

Chronic Critical Illness

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Although advances in intensive care have enabled more patients to survive an acute critical illness, they also have created a large and growing population of chronically critically ill patients with prolonged dependence on mechanical ventilation and other intensive care therapies. Chronic critical illness is a devastating condition: mortality exceeds that for most malignancies, and functional dependence persists for most survivors. Costs of treating the chronically critically ill in the United States already exceed \$20 billion and are increasing. In this article, we describe the constellation of clinical features that characterize chronic critical illness. We discuss the outcomes of this condition including ventilator liberation, mortality, and physical and cognitive function, noting that comparisons among cohorts are complicated by variation in defining criteria and care settings. We also address burdens for families of the chronically critically ill and the difficulties they face in decision-making about continuation of intensive therapies. Epidemiology and resource utilization issues are reviewed to highlight the impact of chronic critical illness on our health care system. Finally, we summarize the best available evidence for managing chronic critical illness, including ventilator weaning, nutritional support, rehabilitation, and palliative care, and emphasize the importance of efforts to prevent the transition from acute to chronic critical illness. As steps forward for the field, we suggest a specific definition of chronic critical illness, advocate for the creation of a research network encompassing a broad range of venues for care, and highlight areas for future study of the comparative effectiveness of different treatment venues and approaches.

Keywords: respirator, artificial; critical illness; chronic disease; respiratory care units

Although advances in intensive care have enabled more patients to survive an acute critical illness, they have also created a large and growing population of patients with prolonged dependence on mechanical ventilation and other intensive care therapies. The term “chronically critically ill” was coined for this group by Girard and Raffin in a 1985 article that asked in its title, “to save or let die”? (1). They focused on patients who survived an initial episode of critical illness but remained dependent on intensive care, neither dying in the acute period

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of intensive care unit (ICU) treatment nor recovering. Estimates indicate that there are more than 100,000 such patients in the United States at any point in time, and increasing numbers in some other countries. Chronic critical illness is a devastating condition for patients and their families and, at a cost exceeding \$20 billion each year, for the U.S. health care system as a whole. Incidence and expenditures are rising as more older adults, who already comprise the majority of chronically critically ill patients, receive aggressive medical and surgical treatments.

In this article, we review clinical features and outcomes of the chronic critical illness syndrome, its impact on the health care system, and the challenges it presents for treatment and decision-making. Data are drawn from a search of the Medline database from 1975 to March 2010 for all English language articles using the terms “chronic critical illness” or “chronically critically ill,” “prolonged critical illness,” “prolonged mechanical ventilation,” “prolonged ventilator weaning,” “post-ICU,” “long-term acute care facility,” “respiratory care unit,” and “tracheostomy” or “tracheotomy”; we also hand-searched reference lists and author files.

CLINICAL FEATURES OF THE CHRONIC CRITICAL ILLNESS SYNDROME

The hallmark of chronic critical illness is respiratory failure requiring prolonged dependence on mechanical ventilation. Although the term “prolonged mechanical ventilation” has been used in the literature to describe periods of ventilator dependence ranging from 2 days to 4 weeks (2–5), this period is usually measured in weeks for the chronically critically ill. Besides prolonged ventilator dependence, evidence suggests that chronic critical illness is a syndrome comprising additional characteristic features. These include profound weakness attributed to myopathy, neuropathy, and alterations of body composition including loss of lean body mass, increased adiposity, and anasarca (6); distinctive neuroendocrine changes including loss of pulsatile secretion of anterior pituitary hormones, contributing to low target organ hormone levels and impaired anabolism (7, 8); increased vulnerability to infection, often with multiresistant microbial organisms (9, 10); brain dysfunction manifesting as coma or delirium that is protracted or permanent (11); and skin breakdown associated with nutritional deficiencies, edema, incontinence, and prolonged immobility (12). Patient reports document significant distress from symptoms including pain, thirst, dyspnea, depression, and anxiety, and from inability to communicate during endotracheal intubation (13). This constellation of features, summarized in Figure 1, serves as a framework for the clinical definition of chronic critical illness. Some of these features (e.g., brain dysfunction, symptom distress) may be present during acute critical illness (or other conditions), but their prolonged duration and intensity in the chronic phase of

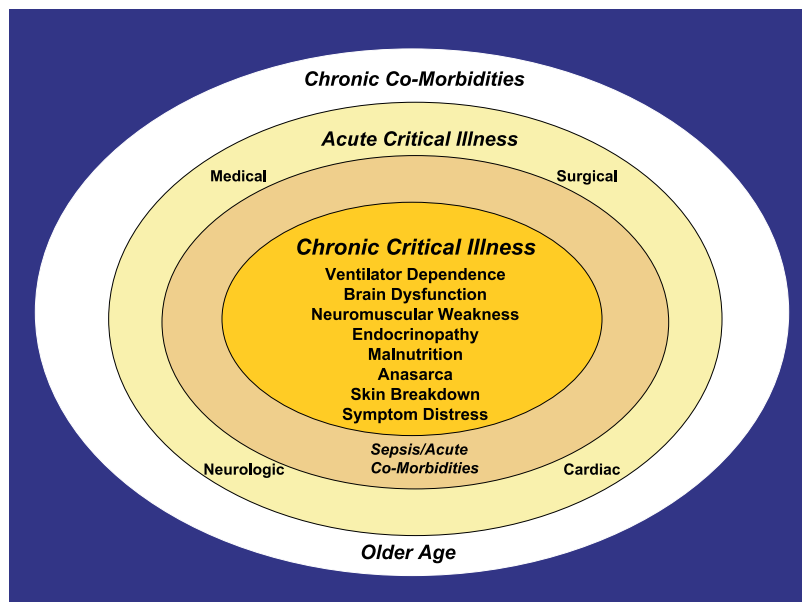


Figure 1. The syndrome of chronic critical illness. Most chronically critically ill patients are older adults who have underlying comorbid conditions and develop sepsis and other acute comorbidities with treatment for acute medical, surgical, neurologic, or cardiac critical illness. Beyond prolonged ventilator dependence, which is its hallmark, increasing evidence indicates that chronic critical illness is a syndrome encompassing other characteristic clinical features and affecting multiple systems and organs.

critical illness are distinctive. Other features (e.g., changes in body composition and neuroendocrine patterns) have been described only in the chronic phase. Chronic critical illness is uniquely characterized by the presence of these features as a clinical constellation in association with prolonged dependence on mechanical ventilation.

