# From the Coronary Care Unit to the Cardiovascular Intensive Care Unit

## The Evolution of Cardiac Critical Care

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**KEYWORDS**

• Cardiac critical care • Cardiovascular intensive care • Multidisciplinary heart care

**KEY POINTS**

- In the 1960s, patients with acute myocardial infarction were sent to the coronary care unit primarily for close monitoring and management of arrhythmias.
- Contemporary cardiovascular intensive care units have adopted the evidence based and multidisciplinary care principles that were the hallmark of general ICUs and had lead to improvements in patient safety and outcomes.
- Modern cardiac critical care will surely evolve as the concept of 'hybrid' cardiac care areas where care is delivered by the 'heart team' becomes standard, and will present opportunities for new areas of research and further improvement in patient outcomes.

*The Times They Are a-Changin'*
*—Bob Dylan, 1963*

### THE EARLY YEARS

Around the time that Bob Dylan penned this song, Hughes Day published a paper "Preliminary Studies of an Acute Coronary Care Area" in the Lancet[1] in February 1963. This article described his experience with 17 acute myocardial infarction (AMI) patients admitted to the first area specifically designed to treat patients with AMI at Bethany Hospital in Kansas City, Kansas. In May 1962, Day had established a monitored area that contained 4 private rooms adjacent to the intensive care unit (ICU). The concept was similar to what was described by Wilburne in an abstract[2] published in the United States in 1961, simultaneous with the publication of Julian's article[3] in the United Kingdom. Both had realized at about the same time that post-AMI ventricular arrhythmias carried significant mortality and that with continuous monitoring in a unit equipped with monitors with alarms, supervision by trained personnel, and the availability of a defibrillator ("AC 440 V or more!")[4] and other appropriate equipment and medications, it was possible to reduce mortality by initiating prompt cardiopulmonary resuscitation (CPR). Such a rapid diffusion of technology was replicated in the 1970s with the enthusiastic adoption of Swan-Ganz catheterization, which originated at the same institution where Wilburne practiced, Cedars of Lebanon Hospital.

Besides improving survival, the coronary care unit (CCU) concept served to fundamentally change how inpatient medicine was practiced in the United States. Up to that point, American

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medicine had established a strict hierarchy, where the doctor dealt with all events and emergencies, outpatient or inpatient, issuing orders for the nurse to follow. However, in the case of life-threatening arrhythmias, like those complicating AMI, there was no time to track down the attending doctor for medical orders. Nurses were empowered to initiate treatment, such as defibrillation and CPR, without waiting for the doctor to enter the unit.

This growth in the CCU model was championed by Corday, also from Cedars of Lebanon Hospital, when he became president of American College of Cardiology in 1965. He helped push legislation in Congress that funded the growth of CCUs as a way to advance care of patients with heart disease.[5] Corday had heard Day speak in Los Angeles in 1962 and became convinced that this was an effective way of reducing mortality in AMI. By 1966 there were more than 200 CCUs in operation in United States. In 1967, Lown published his work, in which he described how he moved myocardial infarction (MI) care from reactive care (defibrillation and CPR) to the prevention and treatment of arrhythmias in his CCU.[6]

## THE MIDDLE AGES

Of course, times kept on changing, and before long there were new, more definitive therapies for myocardial ischemia. As early as 1933, the fibrinolytic activity of hemolytic streptococci had been known,[7] and streptokinase had been used for thrombolysis previously. However, it was not until the publication of the first Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico study in 1986 that thrombolysis became standard for the management of AMI.[8] In 1993, the Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries investigators showed that an accelerated tissue plasminogen activator (tPA) protocol was superior to standard thrombolytic regimens.[9] A quickening of the pulse was palpable; "time is muscle" was the mantra, and "door-to-needle time" entered the lexicon. There were public health programs educating patients to report to the nearest emergency room heralding symptoms of myocardial ischemia. While more people were identified and treated earlier, they were managed in the CCU prior to as well as after coronary angiography.

