



## Reducing Iatrogenic Risks

### ICU-Acquired Delirium and Weakness—Crossing the Quality Chasm

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ICUs are experiencing an epidemic of patients with acute brain dysfunction (delirium) and weakness, both associated with increased mortality and long-term disability. These conditions are commonly acquired in the ICU and are often initiated or exacerbated by sedation and ventilation decisions and management. Despite > 10 years of evidence revealing the hazards of delirium, the quality chasm between current and ideal processes of care continues to exist. Monitoring of delirium and sedation levels remains inconsistent. In addition, sedation, ventilation, and physical therapy practices proven successful at reducing the frequency and severity of adverse outcomes are not routinely practiced. In this article, we advocate for the adoption and implementation of a standard bundle of ICU measures with great potential to reduce the burden of ICU-acquired delirium and weakness. Individual components of this bundle are evidence based and can help standardize communication, improve interdisciplinary care, reduce mortality, and improve cognitive and functional outcomes. We refer to this as the “ABCDE bundle,” for awakening and breathing coordination, delirium monitoring, and exercise/early mobility. This evidence-based bundle of practices will build a bridge across the current quality chasm from the “front end” to the “back end” of critical care and toward improved cognitive and functional outcomes for ICU survivors.

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**Abbreviations:** ABCDE = awakening and breathing coordination, delirium monitoring, and exercise/early mobility; CAM-ICU = confusion assessment method for the ICU; LOS = length of stay; SAT = spontaneous awakening trial; SBT = spontaneous breathing trial

The ICU provides treatment of the sickest hospitalized patients. Advances in intensive care have rescued many who would have previously died. However, many survivors suffer from severe symp-

toms of disease processes acquired or accelerated during the ICU stay. These symptoms typically arise from two common and often unrecognized condi-

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tions that have a significant impact on the quality and quantity of life following critical illness: ICU delirium and ICU-acquired weakness and their chronic sequelae.

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## ICU-ACQUIRED DELIRIUM AND WEAKNESS: PRECURSORS TO POOR PATIENT OUTCOMES

Delirium is an acute, fluctuating change in consciousness and cognition that develops over a brief time period.<sup>1</sup> It can be hyperactive, characterized by agitation and emotional lability (less common), or hypoactive, characterized by apathy and diminished responsiveness (more common), or mixed.<sup>2,3</sup> ICU delirium is a frequent complication of critical care, developing in approximately two-thirds of critically ill patients.<sup>4,6</sup> Despite the high prevalence, without active monitoring, it goes undiagnosed in up to 72% of cases.<sup>7-9</sup> Many patients have preexisting risk factors, including comorbidities (eg, dementia) and acute physiologic derangements present at ICU admission (eg, elevated creatinine, admission severity of illness). Importantly, a substantial proportion of patients acquire additional risk factors while in the ICU that independently predict delirium incidence or amplify preexisting risk factors. Some of these iatrogenic risk factors are modifiable, including both pharmacologic and nonpharmacologic factors. For example, multiple studies highlight the relationship between ICU delirium and the use and management of potent sedative and analgesic agents, with a notable increased risk of delirium with benzodiazepines.<sup>10-12</sup> Nonpharmacologic examples include immobility in the ICU<sup>13,14</sup> and environmental factors (eg, lack of access to daylight) that are both amenable to intervention.<sup>6,15,16</sup> For the purposes of this discussion we refer to newly acquired and potentially modifiable delirium in the critically ill as ICU-acquired delirium. This terminology is selected to bring attention to the potentially modifiable nature of this disorder and to draw parallel with terminology that is increasingly accepted for neuromuscular disease in the critically ill, or ICU-acquired weakness.<sup>17</sup>

ICU-acquired weakness is the acute onset of neuromuscular/functional impairment in the critically ill for which there is no plausible etiology other than critical illness.<sup>18,19</sup> Generalized weakness impairs ventilator weaning and functional mobility. Acute morbidities (eg, acute physiology score, hyperglycemia) and medications (eg, corticosteroid use) are reported risk factors for this condition.<sup>20-23</sup> An additional key risk factor for ICU-acquired weakness is the duration of mechanical ventilation experienced by patients,<sup>24,25</sup> with weakness occurring in up to 58% of patients who receive mechanical ventilation for at least 7 days.<sup>26,27</sup>

Although unique in their clinical presentation, these conditions share important risk factors, outcomes, and evidence-based preventative care processes that are widely available but currently underused. In this article, we review these disorders, propose a preventative bundle of care processes, highlight gaps in quality performance, and provide guiding principles to fill these gaps.