Between 5 and 10% of patients who require mechanical ventilation for acute conditions develop chronic critical illness (14–16). Patients from any type of medical or surgical ICU can be affected. On the basis of data from statewide databases, the mean (SD) age for adult patients is 65 (15) years (17, 18); for those in specialized weaning facilities, it is in the eighth decade (17, 19). Patients are evenly divided according to sex, and comorbidities are common (11, 17–19). Patients with trauma as an admitting diagnosis are usually younger, more likely male, and have fewer comorbidities (18). More than one-third of chronically critically ill patients receive care in teaching hospitals (18).

OUTCOMES

Generalization of outcomes from published reports is complicated by variation in study populations described as chronically critically ill, in definitions of outcomes of interest, and in post-acute care practices that affect hospital use. A threshold period of mechanical ventilation, ranging from 2 to 30 days, has been used to define the majority of cohorts for longitudinal studies (2–5). To limit the heterogeneity of these cohorts and thereby improve comparability of outcomes across different studies, a consensus conference established a formal definition for prolonged mechanical ventilation: at least 21 consecutive days on the ventilator for more than 6 hours/day (2). Other cohort studies have identified chronically critically ill patients by elective placement of a tracheotomy to facilitate prolonged ventilation and weaning efforts (20–23). Referral for tracheotomy reflects the clinician's judgment that the patient will neither wean nor die in the immediate future and thus provides a point of demarcation between acute and chronic critical illness that is both clinically meaningful and practical. In population-based studies, International Classification of Diseases (ICD) coding and Diagnosis-Related Groups (DRGs) have been used, respectively, to identify patients requiring specified threshold periods of mechanical ventilation and those receiving tracheot-

omy for failure to wean from the ventilator (17, 18). One study validated an algorithm defining “prolonged mechanical ventilation” on the basis of coding as either (1) ICD-9-96.72 (mechanical ventilation > 96 h) plus an ICU length of stay of at least 21 days or (2) classification in DRG 541/542 (tracheotomy for a condition other than head, neck, or face disease) (sensitivity, 97.6%; specificity, 96.4%) (17). To address the impact of cohort definition on outcome results, another study compared outcomes of cohorts from the same hospital that were defined either by placement of tracheotomy after at least 96 hours of mechanical ventilation or by ventilation for at least 21 days (24). In that study, patients identified by tracheotomy had higher rates of 1-year survival than those ventilated for at least 21 days (52 vs. 42%), although both definitions captured a group of patients with high resource use and poor clinical outcomes.

Ventilator Liberation

Between 30 and 53% of chronically critically ill patients are liberated from mechanical ventilation (defined as discharged alive and breathing without assistance) in the acute care hospital (14, 25). Average time to ventilator liberation varies with severity and type of illness or injury, but typically ranges from 16 to 37 days after intubation for respiratory failure (14, 17, 24, 25). Most patients who fail to achieve ventilator independence within 60 days do not do so later (26, 27). Better outcomes are reported for some specialized weaning units, but they often select patients with higher potential for ventilator liberation and rehabilitation (10, 26, 28). Reimbursement incentives discourage some weaning facilities from admitting patients who have severe irreversible pulmonary processes, require hemodialysis, or have profound neurologic injuries; outcomes in such facilities may be more favorable because of this admission bias.

Mortality

Although patients who remain ventilator dependent are at higher risk of death, successful weaning does not ensure long-term survival as most patients with chronic critical illness have underlying comorbid conditions, residual organ dysfunction, and intercurrent complications (Table 1). Acute care hospital mortality for unselected patients is generally reported in the range of 20–49% (11, 17, 24, 25). One-year mortality across study populations is 48–68% with little change over the past 20

years (5, 10, 14, 24, 25, 28). Compared with patients requiring short-term ventilation, the risk of death in chronically critically ill patients remains particularly high between 60 and 100 days after initiation of mechanical ventilation (24).

Functional and Cognitive Impairments

Nearly all patients with chronic critical illness leave the hospital with profound impairments of physical function, cognitive status, or both, and most therefore require institutional care (11, 14, 29–31). Hospital readmission rates during the year after hospital discharge exceed 40% (32). Patients discharged to extended care facilities who cannot be sufficiently rehabilitated for return to home by 6 months usually remain institutionalized until death (33). Across multiple studies, fewer than 12% of chronically critically ill patients were alive and independent 1 year after their acute illness (11, 28, 31). Long-term survivors who are able to respond to surveys of health-related quality of life (HRQOL) typically report better emotional and social function than physical function or symptom experience (14, 34). Although these findings are consistent with studies of HRQOL in survivors of acute critical illness, which indicate that some patients can adapt emotionally to profound changes in health status (35), interpretation must be tempered by the fact that the majority of chronically critically ill patients do not survive 1 year and most survivors lack sufficient cognitive function to respond to HRQOL surveys (11).

Family Burdens

Chronic critical illness also imposes heavy burdens on families, who experience high rates of depression and practical and financial hardships (36, 37). Evidence from studies of informal caregivers of patients requiring prolonged mechanical ventilation indicates that depressive symptoms are more severe in this group than among caregivers of patients with Alzheimer's disease or spinal cord injury and that depression continues for months after the patient's discharge from the hospital (37). These caregivers also report a decline in physical health and increase in "caregiving overload" during the postdischarge period (37). In a study of post-ICU caregiver burden, multivariable regression analysis identified the placement of a tracheotomy in the ICU as a significant predictor of lifestyle disruption for informal caregivers of ICU survivors at 1 year after ICU admission (38). Another study, focusing on patients who underwent tracheotomy after at least 4 days of mechanical ventilation or ventilation for at least 21 days, found that 61% of 1-year survivors still required daily assistance from informal

caregivers, who reported "a lot" or "severe" stress from caregiving; 84% of these caregivers had either quit work or significantly changed work hours to accommodate the patient's caregiving needs (39). Several studies have shown that burdens for families are not limited to those who provide the care at home (36, 37); depressive symptoms, caregiving overload, and physical deterioration may actually be more severe among families of patients who are institutionalized than of those who return home (37). In addition, families of patients with protracted critical illness often face significant losses of income and/or savings, even if the patient is insured (40).