Even before the concept of the CCU was described, Sones, a pediatrician who was experimenting with catheter techniques, inadvertently injected the coronary artery and performed the first reported cine coronary arteriography in 1959.[10]

Dotter and Judkins published their report of transluminal angioplasty of the superficial femoral artery (SFA) in 1964.[11] They were able to dilate the SFA by threading successive coaxial catheters into a stenosed SFA. Gruentzig[12] modified the Dotter catheter by adding a balloon at the tip and successfully dilated the iliac artery in 1975. In 1977, he performed the first coronary balloon angioplasty on a severe proximal left anterior descending artery (LAD) stenosis of a 38-year-old insurance salesman in Zurich with a positive stress test. Around this time, US surgeons were opposed to this technology, and in Europe, the management of peripheral vascular disease was the domain of the nonsurgeons. Consequently, catheter techniques were researched and advanced by nonsurgeons, primarily radiologists and cardiologists.[13]

With the increasing utilization of balloon angioplasty, the high rates of abrupt vessel closure and restenosis became apparent. This led to the development of catheter-delivered stents and administration of dual antiplatelet therapy. In the 19th century, an English dentist, Charles Stent, developed a mold to make an impression of the teeth and gums.[14] Thus it came to pass that his name became associated with a device that provided a support for tubular structures and now with the endovascular scaffolding that prevents stenoses. Alexis Carrell, a French surgeon who pioneered vascular suturing techniques, first showed that stenting of a canine aorta with a glass tube did not necessarily lead to thrombosis. Carrell received the Nobel Prize in Medicine for his work in 1912. Dotter built on his previous work and experimented with metal springs/coils to maintain the patency of the vessels that he had succeeded in opening and in 1983 reported on transluminal placement of expandable nitinol coil stents.[15] In 1987, Sigwart and Puel reported on the results of implantation of 24 stents in 19 patients for the management of restenosis, acute closure, and venous bypass grafts.[16] With this, the era of interventional cardiology had arrived, and the further development of future generations of stents continued apace.

In 1997, the GUSTO investigators reported that primary angioplasty provided superior outcomes when compared with thrombolysis for ST elevation MIs (STEMIs).[9] However short-, medium-, and long-term closure and restenosis remained significant problems. By 2003, Andersen and colleagues[17] reported that primary angioplasty with stenting was superior to fibrinolysis in acute STEMIs, especially when delivered within 2 hours. The era of "door-to-balloon time" had arrived. The management of AMI evolved into a hub and spoke

type of public health delivery, where patients with a STEMI were transported to the local percutaneous coronary intervention (PCI)-capable hospital, preferably within 90 minutes of onset of symptoms. CCUs at these PCI-capable hospitals saw more STEMIs and comorbidities and complications that came with the sicker STEMI patients. The heat was being turned up, with catheter laboratory teams that could respond within minutes and high-acuity patients transferred to the CCU at all hours of the day and night.

