Chapter 1
Preventing PICS with the ABCDEF Bundle

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Introduction

Over the last several decades, advances in critical care medicine have led to significant treatment improvements in diseases with high mortality, and in return, an increasing number of patients survive their admission to an intensive care unit (ICU) [1]. With those successes, there is a down-side; increasingly, survivors are burdened with persistent impairments in their cognitive abilities, their physical function, and their mental health. These impairments are identified as part of the post-intensive care unit syndrome (PICS). [2] Most ICU survivors will be impacted by one or more of these impairments after their acute illness, with PICS affecting numerous areas of their lives, including their employment and performance of activities of daily

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living [3–5]. Additionally, a substantial burden is placed on family and caregivers as they help care for these survivors [6, 7]. Family members of critically ill patients and survivors are affected both physically and psychologically, which is described as post-intensive care unit syndrome—family (PICS-F) [8]. These manifestations of PICS, and the risk factors for its development, have transformed the care of the critically ill patient. Preventing PICS has been increasingly understood to begin at the onset of critical illness. Minimizing iatrogenesis, preventing and managing delirium, mobilising early to prevent acute muscle wasting, and engaging families are all evidence-based interventions shown to reduce the numerous complications of critical illness. These individual processes, combined into a synergistic bundle of care called the ABCDEF Bundle, represent the most significant advances in preventing PICS and the sequelae of critical illness in the last two decades.

In response to the growing number of impairments noted in survivors of critical illness, the American College of Critical Care Medicine originally created the Pain, Agitation, and Delirium (PAD) guidelines for the assessment, treatment, and prevention of these concerns in the ICU [9], which were updated in 2018 as the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in the Adult Patients in the ICU (PADIS) Guidelines [10]. A large-scale quality improvement programme, developed by the Society of Critical Care Medicine (SCCM), used these guidelines to create the ABCDEF Bundle, or ICU Liberation Bundle, to address pain, agitation, and delirium in the ICU (Fig. 1.1) [11]. The components of the bundle include the following: **A**ssess, prevent, and manage pain; **B**oth spontaneous awakening trials (SAT) and spontaneous breathing trials (SBT); **C**hoice of analgesia and sedation; **D**elirium— assess, prevent, and manage; **E**arly mobility and Exercise; and **F**amily engagement and empowerment. Each individual component of the bundle is evidence-based and validated in multiple clinical trials, and the bundle combines the individual impact of each intervention into a synergistic process of care that improves ICU outcomes and mitigates the burden of PICS in survivors.

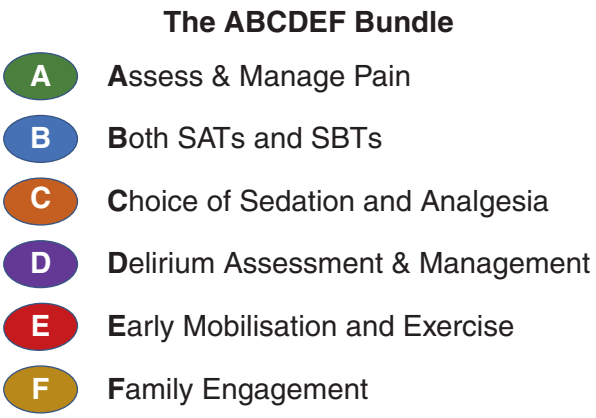

Fig. 1.1 ABCDEF bundle (original graphic adapted with permission from icudelirium.org and Ely [11]); SAT spontaneous awakening trial, SBT spontaneous breathing trial

Assess, Prevent, and Manage Pain

During critical illness, most patients experience pain, with one-half reporting significant pain, while only a minority of patients undergo any assessment and treatment for pain prior to interventions in the ICU [12, 13]. The gold standard for assessing pain in the hospital is self-reported pain using a 1 to 10 numerical rating scale [9]. However, in patients who are unable to provide self-reported pain due to their disease or mechanical ventilation, pain can be assessed using nonverbal pain scales. Two of the most common, validated tools are the Behavioral Pain Scale (BPS) and the Critical Care Pain Observation Tool (CPOT) [14]. For example, the BPS uses facial expression, movement of the upper limbs, and compliance with mechanical ventilation on a scale from zero to 12, with a score of five or higher reflecting uncontrolled pain [15]. Similarly, the CPOT uses components of facial expression, body movement, muscle tension, and compliance with ventilator or vocalization for extubated patients, on a scale from zero to eight, with a score of three or greater indicating uncontrolled pain [16].