Mortality Prediction

Evidence suggests that several patient-related factors contribute significantly to variation in clinical outcomes. Advanced age and residual organ failures, both common characteristics of chronically critically ill patients, are associated with higher mortality, as is poor prior functional status (29, 31, 41). Younger patients with trauma initiating critical illness have had more favorable outcomes (21). Neither the APACHE (Acute Physiology and Chronic Health Evaluation) system nor other models for predicting mortality of acutely critically ill patients are valid for chronic critical illness (41, 42). A simple mortality prediction model was developed to identify chronically critically ill patients at high risk for 3-month and 1-year mortality (25); a multicenter study to provide external validation of this model is ongoing. The mortality model does not address prognosis for functional or cognitive recovery, which many patients and families consider as seriously as prospects for survival (20).

Deficiencies in Physician–Patient–Family Communication

Studies reveal that these clinical outcomes are poorly understood by family decision-makers for chronically critically ill patients and even by physicians. In questionnaire-based interviews conducted shortly after tracheotomy, ICU patients and surrogates reported that key aspects informing the decision to provide prolonged life support were routinely omitted by physicians; for example, 80 and 93% of the respondents received no information about possible functional dependency at hospital discharge or about expected 1-year survival, respectively (20). Similarly, qualitative interviews of family surrogates in another study found that three-quarters lacked accurate estimates of survival, functional status, and caregiving needs for patients requiring prolonged mechanical ventilation; 93% expected that the patient would survive for at least 1 year, and less than 30% anticipated any functional limitation or other

TABLE 1. OUTCOMES OF CHRONIC CRITICAL ILLNESS RELATIVE TO COHORT DEFINITION*

Cohort Definition	Ventilation for ≥ 14 d		Ventilation for ≥ 21 d		Tracheotomy for Prolonged Mechanical Ventilation	
	Combes <i>et al.</i> (34)	Carson <i>et al.</i> (25)	Cox <i>et al.</i> [†] (24)	Cox <i>et al.</i> [†] (24)	Engoren <i>et al.</i> (14)	
Study (reference)	Combes <i>et al.</i> (34)	Carson <i>et al.</i> (25)	Cox <i>et al.</i> [†] (24)	Cox <i>et al.</i> [†] (24)	Engoren <i>et al.</i> (14)	
n	347	200	114	267	347	
Age (yr), median (IQR) or mean \pm SD	63 \pm 14, 67 \pm 13 [‡]	58 (42–69)	66 (47–74)	66 (45–75)	64, 71 [§]	
Duration of ventilation, median (IQR) or mean \pm SD	36 \pm 25, 37 \pm 28 [‡]	35 (26–51)	27 (23–36)	16 (10–24)	23–30	
Hospital length of stay, median (IQR)	—	51 (36–72)	39 (30–52)	29 (22–38)	28–37	
Died in hospital, %	43	41	31	20	22	
Discharged home, %	—	11	4	7	—	
Alive at 12 mo, %	32	48	42	52	50	

* Studies were selected if they were prospective cohort studies published after 2000, enrolled patients in the acute hospital setting who received at least 14 days of mechanical ventilation, and reported 12-month survival for comparison.

[†] Study reporting outcomes of two different cohorts distinguished by definition.

[‡] Mean \pm SD for ICU survivors and for nonsurvivors, respectively.

[§] Median for hospital survivors and for nonsurvivors, respectively.

^{||} Range of medians for hospital survivors who were ventilator dependent, liberated from ventilator but with tracheotomy, or liberated and decannulated; and for nonsurvivors.

impairment of quality of life (39). These expectations diverged dramatically from those held by the patients' physicians, who were less optimistic about chances for 1-year survival (expected by 44% of physicians) and much less so for functional recovery (expected by 6% of physicians). Both families and physicians significantly overestimated the patients' actual outcomes (39).

IMPACT ON HEALTH CARE SYSTEM

Chronic critical illness is a serious and growing problem for the U.S. health care system and an emerging challenge in other countries (23, 43). In population-based studies in the United States, the incidence of respiratory failure requiring mechanical ventilation has been increasing by as much as 5.5% per year (44, 45) and will soon increase at an even faster rate as Baby Boomers pass age 60, when the risk of respiratory failure rises dramatically (46). Numbers of the chronically critically ill, who are mostly older adults, will increase as much or more. Analysis of a state database of hospital discharges showed that the incidence of tracheotomy for prolonged ventilation nearly tripled between 1993 and 2002, from 8.3 per 100,000 population to 24.2 per 100,000 (18). Another population-based study projected that the number of patients requiring mechanical ventilation for at least 7 days in the United States will more than double from 250,000 in 2000 to more than 600,000 in 2020 (44). Although the chronically critically ill account for fewer than 10% of those receiving mechanical ventilation, they consume between 20 and 40% of ICU bed days and other critical care resources (16, 18). Because functional limitations are common, even patients who recover sufficiently to permit discharge from an inpatient facility typically require paid caregiving as outpatients or family members must leave jobs to provide ongoing care. The overall cost to the health care system for the management of chronic critical illness already exceeds an estimated \$20 billion per year (29) and is expected to climb with increases in the incidence of this syndrome and in overall expenditures for critical care, which nearly doubled between 1985 and 2000 and represent 13% of all hospital costs in the United States (47).

Cost-Effectiveness

A cost-effectiveness analysis calculated that providing prolonged mechanical ventilation to Medicare-eligible patients with multiple comorbid conditions exceeds \$200,000 for each quality-adjusted life year gained, as compared with patients who had life-sustaining therapies withdrawn before Day 14 of mechanical ventilation (29). This analysis demonstrated that incremental costs associated with prolonged life support were most sensitive to acute hospital costs (rather than post-acute care facility costs) and hospital readmissions. Innovations to reduce costs in addition to improving clinical outcomes are

needed. A specialized disease management program failed to reduce the risk of readmission for patients ventilated for 3 days or more, but it was associated with a decreased length of stay during rehospitalization from 16 to 11.4 days, yielding an average cost saving of more than \$50,000 per patient (3).

