.: +1-412-6478110
Fax: +1-412-6473791

D. C. Angus
Department of Health Policy and Management,
Graduate School of Public Health,
University of Pittsburgh,
3550 Terrace Street, Pittsburgh, PA,
15261 USA

J. Carlet
Anesthesiology and Emergency Department,
Foundation Hôpital Saint Joseph,
Paris, France

Abstract The traditional goal of intensive care has been to decrease short-term mortality. While worthy, this goal fails to address the issue of what it means to survive intensive care. Key questions include whether intensive care survivors have optimal long-term outcomes and whether ICU care decisions would change if we knew more about these outcomes. The 2002 Brussels Roundtable, "Surviving Intensive care", highlighted these issues, summarizing the available evidence on natural history and risk factors for critical illness and outlining future directions for care and research. Critical illness is associated with a wide array of serious and concerning long-term sequelae that interfere with optimal patient-centered outcomes. Although traditional short-term outcomes, such as hospital mortality, remain extremely important, they are not likely to be adequate surrogates for subsequent patient-centered outcomes. As such, it is important to focus specifically on how critical illness and intensive care affects a patient's and relatives' long-term health and well-being. There are a large number of potential pre-, intra-, and post-ICU factors that may improve or worsen these outcomes, and these factors are subjects for future research. In addition, future clinical trials of ICU therapies should include long-term follow-up of survival, quality of life, morbidity, functional status, and costs of care. Follow-up ought to be for at least six months. The SF-36 and EuroQOL EQ-5D are the best-suited instruments for measuring quality of life in multicenter critical care trials though further methodologic research and instrument design is encouraged. There are also opportunities today to improve care. Key to taking advantage of such opportunities is the need for a global awareness of critical illness as an entity that begins and ends outside the ICU 'box'. Specific interventions that show promise for improving care include ICU discharge screening tools and ICU follow-up clinics.

Keywords Critical care · Intensive care units · Survival rate · Treatment outcome · Long-term outcome · Models of care

Introduction

The traditional goal of intensive care has been to decrease short-term mortality. This is an appropriate and important end-point when caring for critically ill patients. However, less attention has been paid to the issue of what it means to survive intensive care for patients and relatives. Key questions include whether intensive care survivors have good long-term outcomes, whether these outcomes are the best possible results from our care, and whether our care would change if we knew more about outcomes beyond ICU discharge. The 2002 Roundtable was designed to highlight these issues, summarizing the available evidence on natural history and risk factors, and discussing future directions for research and improved care.

Methods

The Roundtable chairs outlined the key questions and developed a syllabus and list of speakers in the late spring of 2001 (see "Appendix"). The syllabus was divided into four sessions: the natural history of critical illness; the predictors and modifiers of long-term outcomes; future research issues, and; approaches to improve long-term outcomes. Speakers were invited in the summer and fall of 2001. Each speaker was given instructions and details regarding their proposed topic and asked to prepare a manuscript and 20-min oral summary. Speakers involved in reviewing the existing literature (the first two sections) were asked to conduct a systematic review as part of their tasks. Manuscripts were circulated to all participants prior to the Roundtable. The Roundtable was held in Brussels 16–18 March 2002. Each participant presented his or her topic followed by a 30-min discussion. At the end of each of the four sessions, further discussion focused on the key themes emerging from that session. At the end of the Roundtable a further 2-h discussion was held to discuss the common themes of the entire Roundtable and summation of key points. These key points were presented at the Opening Session of the 22nd International Symposium on Intensive Care and Emergency Medicine. Following the conference the manuscripts were revised in accordance with thoughts and comments raised during the Roundtable and resubmitted to the two chairs. The entire collection of manuscripts is published under separate cover by Springer-Verlag in the Update in Intensive Care and Emergency Medicine series [1]. This document summarizes the key points emerging from the Roundtable. It was drafted and edited by the Chairs in the spring and summer of 2002 and circulated to all Roundtable participants for feedback and critique. It is organized following the four sessions of the Roundtable.

What do we know about patient-centered outcomes after critical illness?

There are a wide variety of important, serious sequelae in survivors of intensive care. These include late mortality [2, 3], on-going morbidity [3, 4, 5], neurocognitive defects [6], impaired mental health [3, 5, 6], poor functional capabilities [3, 4, 5], decreased quality of life [7], decreased return to work and usual activities [6], burden and stress on families and informal caregivers [8], and economic costs to the patient, the family and society [9].

Several studies have suggested that patients who survive intensive care, such as those surviving severe sepsis, are at a higher risk of death than control cohorts for many years [2, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27]. Furthermore, ICU survivors often report debilitating problems with poor functional status [28, 29, 30, 31, 32]. For example, Montuclard et al. [28] recently reported in a small cohort of elderly ICU survivors that only 41% were alive at 1 year, and 23% had difficulty bathing, 15% had difficulty toileting, 26% had difficulty transferring from chairs or beds, and 19% were incontinent. Even at hospital discharge, many patients have considerable problems. Ely et al. [33] recently demonstrated that almost half of all ICU patients leave the hospital with abnormal mental status. Hopkins et al. [34] showed that neurocognitive problems can persist long after discharge. At 2 years, one-fifth to one-third of acute respiratory distress syndrome (ARDS) survivors demonstrated problems with memory, mental processing, executive decision-making, and attention deficit [35, 36]. ARDS survivors are also likely to have a wide array of symptoms ranging from respiratory problems, such as hoarseness and dyspnea, to general constitutive complaints, such as weakness and fatigue [13]. Herridge [37] has also reported considerable weight loss and debilitation of ARDS survivors, including flexion contractures and heterotopic ossification, presumably due to the prolonged immobilization of protracted ICU stays. These problems impair exercise ability and interfere with the ability to return to work. Indeed, Herridge [37] reported that only 38% of survivors had returned to work 1 year after discharge. It is not surprising, therefore, that numerous studies have demonstrated that ICU survivors and survivors of ARDS or sepsis endure a poorer quality of life than controls [13, 14, 15, 30, 31, 32, 34, 38]. Studies have suggested ICU survivors are more likely to suffer posttraumatic stress disorder and depression with poor quality of life related to both physical and mental domains [32].