ICU delirium is independently predictive of numerous adverse outcomes. Patients experiencing ICU delirium have a 49% increased risk of remaining in the hospital on any given day compared with those without delirium.<sup>28</sup> Among hospital survivors, delirium influences poor long-term outcomes, including cognitive impairment,<sup>29,30</sup> institutional placement,<sup>31</sup> and mortality.<sup>32,33</sup> Two prospective cohort studies similarly revealed that each additional day with delirium was independently associated with a 10% increased risk of death at 6 months (hazard ratio, 1.10; 95% CI, 1.0-1.3)<sup>32</sup> and 1 year (hazard ratio, 1.10; 95% CI, 1.0-1.2),<sup>33</sup> respectively.

ICU-acquired weakness is likewise predictive of poor outcomes. Among patients ventilated more than a week, those with ICU-acquired weakness require approximately 20 additional days of mechanical ventilation<sup>26,34</sup> and have increased mortality (48% vs 19%,  $P = .03$ ).<sup>27,35</sup> Effects of ICU weakness persist well after hospital discharge, with 60% of patients experiencing continued muscle dysfunction up to 1 year after illness.<sup>25</sup>

Delirium and weakness are conditions that are influenced by illness, aggravated by treatment modalities in the ICU, and that interact with each other. Sepsis is a diagnostic prototype that illustrates the synergistic relationship between ICU-acquired delirium and weakness<sup>36,37</sup> and demonstrates the important role of predisposing as well as iatrogenic risk factors (Fig 1). Sepsis-induced endotoxin and cytokine release,<sup>38,39</sup> hypoxemia,<sup>40,41</sup> and endothelial dysfunction<sup>42</sup> present examples of unique mechanisms that reach common final pathways toward weakness and delirium. Patients with sepsis are also exposed to overlapping

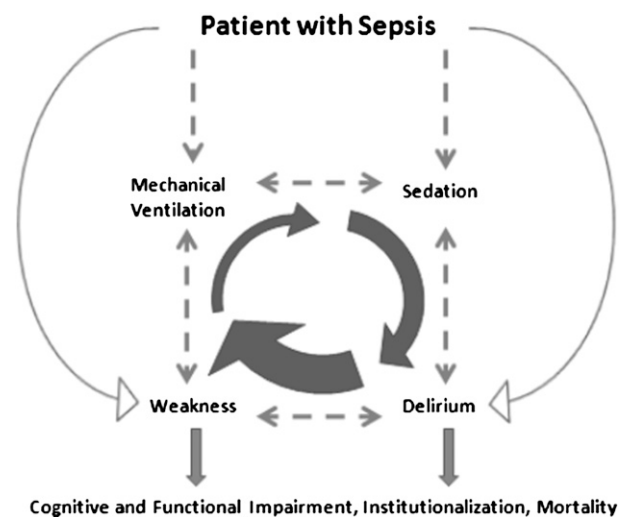


FIGURE 1. Relationship between ICU-acquired delirium and weakness in a patient with sepsis.

risk factors, such as sedation and mechanical ventilation-care processes tightly linked with and potent risk factors for delirium and weakness, respectively.<sup>10,11,24</sup>

Sedation without explicit targets extends mechanical ventilation needs, creating a dynamic feedback loop that aggravates the risks of delirium and weakness.<sup>43</sup> For example, excessive sedation decreases the likelihood a patient can safely perform or pass a spontaneous breathing trial (SBT), leading to additional days of sedation and mechanical ventilation. Even when sedation stops, patients may continue to have delirium. Delirium commonly continues the cycle of prolonged ventilation, acting as a potent barrier to extubation following a successful SBT,<sup>44</sup> once again resulting in additional days of sedation and ventilation.