Venues of Care

Patients with chronic critical illness receive care across a range of venues (Table 2). Besides acute care hospitals, these include long-term acute care facilities, skilled nursing facilities, inpatient rehabilitation facilities, and chronic ventilator facilities, with various resources for the complex needs and dependencies that characterize the chronically critically ill. Diagnosis-Related Groups (DRGs) covering these patients are among the most heavily weighted, supporting relatively high reimbursement to acute care hospitals. Nevertheless, high costs for long-stay outliers are a burden for these hospitals, creating an incentive for transferring chronically critically ill patients to post-acute care facilities for further attempts at weaning and rehabilitation. Such facilities have become profitable to operate, contributing to rapid expansion of the for-profit long-term acute care (LTAC) industry, which grew at a rate of 12% per year between 1993 and 2003 (48). Medicare payments to LTACs, which cover more than 80% of their discharges, have increased by 15% annually (48). Costs over the entire episode of illness are lower for chronically critically ill Medicare beneficiaries who are transferred on mechanical ventilation to LTACs (48), probably because of lower nurse-to-patient ratios and staff salaries, and efficiencies in ventilator weaning and rehabilitation services. Data are inconclusive, however, on whether patient survival is affected by LTAC transfer (48). Reports by individual LTACs suggest that patients are being transferred from acute care hospitals earlier in the course of critical illness, with higher degrees of illness severity (49). If these trends of earlier transfer to LTACs continue, the cost savings associated with care in such facilities may be offset by an increase in rates of subsequent readmissions to acute care hospitals. Congress has mandated reform of payment to post-acute care facilities; this process is currently in the demonstration phase and has expanded to address the role of acute care hospitals in providing care for chronically critically ill patients (50).

TREATMENT CHALLENGES

Even as attention focuses increasingly on chronic critical illness from the perspectives of epidemiologic and health services, empirical research to define effective methods of treatment remains scant. Most data on specific therapeutic approaches derive from descriptive studies conducted in single centers,

TABLE 2. MAIN VENUES FOR CARE OF THE CHRONICALLY CRITICALLY ILL*

	Nursing Intensity/Cost	Patient Acuity	Specialized Rehabilitation Approach
Acute care hospitals			
Intensive care units	+++	+++	+
Critical care stepdown units	++	++	+
Specialized weaning units	++	++	+++
Medical-surgical ward	+	+	+
Long-term acute care (LTAC)	++	++	+++
or long-term care hospitals (LTCH)			
Skilled nursing facilities	+	+	++

* Depending on geographic location and available resources within and outside the acute hospital setting, most chronically critically ill patients in the United States are cared for in acute care hospitals, long-term acute care facilities or, less commonly, skilled nursing facilities. Relative levels of nursing intensity/cost, patient acuity, and availability of specialized rehabilitation are noted for the typical facility in these venue categories, although there is variation within as well as across categories.

leaving clinicians to rely mainly on their own experience and extrapolation of evidence from studies of acutely critically ill patients, which may lack external validity in this setting.

Ventilator Weaning

As shown for ICU patients in prospective, randomized, controlled trials, a before–after study showed the effectiveness of a protocol implemented by respiratory therapists for weaning patients with tracheotomy from prolonged mechanical ventilation in a long-term acute care facility (51). Median time to ventilator liberation was 17 days during an 18-month period after the protocol was implemented, compared with 29 days in a historical control group. Therapists used a rapid shallow breathing index (RSBI) of no more than 80 as an “acceleration step” to advance patients to spontaneous breathing trials. A subsequent prospective observational study found that a higher threshold RSBI of 100 (as used in patients with shorter term ventilation) accelerated weaning without significantly lowering the specificity of the index (52). In many LTACs and other venues, weaning protocols are successfully managed by non-physicians (19, 53). Typically, trials of pressure support at a level (10–15 cm H₂O) that is approximately half of full ventilator support are followed by spontaneous breathing trials, using a “trach collar” or “T-piece approach” for progressively increasing periods (2, 43). Standardized criteria can be used to assess readiness for final removal of a tracheotomy tube (“decannulation”) after ventilator liberation (54).

Nutritional Support

Beyond ventilator weaning, the syndrome of chronic critical illness calls for a broader, multidisciplinary, therapeutic approach that addresses all major clinical features (Figure 2). Strategies have been suggested, but not empirically tested, to address the kwashiorkor-like malnourished state (6). Rational goals of nutritional support reflect a balancing of potential benefits of providing metabolic substrates to minimize further loss of lean body mass against adverse consequences of overfeeding and other risks. For the patient with a functional

gastrointestinal tract, enteral feeding is recommended as first-line therapy, and observational evidence favors placement of a percutaneous endoscopic gastrostomy or jejunostomy for nutritional support to exceed 30 days (55). Stress hyperglycemia, originating during acute critical illness, typically persists and requires insulinization.

Functional and Cognitive Recovery

Integration of physical therapy in a comprehensive rehabilitative model for care is supported by a consensus of expert opinion (2) and by evidence emerging from the setting of acute critical illness, which indicates that early mobilization may mitigate development, severity, and/or duration of post-ICU muscle weakness (56). Initiation of this approach during the chronic phase of critical illness, when the patient is already cachectic, profoundly weak, and debilitated, has not yet been specifically studied. Biochemical evidence supports treatment with calcitriol and pamidronate to attenuate accelerated bone loss (22), but clinical implications for recovery of strength or function remain unclear. Although some data suggest that sedation and analgesia can be reduced after tracheotomy (57), it is not known whether this will decrease the prevalence or prolonged duration of brain dysfunction. Extrapolation from the acute ICU setting suggests that, because of their delirigenic potential (58, 59), benzodiazepines should be avoided as possible. Haloperidol and newer atypical antipsychotics such as ziprasidone have been recommended for control of agitation or delirium in the ICU, but data are limited regarding their efficacy in reducing delirium, especially the hypoactive form (60).

Preventing Complications

Attempts to prevent and treat infectious and other complications, which cause morbidity, mortality, and persistent ventilatory insufficiency (61), require assiduous efforts. Patients face a “triple threat” of risk of infection, the most common complication (10): barrier breaches, such as intravenous catheterization and skin breakdown; exposure to virulent and re-