These poor long-term outcomes likely place significant toll on spouses and families. Although there are no studies of the long-term impact of ICU care on informal caregivers [8], evidence from stroke survivors suggest that stroke caregivers (spouses and families) are three times more likely to develop depression [39]. This appears to be particularly problematic among women [40]. Based on studies in the care of other chronically ill patients, the ramifications for informal caregivers of ICU survivors might well include impaired physical and mental health, social isolation, impaired sexual relations, and forced loss of earnings [8]. In addition, families may experience serious psychological sequelae from a bad experience with the patient stay in the ICU.

What are the causes and modifiers of the poor patient-centered outcomes after intensive care?

Despite the importance of this question, the answers are generally complicated and poorly understood. Problems include delineating post-ICU sequelae that are due to the ICU course vs. part of the underlying illness, separating the myriad potential variables that might influence outcome and interact with each other, and a lack of comprehensive data. To consider this question, therefore, it is helpful to first create a conceptual model of critical illness. We propose that an episode of critical illness is not just the period of time a patient spends in an ICU but is the period of time that begins with the onset of the acute deterioration and ends when a patient's risk of late sequelae, such as on-going mortality, has returned to the baseline risk of a similar patient who had not incurred the acute critical illness [41]. This is represented graphically in Fig. 1.

Imposed upon this model, one can begin to delineate and classify some of the potential variables and their interactions that might influence subsequent patient-centered outcomes. We propose such a classification with illustrative examples in Table 1. Many of these pre- and intra-ICU factors have been studied previously. However, in many instances, the studies have only explored the relationship with short-term outcome using association analysis. For example, there are many observational studies suggesting that full-time intensivists improve hospital mortality but no prospective studies [42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67]. The same holds true for the use of many interventions in the ICU and obviously for variables suspected of causing harm. The relationship between nosocomial pneumonia and outcome will only be studied by association analysis because one would not prospectively assign a patient to develop a pneumonia.

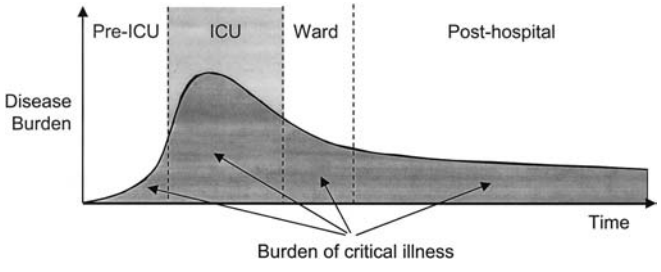

Fig. 1 The episode of critical illness. The figure shows that an episode of critical illness is not just the period of time a patient spends in an ICU but is the period of time that begins with the onset of the acute deterioration and ends when a patient's risk of late sequelae, such as on-going mortality, has returned to the baseline risk of a similar patient who had not incurred the acute critical illness. (Adapted with permission from [41])

The best approach to understand causality in clinical medicine is to conduct a prospective randomized trial. However, even variables that can be studied using prospective randomized trials, such as ICU therapies [68] and protocols [69, 70, 71], have typically not evaluated the effect on long-term outcomes. Research in this area is also complicated by the inherent difficulties of isolating pre-ICU factors in patients who are often only identified once they have been admitted to the ICU. Similarly, obtaining long-term follow-up can be difficult and expensive.

Given the difficulties of measuring long-term outcomes, and the existing and comprehensive focus on short-term outcomes, it would be appealing to believe that these short-term outcomes would be valuable proxies for subsequent outcomes. This, however, is a very dangerous assumption. As shown in Table 2, there are many examples from many diseases where an intervention appeared to engender a good short-term outcome yet was subsequently shown to have no effects or even harmful effects on long-term outcomes. Indeed, Clermont et al. recently showed that, in patients surviving a hospitaliza-

Table 1 Variables potentially influencing long-term outcomes after critical illness

Variable	Examples
Pre-ICU	
Underlying illness	Chronic obstructive lung disease, preillness quality of life
Reason for ICU admission	Respiratory failure, trauma
Pre-ICU management	Resuscitation, antibiotics
Access to the ICU	Bed availability, physician referral patterns, health insurance
Intra-ICU	
Patient course and events	Organ dysfunction, sepsis
Treatments	Sedation, feeding, transfusions
Organization	Staffing patterns, protocol use
Iatrogenesis and environment	Pneumothorax, noise pollution
Patient-healthcare interactions	
Sleep disturbance and delirium	Patient-ventilator asynchrony and sedation use

Table 2 Paradoxical short- and long-term effects after certain interventions (*CHF* congestive heart failure, *AMI* acute myocardial infarction) (Adapted with permission from [91]

Intervention	Disease	Positive early effect	Negative late effect
Milrinone	CHF	Increased cardiac output and exercise	Higher mortality [92]
Flecanide	Post-AMI	Decreased arrhythmias	Higher mortality [93]
Growth hormone	Critical illness	Improved nitrogen balance	Higher mortality [94]
Transfusion	ICU anemia	Increased hematocrit	Higher mortality [71]
Postnatal steroids	Premature respiratory failure	Decreased lung disease [95]	Impaired neurodevelopment [96, 97]

tion for community-acquired pneumonia, the degree of acute organ dysfunction (as a measure of the 'burden of critical illness') was not an independent predictor of subsequent patient-centered outcomes [72].

In other words, although we are very concerned about the poor long-term outcomes of ICU survivors, it is not clear to what extent these outcomes are due to the ICU care, the ICU disease, or underlying characteristics of the types of patients who develop critical illness. These are crucial distinctions that must be addressed in future research if we are to optimize long-term outcomes after critical illness.

What are the implications for future research?

We organized our recommendations for future research into four areas: observational studies, conduct of future ICU interventional trials, innovations to improve long-term outcomes, and methodological research.

