

# AACN Practice Alert

## Assessment and Management of Delirium Across the Life Span

### Scope and Impact of the Problem

Delirium is an acute change in consciousness that is accompanied by inattention and either a change in cognition or perceptual disturbance.<sup>1</sup> Patients can have hyperactive delirium (agitation, restlessness, attempting to remove catheters, and/or emotional lability), hypo-active delirium (flat affect, withdrawal, apathy, lethargy, and/or decreased responsiveness), or a combination of both.<sup>1</sup> Delirium affects up to 80% of patients in the intensive care unit (ICU), and it is estimated that ICU costs associated with delirium equal between \$4 billion and \$16 billion annually in the United States.<sup>2-6</sup>

This form of acute brain dysfunction is associated with increased length of ICU and hospital stays, time receiving mechanical ventilation, mortality, and long-term cognitive impairment.<sup>7-9</sup> Despite this high prevalence and the adverse outcomes, delirium in the ICU goes undetected and, thus, untreated in scores of patients.<sup>10</sup> Iatrogenic risk factors are often modifiable and are referred to as precipitating factors.<sup>3,11</sup>

### Expected Nursing Practice

1. Evaluate patients for potential risk factors for delirium, including a review of medications. [level B]
2. Assess all critically ill patients for delirium by using validated tools. [level B]
3. Create strategies to decrease delirium risk factors, including early progressive mobility. [level B]



### AACN Levels of Evidence

- Level A** Meta-analysis of quantitative studies or metasynthesis of qualitative studies with results that consistently support a specific action, intervention, or treatment (including systematic review of randomized controlled trials)
- Level B** Well-designed, controlled studies with results that consistently support a specific action, intervention, or treatment
- Level C** Qualitative studies, descriptive or correlational studies, integrative reviews, systematic reviews, or randomized controlled trials with inconsistent results
- Level D** Peer-reviewed professional and organizational standards with the support of clinical study recommendations
- Level E** Multiple case reports, theory-based evidence from expert opinions, or peer-reviewed professional organizational standards without clinical studies to support recommendations
- Level M** Manufacturer's recommendations only

4. Collaborate with providers to administer benzodiazepines cautiously, developing strategies to give only what is needed. [level C]
5. Use antipsychotic medications cautiously, monitoring for prolongation of QTc. [level C]
6. Collaborate with the interprofessional team to prevent and manage delirium. [level D]
7. Involve family in nonpharmacological management strategies. [level C]

### Supporting Evidence

#### Identification and Modification of Risk Factors

1. *Pediatrics*. Risk factors for delirium in critically ill children are understudied, with one single-center prospective report<sup>12</sup> currently available. Large-scale, multisite research is needed to

further discern the risk factors for delirium specific to the pediatric ICU population. Current risk factors associated with the diagnosis of delirium in the pediatric ICU include

- Presence of developmental delay
- Need for mechanical ventilation
- Age 2-5 years

2. *Adults and Older Adults.* Risk factors for delirium in critically ill adults are consistently reported as older age, preexisting dementia, hypertension, pre-ICU emergency surgery or trauma, high severity of illness, mechanical ventilation, metabolic acidosis, delirium on the prior day, coma, and multiple organ failure.<sup>13</sup>

Although immobility has not been reported as a risk factor for the development of delirium in the ICU, it has been reported in non-ICU cohorts.<sup>14</sup> Researchers in recent studies<sup>15,16</sup> have reported that early mobility in critically ill patients results in not only improved physical function, but also improved cognitive function, reducing the duration of delirium by 2 days. “Early” is defined by these protocols as within the first 3 days of the ICU stay and focuses on progressive mobility pathways, starting with passive range-of-motion exercises and progressing to active range-of-motion exercises, sitting on the side of the bed, and ambulating as tolerated.<sup>17</sup> Mobilize ICU patients early, whenever feasible, to reduce the incidence and duration of delirium and improve physical outcomes.<sup>18</sup>

Sedative use has been the only consistently identified modifiable risk factor for ICU delirium.