Finally, emerging evidence suggests that physical performance and cognitive performance influence each other, further potentiating the feedback loop.<sup>14,45,46</sup> A preventative strategy must take advantage of shared and reinforcing features outlined above (and in Fig 1) to be more efficient and effective in minimizing delirium, weakness, and additional adverse outcomes.

#### ABCDE: A UNIFYING STRATEGY TO MITIGATE ICU-ACQUIRED DELIRIUM AND WEAKNESS

Improving outcomes in patients experiencing ICU-acquired delirium and weakness can be achieved by aligning and supporting the people, processes, and technology already existing in ICUs. Not only are advanced machines, expensive medications, and addi-

tional provider technical skills not required, but technology can be reduced, medications adjusted, and teamwork improved to minimize the burden of provider tasks. Such improvements may result from implementing a set of practices such as: awakening and breathing coordination, delirium monitoring, and exercise/early mobility—the ABCDE bundle (Fig 2). ABCDE is a multicomponent process that is intentionally interdependent and designed to: (1) improve collaboration among clinical team members, (2) standardize care processes, and (3) break the cycle of oversedation and prolonged ventilation, which appear causative to delirium and weakness.

#### *Awaken the Patient Daily: Sedation Cessation*

Sedative selection and management are leading modifiable risk factors for preventing delirium in the ICU.<sup>10,11</sup> Sedative drugs, universally used in critically ill patients, reduce the work of breathing and alleviate agitation. Evidence suggests that benzodiazepines pose the highest risk. Although withholding benzodiazepines may not eliminate delirium, strong evidence suggests that increasing doses dramatically increases the risk of delirium in a dose-dependent fashion (Fig 3)<sup>10,12</sup> and simultaneously prevents patient mobility.<sup>24</sup> In multiple studies, daily spontaneous awakening trials (SATs) facilitate the transition from drug-induced coma to consciousness, reduce the duration of mechanical ventilation, and reduce ICU complications as well as costs.<sup>47-49</sup> Although the benefits of protocolized SATs have been reported among broad populations, the benefits may not be realized by some specific populations, most notably those experiencing alcohol