The PADIS guidelines recommend frequent pain assessment and treatment, assessing pain using any of the previous tools at least four times per shift and as needed, such as before using sedative or prior to procedures [10]. The recommended pharmacologic treatment is parenteral opioids for non-neuropathic pain with the use of gabapentin or carbamazepine in cases of neuropathic pain. These should be used as a component of a multimodal approach with adjunctive nonopioid analgesics, such as acetaminophen or nonsteroidal anti-inflammatory drugs, and nonpharmacologic interventions, such as repositioning and use of heat/cold, to reduce opioid requirement. Other modalities, such as regional analgesia, can be used in special circumstances, such as post-operative populations and patients with traumatic rib fractures [9].

Poorly managed pain puts patients at risk for multiple complications. For example, undertreated pain and excessive use of opioids are risk factors for delirium [9]. Untreated pain also potentially limits the ability of patients to mobilise and participate in early exercise during critical illness. It can also limit inspiratory effort, further complicating weaning from mechanical ventilation. All of these circumstances, through a cascading series of events, can increase the risk of PICS for patients. It is vital to actively assess, prevent, and manage pain, not only for improving patient comfort and reducing suffering, but to also prevent and manage several risk factors for the development of PICS.

Both Spontaneous Awakening Trials and Spontaneous Breathing Trials

Spontaneous awakening trials (SATs), or daily sedative interruptions, are a recommended approach to sedation management and minimization in the ICU. Practically, it is a nurse-driven protocol involving a safety checklist for sedation cessation.

Should patients pass the safety screen as administered by the bedside nurse, then all continuous sedative infusions are stopped and the patient is carefully monitored. If needed, such as for significant agitation or tachypnoea, sedation and analgesia are started at half the previous dose [17]. In a single-centre, randomized controlled trial of 128 mechanically ventilated patients, daily SATs reduced duration of mechanical ventilation by 2 days and ICU length of stay by 3.5 days, as well as reduced ventilator-associated pneumonia (VAP) and complications [18, 19]. Additionally, with regard to the safety and long-term outcomes, patients who underwent daily SATs reported fewer signs of PTSD with similar rates of anxiety and depression at follow-up after critical illness [20].

Once a patient passes an SAT, respiratory therapists or critical care physicians then perform a spontaneous breathing trial (SBT) following a safety screen [17]. Routine performance of daily SBTs has been shown to reduce the median of days of mechanical ventilation [21]. SBTs are performed either by placing the ventilator in a spontaneous breathing mode such as pressure support ventilation or by attachment of a T-piece. Once a patient has tolerated an SBT for at least 30 minutes without adverse response, such as hypoxia, tachycardia, or tachypnoea, they meet criteria for extubation [22, 23]. SBTs have been studied with varying time frames, from 30 minutes to 2 hours, with 30-minute trials showing similar efficacy and fewer adverse events than two-hour trials. Notably, Subira and colleagues demonstrated that patients that underwent 30-minute SBTs as compared to two-hour T-piece trials were more likely to remain successfully extubated [24].

While SATs and SBTs have improved outcomes as individual practices in mechanical ventilation, the daily, paired coordination of both SATs and SBTs has demonstrated even greater success in liberating patients from mechanical ventilation (Fig. 1.2). In the multicentre, randomized controlled Awake and Breathing Controlled (ABC) Trial, when pairing both SATs and SBTs compared to standard sedation and daily SBT, patients were extubated 3 days sooner, ICU and hospital length of stay were reduced by 4 days, and there was a 14% absolute reduction in mortality at 1 year with number needed to treat of 7 [25]. Pairing of both SATs and SBTs represents a significant advance in our approach to mechanical ventilation and represents the standard of care in liberating patients from the ventilator. Using best practices to facilitate prompt liberation from mechanical ventilation reduces the downstream complications of mechanical ventilation, including muscle weakness, delirium, and prolonged ventilation, limiting the physical deficits so often manifested in ICU survivors with PICS.