Future observational studies of long-term outcomes

Quality of life, function, morbidity, and survival in different ICU populations

Although we have considerable information on the natural history of critical illness, there is still a need for better observational study to catalog the potential sequelae more carefully. For example, although there are a number of studies of quality of life following ARDS, the general rigor is poor and inconsistent [73, 74]. And, there are still very few studies cataloging functional status and on-going morbidity. We would therefore urge investigators to better study the quality of life, functional status, morbidity, and survival in different ICU populations.

Neurocognitive abnormalities in ICU survivors

The recent reports of neurocognitive abnormalities in ICU survivors are particularly concerning [6, 33, 34, 75, 76, 77]. We use a wide array of powerful neurosedative and neurotropic agents in the ICU and there is a distinct possibility that our use of such agents and management of delirium in the ICU could be influencing subsequent neurocognitive function. We therefore strongly recommend greater study in this area.

Burden on family and other informal caregivers of ICU survivors

Many ICU survivors incur poor patient-centered outcomes akin to those suffered by patients with many chronic and debilitating conditions. Informal caregiver burden is considerable in the latter instance yet there is essentially no evaluation of the burden and stress on informal caregivers of ICU survivors [8].

Long-term economic costs

There are no studies of the long-term costs following ICU discharge. It is likely that these costs could be high, given the potential for numerous debilitating sequelae. If so, there may be a considerable financial impetus to find alternative treatment strategies that improve outcomes and decrease these costs. Alternatively, new strategies may improve outcomes but only at considerable increase in cost. If so, determining the value or cost-effectiveness of these strategies will be important when evaluating whether such interventions can be adopted [78].

Future interventional trials (e.g., antisepsis trials)

New interventions in intensive care are commonly studied in large, multicenter (and frequently multinational) randomized trials. To better understand the long-term ramifications of these interventions, yet not unduly burden the study with excessive additional data collection, we recommend the following.

Prolong follow-up for survival to at least 6 months

Clinical trials would ideally include a follow-up period that is comparable to the time interval of risk [2]. Based on survival curves from prior studies [10] and in keeping with the recommendations of the International Working Party on clinical trials in sepsis convened by the UK Medical Research Council [79], we recommend that all ICU interventional trials designed to test efficacy include survival follow-up to at least 6 months (and ideally longer, especially for those enrolled early in the trial).

Telephone-based assessment of quality of life

Survival alone is an inadequate measure of patient-centered outcome [7, 80, 81, 82]. We would therefore recommend also assessing quality of life. We recommend using a standard, well-validated instrument that is straightforward and appropriate to administer by telephone (given the complexities of long-term follow-up in a multicenter study) and, ideally, is applicable in different countries and languages. The SF-36 [83] is an example of a comprehensive instrument that meets these criteria while the EQ-5D by the EuroQOL group [84] is an example of a simple instrument that meets these criteria [7, 78, 80]. The EQ-5D provides a measure of both quality of life and utility, the latter being necessary for the calculation of quality-adjusted survival, a key measure of health effect for cost-effectiveness assessments [85]. Recently, Brazier et al. demonstrated a method to calculate utilities from the SF-36 as well [86]. Consistent adoption of common instruments across studies would also facilitate interstudy comparisons [74].

Telephone-based assessment of function, morbidity, resource use, return to work and usual activities, and other domains

Quality of life is not the only important long-term outcome. If researchers are conducting a telephone-based assessment of quality of life, we would recommend the interview be complimented with additional questions relating to the other domains listed above [9, 78]. Instruments are less well-standardized in this arena and may require tailoring to specific diseases or interventions. Nevertheless, a short set of additional questions could add valuable information at little additional cost to the study.

Innovations to improve long-term outcomes

When data characterizing the nature and extent of decreases in long-term patient-centered outcomes after intensive care are still somewhat lacking, it is difficult to articulate a list of specific interventions directed at improving care. Nevertheless, there are examples of potential interventions that might be developed with reasonable ease. One example is the ICU follow-up clinic. [87] Such clinics already exist sporadically in some countries [88]. The organization and purpose of these clinics is quite varied but generally conducted at least in part by intensive care staff. The premise for these clinics is that: (a) there are sequelae following intensive care that can be identified and potentially improved, and (b) specific post-ICU follow-up is better suited to detecting and treating these sequelae than general medical care. However, there is little formal evaluation at this point and a number of questions regarding the benefits and costs of such follow-up are unanswered.

Perhaps complimentary to ICU follow-up clinics, a second idea is that of ICU discharge screening [89]. It is certainly possible that there are key risk factors potentially identifiable at ICU discharge for important sequelae. Screening for such risk factors may allow more targeted post-ICU care. Again, however, although the idea appears worthy, there are no data currently.

Methodological research

There are a number of methodological issues relating to the adequate capture of post-ICU patient-centered outcomes. For example, what are the best quality of life instruments? Are existing instruments suitable for capturing important nuances of post-ICU sequelae or should disease-specific instruments be captured? Although the panel has made recommendations for the use of such instruments above, we recognize there are limitations and would encourage investigators to continue evaluation of new instruments. Specific challenges, for example, include developing instruments that can adequately capture neurocognitive defects post-ICU in environments such as large multicenter trials where exhaustive neuropsychological testing may be impractical. Similar issues relate to tracking long-term economic costs, especially in multinational studies. Of course, some of these issues are not specific to intensive care and it is key that we take advantage of methodological breakthroughs in related fields as they occur.

How could we change care now?

Although there is considerable need for on-going research, there was a general perception among the panelists that there is adequate empirical evidence to support changing practice today. Indeed, attention to many common elements of ICU practice may improve long-term outcomes. However, even within the experience of the

Table 3 Examples of common ICU problems, potential late sequelae, and simple interventions

ICU problem	Potential long-term sequelae	Simple ICU interventions
Intra-ICU weight loss	Impaired recovery of strength and functional capabilities; delayed return to work or usual activities.	Attention to adequate feeding Referral to rehabilitation for strength training
Immobilization, critical illness polyneuropathy and entrapment neuropathies	Prolonged neuromuscular weakness; impaired functional recovery; delayed returnto work or usual activities.	Physical therapy in and after ICU
Patient and family anxiety	Poor patient and family satisfaction with care; residual anger, resentment and mistrust.	Communication program "Discharge" interview
Oversedation and delirium	Impaired or delayed neurocognitive function/recovery	Daily awakening

panel, there was wide variation in current practice patterns with regard to simple, and presumably straightforward, practice recommendations. Table 3 presents some examples of common problems that develop in the ICU, the potential long-term sequelae, and some relatively simple changes in care, or the focus of care, that could minimize unwanted sequelae.