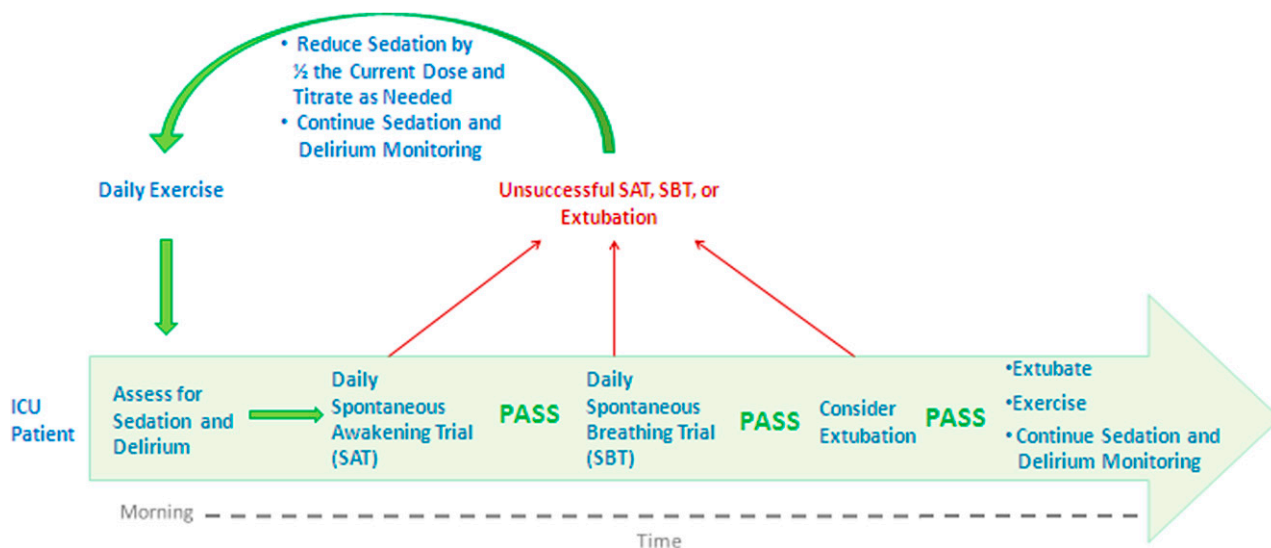


FIGURE 2. ABCDE is an ICU-acquired delirium and weakness mitigation strategy. This strategy is a protocolized bundle performed daily on mechanically ventilated and/or sedated patients in the ICU. This strategy is interdisciplinary by design and most effective when implemented by nursing, respiratory therapy, and physical therapy personnel working together as an ICU team. ABCDE = awakening and breathing coordination, delirium monitoring, and exercise/early mobility.

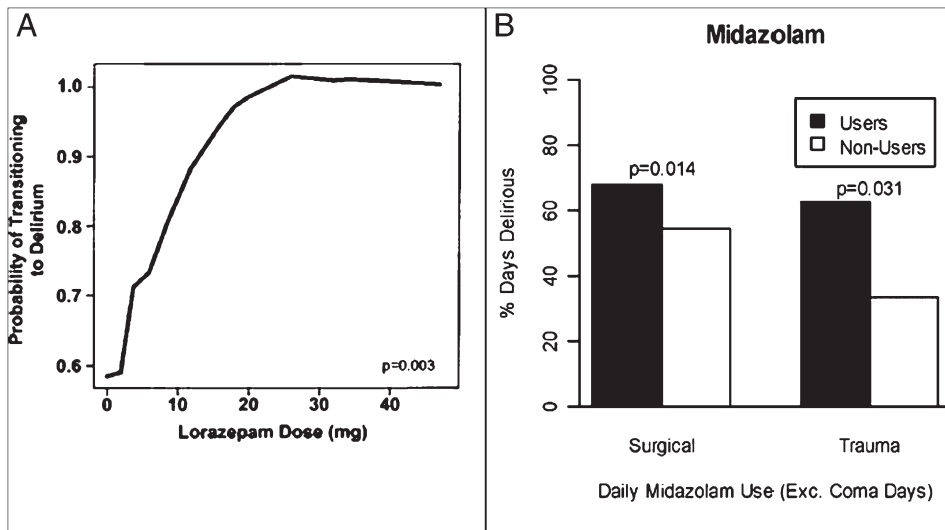


FIGURE 3. A, Data from Pandharipande et al<sup>10</sup> indicate that lorazepam dose in the preceding 24 h is an independent predictor for transitioning to delirium in the ICU. The effect rapidly increased up to doses of 20 mg/d, at which point the effect plateaued at near 100% probability of transition to delirium. B, Data from Pandharipande et al<sup>12</sup> demonstrate that in both surgical and trauma ICU patients, users of midazolam have statistically increased number of days of delirium.

withdrawal and delirium tremens, or those already maintained at a very light level of sedation.<sup>50,51</sup>

#### Breathing: Daily Interruptions of Mechanical Ventilation

Terminating mechanical ventilation requires objective assessment for patient readiness, best performed by daily SBTs in patients meeting established safety criteria, such as being on  $\leq 50\%$  FIO<sub>2</sub> and positive end-expiratory pressure  $< 8$  cm H<sub>2</sub>O. The first randomized trial of a spontaneous breathing protocol with a control group of which we are aware established decreased ventilator days and complications of mechanical ventilation.<sup>52</sup> Later reports confirmed that nonphysician protocolized management (eg, using respiratory therapists) of SBTs resulted in no loss of safety, while simultaneously increasing nonphysician provider autonomy.<sup>53</sup> In addition, these trials highlighted the importance of interdisciplinary coordination of sedation and ventilation between respiratory therapists and nurses.