- a. Benzodiazepines. Benzodiazepines are an independent risk factor for the transition to delirium.<sup>19,20</sup> Use of benzodiazepines is not suggested for ICU patients with delirium unrelated to alcohol or benzodiazepine withdrawal.<sup>18</sup>
- b. Dexmedetomidine. Two recent studies, “Maximizing Efficacy of Targeted Sedation and Reducing Neurological Dysfunction (MENDS)” and “Safety and Efficacy of Dexmedetomidine Compared with Midazolam (SEDCOM),” showed a significant reduction

in delirium duration in patients receiving dexmedetomidine when compared with benzodiazepines (lorazepam and midazolam, respectively).<sup>21,22</sup> Both studies used dexmedetomidine at higher doses and for longer durations than the current Food and Drug Administration (FDA) labeling approval, which is a maximum dose of 0.7 mcg/kg per hour for a 24-hour duration. Patients sedated with dexmedetomidine have a lower prevalence of delirium than do patients sedated with benzodiazepines, along with other improved outcomes (eg, duration of mechanical ventilation, ICU length of stay).<sup>18</sup>

- c. Opioids and propofol. The data concerning opioids are difficult to interpret, because some studies show a dose-dependent relationship, while other studies indicate no relationship between the use of these drugs and development of delirium in the ICU.<sup>3,19,23-25</sup> Only 1 study has explicitly addressed propofol, and those researchers report no significant relationship between propofol and ICU delirium.<sup>20,24</sup> More research is needed with both propofol and opioids to fully understand their relationship to the development and duration of delirium.

### Delirium Assessment Tools

In the absence of a validated tool, delirium goes undetected by both physicians and nurses in more than 65% of ICU patients.<sup>10,26-28</sup> Reports underscore the need for systematic utilization of standardized assessment tools, which is in concert with the recommendations from both national and international guidelines.<sup>18,29-31</sup> Recent Society of Critical Care Medicine guidelines recommend all adult ICU patients be routinely assessed for delirium.<sup>18</sup> Routine assessment reduces the likelihood of delirium going undetected and consequently untreated. ICU delirium assessment tools are available for both adults and children.

1. *Pediatrics.* The Pediatric Confusion Assessment Method for the ICU (pCAM-ICU for ages  $\geq 5$  years),<sup>32</sup> Cornell Assessment of Pediatric Delirium (CAP-D for ages 1-17 years),<sup>33</sup> and

the Pediatric Anesthesia Emergence Delirium Scale (PAED, for ages 1-17 years)<sup>34</sup> are valid and reliable tools for assessing delirium in pediatric ICU patients. A PreSchool Confusion Assessment Method for the ICU (psCAM-ICU) for children 6 months to 5 years of age also has been validated for use.<sup>35</sup>

2. *Adults and Older Adults.* The Confusion Assessment Method for the ICU (CAM-ICU)<sup>36,37</sup> and the Intensive Care Delirium Screening Checklist (ICDSC)<sup>38</sup> are the most valid and reliable tools to assess delirium in adult and older adult ICU patients.<sup>14</sup> Implementation of both tools has been described; both have high accuracy and favorable compliance, and each requires minimal education.<sup>39-43</sup>

### Medical Management

1. Fundamentally, prevention and management strategies for children and adults should focus first on disease-related interventions. The Society of Critical Care Medicine suggests identification of the cause as the first step in delirium management.<sup>18</sup> The following THINK mnemonic may be helpful in determining the cause when delirium is present:

#### Toxic situations

- Congestive heart failure, shock, dehydration
- Deliriogenic medications (tight titration of sedatives)
- New organ failure (eg, liver, kidney)

#### Hypoxemia

Infection/sepsis (hospital-acquired),  
Immobilization

Nonpharmacological interventions (Are these being neglected?)

- Hearing aids, glasses, sleep protocols, music, noise control, ambulation

#### K<sup>+</sup> or electrolyte problems

2. Additional Management Strategies for Older Adults
  - a. Older adults are likely to have more non-modifiable risk factors for delirium upon presentation to the hospital. Mitigation

of modifiable risk factors becomes extremely important.