## THE CONTEMPORARY CICU

The hectic pace of innovation radically changed the function and acuity of the CCU. It had evolved from managing AMIs with monitoring and defibrillation/CPR in the event of ventricular tachycardia (VT)/ventricular fibrillation (VF) to actively managing relatively acute and unstable patients with active hemodynamic, cardiovascular, and respiratory complications. In the first 30 or so years, remarkable improvements in survival were noted, as close monitoring and early resuscitation became ubiquitous. Killip reported that the mortality in MI in his CCU decreased from 26% to 7% over a 2-year period from January 1965 to 1967.[18] Patients were no longer dying from sudden arrhythmias but from pump failure. However, the low hanging fruit had been picked. In their remarkable review of the changing epidemiology in their CCU[19] over a 17-year period from 1989 to 2006, Katz and colleagues were unable to replicate this reduction in mortality. At the same time that rapid advancements in technology were leading to a decrease in AMI mortality, the burden of patients with ischemic cardiomyopathy and advanced heart failure was increasing. This was reflected in the increase in such patients in their CCU. To manage these patients, improved therapies, both pharmacologic as well as mechanical circulatory support, were being increasingly utilized. These patients were older and sicker and had many more comorbid medical conditions requiring a broader knowledge and experience base and a wider therapeutic armamentarium. This was clearly shown in Katz's study of the changing trends in pathophysiology of CCU patients. He documented a pattern of increasing patient complexity, evolving critical illness, and accelerated resource utilization. Over the 17-year period, he noted a significant decrease in patients with STEMI, and a significant increase in patients with non-STEMI (NSTEMI) and cardiogenic shock. There was a significant increase in the number of patients with pneumonia, sepsis and septic shock, acute and chronic kidney failure, acute and chronic respiratory failure, and prolonged ventilation. More invasive procedures such as central venous catheterization, gastrointestinal endoscopy, bronchoscopy, and renal replacement therapies were performed. Interestingly, despite the increased case mix and Charlson comorbidity indices, there was no significant increase in CCU length of stay or unadjusted in-hospital and CCU mortality. This was attributed to a better understanding and prophylaxis of potential complications of ongoing critical care.

Practitioners at Mount Sinai have noted a similar increase in severity of illness in the CCU. Most PCI patients today are discharged the same day, and those who are admitted go to a step-down monitored unit. Increasingly the CCU of today is becoming more like a general ICU with a focus on cardiac patients. **Table 1** highlights this severity and complexity in 1370 admissions in 2012.

The coronary care units of the 1970s have evolved into the cardiovascular ICUs (CICUs) of the 21st century and this evolution will certainly continue. As the modern CICU develops, it must follow the trends that have been evolving in the more organized general critical care realm. The principles of the approach to intensive care are evidence-based and can be examined in the context of 3 domains, which will be discussed in the next sections.

**Table 1**
**The distribution of 1370 consecutive admissions to Mount Sinai CCU, from Jan. 1, 2012 to Dec. 1, 2012**

| Primary Reason | Number of Patients |
|---|---|
| PCI | 624 |
| Structural interventions | 167 |
| EP interventions | 220 |
| Heart failure | |
| Acute heart failure | 133 |
| Cardiogenic shock | 30 |
| LVAD | 6 |
| Peripheral vascular interventions | 11 |
| Carotid artery interventions | 15 |
| Other | |
| Hypothermia for cardiac arrest | 11 |
| Miscellaneous (sepsis, gastrointestinal bleed, and others) | 153 |
| Total | 1370 |

### *Quality, Safety, and Resource Utilization*

The modern patient safety movement began with the Harvard Medical Practice Study (MPS), which was published in 1991 and found that 3.7% of hospitalized patients suffered an adverse event, of which 69% were preventable, and 14% were fatal.[20] Although this study also ran as a front-page article in the New York Times, it was essentially ignored. Only in 1996 did the American Medical Association (AMA) join the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO), the American Academy of Arts and Sciences, and the Annenberg Foundation to host the first ever conference on medical errors in California.[21] The patient safety movement gathered further steam after the 1999 Institute of Medicine report "To Err is Human," which estimated that medical errors were the cause of up to 98,000 preventable deaths per year.[22] The focus also shifted from a culture of blame to a problem of defective processes and systems. Since then, various agencies have established organizations focused on increasing patient safety and improving the quality of care. Some of these agencies are the Centers for Medicare and Medicaid Services (CMS), the National Quality Forum (NQF), JCAHO, the Agency for Healthcare Research and Quality (AHRQ), the AMA, through its National Patient Safety Foundation, and the Institute for Healthcare Improvement (IHI). The Society of Critical Care Medicine (SCCM) collaborates with most of these organizations to promote evidence-based care in the ICU. The SCCM also collaborates with the National Institutes of Health's (NIH) United States Critical Illness and Injury Trial (USCIIT) Group, to study organizational structure, processes of care, use of protocols, and outcomes in ICUs and determine which of these structures and processes of care and other factors might be associated with patient outcomes.[23] To date, more than 200 USCIIT Group investigators have enrolled more than 10,000 patients from more than 30 academic and community hospitals in studies during the last 3 years.[24]

The modern CICU must be cognizant of and incorporate these structures and processes into daily work flow. These processes will be discussed briefly.