Choice of Analgesia and Sedation

Frequent assessment of pain and sedation targets for goal-directed use of sedative agents is the current standard of care in critically ill patients needing such interventions [10]. It is recommended to use the validated sedation and level of arousal assessment tools, such as the Richmond Agitation-Sedation Scale (RASS) and the

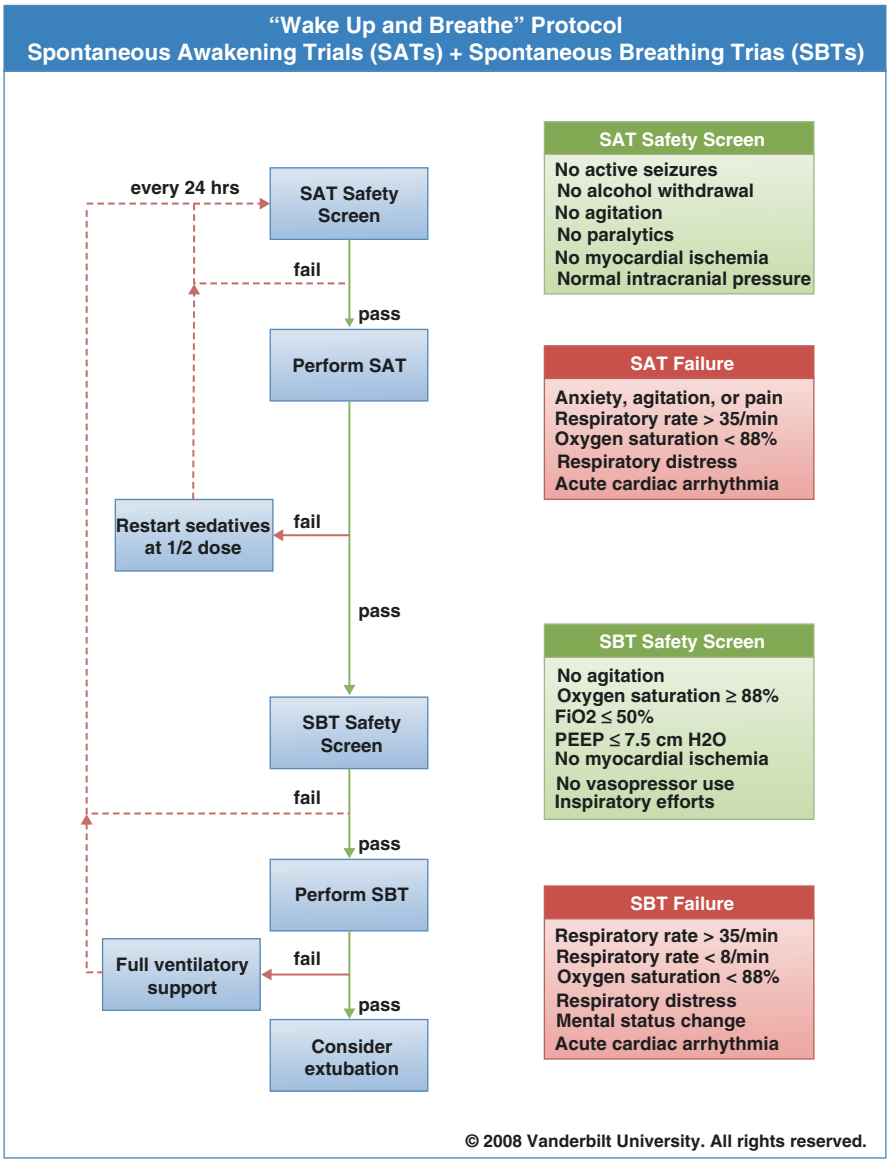

Fig. 1.2 "Wake Up and Breathe Protocol"—paired SATs and SBTs. (Adapted with permission from ICU Delirium, Vanderbilt University Medical Center—icudelirium.org); FiO2 fraction of inspired oxygen, PEEP positive-end expiratory pressure