- b. Additional nonpharmacological interventions to prevent and manage delirium in critically ill older adults include, but are not limited to<sup>18,29-31,44</sup>

- Avoid malnutrition
- Avoid use of restraints
- Discontinue or remove all unnecessary catheters, tubes, and equipment
- Keep environment calm and uncluttered; avoid overstimulation
- Consider “camouflaging” catheters and tubes
- Early and frequent mobilization and participation in activities of daily living
- Treat pain
- Provide cognitively stimulating activities adapted for patient

### Medications and Delirium

1. No drug has been approved by the FDA to treat delirium in children or adults.
2. *Pediatric.* No guidelines for pharmacological treatment of delirium in children are currently available. In single-center retrospective studies,<sup>45,46</sup> atypical antipsychotic administration (ie, olanzapine, risperidone, quetiapine) appeared to be effective and safe for managing delirium in children. Further prospective and placebo-controlled studies of pharmacological treatment of critically ill children with delirium is required to determine the efficacy of those drugs.
3. *Adults and Older Adults.* Current clinical practice guidelines for critically ill adults state that no published evidence indicates that treatment with haloperidol reduces the duration of delirium in adult ICU patients; however, atypical antipsychotics may reduce the duration of delirium.<sup>18</sup> In the past, clinical practice guidelines have recommended antipsychotics as the medication class of choice for delirium, yet very little evidence exists to support this internationally adopted treatment.<sup>47-49</sup> Review of the literature reveals few placebo-controlled investigations on the efficacy of antipsychotic agents

for the treatment of ICU delirium. Two such studies<sup>50,51</sup> demonstrated no difference in antipsychotic treatment versus placebo. Another pilot study<sup>52</sup> indicated that treatment with quetiapine may reduce delirium duration. These studies are the first steps in understanding the best pharmacological treatment; however, larger trials are needed to confirm these findings in order to systematically direct the choice for delirium treatment.

All patients receiving antipsychotics (haloperidol or any of the atypical antipsychotics) should be routinely and systematically monitored for side effects, especially QT prolongation. Guidelines suggest withholding antipsychotic agents in patients at risk for arrhythmia (eg, baseline QT prolongation, history of torsades de pointes, administration of concomitant medications known to prolong QT interval).<sup>18</sup>

Rivastigmine, a cholinesterase inhibitor, is not superior to placebo for the treatment of ICU delirium. A large European trial was stopped prematurely because of increased mortality in the rivastigmine group.<sup>53</sup>

The FDA has issued an alert that atypical antipsychotic medications (second-generation antipsychotic agents such as olanzapine, risperidone, quetiapine) are associated with mortality risk among older patients, and another analysis indicated that haloperidol use had an even higher mortality risk in non-ICU older patients than did atypical antipsychotics.<sup>54</sup>

### Interprofessional Collaboration, Including Family

Several reviews<sup>55-57</sup> have described the idea of implementing a core model of care that combines multiple evidence-based practice strategies subsequently incorporated into routine daily care for the purpose of improving overall outcomes for patients and allowing a systematic reduction in the modifiable risk factors for delirium. The ABCDEF bundle includes spontaneous awakening and breathing trial coordination, careful sedation choice, delirium monitoring, early progressive mobility and exercise, and family engagement and empowerment. The intent of

combining and coordinating these individual strategies is to “(1) improve collaboration among clinical team members and the family, (2) standardize care processes, and (3) break the cycle of oversedation and prolonged ventilation, which appear causative to delirium and weakness.”<sup>55</sup>

The ABCDEF bundle is a helpful paradigm for critical care nurses to consider when implementing strategies to improve patient care as a means to reduce modifiable delirium risk factors and improve quality of life for patients and their families. Studies evaluating the effectiveness and safety of the bundle have reported reductions in duration of mechanical ventilation, delirium incidence, and length of stay along with increases in the occurrence of mobilization—all with no significant increased risk of adverse events.<sup>16,58,59</sup> Components of the ABCDEF bundle are

**Assess and manage pain**

**Both** awakening and breathing trials (Wake up and Breathe protocol)

**Choice** of sedation and analgesia (attention to these medications)

**Delirium** assessment and management

**Early** progressive mobility

**Family** engagement and empowerment

- Consider having patients’ family members keep an intensive care diary, which can reduce the new onset of posttraumatic stress disorder following critical illness.<sup>60</sup>
- Family members can be helpful in preventing, recognizing, and mitigating delirium. Family and friends can help ICU patients by using the following techniques:
  - Communication: use simple words, be concrete, and take your time
  - Remind patient of day, date, surroundings
  - Talk about family and friends
  - Address patients’ concerns (eg, bills, pets, work)
  - Bring glasses or hearing aids
  - Decorate the room with familiar items that may be reminders of home
  - Encourage patient to perform range-of-motion exercises at discretion of clinical staff