These examples highlight the potential simplicity of the steps that could be taken to optimize long-term outcomes. At the same time, they also highlight the need to have a global awareness of critical illness both within and outside the ICU "box." This is illustrated in Fig. 2, which demonstrates the traditional "within the box" model of intensive care delivery (Fig. 2A) and an alternative role for the critical care team that thinks "outside the box" (Fig. 2B).

Encouraging this paradigm shift is not necessarily easy. As with many other quality improvement initiatives, we would recommend that intensivists begin with small, simple measures that are likely to work locally [87, 90]. We also recognize that care before and after the ICU is already provided by other medical disciplines [87, 90]. We do not suggest that intensivists should assume this expanded responsibility alone. Rather, we would suggest that intensivists seek to create partnerships with other caregivers. For example, primary care physicians may be very willing to screen for the late sequelae of ARDS, and simply require education regarding what to look for. Similarly, rehabilitation medicine is a well-established field that plays a key role in aiding recovery after a wide variety of conditions such as stroke or traumatic brain injury. Creating partnerships with rehabilitation services to promote follow-up of debilitated, underweight ICU survivors could foster improved outcomes at minimal expense. Changing the focus of the ICU team to consider long-term patient-centered outcomes, such as whether a patient will successfully return to work, may have the added advantage of facilitating communication with family members.

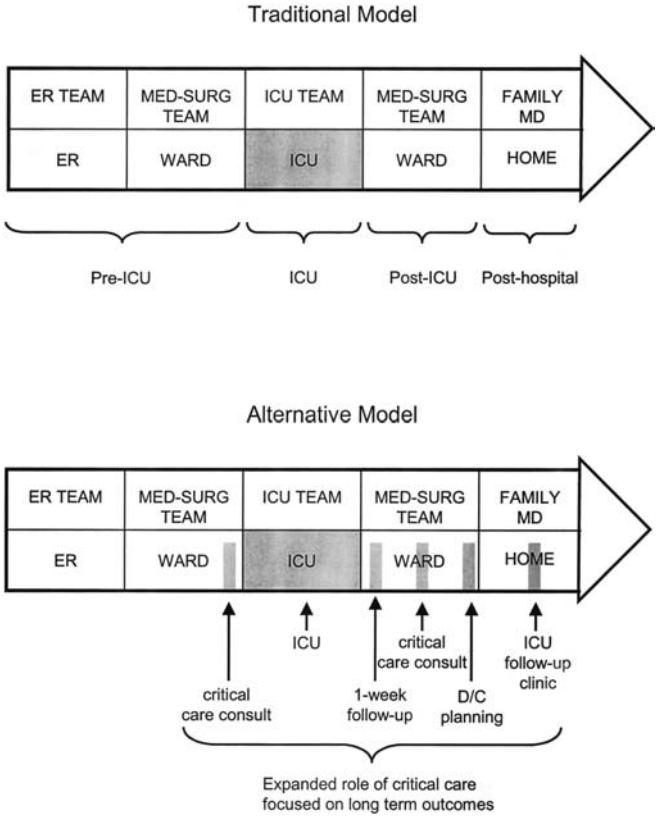

Fig. 2 Traditional and alternative models of intensive care delivery to the critically ill. In the traditional model of critical illness, critical care is delivered only by ICU clinicians in the ICU. Patient management is delivered according to distinct clinical roles during distinct, usually short-term, episodes of illness. In the alternative model, critical illness is viewed on a continuum. Patient management related to critical illness is offered at several points in the illness continuum. The focus is on optimizing long-term outcomes. *ER* Emergency room; *D/C* discharge. (Adapted with permission from [87])

Summary

This year's Roundtable represented an opportunity to take stock of an existing literature base, debate conceptual issues regarding the focus and purpose of critical care, and recommend future steps for research and clinical care. It was very apparent that critical illness is associated with a wide array of serious and concerning long-term sequelae that interfere with optimal patient-centered outcomes. Although traditional short-term outcomes, such as hospital mortality, remain extremely important, they are not likely to be adequate surrogates for subsequent patient-centered outcomes. As such, it is important to focus specifically on how critical illness and intensive care affects a patient's and relatives' long-term health and well-being. Clearly, there are a large number of potential pre-, intra-, and post-ICU factors that may improve or worsen these outcomes, and delineating these effects sets the stage for a rich research agenda. At the same time, there are opportunities today to improve care. Key to taking advantage of such opportunities is the need to embrace a global awareness of critical illness as an entity that begins and ends outside the ICU "'box."

Acknowledgements The authors thank Veronique de Vlaeminck for her indispensable help with organization of the Roundtable, Karen Pickett for her assistance with editing, Tony Dremsizov, MBA, for his assistance with manuscript preparation, and Gordon Rubenfeld, MD, MSc, and Deborah Cook, MD, for their permission to use Table 2 and Fig. 2.