The Centers for Disease Control and Prevention (CDC), The Joint Commission (TJC), the IHI, and several state departments of health all have rigorous protocols for the prevention and monitoring of central line-associated blood stream infections (CLABSIs). Similar protocols and requirements exist for the prevention of catheter-associated urinary tract infections (CAUTIs), *Clostridium difficile*-associated diarrhea (CDAD), ventilator-associated pneumonia (VAP), and coronary artery bypass grafting (CABG) surgical site infections.

The IHI promotes comprehensive protocols such as the ventilator bundle, central line bundle, and methicillin-resistant Staphylococcus aureus (MRSA) prevention and best practices to reduce patient harm from sedation, immobility, and delirium. All of these are germane to the practice of modern cardiac critical care.

TJC and the CMS collaborate to monitor core measure sets that standardize the use of evidence-based interventions to maximize patient safety and outcomes. Some of the core measure sets relevant to cardiac critical care include

1. Venous thromboembolism
2. Heart failure
3. Surgical care improvement project
4. Tobacco treatment
5. Pneumonia and influenza vaccination
6. Acute Myocardial Infarction
7. Stroke

On its Web site www.medicare.gov/hospitalcompare, CMS posts various data points relating to care delivered to its Medicare recipients. Some of these are

1. Hospital Consumer Assessment of Health Care Providers and Systems (HCAHPS), which collects patient feedback on 10 important hospital quality topics in recently discharged hospitalized Medicare patients
2. Measures of timely care such as for heart attack, heart failure, pneumonia, and surgical management
3. 30-day mortality and readmission rates
4. Medicare payment

The CMS also has the authority to deny payment to hospitals for hospital-acquired conditions (HACs, also known as "not present on admission"), which obviously has implications for resource management for the hospital and its ICUs. For 2013, there are 14 HACs for which CMS can deny payment (http://www.cms.gov/Medicare/ Medicare-Fee-for-Service-Payment/ HospitalAcqCond/Downloads/FY_2013_ Final_ HACsCodeList.pdf). Those relevant to cardiac critical care are

1. Foreign object retained after surgery
2. Air embolism
3. Blood incompatibility
4. Stage 3 and 4 pressure ulcers
5. Falls and trauma

6. Manifestations of poor glycemic control
7. Catheter-associated urinary tract infection
8. Central line-associated blood stream infection
9. Deep vein thrombosis/pulmonary embolism
10. Iatrogenic pneumothorax
11. Surgical site infection and mediastinitis following CABG
12. Surgical site infection following implantable cardiac electronic device

## THE MULTIDISCIPLINARY APPROACH TO INCREASINGLY COMPLEX PATIENTS

The first steps toward multidisciplinary care were taken in the earliest CCUs with the empowerment of specially trained nurses to initiate emergency protocols for medical care. As complexity has increased and CCUs have come to resemble general ICUs, the importance of multidisciplinary care has become evident. The increasing complexity of pharmacotherapy and attention to adverse drug events and drug–drug interactions mean that pharmacists must become an integral part of the multidisciplinary critical care team.[25] Similarly, the focus on maintaining optimal nutritional status, specific blood glucose targets, and the use of complex nutritional products make dieticians a valuable part of the team as well.[26] Respiratory therapists who ensure daily sedation interruption and daily evaluation for early liberation from mechanical ventilation and the emerging evidence for early mobilization and rehabilitation make the role of physical therapists critical to the multidisciplinary team.[27,28] Social workers contribute to ensuring that the patient's and family's social situations are assessed and social needs met, to promote early and appropriate progression through the next continuum of care and decrease length of stay.[29]