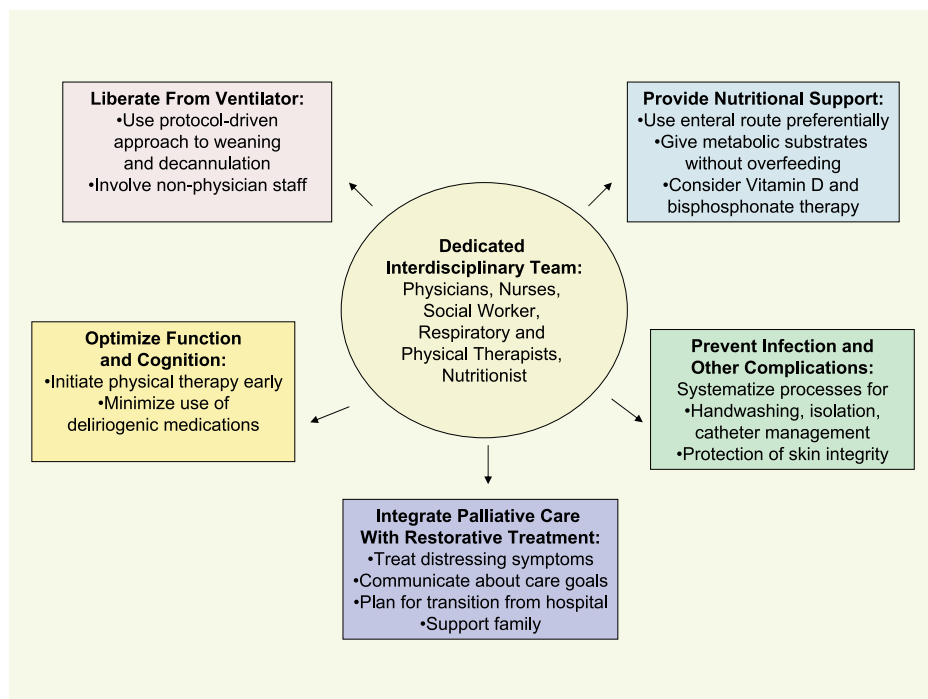


Figure 2. Comprehensive care for the chronically critically ill. Comprehensive care for the chronically critically ill includes multiple components, as illustrated here and discussed more fully in text, with five key goals: ventilator liberation, nutritional support, cognitive and functional recovery, prevention of complications, and attention to palliative needs. Given the unique and complex challenges, a dedicated interdisciplinary team of professionals may be best equipped to provide this care.

sistant pathogens in ICU and post-ICU care environments; and postulated “immune exhaustion” from recent critical illness and comorbidities (9). Processes of care should be systematized to maximize use of essential preventive measures such as hand-washing, isolation, removal of unnecessary indwelling catheters, restriction of antibiotic use, and best practices for maintaining skin integrity (12). Source identification and control should focus first on possible line sepsis, pneumonia, and *Clostridium difficile* colitis, which account for the majority of infections (9).

Care Models

Effective and efficient care can be provided to the chronically critically ill outside of the ICU, either in specialized in-hospital units or free-standing facilities, with lower levels of nursing intensity, technology, and ancillary care (62). In these venues, nurses have played a key role in structuring and managing care by an interdisciplinary team that is dedicated to the special needs of this resource-intensive patient group (12, 62). A “mobile” team led by advanced practice nurses using a protocol-based approach improved outcomes and reduced costs for ICU patients requiring mechanical ventilation for more than 3 days (63).

Tracheotomy Timing and Other Issues

Although placement of a tracheotomy for patients with prolonged weaning failure is a clinical marker of the transition between the acute and chronic phases of critical illness, there is debate about whether earlier placement of a tracheotomy can reduce ventilator days and therefore reduce the likelihood of complications that can lead to chronic critical illness (64). Multicenter trials designed to help resolve this debate are ongoing, while the average time from initiation of mechanical ventilation to tracheotomy placement is decreasing in clinical practice (18, 65). It is likely that other evidence-based practices that reduce ventilator days for patients in the acute ICU setting will help to decrease the incidence of chronic critical illness when applied systematically during the acute phase. Efficient liberation from mechanical ventilation requires organized ICU management practices, preferably directed by certified intensivists in a “closed” ICU model (66, 67). Weaning protocols should include daily spontaneous breathing trials (68), daily lightening of continuous sedatives (69), and avoidance of long-acting sedatives (70), as all of these strategies shorten duration of mechanical ventilation and ICU length of stay. Systematic approaches to prevention of ventilator-associated pneumonia and central line-associated bloodstream infections are supported by existing evidence (71).

Palliative Care

Palliative care is an essential component of comprehensive treatment for all chronically critically ill patients, including those receiving life-prolonging therapies. This care includes sensitive, effective, proactive, and ongoing communication with patients and families about prognosis, achievable goals of treatment, and alternatives to continuation of critical care (20). Ideally, goals should be defined by the patient’s preferences for treatment and views of acceptable function and quality of life, but most chronically critically ill patients are unable to participate directly in discussions or decision-making and few have designated a surrogate decision-maker or prepared another advance directive (72). A prospective study showed that treatment and decision-making in chronic critical illness generally proceeded without direct input from the patient (most lacked capacity when critical illness became chronic and 85% lacked an advance directive expressing

treatment preferences) (72). Limitation (withholding or withdrawal) of life-supporting therapies (mechanical ventilation, renal replacement therapy, artificial nutrition, intravenous hydration, or vasopressors) was rare—fewer than 1 in 5 (39 of 203) patients—and late in the course (median, 39 d from hospital admission), when the patient was near death. In another study, one-third of family surrogates denied any role in deciding to continue mechanical ventilation for a prolonged period, stating their understanding that this decision was made exclusively by the physician (39).

To ensure meaningful participation by patients and families who wish to share in decision-making, clinicians should engage them in a mutual exchange, providing relevant medical information in terms that are clear and understandable to a layperson, while investigating the patient’s values and goals. A new model based on four simple measures may be useful to estimate 1-year survival of patients requiring prolonged mechanical ventilation (25). The use of objective mortality prediction models for guiding discussions of prognosis and goals of care is controversial. The SUPPORT (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments) study, which tested communication of model-derived prognostic information from physicians to patients through a research nurse intermediary, did not favorably alter physician behavior or clinical outcomes for seriously ill patients hospitalized with acute illness (73). It is possible, however, that a simpler model designed to identify chronically critically ill patients who are at the greatest risk for mortality with a high degree of specificity will allow clinicians to be more confident in discussing poor prognoses directly. Patients, families, and even clinicians may fail to appreciate the ongoing risks of death or severe disability when the patient has just survived the acute phase of critical illness (20, 39). A new brochure about chronic critical illness is available as an adjunct to direct clinician counseling for education of patients and families (74); the value of printed informational materials for this purpose has been shown in randomized, controlled trials (75, 76). In a randomized, controlled, multicenter trial that is newly funded by the National Institutes of Health, this brochure will be given to families of chronically critically ill patients in both the control and intervention groups; in addition, a “Supportive Information Team” including a palliative care physician and nurse, which the ICU attending physician will have the option to join, will conduct proactive meetings with families in the intervention group.

Interdisciplinary support addressing families’ emotional, spiritual, and practical needs is helpful as a framework for discussions and decision-making about continuation of intensive care therapies when critical illness enters a chronic phase. Palliative care consultants are increasingly available to help with communication challenges and provide other support for patients and families, as well as to optimize symptom control and transitional planning. Early integration of palliative care with treatments for cure or longer life, ideally from admission to the ICU and through the chronic phase, is recommended.