Appendix: list of participants in the Surviving Intensive Care Roundtable, Brussels, March 2002

Co-chairs:

- Derek C. Angus, MB, ChB, MPH; the CRISMA Laboratory, Department of Critical Care Medicine, School of Medicine, and the Department of Health Policy and Management, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pa, USA
- Jean Carlet, MD; Foundation Hôpital Saint Joseph, Paris, France

Members

- Elie Azoulay, MD; Service de Réanimation Médicale, Hôpital St Louis and Paris 7 University, Paris, France
- Julian F. Bion, MD; Department of Anaesthetics and Intensive Care Medicine, The University of Birmingham, Department of Intensive Care Medicine, Birmingham, UK
- Stephen Brett, MD, FRCA; Department of Anesthesia and Intensive Care Medicine, Hammersmith Hospital, London, UK
- Christian Brun-Buisson, MD; Medical ICU, Hôpital Henri-Mondor, Creteil, France
- Deborah J. Cook, MD; Department of Medicine and the Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada
- J. Randall Curtis, MD, MPH; Division of Pulmonary and Critical Care Medicine, University of Washington, Seattle, Wash., USA
- E. Wesley Ely, MD, MPH; Allergy, Pulmonary and Critical Care Medicine Division, Vanderbilt University, Nashville, Tenn., USA
- Jesse Hall, MD; Department of Medicine, the University of Chicago, Chicago, Ill., USA
- Margaret Herridge, MD, MPH; Department of Medicine, Toronto General Hospital, Toronto, Canada
- Ramona O. Hopkins, PhD; Psychology Department and Neuroscience Center, Brigham Young University, Provo, Utah, and Department of Medicine, Pulmonary and Critical Care Divisions, LDS Hospital, Salt Lake City, Utah, USA
- Sean Keenan, MD, MSc; Intensive Care Unit and Department of Medicine, Royal Columbian Hospital, New Westminster, British Columbia, Canada
- Mitchell Levy, MD; Department of Pulmonary and Critical Care Medicine, Brown University and Rhode Island Hospital, Providence, R.I., USA
- Walter T. Linde-Zwirble; Health Process Management, LLC, Doylestown, Pa., USA
- Rui Moreno, MD; Department of Intensive Care, Hospital de St. Antonio dos Capuchos, Lisbon, Portugal
- Peter J. Pronovost, MD, PhD; The Johns Hopkins University School of Medicine, Bloomberg School of Public Health, Baltimore, Md., USA
- Adrienne Randolph, MD; Department of Anesthesia and Pediatrics, Children's Hospital of Boston and Harvard University Medical School, Boston, Mass., USA
- Marco Ranieri, MD; Division of Anesthesiology and Critical Care Medicine, Ospedale S. Giovanni Battista, Turin, Italy
- Kathy Rowan, DPhil; Intensive Care National Audit and Research Centre, London, UK
- Gordon D. Rubenfeld, MD, MSc; Division of Pulmonary and Critical Care Medicine, University of Washington, Seattle, Wash., USA
- William J. Sibbald, MD; Department of Medicine, Sunnybrook & Women's College Health Science Center, Toronto, Ontario, Canada
- Charles Sprung, MD, JD; Department of Anesthesiology, Hadassah University Medical Center, Jerusalem, Israel
- Martine Van Glabbeke; European Organization for Research and Treatment of Cancer, Data Centre, Brussels, Belgium
- Ben A. van Hout, MSc, PhD; Julius Center for General Practice and Patient Oriented Research, University Medical Center, Utrecht, The Netherlands
- Jean-Louis Vincent, MD, PhD; Department of Intensive Care, Erasme University Hospital, Free University of Brussels, Brussels, Belgium