### *Human Resource Management*

#### *Special skills*

While the early CCUs essentially required personnel to be trained for rhythm monitoring, defibrillation and initiation of CPR, the skill sets required today are significantly more complex. The modern CICU should be staffed by people who are comfortable and trained to manage

- Respiratory support devices such as invasive and noninvasive positive pressure ventilation
- Insertion of central venous and pulmonary artery catheters, intra-arterial lines, and devices
- Cardiac support with percutaneous devices (eg, Intra-Aortic Balloon Pump, Impella, Tandem Heart) and implanted devices (LVADs, Syncardia Total Artificial Heart)
- Cardiopulmonary support with extracorporeal membrane oxygenation (ECMO), Cardiohealth, Centrimag
- Neurologic support, including sedation monitoring and interruption, delirium management, hypothermia devices, and continuous electroencephalogram (EEG) monitors
- Renal support with various hemodialysis and ultrafiltration protocols
- Multiple vasoactive, sedative–hypnotic and paralytic agents delivered by intravenous drip
- Bedside imaging with vascular ultrasound and transthoracic and transesophageal echocardiography

Similarly, skill and staffing levels should be sufficient to competently manage patients who have undergone complex PCI, complex electrophysiology, and structural heart interventions or are in various shock states.

Personnel skill should also extend to a competent understanding of palliative and end-of-life issues, as many of these patients have complex and advanced multiorgan illnesses.[30] Familiarity with standardized approaches such as the Improving Palliative Care in the ICU tools and specific CICU issues such as deactivation of implantable cardioverter-defibrillator (ICDs) and LVADs is essential.[31]

Finally, CICU professionals must realize that research in this growing subspecialty is integral to promoting both patient outcomes and the body of knowledge. The interested reader is referred to a "call to action" article by van Diepen and colleagues,[32] in which areas of, and solutions to CICU research are identified (**Table 2**).

#### *Staffing requirements*

The preceding paragraphs lay out a landscape that demands patient management by an experienced multidisciplinary team led by a clinician who has significant training or experience in both intensive care and cardiovascular medicine. This marriage of skills is unlikely to be present in a person who is not practicing such medicine for the majority of his or her time and is not based in the CICU. Morrow and colleagues[33] address this issue in great detail in an AHA scientific statement. How one trains such physicians has moved beyond the debate stage; at least 1 large academic center in New York is adding an additional year to enable either a cardiology or critical care fellowship trained physician to seek further training and expertise (V. Kvetan, MD, personal communication, 2013) in this area.

The Leapfrog Group, a group of large purchasers of health care services, seeks to promote

**Table 2**
**Urgent areas for cardiac critical care research**

| | |
|---|---|
| Shock in the Cardiac Patient | • Defining the best fluid and vasoactive pharmacologic management strategies in cardiogenic shock<br>• Managing septic shock and inflammatory response syndromes in patients with heart failure |
| Cardio-renal Syndrome | • Timing preventive and therapeutic interventions for cardio-renal syndromes |
| Cardiac Arrest Care | • Improving systems of care and identifying therapies beyond hypothermia that can improve postcardiac arrest neurologic outcomes and survival |
| Delivery of Care | • Evaluating whether institutional or physician volumes and regionally centralized care affect the outcomes of critically ill cardiac patients<br>• Evaluating whether electronic medical record systems and clinical decision support systems can reduce errors and improve safety<br>• Examining the role of cardiology and intensive care cross-training |
| Measurement | • Establishing standardized definitions, processes of care, and outcome measures for patients with advanced cardiac disease and critical illness through registry platforms and databases |
| Palliative Care | • Enhancing support of patients and families to ensure optimal decision making about end-of-life care, including admiration, withholding or withdrawal of advanced cardiac and other critical care technologies, and integrating palliative care into both the in-patient and out-patient settings |
| Training | • Cross-fertilizing in clinical practice and clinical research for cardiology and critical care trainees |