- Keep in mind that critical illness affects patients *and* their support system. It is important to recognize needs of the patient's family as well as needs of the patient. Family needs may include education, social and emotional support, and access to helpful resources. Education should include expectations for the patient during and after critical illness (eg, post-intensive care syndrome, posttraumatic stress disorder, depression). Last, encourage family members to attend to basic personal needs without guilt.

## Implementation/Organizational Support for Practice

**Ensure** consistent practice for delirium assessment: at least once per shift or with each change of caregiver, assess delirium for all critically ill patients, using a validated tool (eg, CAM-ICU, ICDSC, or pediatric assessment tool).

**Support** collaboration with the interprofessional team to decrease benzodiazepine use, including titration strategies (eg, sedation scale, targeted sedation protocols, and daily awakening trials) or use of alternative sedatives (eg, dexmedetomidine or propofol).

**Develop** a protocol that incorporates early progressive mobility and exercise for all critically ill patients. Involve the patient's family in mobility as indicated.

**Review** and update policies allowing patients' families to be present with patients.

## Need More Information or Help?

1. Contact a clinical practice specialist for additional information: go to [www.aacn.org](http://www.aacn.org) then select Practice Resource Network.
2. See [www.ICUdelirium.org](http://www.ICUdelirium.org) for materials about delirium teaching and implementation of assessment tools, including downloadables and videos.
3. See [www.ICULiberation.org](http://www.ICULiberation.org) for information on implementation of the 2013 Clinical Practice Guidelines for the management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit.

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## References

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM 5*. Arlington, VA: American Psychiatric Association; 2013.
2. Pisani MA, Murphy TE, Van Ness PH, Araujo KL, Inouye SK. Characteristics associated with delirium in older patients in a medical intensive care unit. *Arch Intern Med*. 2007;167(15):1629-1634.
3. Pandharipande P, Cotton BA, Shintani A, et al. Prevalence and risk factors for development of delirium in surgical and trauma intensive care unit patients. *J Trauma*. 2008;65(1):34-41.
4. McNicoll L, Pisani MA, Zhang Y, Ely EW, Siegel MD, Inouye SK. Delirium in the intensive care unit: occurrence and clinical course in older patients. *J Am Geriatr Soc*. 2003;51(5):591-598.
5. Milbrandt EB, Deppen S, Harrison PL, et al. Costs associated with delirium in mechanically ventilated patients. *Crit Care Med*. 2004;32(4):955-962.
6. Leslie DL, Marcantonio ER, Zhang Y, Leo-Summers L, Inouye SK. One-year health care costs associated with delirium in the elderly population. *Arch Intern Med*. 2008;168(1):27-32.
7. Ely EW, Shintani A, Truman B, et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *JAMA*. 2004;291(14):1753-1762.
8. Ely EW, Gautam S, Margolin R, et al. The impact of delirium in the intensive care unit on hospital length of stay. *Intensive Care Med*. 2001;27(12):1892-1900.
9. Pandharipande PP, Girard TD, Jackson JC, et al. Long-term cognitive impairment after critical illness. *N Engl J Med*. 2013;369(14):1306-1316.
10. Spronk PE, Riekerk B, Hofhuis J, Rommes JH. Occurrence of delirium is severely underestimated in the ICU during daily care. *Intensive Care Med*. 2009;35(7):1276-1280.
11. Inouye SK. Predisposing and precipitating factors for delirium in hospitalized older patients. *Dement Geriatr Cogn Disord*. 1999;10(5):393-400.
12. Silver G, Traube C, Gerber LM, et al. Pediatric delirium and associated risk factors: a single-center prospective observational study. *Pediatr Crit Care Med*. 2015;16(4):303-309.
13. Zaal JJ, Devlin JW, Peelen LM, Slooter AJ. A systematic review of risk factors for delirium in the ICU. *Crit Care Med*. 2015;43(1):40-47.
14. Elie M, Cole MG, Primeau FJ, Bellavance F. Delirium risk factors in elderly hospitalized patients. *J Gen Intern Med*. 1998;13(3):204-212.
15. Schweickert WD, Pohlman MC, Pohlman AS, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet*. 2009;373(9678):1874-1882.
16. Needham DM, Korupolu R, Zanni JM, et al. Early physical medicine and rehabilitation for patients with acute respiratory failure: a quality improvement project. *Arch Phys Med Rehabil*. 2010;91(4):536-542.
17. Ross AG, Morris PE. Safety and barriers to care. *Crit Care Nurse*. 2010;30(2):S11-S13.
18. Barr J, Fraser GL, Puntillo K, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med*. 2013;41(1):263-306.
19. Pisani MA, Murphy TE, Araujo KL, 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(1):177-183.
20. Pandharipande P, Shintani A, Peterson J, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. *Anesthesiology*. 2006;104(1):21-26.
21. Pandharipande PP, Pun BT, Herr DL, et al. Effect of sedation with dexmedetomidine vs lorazepam on acute brain dysfunction in mechanically ventilated patients: the MENDS randomized controlled trial. *JAMA*. 2007;298(22):2644-2653.
22. Riker RR, Shehabi Y, Bokesch PM, et al. Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial. *JAMA*. 2009;301(5):489-499.
23. Ouimet S, Kavanagh BP, Gottfried SB, Skrobik Y. Incidence, risk factors and consequences of ICU delirium. *Intensive Care Med*. 2007;33(1):66-73.
24. Van Rompaey B, Elseviers MM, Schuurmans MJ, Shortridge-Baggett LM, Truijzen S, Bossaert L. Risk factors for delirium in intensive care patients: a prospective cohort study. *Crit Care*. 2009;13(3):R77.
25. Dubois MJ, Bergeron N, Dumont M, Dial S, Skrobik Y. Delirium in an intensive care unit: a study of risk factors. *Intensive Care Med*. 2001;27(8):1297-1304.