References

1. Angus DC, Carlet J (eds) (2002) Surviving intensive care. Update in intensive care and emergency medicine, no 39. Springer, Berlin Heidelberg New York
2. Keenan SP, Dodek P (2002) Survival as an outcome for ICU patients. In: DC Angus, J Carlet (eds) Surviving intensive care. Update in intensive care and emergency medicine, no 39. Springer, Berlin Heidelberg New York
3. Ely EW (2002) Understanding outcomes of critically ill older patients. In: DC Angus, J Carlet (eds) Surviving intensive care. Update in intensive care and emergency medicine, no 39. Springer, Berlin Heidelberg New York
4. Herridge MS (2002) Morbidity and functional limitations in survivors of ARDS. In: DC Angus, J Carlet (eds) Surviving intensive care. Update in intensive care and emergency medicine, no 39. Springer, Berlin Heidelberg New York
5. Randolph AG, Graham R (2002) Measuring the health status of pediatric ICU survivors. In: DC Angus, J Carlet (eds) Surviving intensive care. Update in intensive care and emergency medicine, no 39. Springer, Berlin Heidelberg New York
6. Sukantarat KT, Brett S (2002) The neuropsychological consequences of intensive care. In: DC Angus, J Carlet (eds) Surviving intensive care. Update in intensive care and emergency medicine, no 39. Springer, Berlin Heidelberg New York
7. Rowan K, Jenkinson C, Black N (2002) Health-related quality of life. In: DC Angus, J Carlet (eds) Surviving intensive care. Update in intensive care and emergency medicine, no 39. Springer, Berlin Heidelberg New York
8. Levy MM (2002) The burden of caregiving on families of ICU survivors. In: DC Angus, J Carlet (eds) Surviving intensive care. Update in intensive care and emergency medicine, no 39. Springer, Berlin Heidelberg New York
9. Kalassian KG, Angus DC (2002) Long-term economic consequences of surviving intensive care. In: DC Angus, J Carlet (eds) Surviving intensive care. Update in intensive care and emergency medicine, no 39. Springer, Berlin Heidelberg New York
10. Quartin AA, Schein RM, Kett DH, Peduzzi PN, for the Department of Veterans Affairs Systemic Sepsis Cooperative Studies Group (1997) Magnitude and duration of the effect of sepsis on survival. JAMA 277:1058–1063
11. Keenan SP, Dodek P, Chan K, Hogg RS, Craib KJP, Anis AH, Spinelli JJ (2002) Intensive care unit admission has minimal impact on long-term mortality. Crit Care Med 30:501–507
12. Kaplan V, Clermont G, Griffin MF, Kasal J, Watson RS, Linde-Zwirble WT, Angus DC (2002) Pneumonia-still the old man's friend? Arch Intern Med (in press)
13. Angus DC, Musthafa AA, Clermont G, Griffin MF, Linde-Zwirble WT, Dremsizov TT, Pinsky MR (2001) Quality-adjusted survival in the first year after the acute respiratory distress syndrome. Am J Respir Crit Care Med 163:1389–1394
14. Davidson TA, Rubenfeld GD, Caldwell ES, Hudson LD, Steinberg KP (1999) The effect of acute respiratory distress syndrome on long-term survival. Am J Respir Crit Care Med 160:1838–1842
15. Perl TM, Dvorak L, Hwang T, Wenzel RP (1995) Long-term survival and function after suspected gram-negative sepsis. JAMA 274:338–345
16. Parno JR, Teres D, Lemeshow S, Brown RB (1982) Hospital charges and long-term survival of ICU versus non-ICU patients. Crit Care Med 10:569–574
17. Thibault GE, Mulley AG, Barnett GO, Goldstein RL, Reder VA, Sherman EL, Skinner ER (1980) Medical intensive care: indications, interventions, and outcomes. N Engl J Med 302:938–942
18. Bams JL, Miranda DR (1985) Outcome and costs of intensive care: a follow-up study on 238 ICU-patients. Intensive Care Med 11:234–241
19. Jacobs CJ, van der Vliet JA, van Roozendaal MT, van der Linden CJ (1988) Mortality and quality of life after intensive care for critical illness. Intensive Care Med 14:217–220
20. Mundt DJ, Gage RW, Lemeshow S, Pastides H, Teres D, Avrunin JS (1989) Intensive care unit patient follow-up. Mortality, functional status, and return to work at six months. Arch Intern Med 149:68–72
21. Ridley S, Jackson R, Findlay J, Wallace P (1990) Long term survival after intensive care. BMJ 301:1127–1130
22. Ridley S, Plenderleith L (1994) Survival after intensive care. Comparison with a matched normal population as an indicator of effectiveness. Anaesthesia 49:933–935
23. Niskanen M, Kari A, Halonen P (1996) Five-year survival after intensive care-comparison of 12:180 patients with the general population. Finnish ICU Study Group. Crit Care Med 24:1962–1967
24. Capuzzo M, Bianconi M, Contu P, Pavoni V, Gritti G (1996) Survival and quality of life after intensive care. Intensive Care Med 22:947–953
25. Short TG, Buckley TA, Rowbottom MY, Wong E, Oh TE (1999) Long-term outcome and functional health status following intensive care in Hong Kong. Crit Care Med 27:51–57
26. Eddleston JM, White P, Guthrie E (2000) Survival, morbidity, and quality of life after discharge from intensive care. Crit Care Med 28:2293–2299
27. Flaatten H, Kvale R (2001) Survival and quality of life 12 years after ICU. A comparison with the general Norwegian population. Intensive Care Med 27:1005–1011
28. Montuclard L, Garrouste-Orgeas M, Timsit JF, Misset B, De Jonghe B, Carlet J (2000) Outcome, functional autonomy, and quality of life of elderly patients with a long-term intensive care unit stay. Crit Care Med 28:3389–3395
29. Tsevat J, Cook EF, Green ML, Matchar DB, Dawson NV, Broste SK, Wu AW, Phillips RS, Oye RK, Goldman L (1995) Health values of the seriously ill. SUPPORT investigators. Ann Intern Med 122:514–520
30. McHugh LG, Milberg JA, Whitcomb ME, Schoene RB, Maunder RJ, Hudson LD (1994) Recovery of function in survivors of the acute respiratory distress syndrome. Am J Respir Crit Care Med 150:90–94
31. Weinert CR, Gross CR, Kangas JR, Bury CL, Marinelli WA (1997) Health-related quality of life after acute lung injury. Am J Respir Crit Care Med 156:1120–1128
32. Schelling G, Stoll C, Haller M, Briegel J, Manert W, Hummel T, Lenhart A, Heyduck M, Polasek J, Meier M, Preuss U, Bullinger M, Schuffel W, Peter K (1998) Health-related quality of life and posttraumatic stress disorder in survivors of the acute respiratory distress syndrome. Crit Care Med 26:651–659
33. Ely EW, Inouye SK, Bernard GR, Gordon S, Francis J, May L, Truman B, Speroff T, Gautam S, Margolin R, Hart RP, Dittus R (2001) Delirium in mechanically ventilated patients-Validity and reliability of the Confusion Assessment Method for the intensive care unit (CAM-ICU). JAMA 286:2703–2710