*From* van Diepen Cook DJ, Jacka M, Granger CB. Critical care cardiology research: a call to action. Circ Cardiovasc Qual Outcomes 2013;6(2):238; with permission.

high-value health care through its purchasing power and has recommendations on ICU physician staffing as one of its initiatives. The Leapfrog Group's benchmark is that the ICU be managed or comanaged by intensivists who are present during clinical hours and provide clinical care exclusively in the ICU, and when not present be available at least 95% of the time within 5 minutes. Given the well-recognized shortage of dedicated intensivists, this is an unrealistic goal for all CICUs to meet in the short term.[34] In the authors' experience, collaboration between an intensivist and a cardiologist to serve as physician leadership of the CICU makes sense as the CICU becomes populated by patients with increasingly complex cardiovascular and multiorgan illness. The authors' CICU is best described as a transitional unit, in which 1 of 4 subspecialty (interventional, EP, heart failure/transplant, or cardiac intensivist) physicians is the primary attending for the CICU patients, and a cardiac intensivist is present. Morrow's article discusses in detail both the physician staffing paradigms as well as a proposal for categorization of CICUs. Finally given the duty hour regulations and increasing primary care focus of house staff training programs, the presence of physician extenders in ICUs is growing and is a welcome trend.

## SUMMARY

There has been a remarkable transformation of cardiac intensive care. Gone are the days when patients suffering from AMI were sent to the CCU primarily for close monitoring. The incredible progress made in patient care in the past 50 years has dramatically changed the landscape. The CICU patient of the modern era is admitted for a wide variety of reasons, ranging from well-defined pathologies such as decompensated heart failure, AMI or ventricular arrhythmias, to newer indications such as complications from modern percutaneous procedures, therapeutic hypothermia for neuroprotection after cardiac arrest, or the advanced management of cardiogenic shock. Cardiovascular pathologies are now seen as a part of a spectrum of illness, including all other comorbidities from which the patient suffers. This has put new demands on health care delivery, resource utilization, clinician training, and physician staffing in the CICU. Clearly this trend toward increasing complexity, and subspecialty expertise

with emerging technologies will continue. Clinicians should be prepared to address the issues that will arise.