CONCLUSION

In their 1985 article, Girard and Raffin asked whether we should attempt to save the chronically critically ill or let them die (1). This question remains immediately relevant, but the present state of the evidence, 25 years later, does not yet support a definite response. Various factors have made it difficult for research on chronic critical illness to progress more quickly. The successes of acute critical care in achieving short-term survival have partly obscured the scope and severity of the

problem of chronic critical illness, delaying the emergence of this area as an important focus of scientific investigation. Another barrier is the diversity of venues in which care is currently provided to the chronically critically ill, compounding the problem of generalization from one setting to another while also increasing the challenge of recruiting large cohorts for research. To move forward at a pace that matches the increasing incidence of this condition and the magnitude of its impact, the field needs consensus on a definition. We suggest that placement of a tracheotomy after at least 10 days of mechanical ventilation be used to define the onset of chronic critical illness because this definition incorporates the clinician's judgment that the patient is not expected to die or to wean from the ventilator in the immediate future. Although it may not be necessary or possible for all studies of chronic critical illness to conform exactly to this definition (e.g., studies using administrative data as currently classified) (17), a common definition would be beneficial for interventional studies in which patients are prospectively enrolled. We also suggest that federal funds be dedicated to support the development of a large research network encompassing a broad range of venues for care of the chronically critically ill. Pathobiology and pathophysiology of chronic as distinct from acute critical illness deserve further scientific investigation. We also need well-designed trials testing approaches to the many clinical challenges, from management of prolonged mechanical ventilation to nutritional support to treatment of delirium, symptom distress, and physical weakness. Regarding appropriate venues for care, current evidence lags far behind trends in practice. Comparative effectiveness research that includes detailed economic analyses should be conducted to compare the cost-effectiveness of transferring chronically critically ill patients from acute hospitals to specialized facilities (77). Whereas existing evidence for optimal management strategies remains limited, data on long-term outcomes are available and clear. These data should not be ignored during discussions with patients and their families about appropriate goals of continuing intensive care therapies when critical illness becomes chronic.

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References

- Girard C, Raffin TA. The chronically critically ill: to save or let die? *Respir Care* 1985;30:339–347.
- MacIntyre NR, Epstein SK, Carson S, Scheinhorn D, Christopher K, Muldoon S. Management of patients requiring prolonged mechanical ventilation: report of a NAMDRC consensus conference. *Chest* 2005; 128:3937–3954.
- Daly BJ, Douglas SL, Kelley CG, O'Toole E, Montenegro H. Trial of a disease management program to reduce hospital readmissions of the chronically critically ill. *Chest* 2005;128:507–517.
- Chelluri L, Im KA, Belle SH, Schulz R, Rotondi AJ, Donahoe MP, Sirio CA, Mendelsohn AB, Pinsky MR. Long-term mortality and quality of life after prolonged mechanical ventilation. *Crit Care Med* 2004;32: 61–69.
- Gracey DR, Naessens JM, Krishan I, Marsh HM. Hospital and post-hospital survival in patients mechanically ventilated for more than 29 days. *Chest* 1992;101:211–214.
- Hollander JM, Mechanick JI. Nutrition support and the chronic critical illness syndrome. *Nutr Clin Pract* 2006;21:587–604.
- Van den Berghe G, de Zegher F, Veldhuis JD, Wouters P, Awouters M, Verbruggen W, Schetz M, Verwaest C, Lauwers P, Bouillon R, et al. The somatotrophic axis in critical illness: effect of continuous growth hormone (GH)-releasing hormone and GH-releasing peptide-2 infusion. *J Clin Endocrinol Metab* 1997;82:590–599.
- Van den Berghe G, de Zegher F, Veldhuis JD, Wouters P, Gouwy S, Stockman W, Weekers F, Schetz M, Lauwers P, Bouillon R, et al. Thyrotrophin and prolactin release in prolonged critical illness: dynamics of spontaneous secretion and effects of growth hormone-secretagogues. *Clin Endocrinol (Oxf)* 1997;47:599–612.
- Kalb TH, Lorin S. Infection in the chronically critically ill: unique risk profile in a newly defined population. *Crit Care Clin* 2002;18:529–552.
- Scheinhorn DJ, Hassenpflug MS, Votto JJ, Chao DC, Epstein SK, Doig GS, Knight EB, Petrak RA. Post-ICU mechanical ventilation at 23 long-term care hospitals: a multicenter outcomes study. *Chest* 2007; 131:85–93.
- Nelson JE, Tandon N, Mercado AF, Camhi SL, Ely EW, Morrison RS. Brain dysfunction: another burden for the chronically critically ill. *Arch Intern Med* 2006;166:1993–1999.
- Carasa M, Polycarpe M. Caring for the chronically critically ill patient: establishing a wound-healing program in a respiratory care unit. *Am J Surg* 2004;188:18–21.
- Nelson JE, Meier DE, Litke A, Natale DA, Siegel RE, Morrison RS. The symptom burden of chronic critical illness. *Crit Care Med* 2004; 32:1527–1534.
- Engoren M, Arslanian-Engoren C, Fenn-Buderer N. Hospital and long-term outcome after tracheostomy for respiratory failure. *Chest* 2004; 125:220–227.
- Seneff MG, Zimmerman JE, Knaus WA, Wagner DP, Draper EA. Predicting the duration of mechanical ventilation: the importance of disease and patient characteristics. *Chest* 1996;110:469–479.
- Wagner DP. Economics of prolonged mechanical ventilation. *Am Rev Respir Dis* 1989;140:S14–S18.
- Kahn JM, Carson SS, Angus DC, Linde-Zwirble WT, Iwashyna TJ. Development and validation of an algorithm for identifying prolonged mechanical ventilation in administrative data. *Health Serv Outcomes Res Methodol* 2009;9:117–132.
- Cox CE, Carson SS, Holmes GM, Howard A, Carey TS. Increase in tracheostomy for prolonged mechanical ventilation in North Carolina, 1993–2002. *Crit Care Med* 2004;32:2219–2226.
- Scheinhorn DJ, Hassenpflug MS, Votto JJ, Chao DC, Epstein SK, Doig GS, Knight EB, Petrak RA. Ventilator-dependent survivors of catastrophic illness transferred to 23 long-term care hospitals for weaning from prolonged mechanical ventilation. *Chest* 2007;131:76–84.
- Nelson JE, Mercado AF, Camhi SL, Tandon N, Wallenstein S, August GI, Morrison RS. Communication about chronic critical illness. *Arch Intern Med* 2007;167:2509–2515.
- Engoren M, Arslanian-Engoren C. Hospital and long-term outcome of trauma patients with tracheostomy for respiratory failure. *Am Surg* 2005;71:123–127.
- Nierman DM, Mechanick JI. Biochemical response to treatment of bone hyperresorption in chronically critically ill patients. *Chest* 2000;118: 761–766.
- Estensoro E, Reina R, Canales HS, Saenz MG, Gonzalez FE, Aprea MM, Laffaire E, Gola V, Dubin A. The distinct clinical profile of chronically critically ill patients: a cohort study. *Crit Care* 2006;10: R89.
- Cox CE, Carson SS, Lindquist JH, Olsen MK, Govert JA, Chelluri L. Differences in one-year health outcomes and resource utilization by definition of prolonged mechanical ventilation: a prospective cohort study. *Crit Care* 2007;11:R9.
- Carson SS, Garrett J, Hanson LC, Lanier J, Govert J, Brake MC, Landucci DL, Cox CE, Carey TS. A prognostic model for one-year mortality in patients requiring prolonged mechanical ventilation. *Crit Care Med* 2008;36:2061–2069.
- Bigatello LM, Stelfox HT, Berra L, Schmidt U, Gettings EM. Outcome of patients undergoing prolonged mechanical ventilation after critical illness. *Crit Care Med* 2007;35:2491–2497.
- MacIntyre NR, Cook DJ, Ely EW Jr, Epstein SK, Fink JB, Heffner JE, Hess D, Hubmayer RD, Scheinhorn DJ. Evidence-based guidelines for weaning and discontinuing ventilatory support: a collective task force facilitated by the American College of Chest Physicians; the American Association for Respiratory Care; and the American College of Critical Care Medicine. *Chest* 2001;120:375S–395S.