34. Hopkins RO, Weaver LK, Pope D, Orme JF, Bigler ED, Larson-Lohr V (1999) Neuropsychological sequelae and impaired health status in survivors of severe acute respiratory distress syndrome. Am J Respir Crit Care Med 160:50–56
35. Hopkins RO, Gale SD, Pope D, Weaver LK, Bigler ED (2000) Ventricular enlargement in patients with acute respiratory distress syndrome (abstract). J Int Neuropsychol Soc 6:229
36. Hopkins RO (2001) Brain imaging, neurocognitive sequelae and health related quality of life following acute respiratory distress syndrome. In: SG Pandalai (ed) Recent research developments in respiratory and critical care medicine. Research Signpost, Kerala, pp 209–222
37. Herridge MS (2002) Long-term outcomes after critical illness. Curr Opin Crit Care 8:331–336
38. Davidson TA, Caldwell ES, Curtis JR, Hudson LD, Steinberg KP (1999) Reduced quality of life in survivors of acute respiratory distress syndrome compared with critically ill control patients. JAMA 281:354–360
39. Woods NF, Haberman MR, Packard NJ (1993) Demands of illness and individual, dyadic, and family adaptation in chronic illness. West J Nurs Res 15:10–30
40. Donelan K, Falik M, DesRoches CM (2001) Caregiving: challenges and implications for women's health. Womens Health Issues 11:185–200
41. Angus DC (1997) Understanding the incidence and long-term outcome of ARDS. In: Gullo A (ed) Anaesthesia, pain, intensive care and emergency medicine: scientific report. Springer, Berlin Heidelberg New York, pp 289–298
42. Pronovost PJ, Jencks M, Dorman T, Garrett E, Rosenfeld BA, Breslow MJ, Lipsett PA, Bass EB (1999) Organizational characteristics of intensive care units related to outcomes of abdominal aortic surgery. JAMA 281:1310–1312
43. Brown JJ, Sullivan G (1989) Effect on ICU mortality of a full-time critical care specialist. Chest 96:127–129
44. Baldock G, Foley P, Brett S (2001) The impact of organisational change on outcome in an intensive care unit in the United Kingdom. Intensive Care Med 27:865–872
45. Kuo HS, Tang GJ, Chuang JH, Lee CH, Lui WY, Lee TY, P'eng FK (2000) Changing ICU mortality in a decade-effect of full-time intensivist. Crit Care Shock 3:57–61
46. Multz AS, Chalfin DB, Samson IM, Dantzker DR, Fein AM, Steinberg HN, Niederman MS, Scharf SM (1998) A "closed" medical intensive care unit (MICU) improves resource utilization when compared with an "open" MICU. Am J Respir Crit Care Med 157:1468–1473
47. Reynolds HN, Haupt MT, Thill-Baharozian MC, Carlson RW (1988) Impact of critical care physician staffing on patients with septic shock in a university hospital medical intensive care unit. JAMA 260:3446–3450
48. Al-Asadi L, Dellinger RP, Deutch J, Nathan SS (1996) Clinical impact of closed versus open provider care in a medical intensive care unit (abstract). Am J Respir Crit Care Med 153:A360
49. Carson SS, Stocking C, Podsadecki T, Christenson J, Pohlman A, MacRae S, Jordan J, Humphrey H, Siegler M, Hall J (1996) Effects of organizational change in the medical intensive care unit of a teaching hospital: a comparison of 'open' and 'closed' formats. JAMA 276:322–328
50. Ghorra S, Reinert SE, Cioffi W, Buczko G, Simms HH (1999) Analysis of the effect of conversion from open to closed surgical intensive care unit. Ann Surg 229:163–171
51. Li TC, Phillips MC, Shaw L, Cook EF, Natanson C, Goldman L (1984) On-site physician staffing in a community hospital intensive care unit. Impact on test and procedure use and on patient outcome. JAMA 252:2023–2027
52. Jacobs MC, Hussain E, Hanna A, Ruskin G, Weiss S, Skrzpiec W, Sison C, Cohn E (1998) Improving the outcome and efficiency of surgical intensive care: the impact of full time medical intensivists (abstract). Chest 114:276S-277S
53. Manthous CA, Amoateng-Adjepong Y, al-Kharrat T, Jacob B, Alnuaimat HM, Chatila W, Hall JB (1997) Effects of a medical intensivist on patient care in a community teaching hospital. Mayo Clin Proc 72:391–399
54. Marini CP, Nathan IM, Ritter G, Rivera L, Jurkiewicz A, Cohen JR (1995) The impact of full-time surgical intensivists on ICU utilization and mortality (abstract). Crit Care Med 23:A235
55. Pollack MM, Katz RW, Ruttimann UE, Getson PR (1988) Improving the outcome and efficiency of intensive care: the impact of an intensivist. Crit Care Med 16:11–17
56. Reich HS, Buhler L, David M, Whitmer G (1998) Saving lives in the community. Impact of intensive care leadership (abstract). Crit Care Med 25:A44
57. Tai DYH, Goh SK, Eng PCT, Wang YT (1998) Impact on quality of patient care and procedure use in the medical intensive care unit (MICU) following reorganisation. Ann Acad Med Singapore 27:309–313
58. Pollack MM, Cuerdon TT, Patel KM, Ruttimann UE, Getson PR, Levetown M (1994) Impact of quality-of-care factors on pediatric intensive care unit mortality. JAMA 272:941–946
59. DiCosmo BF (1999) Addition of an intensivist improves ICU outcomes in a non-teaching community hospital (abstract). Chest 116:238S
60. Dimick JB, Pronovost PJ, Heitmiller RF, Lipsett PA (2001) Intensive care unit physician staffing is associated with decreased length of stay, hospital cost, and complications after esophageal resection. Crit Care Med 29:753–758
61. Dimick JB, Pronovost PJ, Lipsett PA (2000) The effect of ICU physician staffing and hospital volume on outcomes after hepatic resection (abstract). Crit Care Med 28:A77
62. Rosenfeld BA, Dorman T, Breslow MJ, Pronovost P, Jenckes M, Zhang N, Anderson G, Rubin H (2000) Intensive care unit telemedicine: alternate paradigm for providing continuous intensivist care. Crit Care Med 28:3925–3931
63. Diringer MN, Edwards DF (2001) Admission to a neurologic/neurosurgical intensive care unit is associated with reduced mortality rate after intracerebral hemorrhage. Crit Care Med 29:635–640
64. Goh AYT, Lum LCS, Abdel-Latif MEA (2001) Impact of 24 hour critical care physician staffing on case-mix adjusted mortality in paediatric intensive care. Lancet 357:445–446
65. Blunt MC, Burchett KR (2000) Out-of-hours consultant cover and case-mix-adjusted mortality in intensive care. Lancet 356:735–736
66. Topeli A (2000) Effect of changing organization of intensive care unit from "open policy without critical care specialist" to "closed policy with critical care specialist" (abstract). Am J Respir Crit Care Med 161:A397
67. Hanson CW, Deutschman CS, Anderson HL, Reilly PM, Behringer EC, Schwab CW, Price J (1999) Effects of an organized critical care service on outcomes and resource utilization: a cohort study. Crit Care Med 27:270–274