## REFERENCES


1. Day HW. Preliminary studies of an acute coronary care area. J Lancet 1963;83:53–5.
2. Wilburne M. Coronary care unit: new approach to treatment of acute coronary occlusion [abstract]. Circulation 1961;24:1071.
3. Julian D. Treatment of cardiac arrest in acute myocardial ischemia and infarction. Lancet 1961;2: 840–4.
4. Wilburne M, Fields J. Cardiac resuscitation in coronary artery disease: a central coronary care unit. JAMA 1963;184(6):453–7.
5. Fye WB. Resuscitating a circulation abstract to celebrate the 50th anniversary of the coronary care unit concept. Circulation 2011;124(17):1886–93.
6. Lown B, Fakhro AM, Hood WB Jr, et al. The coronary care unit: new perspectives and directions. JAMA 1967;199(3):188–98.
7. Tillett WS, Garner RL. The fibrinolytic activity of hemolytic streptococci. J Exp Med 1933;58(4): 485–502.
8. Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI). Lancet 1986;1(8478):397–402.
9. The GUSTO Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. N Engl J Med 1993; 329(10):673–82.
10. Sones FM Jr, Shirey EK, Proudfit WL, et al. Cine coronary arteriography [abstract]. Circulation 1959;20:773.
11. Dotter CT, Judkins MP. Transluminal treatment of arteriosclerotic obstruction: description of a new technic and a preliminary report of its application. Circulation 1964;30(5):654–70.
12. Gruentzig A, Myler R, Hanna R, et al. Coronary transluminal angioplasty [abstract]. Circulation 1977;56:84.
13. King SB. Angioplasty from bench to bedside to bench. Circulation 1996;93(9):1621–9.
14. Ruygrok PN, Serruys PW. Intracoronary stenting: from concept to custom. Circulation 1996;94(5):882–90.
15. Dotter CT, Buschmann RW, McKinney MK, et al. Transluminal expandable nitinol coil stent grafting: preliminary report. Radiology 1983;147(1):259–60.
16. Sigwart U, Puel J, Mirkovitch V, et al. Intravascular stents to prevent occlusion and restenosis after transluminal angioplasty. N Engl J Med 1987; 316(12):701–6.
17. Andersen HR, Nielsen TT, Rasmussen K, et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med 2003;349(8):733–42.
18. Killip T, Kimball JT. Treatment of myocardial infarction in a coronary care unit: a two year experience with 250 patients. Am J Cardiol 1967;20(4): 457–64.
19. Katz JN, Shah BR, Volz EM, et al. Evolution of the coronary care unit: clinical characteristics and temporal trends in healthcare delivery and outcomes. Crit Care Med 2010;38(2):375–81.
20. Brennan TA, Leape LL, Laird NM, et al. Incidence of adverse events and negligence in hospitalized patients. N Engl J Med 1991;324(6):370–6.
21. Leape LL. Scope of problem and history of patient safety. Obstet Gynecol Clin North Am 2008;35(1): 1–10.
22. Kohn LT, Corrigan JM, Donaldson MS, editors. To err is human: building a safer health system. Washington, DC: National Academy Press; 1999.
23. Cobb JP, Cairns CB, Bulger E, et al. The United States critical illness and injury trials group: an introduction. J Trauma 2009;67(Suppl 2):S159–60.
24. Blum JM, Morris PE, Martin GS, et al. United states critical illness and injury trials group. Chest 2013; 143(3):808–13.
25. Horn E, Jacobi J. The critical care clinical pharmacist: evolution of an essential team member. Crit Care Med 2006;34(3):S46–51.
26. Roberts SR, Kennerly DA, Keane D, et al. Nutrition support in the intensive care: unit adequacy, timeliness, and outcomes. Crit Care Nurse 2003;23(6): 49–57.
27. Morris PE, Goad A, Thompson C, et al. Early intensive care unit mobility therapy in the treatment of acute respiratory failure. Crit Care Med 2008;36(8): 2238–43.
28. Truong AD. Bench-to-bedside review: mobilizing patients in the intensive care unit—from pathophysiology to clinical trials. Crit Care 2009; 13(4):216.
29. Carr DD. Building collaborative partnerships in critical care: the RN case manager/social work dyad in critical care. Prof Case Manag 2009; 14(3):121–32 [quiz: 133–4].
30. Penrod JD, Pronovost PJ, Livote EE, et al. Meeting standards of high-quality intensive care unit palliative care: clinical performance and predictors. Crit Care Med 2012;40(4):1105–12.
31. Allen LA, Stevenson LW, Grady KL, et al. Decision making in advanced heart failure: a scientific statement from the American Heart Association. Circulation 2012;125(15):1928–52.
32. van Diepen S, Cook DJ, Jacka M, et al. Critical care cardiology research: a call to action. Circ Cardiovasc Qual Outcomes 2013;6(2):237–42.
33. Morrow DA, Fang JC, Fintel DJ, et al. Evolution of critical care cardiology: transformation of the

cardiovascular intensive care unit and the emerging need for new medical staffing and training models: a scientific statement from the American Heart Association. Circulation 2012;126(11):1408–28.

34. Angus DC, Shorr AF, White A, et al. Critical care delivery in the United States: distribution of services and compliance with Leapfrog recommendations. Crit Care Med 2006;34(4):1016–24.