26. van Eijk MM, van Marum RJ, Klijn IA, de Wit N, Kesecioglu J, Slooter AJ. Comparison of delirium assessment tools in a mixed intensive care unit. *Crit Care Med*. 2009;37(6):1881-1885.
27. Truman B, Ely EW. Monitoring delirium in critically ill patients. Using the Confusion Assessment Method for the Intensive Care Unit. *Crit Care Nurse*. 2003;23(2):25-36; quiz 37-28.
28. Devlin JW, Fong JJ, Schumaker G, O'Connor H, Ruthazer R, Garpestad E. Use of a validated delirium assessment tool improves the ability of physicians to identify delirium in medical intensive care unit patients. *Crit Care Med*. 2007;35(12):2721-2724; quiz 2725.
29. Borthwick M. *Detection, Prevention and Treatment of Delirium in Critically Ill Patients*. Oadby, UK: United Kingdom Clinical Pharmacy Association; 2006.
30. Young J, Anderson D, Gager M. *Delirium: Diagnosis, Prevention, and Management*. London, England: National Institute for Health and Care Excellence; 2010.
31. Martin J, Heymann A, Basell K, et al. Evidence and consensus-based German guidelines for the management of analgesia, sedation and delirium in intensive care: short version. *Ger Med Sci*. 2010;8:Doc02.
32. Smith HA, Boyd J, Fuchs DC, et al. Diagnosing delirium in critically ill children: validity and reliability of the Pediatric Confusion Assessment Method for the Intensive Care Unit. *Crit Care Med*. 2011;39(1):150.
33. Traube C, Silver G, Kearney J, et al. Cornell Assessment of Pediatric Delirium: a valid, rapid, observational tool for screening delirium in the PICU. *Crit Care Med*. 2014;42(3):656-663.
34. Sikich N, Lerman J. Development and psychometric evaluation of the pediatric anesthesia emergence delirium scale. *J Am Soc Anesthesiol*. 2004;100(5):1138-1145.
35. Smith HA, Gangopadhyay M, Goben CM, et al. The Preschool Confusion Assessment Method for the ICU: valid and reliable delirium monitoring for critically ill infants and children. *Crit Care Med*. 2016;44(3):592-600.
36. Ely EW, Margolin R, Francis J, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med*. 2001;29(7):1370-1379.
37. Ely EW, Inouye SK, Bernard GR, et al. Delirium in mechanically ventilated patients: validity and reliability of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *JAMA*. 2001;286(21):2703-2710.
38. Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y. Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. *Intensive Care Med*. 2001;27(5):859-864.
39. Pun BT, Gordon SM, Peterson JF, et al. Large-scale implementation of sedation and delirium monitoring in the intensive care unit: a report from two medical centers. *Crit Care Med*. 2005;33(6):1199-1205.
40. Devlin JW, Marquis F, Riker RR, et al. Combined didactic and scenario-based education improves the ability of intensive care unit staff to recognize delirium at the bedside. *Crit Care*. 2008;12(1):R19.