#### Coordination: Daily Awakening and Daily Breathing

Recognizing the benefit of both protocolized interruptions of sedation and mechanical ventilation, Girard et al<sup>54</sup> combined these approaches in what is known as the Awakening and Breathing Controlled trial, or the ABC trial. Daily SATs coordinated with daily SBTs decreased adverse cognitive outcomes, reduced hospital length of stay (LOS) by 4 days, and reduced death at 1 year by 14% (Fig 4). The processes

were synergistic, yielding outcome reductions in excess of what has been shown when the protocols were delivered independently (ie, 4 days improvement in LOS vs 2 days when done independently).<sup>47,52,54</sup>

#### Delirium Monitoring

Delirium monitoring is a guideline-recommended practice.<sup>55</sup> Instruments such as the Intensive Care Delirium Screening Checklist<sup>56</sup> and the confusion

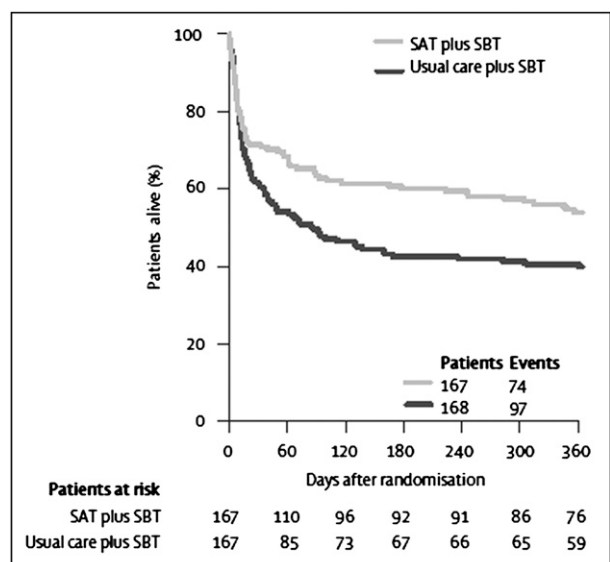


FIGURE 4. One-year survival analysis of the Awakening and Breathing Controlled Trial from Girard et al.<sup>54</sup> Survival was 14% higher at 1 year among the intervention group (spontaneous awakening trial coordinated with spontaneous breathing trial) vs the control group (usual care plus spontaneous breathing trial). SAT = spontaneous awakening trial; SBT = spontaneous breathing trial.