Riker Sedation-Agitation Scale (SAS). The RASS is a 10-point scale with four levels of agitation (+1 to +4), one level of calm and alert (0), and three levels of sedation (−1 to −3), and two levels of coma (−4 to −5). The SAS is a 7-point scale ranging from coma (1) to severe agitation (7) [26]. These scales perform well at the

bedside and are convenient. For example, the RASS has been shown to be easily performed by nurses, taking less than 20 seconds to perform, with high inter-rater reliability [27].

Analgesics, predominantly parenteral opioids, should be used as first-line agents prior to use of sedative medications to target and achieve a RASS of −2 to 0 or SAS of 3 to 4 with a goal of patients purposely following commands without agitation. If patients are over-sedated, sedatives should be held until the level of consciousness is at target and then only restarted at half the previous dose [9]. Critical care practice has migrated away from deep sedation due to evidence that inappropriate deep sedation is associated with poor outcomes. Early deep sedation in the ICU is associated with longer ventilation times, increased length of stay, and higher rates of mortality [28]. Similarly, targeting lighter sedation is associated with more delirium-free days and less use of restraints with no difference in self-extubation rates [29].

For sedation, the PADIS guidelines recommend using either propofol or dexmedetomidine (DEX) over benzodiazepines, which are associated with worse outcomes, specifically an increased risk of delirium in a dose-dependent fashion [30]. There has been increasing interest as well in central α-2 agonists as sedation agents in the critically ill. In the MIDEX and PRODEX trials, dexmedetomidine was non-inferior to midazolam and propofol for time to target sedation and associated with decreased duration of mechanical ventilation compared to midazolam, though not propofol [31]. There have been two other trials evaluating the α-2 agonist dexmedetomidine to benzodiazepines. The MENDS study (Maximizing Efficacy of Targeted Sedation and Reducing Neurologic Dysfunction) compared dexmedetomidine to lorazepam, and patients receiving dexmedetomidine had 4 more days alive without delirium or coma and were more often at target-level sedation without differences in mortality or ventilator-free days [32]. However, the subgroup of patients with sepsis receiving dexmedetomidine had shorter durations of delirium and coma, lower probability of incident delirium, decreased time on the ventilator, and a 70% decrease in mortality [33]. In the SEDCOM trial (Safety and Efficacy of Dexmedetomidine Compared with Midazolam), there was a lower prevalence of delirium and two fewer days of mechanical ventilation with DEX compared to midazolam [34]. Regardless of sedative choice, targeting light sedation should be achieved through use of analgosedation with a focus on treating pain first and then adding sedation medication as needed. Focusing on light sedation is an important aspect of the ABCDEF bundle and its impact on PICS, as it limits immobilisation and helps reduce delirium. Future investigation is needed to determine the optimal sedative agent for improving outcomes.

Delirium Assessment, Prevention, and Management

Delirium is a devastating and serious complication of critical illness. It is defined by an acute change in attention and awareness that develops over a short period of time with a waxing and waning course, which can be categorized into hypoactive

delirium with reduced level of consciousness, hyperactive delirium with increased levels of agitation, or mixed delirium with elements of both [35]. It is vital to screen for the disease because it affects 60–80% of mechanically ventilated patients and is associated with long-term cognitive impairment and increased disability, both cardinal features of PICS [4, 36–38].

There are two validated tools used for assessing and screening for delirium: the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC) [10]. The ICDSC is an eight-item screening tool, and a score of 4 or greater is positive for delirium with sensitivity and specificity of 74% and 82%, respectively, compared to the CAM-ICU that has sensitivity and specificity of 80% and 96%, respectively [39]. The CAM-ICU is composed of four features: (1) acute onset of mental status changes or fluctuating course, (2) inattention, (3) disorganized thinking, and (4) altered level of consciousness, and a patient is considered CAM positive for delirium if components 1 and 2 in addition to either 3 or 4 are present (Fig. 1.3) [40].