68. Bernard GR, Vincent JL, Laterre PF, LaRosa SP, Dhainaut JF, Lopez-Rodriguez A, Steingrub JS, Garber GE, Helterbrand JD, Ely EW, Fisher CJ Jr, for the PROWESS Study Group (2001) Efficacy and safety of recombinant human activated protein C for severe sepsis. N Engl J Med 344:699–709
69. Kress JP, Pohlman AS, O'Connor MF, Hall JB (2000) Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med 342:1471–1477
70. Ely EW, Baker AM, Dunagan DP, Burke HL, Smith AC, Kelly PT, Johnson MM, Browder RW, Bowton DL, Haponik EF (1996) Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. N Engl J Med 335:1864–1869
71. Hebert PC, Wells G, Blajchman MA, Marshall J, Martin C, Pagliarello G, Tweeddale M, Schweitzer I, Yetisir E (1999) A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. N Engl J Med 340:409–417
72. Clermont G, Angus DC, Linde-Zwirble WT, Griffin MF, Fine MJ, Pinsky MR (2002) Does acute organ dysfunction predict patient-centered outcomes? Chest 121:1963–1971
73. Heyland DK, Guyatt G, Cook DJ, Meade M, Juniper E, Cronin L, Gafni A (1998) Frequency and methodologic rigor of quality-of-life assessments in the critical care literature. Crit Care Med 26:591–598
74. Black NA, Jenkinson C, Hayes JA, Young D, Vella K, Rowan KM, Daly K, Ridley S (2001) Review of outcome measures used in adult critical care. Crit Care Med 29:2119–2124
75. Rothenhausler HB, Ehrentraut S, Stoll C, Schelling G, Kapfhammer HP (2001) The relationship between cognitive performance and employment and health status in long-term survivors of the acute respiratory distress syndrome: results of an exploratory study. Gen Hosp Psychiatry 23:88–94
76. Marquis KA, Curtis JR, Caldwel ES, et al (2000) Neuropsychologic sequelae in survivors of ARDS compared with critically ill control patients (abstract). Am J Respir Crit Care Med 16:A383
77. Hopkins RO (2002) How should we assess neuropsychological sequelae of critical illness? In: DC Angus, J Carlet (eds) Surviving intensive care. Update in intensive care and emergency medicine, no 39. Springer, Berlin Heidelberg New York
78. van Hout B, Angus DC (2002) How should we measure the economic consequences of critical illness? In: DC Angus, J Carlet (eds) Surviving intensive care. Update in intensive care and emergency medicine, no 39. Springer, Berlin Heidelberg New York
79. Cohen J, Guyatt G, Bernard GR, Calandra T, Cook D, Elbourne D, Marshall J, Nunn A, Opal S, on behalf of a UK Medical Research Council International Working Party (2001) New strategies for clinical trials in patients with sepsis and septic shock. Crit Care Med 29:880–886
80. Curtis JR (2002) Measuring health status after critical illness: where are we and where do we go from here? In: DC Angus, J Carlet (eds) Surviving intensive care. Update in intensive care and emergency medicine, no 39. Springer, Berlin Heidelberg New York
81. Angus DC, Rubenfeld GD, Roberts MS, Curtis JR, Connors AFJ, Cook DJ, Lave JR, Pinsky MR (2002) Understanding costs and cost-effectiveness in critical care: report from the Second American Thoracic Society Workshop on Outcomes Research. Am J Respir Crit Care Med 165:540–550
82. Rubenfeld GD, Angus DC, Pinsky MR, Curtis JR, Connors AFJ, Bernard GR, and the members of the Outcomes Research Workshop (1999) Outcomes research in critical care: results of the American Thoracic Society Critical Care Assembly Workshop on Outcomes Research. Am J Respir Crit Care Med 160:358–367
83. Ware JE Jr, Sherbourne CD (1992) The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 30:473–483
84. The EuroQol Group (1990) EuroQol – a new facility for the measurement of health-related quality of life. Health Policy 16:199–208
85. Gold MR, Russell LB, Seigel JE, Weinstein MC (1996) Cost-effectiveness in health and medicine. Oxford University Press, New York
86. Brazier J, Roberts J, Deverill M (2002) The estimation of a preference-based measure of health from the SF-36. J Health Econ 21:271–292
87. McMullin J, Cook DJ (2002) Changing ICU behavior to focus on long-term outcomes. In: DC Angus, J Carlet (eds) Surviving intensive care. Update in intensive care and emergency medicine, no 39. Springer, Berlin Heidelberg New York
88. Young C, Millo JL, Salmon J (2002) Reduction in post-ICU, in-hospital mortality following the introduction of an ICU nursing outreach service (abstract). Critical Care 6 [Suppl 1]:S117
89. Pronovost P, Wu A, Holzmueller CG (2002) Defining success in ICU care. In: DC Angus, J Carlet (eds) Surviving intensive care. Update in intensive care and emergency medicine, no 39. Springer, Berlin Heidelberg New York
90. Hartleib M, Sibbald WJ (2002) Reorganizing health care systems to optimize critical care outcomes. In: DC Angus, J Carlet (eds) Surviving intensive care. Update in intensive care and emergency medicine, no 39. Springer, Berlin Heidelberg New York
91. Rubenfeld GD et al. (2003) Surrogate measures of patient-centered outcomes. In: Angus, Carlet (eds) Surviving intensive care. Update in intensive care and emergency medicine, no 39
92. Packer M (1992) Effect of oral milrinone on mortality in severe chronic heart-failure. Verh Dtsch Ges Herz Kreislaufforsch 24:276
93. Echt DS, Liebson PR, Mitchell LB, Peters RW, Obias-Manno D, Barker AH, Arensberg D, Baker A, Friedman L, Greene HL (1991) Mortality and morbidity in patients receiving encainide, flecainide, or placebo. The Cardiac Arrhythmia Suppression Trial. N Engl J Med 324:781–788
94. Takala J, Ruokonen E, Webster NR, Nielsen MS, Zandstra DF, Vundelinckx G, Hinds CJ (1999) Increased mortality associated with growth hormone treatment in critically ill adults. N Engl J Med 341:785–792
95. Garland JS, Alex CP, Pauly TH, Whitehead VL, Brand J, Winston JF, Samuels DP, McAuliffe TL (1999) A three-day course of dexamethasone therapy to prevent chronic lung disease in ventilated neonates: a randomized trial. Pediatrics 104:91–99
96. Taylor HG, Klein N, Hack M (2000) School-age consequences of birth weight less than 750 g: a review and update. Dev Neuropsychol 17:289–321
97. O'Shea TM, Kothadia JM, Klinepeter KL, Goldstein DJ, Jackson BG, Weaver RG, Dillard RG (1999) Randomized placebo-controlled trial of a 42-day tapering course of dexamethasone to reduce the duration of ventilator dependency in very low birth weight infants: outcome of study participants at 1-year adjusted age. Pediatrics 104:15–21