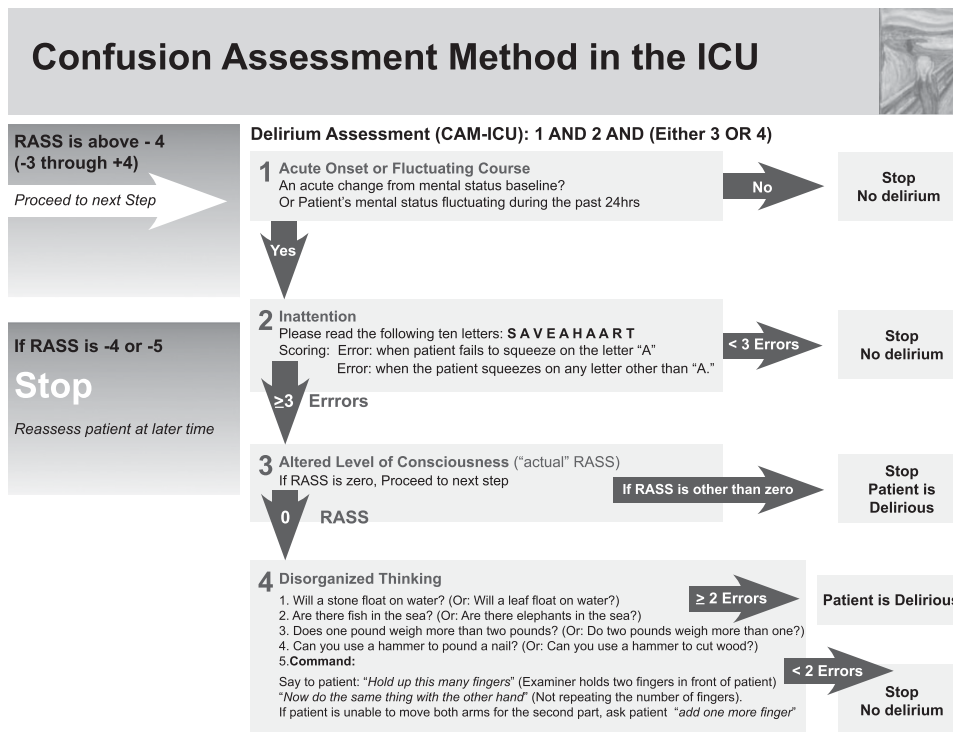


FIGURE 5. CAM-ICU. Available at [www.icudelirium.org](http://www.icudelirium.org). This stepwise approach integrates information from the any sedation scale into the delirium assessment. CAM-ICU = confusion assessment method for the ICU<sup>5,56</sup>; RASS = Richmond Agitation-Sedation Score.<sup>60</sup> Republished with permission from the American Medical Association.<sup>5</sup>

assessment method for the ICU (CAM-ICU)<sup>5,57</sup> offer highly sensitive and specific tools for delirium detection. Both tools have been validated across populations of mechanically ventilated and nonventilated patients and are in use in > 20 countries and languages. Of course, monitoring delirium alone may not be sufficient to change outcomes. Similar to other modes of physiologic monitoring in the ICU, it is what one does with the information that matters. Using such tools to identify delirium prompts providers to investigate and treat underlying conditions that may otherwise be delayed or missed altogether.

Sedation monitoring can likewise be achieved with simple instruments validated in the ICU. Sedation scales (eg, Sedation Agitation Scale,<sup>58</sup> Ramsay Score,<sup>59</sup> Richmond Agitation-Sedation Score,<sup>60</sup> Minnesota Sedation Assessment Tool<sup>61</sup>) should be integrated with, and used complementary to, delirium instruments (eg, Intensive Care Delirium Screening Checklist,<sup>56</sup> CAM-ICU<sup>5</sup>). Figure 5 illustrates an example of this.<sup>57</sup> Use of sedation assessment tools provides a shared language to assess and communicate sedation across providers, thus clarifying sedation indications, goals, and outcomes. In the absence of reliable measures of sedation, clinicians risk both oversedation and undersedation. This can lead to severe adverse consequences of the potent medications, including prolonged mechan-

ical ventilation, immobility, and delirium. In contrast, objective measures of sedation, rather than clinician judgment alone, can lead to reduced mechanical ventilation time and complications.<sup>62,63</sup>

### Exercise/Early Mobility

Early mobilization of ICU patients reduces acute cognitive and physical dysfunction. Multiple studies have demonstrated the feasibility of early mobilization among patients with respiratory failure.<sup>13,14,64,65</sup> In addition, early physical therapy has been shown to independently reduce hospital LOS up to 3 days,<sup>13,65</sup> reduce delirium incidence,<sup>13,14</sup> and increase return to independent functioning.<sup>13,14</sup> Although not yet a part of formal guidelines, the compelling body of evidence suggests that early physical exercise should be considered strongly as a routine part of ICU care.

The relationship between ICU-acquired delirium and long-term cognitive impairment, and subsequent risks to patient safety and quality of life, demands that cognitive rehabilitation also be considered.<sup>28,29</sup> Cognitive rehabilitation improves neuropsychologic abilities, such as attention, memory, and executive function,<sup>66,67</sup> for multiple conditions associated with acute brain injury, although these techniques of cognitive rehabilitation have not been formally tested in

general medical/surgical ICU survivors. Patients at high risk for acquired and long-lasting cognitive dysfunction (ie, prolonged delirium, sepsis) or with measured cognitive deficits may be considered for referral to cognitive rehabilitation, especially with attention toward executive and memory deficits.