There are many risk factors for delirium, including sedating medications (most notably benzodiazepines), hypoxemia, sepsis, preexisting cognitive impairment, advanced age, mechanical ventilation, untreated pain, prolonged immobilisation, sleep deprivation, and multiple medical conditions [41]. When delirium is identified, the first step is to search for all reversible causes. These include unrecognized disease or infection and removing offending drugs. Additionally, performing

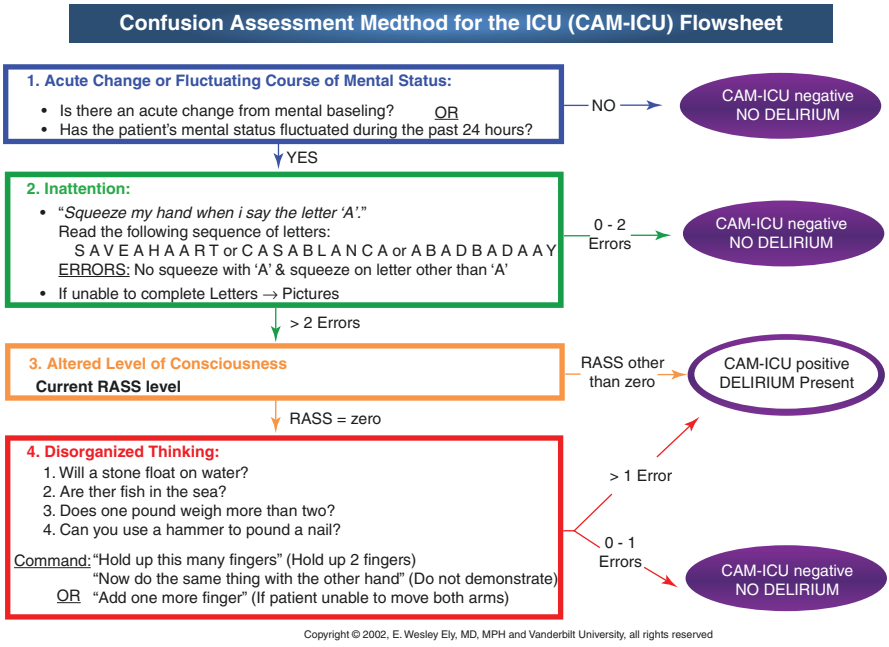

Fig. 1.3 Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). (Courtesy of E. Wesley Ely, MD, MPH and Vanderbilt University Medical Center, Nashville, TN)

nonpharmacologic interventions, such as early mobilisation, frequent reorientation of the patient, and promoting appropriate sleep–wake cycles, are important management strategies as well.

Antipsychotics were previously used and recommended for the treatment of delirium; however, based on evidence from multiple RCTs, there is no definitive evidence supporting the treatment of delirium with antipsychotics [42, 43]. Girard and colleagues performed the MIND-USA trial (Modifying the Impact of ICU-Induced Neurologic Dysfunction-USA), a multicentre, randomized, placebo-controlled trial comparing haloperidol and ziprasidone versus placebo in treating delirium. The authors found no difference in duration of delirium or adverse outcomes, including mechanical ventilation, ICU length of stay, and mortality [44]. Based on this and similar trials showing no treatment benefit with antipsychotics [43, 45], the PADIS guidelines do not currently recommend the use of antipsychotics to treat delirium. There remains a role for these drugs in the management of agitation, which can be seen in hyperactive delirium, but the medication does not treat the underlying disease but instead manages the symptoms. There remains an unmet need for further investigation into pharmacological treatment options for delirium.

Early Mobility and Exercise

Prolonged immobilisation is common during critical illness, most often due to due to disease severity and regular interventions in the ICU such as mechanical ventilation. It causes muscle wasting and weakness and can eventually lead to ICU-acquired weakness. It affects 25–60% of critically ill patients and is associated with worse outcomes, including prolonged mechanical ventilation, increased hospital length of stay, and greater mortality [46–49]. This weakness can last years and is associated with disability at one and 5 years in patients with acute respiratory distress syndrome [50, 51]. ICU-acquired weakness and its link to poor physical functioning contribute to the development of PICS in survivors of critical illness.