28. Stoller JK, Xu M, Mascha E, Rice R. Long-term outcomes for patients discharged from a long-term hospital-based weaning unit. *Chest* 2003;124:1892–1899.
29. Cox CE, Carson SS, Govert JA, Chelluri L, Sanders GD. An economic evaluation of prolonged mechanical ventilation. *Crit Care Med* 2007;35:1918–1927.
30. Douglas SL, Daly BJ, Gordon N, Brennan PF. Survival and quality of life: short-term versus long-term ventilator patients. *Crit Care Med* 2002;30:2655–2662.
31. Carson SS, Bach PB, Brzozowski L, Leff A. Outcomes after long-term acute care. An analysis of 133 mechanically ventilated patients. *Am J Respir Crit Care Med* 1999;159:1568–1573.
32. Douglas SL, Daly BJ, Brennan PF, Gordon NH, Uthris P. Hospital readmission among long-term ventilator patients. *Chest* 2001;120:1278–1286.
33. Nasraway SA, Button GJ, Rand WM, Hudson-Jinks T, Gustafson M. Survivors of catastrophic illness: outcome after direct transfer from intensive care to extended care facilities. *Crit Care Med* 2000;28:19–25.
34. Combes A, Costa M-A, Trouillet J-L, Baudot J, Mokhtari M, Gibert C, Chastre J. Morbidity, mortality, and quality-of-life outcomes of patients requiring ≥ 14 days of mechanical ventilation. *Crit Care Med* 2003;31:1373–1381.
35. Hofhuis JGM, van Stel HF, Schrijvers AJP, Rommes JH, Bakker J, Spronk PE. Conceptual issues specifically related to health-related quality of life in critically ill patients. *Crit Care* 2009;13:118.
36. Van Pelt DC, Milbrandt EB, Qin L, Weissfeld LA, Rotondi AJ, Schulz R, Chelluri L, Angus DC, Pinsky MR. Informal caregiver burden among survivors of prolonged mechanical ventilation. *Am J Respir Crit Care Med* 2007;175:167–173.
37. Douglas SL, Daly BJ. Caregivers of long-term ventilator patients: physical and psychological outcomes. *Chest* 2003;123:1073–1081.
38. Van Pelt DC, Schulz R, Chelluri L, Pinsky MR. Patient-specific, time-varying predictors of post-ICU informal caregiver burden: the caregiver outcomes after ICU discharge project. *Chest* 2010;137:88–94.
39. Cox CE, Martinu T, Sathy SJ, Clay AS, Chia J, Gray AL, Olsen MK, Govert JA, Carson SS, Tulskey JA. Expectations and outcomes of prolonged mechanical ventilation. *Crit Care Med* 2009;37:2888–2894.
40. Swoboda SM, Lipsett PA. Impact of a prolonged surgical critical illness on patients' families. *Am J Crit Care* 2002;11:459–466.
41. Dematte D'Amico JE, Donnelly HK, Mutlu GM, Feinglass J, Jovanovic BD, Ndukwu IM. Risk assessment for inpatient survival in the long-term acute care setting after prolonged critical illness. *Chest* 2003;124:1039–1045.
42. Carson SS, Bach PB. Predicting mortality in patients suffering from prolonged critical illness: an assessment of four severity-of-illness measures. *Chest* 2001;120:928–933.
43. Schonhofer B, Euteneuer S, Nava S, Suchi S, Kohler D. Survival of mechanically ventilated patients admitted to a specialised weaning centre. *Intensive Care Med* 2002;28:908–916.
44. Zilberberg MD, de Wit M, Pirone JR, Shorr AF. Growth in adult prolonged acute mechanical ventilation: implications for healthcare delivery. *Crit Care Med* 2008;36:1451–1455.
45. 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;21:173–182.
46. Behrendt CE. Acute respiratory failure in the United States: incidence and 31-day survival. *Chest* 2000;118:1100–1105.
47. 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;32:1254–1259.
48. Medicare Payment Advisory Commission (MEDPAC). Report to the Congress: new approaches in Medicare, Chapter 5: Defining long-term care hospitals. Washington DC: MEDPAC; 2004. Accessed June 1, 2010. Available at www.medpac.gov/publications%5Ccongressional_reports%5CJune04_ch5.pdf
49. Scheinhorn DJ, Chao DC, Stearn-Hassenpflug M, LaBree LD, Heltsley DJ. Post-ICU mechanical ventilation: treatment of 1,123 patients at a regional weaning center. *Chest* 1997;111:1654–1659.
50. RTI International. Medicare post-acute care payment reform demonstration. Accessed June 1, 2010. Available at: <http://www.pacdemo.rti.org>
51. Scheinhorn DJ, Chao DC, Stearn-Hassenpflug M, Wallace WA. Outcomes in post-ICU mechanical ventilation: a therapist-implemented weaning protocol. *Chest* 2001;119:236–242.
52. Chao DC, Scheinhorn DJ. Determining the best threshold of rapid shallow breathing index in a therapist-implemented patient-specific weaning protocol. *Respir Care* 2007;52:159–165.
53. Carasa M, Nespoli G. Nursing the chronically critically ill patient. *Crit Care Clin* 2002;18:493–507.
54. Ceriana P, Carlucci A, Navalesi P, Rampulla C, Delmastro M, Piaggi G, De Mattia E, Nava S. Weaning from tracheotomy in long-term mechanically ventilated patients: feasibility of a decisional flowchart and clinical outcome. *Intensive Care Med* 2003;29:845–848.
55. Dwolatzky T, Berezovski S, Friedmann R, Paz J, Clarfield AM, Stessman J, Hamburger R, Jaul E, Friedlander Y, Rosin A, et al. A prospective comparison of the use of nasogastric and percutaneous endoscopic gastrostomy tubes for long-term enteral feeding in older people. *Clin Nutr* 2001;20:535–540.
56. Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, Spears L, Miller M, Franczyk M, Deprieto D, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet* 2009;373:1874–1882.
57. Nieszkowska A, Combes A, Luyt C-E, Ksibi H, Trouillet J-L, Gibert C, Chastre J. Impact of tracheotomy on sedative administration, sedation level, and comfort of mechanically ventilated intensive care unit patients. *Crit Care Med* 2005;33:2527–2533.
58. Pisani MA, Murphy TE, Araujo KLB, Slattum P, Van Ness PH, Inouye SK. Benzodiazepine and opioid use and the duration of intensive care unit delirium in an older population. *Crit Care Med* 2009;37:177–183.
59. Pandharipande P, Shintani A, Peterson J, Pun BT, Wilkinson GR, Dittus RS, Bernard GR, Ely EW. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. *Anesthesiology* 2006;104:21–26.
60. Girard TD, Pandharipande PP, Carson SS, Schmidt GA, Wright PE, Canonic AE, Pun BT, Thompson JL, Shintani AK, Meltzer HY, et al. Feasibility, efficacy, and safety of antipsychotics for intensive care unit delirium: the MIND randomized, placebo-controlled trial. *Crit Care Med* 2010;38:428–437.
61. Gracey DR. Ventilator care beyond the intensive-care unit. *Mayo Clin Proc* 1995;70:595–597.
62. Rudy EB, Daly BJ, Douglas S, Montenegro HD, Song R, Dyer MA. Patient outcomes for the chronically critically ill: special care unit versus intensive care unit. *Nurs Res* 1995;44:324–331.
63. Burns SM, Earven S, Fisher C, Lewis R, Merrell P, Schubart JR, Truitt JD, Bleck TP. Implementation of an institutional program to improve clinical and financial outcomes of mechanically ventilated patients: one-year outcomes and lessons learned. *Crit Care Med* 2003;31:2752–2763.
64. Griffiths J, Barber VS, Morgan L, Young JD. Systematic review and meta-analysis of studies of the timing of tracheostomy in adult patients undergoing artificial ventilation. *BMJ* 2005;330:1243.
65. Freeman BD, Borecki IB, Coopersmith CM, Buchman TG, Freeman BD, Borecki IB, Coopersmith CM, Buchman TG. Relationship between tracheostomy timing and duration of mechanical ventilation in critically ill patients. *Crit Care Med* 2005;33:2513–2520.
66. 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;288:2151–2162.
67. Carson SS, Stocking C, Podsadecki T, Christenson J, Pohlman A, MacRae S, Jordan J, Humphrey H, Siegler M, Hall J. Effects of organizational change in the medical intensive care unit of a teaching hospital: a comparison of “open” and “closed” formats. *JAMA* 1996;276:322–328.
68. Ely EW, Baker AM, Dunagan DP, Burke HL, Smith AC, Kelly PT, Johnson MM, Browder RW, Bowton DL, Haponik EF. Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. *N Engl J Med* 1996;335:1864–1869.
69. Kress JP, Vinayak AG, Levitt J, Schweickert WD, Gehlbach BK, Zimmerman F, Pohlman AS, Hall JB, Kress JP, Vinayak AG, et al. Daily sedative interruption in mechanically ventilated patients at risk for coronary artery disease. *Crit Care Med* 2007;35:365–371.
70. Carson SS, Kress JP, Rodgers JE, Vinayak A, Campbell-Bright S, Levitt J, Bourdet S, Ivanova A, Henderson AG, Pohlman A, et al. A randomized trial of intermittent lorazepam versus propofol with daily