### ABCDEs: SIMPLE DOES NOT MEAN EASY

The Institute of Medicine's 2001 landmark report, *Crossing the Quality Chasm: A New Health System for the 21st Century*, stated that "health care today harms too frequently and routinely fails to deliver potential benefits."<sup>68</sup> Although great strides have been made in improving the quality and safety of critical care, adherence to recommended strategies of ICU care remains inadequate. The ABCDE intervention bundle is one important approach to cross this quality chasm.

#### *Implementing Awakening and Breathing Coordination*

Despite the benefit from SATs, only 40% of ICU providers reported using daily sedation interruptions, and among those, only 63% did so for all patients.<sup>69</sup> A more recent survey of intensivists revealed < 50% reported using SATs.<sup>70</sup> Use of SBTs is also lagging. Kahn et al<sup>71</sup> found that among academic ICUs, the rates of SBTs ranged from 31% to 42%, despite high levels of intensivist staffing. In a recently published Canadian survey, only 20% of intensivists reported always performing an SBT (or assessing for readiness).<sup>72</sup>

#### *Implementing Delirium Monitoring*

Monitoring for delirium is an emerging component of modern ICUs over the past 10 years. A Canadian survey in 2001 found that only 4% of intensivists used a delirium scoring system,<sup>69</sup> whereas 5 years later a US survey in 2006 found that 33% of intensivists use a validated delirium tool.<sup>70</sup> The use of validated sedation monitoring scales is also inadequate. In one study, sedation scales were routinely used in approximately 50% of ICUs.<sup>69</sup> For institutions using a scale, it was common to choose unvalidated scales over scales specifically validated for use in the ICU. More recent surveys revealed that 30% to 40% of intensivists continue to manage sedation without a specific monitoring instrument.<sup>70,73</sup>

#### *Implementing Exercise/Early Mobility*

Use of physical therapy targeted toward ICU patients is increasingly common, yet not uniform, and faces many barriers, including competing processes of care, lack of early mobilization care planning, and inadequate technology and/or collaboration.<sup>64</sup> Morris et al,<sup>65</sup>

reported that among 165 patients in a "usual care" arm of a trial testing early ICU mobilization, only 47% of patients had any physical therapy. In another study of critically ill patients, 20% received no physical activity, and 15% more only received passive range of motion exercises during the ICU stay.<sup>74</sup>

### CROSSING THE QUALITY GAP WITH ABCDE: KEY IMPLEMENTATION PRINCIPLES

Implementation of new discoveries into practice is commonly delayed. The gaps in process performance to prevent and/or mitigate ICU-acquired delirium and weakness are not unexpected, as the most appropriate care is often provided only half of the time.<sup>75</sup> Similar to other conditions, reversing the epidemic of ICU-acquired delirium and weakness will not depend solely on new evidence. Application of current evidence into routine practice should yield great benefit. To do so, we provide seven guiding principles:

1. Cognitive and functional decline in the ICU must change from being viewed as "part of the inevitable consequences of critical illness" to a modifiable condition. Central line-associated bloodstream infections were once considered part of the unavoidable complications of ICU care. We now know this is not so. With rigorous adherence to infection control techniques, coupled with simulation-based training, such infections can be nearly eliminated.<sup>76-78</sup> An analogous transformation must occur in approaches to ICU-acquired delirium and weakness. Although these conditions may occur in the absence of specific modifiable risk factors (Fig 3), ICU provider teams must recognize the important role that modifiable risk factors play and use process improvement methods to achieve reductions believed unimaginable today. In fact, government stakeholders already view delirium through the lens of quality and safety, having recently proposed its inclusion as an avoidable hospital-acquired condition.<sup>79</sup>
2. Improvement requires evolution in critical care team roles. Repeated studies demonstrate that nurses and respiratory therapists can successfully use sedation and mechanical ventilation protocols<sup>53,54,63,65</sup> and streamline the process of care from a minimum of three separate processes to one unifying process. Although physician expertise and judgment is critical in ICU management, mounting evidence suggests that a team-based, evidence-based, and systematic approach to care delivery is required.
3. Teams must shift from multidisciplinary to interdisciplinary care. Implementation of ABCDE cannot succeed with multidisciplinary silos.