Early mobilisation refers to the initiation of rehabilitation and physical activity at the beginning of critical illness, even when patients are receiving invasive support. For example, early mobilisation has been shown to be safe in patients receiving advanced support, including mechanical ventilation and extracorporeal cardiopulmonary support with low risk of complications [52, 53]. It has also been shown to be one of the few interventions that reduces duration of delirium [54, 55]. Similarly, in a related prospective cohort study, patients receiving treatment with a dedicated mobility team compared to usual care were more likely to receive physical therapy in the ICU, were out of bed 6 days earlier, and were discharged from the ICU and hospital earlier [56]. When paired with SATs, early mobilisation within 3 days of mechanical ventilation reduced duration of delirium, increased days breathing without assistance, and improved return to independent functional status at discharge [55]. However, when mobilisation occurred four or more days after initiation of

mechanical ventilation, there was no difference in long-term function [57], suggesting that the benefit to early rehabilitation may be seen predominantly in the early phases of critical illness. As such, mobility interventions need to be timed early during critical illness to optimize the impact on ICU recovery and be effective in reducing ICU-acquired weakness and PICS.

Given its impact on delirium and physical function, early mobilisation and exercise are foundational to the success of the ABCDEF bundle and synergistic in promoting the other components of the intervention. Needham and colleagues demonstrated that a focused quality improvement process to improve sedation practices and increase mobilisation resulted in decreased prescriptions of benzodiazepines, lower doses of narcotics, increased number of physical and occupational therapy treatments, doubled amount of days without delirium, and patients were awake and alert on twice as many ICU days [58]. These outcomes are integral to minimizing the iatrogenic causes of PICS with early mobility as the core preventative measure.

Family Engagement and Empowerment

The ABCDE bundle, as it initially began, evolved to include the letter "F" to represent family engagement as a core pillar of the bundle in facilitating patient-centred care. Incorporation of family engagement at the bedside allowed for wishes, questions, and concerns to be addressed, which is especially important when the patients are unable to communicate due to their underlying illness and medical interventions. Without family engagement, these patient preferences and values would otherwise fail to respect patient dignity and be a missed opportunity for shared decision-making [59].

Family presence on rounds is one way to promote family engagement in their loved one's care. In pediatric ICUs, such presence did not interfere with education or communication and results in families having increased feelings of inclusion, respect, and increased understanding of the patient's care. It also increased nurse satisfaction with team communication [60]. In adult ICUs, family rounds were associated greater satisfaction with care [61]. Additionally, family satisfaction with medical care was higher when they felt included with their loved one's care, as well as with clinician facilitated family conferences [62, 63].

Critical illness impacts both the patient and their entire family and support system and can lead to psychological distress. Although a directed family-support intervention for surrogates, which included providing emotional support by trained nurses and ensuring frequent clinician-family communication, did not decrease this distress, it did increase perception of quality communication and patient and family-centred care, as well as a reduction in ICU length of stay [64]. Studies of patient and family ICU diaries suggest an association with reduced symptoms of post-traumatic stress disorder (PTSD) in both patients and families [65, 66]. However, a recent study of ICU diaries did not show a significant reduction in PTSD symptoms at

3 months, so more investigation is needed to find the most effective way to reduce patient and family suffering [67]. Additionally, family presence during CPR did not interfere with medical efforts and was associated with fewer symptoms of anxiety and depression amongst family members [68].

Ultimately, in patients who do not have survivable illness, increased focused communication with the family through routine ICU family conference and palliative care consultation can facilitate family decision to transition to comfort-focused care and forgo life-sustaining treatment [69, 70]. This is important to preserve patient's dignity and autonomy while also ensuring they have minimal discomfort. Ultimately, family engagement is fundamental to promoting the care of the whole patient as well as their family members, and this synergy is at the core of the ABCDEF bundle. Future investigations will be needed to clarify the best practices of family engagement and their impact on both PICS and other important patient-centred outcomes.