- interruption in mechanically ventilated patients. *Crit Care Med* 2006; 34:1326–1332.
71. Pronovost P, Needham D, Berenholtz S, Sinopoli D, Chu H, Cosgrove S, Sexton B, Hyzy R, Welsh R, Roth G, *et al*. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med* 2006;355:2725–2732.
72. Camhi SL, Mercado AF, Morrison RS, Du Q, Platt DM, August GI, Nelson JE. Deciding in the dark: advance directives and continuation of treatment in chronic critical illness. *Crit Care Med* 2009;37: 919–925.
73. SUPPORT Principal Investigators. A controlled trial to improve care for seriously ill hospitalized patients. *JAMA* 1995;274:1591–1598.
74. Society of Critical Care Medicine. Chronic critical illness in adults requiring prolonged mechanical ventilation [support brochure]. Accessed June 1, 2010. Available at http://www.mycucare.org/Support_Brochures/Pages/ChronicCriticalIllness.aspx
75. Lautrette A, Darmon M, Megarbane B, Joly LM, Chevret S, Adrie C, Barnoud D, Bleichner G, Bruel C, Choukroun G, *et al*. A communication strategy and brochure for relatives of patients dying in the ICU. *N Engl J Med* 2007;356:469–478.
76. Azoulay E, Pochard F, Chevret S, Jourdain M, Bornstain C, Wernet A, Cattaneo I, Annane D, Brun F, Bollaert P-E, *et al*. Impact of a family information leaflet on effectiveness of information provided to family members of intensive care unit patients: a multicenter, prospective, randomized, controlled trial. *Am J Respir Crit Care Med* 2002;165: 438–442.
77. Kahn JM. The evolving role of dedicated weaning facilities in critical care. *Intensive Care Med* 2010;36:8–10.