ABCDE requires each team member to provide and receive constant bidirectional feedback facilitated by common assessment tools that describe complex constructs of sedation and delirium. The very nature of ABCDE combines processes with intentional synergy, wherein the success of one depends and augments the success of others. For example, communication across physicians, nurses, respiratory therapists, and physical therapists is facilitated with standardized sedation and delirium measures. SBTs cannot begin until nurses perform and communicate safe completion of SATs. Safe extubation cannot occur without SAT and SBT results communicated to the physician. Participation in physical therapy requires appropriately targeted sedation.

4. ABCDE should become the default practice. Patients cannot afford to wait for physicians to make decisions regarding initiation of an SAT, SBT, or physical therapy, especially when nurses or respiratory therapists may be present at the bedside more often and have an even better ability to manage processes of care and monitor for subsequent improvements or decline. ABCDE practices must be structured as a daily part of care with clearly laid out safety guidelines. The components of this bundle are safe, reliable, and save lives.<sup>14,54</sup>
5. Patients will wake up, breath, and exercise if we allow them. First, although sedative administration is a common practice, it may not always be required. In a randomized, controlled trial comparing a standard sedation protocol vs an analgesia-sedation protocol, Strøm et al<sup>80</sup> demonstrated that critically ill patients can safely tolerate an analgesia-sedation strategy and experience reductions in the duration of mechanical ventilation. Second, implementation of daily SATs and SBTs raises appropriate concerns about inadequate rest and potential psychologic trauma, yet, to date there is no strong evidence to suggest either occurs.<sup>79,81</sup> Despite a documented increased risk of self-extubation with paired SATs and SBTs, there is no evidence of increased reintubations among the same patients.<sup>54</sup> Finally, in the case of protocolized exercise, not only did patients walk 5 days earlier when prompted by a protocol, but they did so without excess unplanned extubation or equipment removal.<sup>14,65</sup> Qualitative data from patient interviews highlight perceived benefits of early exercise without evidence of serious psychologic side effects (see patient interview at [www.hopkinsmedicine.org/oacis](http://www.hopkinsmedicine.org/oacis)).
6. Checklists and daily goals should be used; not elegant, but effective. Prior studies have demonstrated the benefits of using a checklist in patient

safety.<sup>76,77</sup> A five-step checklist reduced the central line-associated bloodstream infection rate to near zero across 108 Michigan hospitals.<sup>77</sup> A similar approach applied to ABCDE interventions may yield analogous benefits in preventing ICU-acquired delirium and weakness.

7. Incorporate process and outcomes monitoring. ICUs must strive to monitor their adherence with SATs, SBTs, and exercise/early mobility protocols. Such monitoring must include rates of delirium, sedation levels in comparison with process targets, and important outcomes of care (eg, duration of mechanical ventilation, mortality). Tracking performance offers the only chance to assess current performance, understand improvement barriers, and generate new targets for improvement.

## CONCLUSIONS

ICU-acquired delirium and weakness are disorders of epidemic proportions and should be viewed as potentially preventable and/or modifiable outcomes for ICU survivors. Currently available processes of care can dramatically reduce this burden of disease. We propose implementation of a bundle of processes—awakening and breathing coordination, delirium monitoring, and exercise/early mobility—or the ABCDE bundle, to achieve this goal. The bundle requires minimal additional resources yet mandates an important investment in changing the operational culture of the ICU. Delirium and weakness must now be viewed as urgent issues affecting the immediate and long-term quality and safety of our sickest patients. ABCDE processes should be protocolized and all ICU team members empowered, including physicians, nurses, respiratory therapists, and physical therapists. Through constant measurement, analysis, and process improvement cycles, the critical care team can understand quality gaps, identify best practices, and continue to work toward the liberation of patients from harmful effects of prolonged sedation, mechanical ventilation, and bed rest. Indeed, patients' survival and long-term quality of life depend on it.

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