The ABCDEF Bundle—Evidence and Implementation

Each of the previously mentioned interventions, from light sedation to delirium assessment to family engagement, has been validated in multiple critical care trials in improving both short- and long-term outcomes in critically ill patients. Combining these evidence-based interventions into a singular care philosophy, the ABCDEF bundle is a multidisciplinary, synergistic approach to improving ICU outcomes and preventing complications of ICU care.

In addition to the evidence for individual components, there have been multiple studies examining the impact of the bundle in totality [71–74]. For example, in a prospective single-centre cohort study including almost 300 patients, after implementation of the ABCDE bundle, patients spent three more days without mechanical ventilation and had almost half the odds of patients having delirium and increased odds of mobilising out of bed. Notably, there was no difference in self-extubation or reintubation rates [71]. A prospective multicentre cohort study including 6000 patients across seven community hospitals in California demonstrated the dose–response of the ABCDEF bundle in improving outcomes [72]. They found that with each 10% increase in bundle compliance, the odds of hospital survival increased by 7%, and for every 10% increase in partial bundle compliance, there was a 10% increase in hospital survival. Both findings were more pronounced when removing patients identified as receiving palliative care (12% and 23%, respectively) [72]. In addition, with both partial and total bundle compliance, patients had more days alive and free of delirium and coma. In a related prospective multicentre cohort study of 15,000 patients across 68 academic, community, and federal ICUs, compliance with the ABCDEF bundle was associated with a higher likelihood of ICU and hospital discharge and a lower likelihood of death, mechanical ventilation, coma, delirium, physical restraint, ICU readmission, and discharge to a destination other

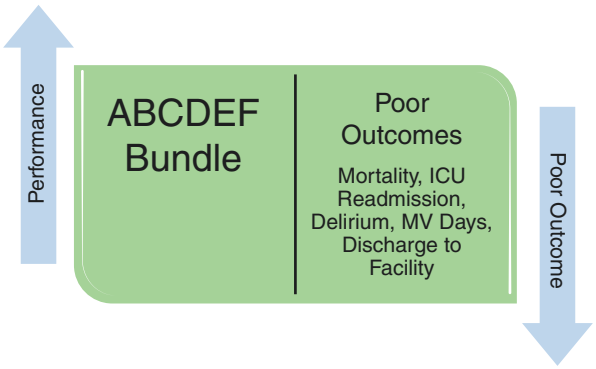

Fig. 1.4 Association between proportional performance of the ABCDEF bundle and poor ICU outcomes. Based on data from Pun et al. and Barnes-Daly et al, there is a significant dose–response showing that increasing percentile performance of the bundle is associated with reduced mortality, delirium, days of mechanical ventilation, and decreased likelihood of discharge to a facility. Abbreviations: MV mechanical ventilation

than home when compared with patients who did not receive 100% of possible bundle elements [73]. (Fig. 1.4) In addition, there is a dose–response related to bundle performance with a greater percentage of eligible bundle components associated with similar findings of increased likelihood of ICU and hospital discharge and lower likelihood of death, mechanical ventilation, coma, delirium, and physical restraint [70]. However, the increased dose is also associated with more significant pain episodes, which was not seen in the complete bundle performance analysis, highlighting the complex and interconnected nature of the bundle.

The ABCDEF bundle has been developed to uniquely combine interventions that are complementary. In a survey across 51 Michigan ICUs, ICUs that completed both SATs and delirium assessments were 3.5 times more likely to exercise ventilated patients, whereas those who completed SATs but not delirium assessments were no more likely to achieve exercise outcomes compared to other incomplete implementers of the bundle [74]. The authors of this study note that their findings support the idea that "the whole truly is greater than the sum of its individual parts" [74]. The multifactorial nature of PICS necessitates a multifactorial treatment philosophy, which the ABCDEF bundle addresses.

The ABCDEF bundle has demonstrated significant improvements in outcomes in clinical trials. To reach its full impact, consistent implementation of the bundle across ICUs is needed to improve ICU outcomes and help prevent PICS. One recent attempt at improved implementation is the Society of Critical Care Medicine's ICU Liberation ABCDEF Bundle Improvement Collaborative, which aims to improve bundle implementation [75]. Through research focused on identifying implementation difficulties, they noted that common barriers that were encountered included issues with electronic health records, inaccurate/unreliable assessments, staffing ratios and high turnover rates, challenging patient populations, communication and care coordination, data collection and documentation burden, no formal protocols,

and lack of administrative buy-in. Various implementation approaches were used to identify these barriers and potential solutions. Possible solutions include forming interprofessional teams to engage and empower leaders, establishing quality improvement methods to implement the bundle elements, utilizing small tests of change, eliciting feedback through discussions or surveys, scheduling frequent coaching calls and meetings, providing multimodal educational offerings, sharing bundle-related protocols, sharing former family and patient stories and cases to highlight bundle-related successes, and using auditing and feedback [75]. Providing standardized assessment, documentation, and communication of each bundle component in the electronic health record and on ICU rounds is also essential to implementation [76]. This requires interdisciplinary teams to work together and engaging patients' families during mobility and on rounds [77]. When all stakeholders are committed, change can be made with one or two patients at time, building upon small quality improvement cycles that set the foundation for successful implementation of the ABCDEF bundle and culture change promoting ICU liberation. Read more about the SCCM ICU Liberation Campaign and find resources and implementation tools at http://www.iculiberation.org.

Example Case

An instructive example of the implementation of the ABCDEF bundle is as follows: A 65-year-old man is admitted to the ICU for respiratory failure requiring mechanical ventilation due to streptococcal pneumonia. The nursing staff use the CPOT to frequently assess for pain and use as needed pain medications, target light sedation with dexmedetomidine for a RASS goal of −2 to 0, and monitor for delirium using the CAM-ICU, and the physical therapy team is engaged within the first 48 hours for early mobilisation. The patient's family is present on ICU rounds to participate in decision-making, as well as at the bedside with nursing and physical therapy to help comfort and orient the patient. Every morning, per the nursing protocol, sedation is stopped for a spontaneous awakening trial (SAT), and if passed, respiratory therapy performs a spontaneous breathing trial (SBT). After 3 days of mechanical ventilation, he passes his SAT and SBT and is liberated from the ventilator. Nursing continues to assess for pain and delirium, physical therapy mobilises and gets him out of bed and walking in the hallway, and his family is at the bedside to support him. He is transferred to the medical floor, and after a few more days in the hospital, he is discharged home with the ongoing assistance of home physical therapy and his family. Given his critical illness, he follows up in the ICU recovery clinic, where he undergoes a full assessment of his post-ICU recovery and any impairments, including physical, cognitive, and psychological symptoms. As his needs are identified, the ICU recovery clinic assists in coordinating further care, resources, and therapy the patient needs and provides the patient and family with educational resources and support groups [78].

Conclusion

There continues to be significant urgency to elucidate targets for intervention to prevent PICS, including optimal strategies and agents for pain and sedation, effective pharmacological treatments for delirium, and the optimal methods to engage families and reduce suffering. In addition, with the assistance of ICU recovery clinics, further investigation is needed into the long-term outcomes of the ABCDEF bundle in a prospective manner, as well as the most effective strategy for improving post-ICU recovery. The role of post-ICU clinics and various interventions in the post-discharge arena require further study to optimize outcomes for patients.

We have seen a substantial shift in the culture of critical care medicine. No longer are we only treating only the pathology, but instead we are focusing on the outcomes for the entire person, from physical to cognitive. A substantial and integral part of this culture change is made manifest in the ABCDEF bundle. Moving forward, as we understand in increasing depth the mechanisms of PICS and the best practices that prevent those sequelae, the bundle will continue to evolve, and ICU clinics will be able to address improving ICU recovery. As these advances are made, the ABCDEF bundle will remain on the front line in cultivating a holistic philosophy of ICU care that directly addresses the causes and risks for PICS, ultimately leading to improved post-ICU outcomes.

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