41. Soja SL, Pandharipande PP, Fleming SB, et al. Implementation, reliability testing, and compliance monitoring of the Confusion Assessment Method for the Intensive Care Unit in trauma patients. *Intensive Care Med*. 2008;34(7):1263-1268.
42. Riekerk B, Pen EJ, Hofhuis JG, Rommes JH, Schultz MJ, Spronk PE. Limitations and practicalities of CAM-ICU implementation, a delirium scoring system, in a Dutch intensive care unit. *Intensive Crit Care Nurs*. 2009;25(5):242-249.
43. Page VJ, Navarange S, Gama S, McAuley DF. Routine delirium monitoring in a UK critical care unit. *Crit Care*. 2009;13(1):R16.
44. Balas MC, Rice M, Chaperon C, Smith H, Disbot M, Fuchs B. Management of delirium in critically ill older adults. *Crit Care Nurse*. 2012;32(4):15-26.
45. Turkel SB, Jacobson J, Munzig E, Tavare CJ. Atypical antipsychotic medications to control symptoms of delirium in children and adolescents. *J Child Adolesc Psychopharmacol*. 2012;22(2):126-130.
46. Joyce C, Witcher R, Herrup E, et al. Evaluation of the safety of quetiapine in treating delirium in critically ill children: a retrospective review. *J Child Adolesc Psychopharmacol*. 2015;25(9):666-670.
47. Jacobi J, Fraser GL, Coursin DB, et al. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med*. 2002;30(1):119-141.
48. Lonergan E, Britton AM, Luxenberg J, Wyller T. Antipsychotics for delirium. *Cochrane Database Syst Rev*. 2007(2):CD005594.
49. Campbell N, Boustani MA, Ayub A, et al. Pharmacological management of delirium in hospitalized adults: a systematic evidence review. *J Gen Intern Med*. 2009;24(7):848-853.
50. Girard TD, Pandharipande PP, Carson SS, et al. Feasibility, efficacy, and safety of antipsychotics for intensive care unit delirium: the MIND randomized, placebo-controlled trial. *Crit Care Med*. 2010;38(2):428-437.
51. Page VJ, Ely EW, Gates S, et al. Effect of intravenous haloperidol on the duration of delirium and coma in critically ill patients (Hope-ICU): a randomised, double-blind, placebo-controlled trial. *Lancet Respir Med*. 2013;1(7):515-523.
52. Devlin JW, Roberts RJ, Fong JJ, et al. Efficacy and safety of quetiapine in critically ill patients with delirium: a prospective, multicenter, randomized, double-blind, placebo-controlled pilot study. *Crit Care Med*. 2010;38(2):419-427.
53. van Eijk MM, Roes KC, Honing ML, et al. Effect of rivastigmine as an adjunct to usual care with haloperidol on duration of delirium and mortality in critically ill patients: a multicentre, double-blind, placebo-controlled randomised trial. *Lancet*. 2010;376(9755):1829-1837.
54. Meyer-Massetti C, Cheng CM, Sharpe BA, Meier CR, Guglielmo BJ. The FDA extended warning for intravenous haloperidol and torsades de pointes: how should institutions respond? *J Hosp Med*. 2010;5(4):E8-E16.
55. Vasilevskis EE, Ely EW, Speroff T, Pun BT, Boehm L, Dittus RS. Reducing iatrogenic risks: ICU-acquired delirium and weakness—crossing the quality chasm. *Chest*. 2010;138(5):1224-1233.
56. Vasilevskis EE, Pandharipande PP, Girard TD, Ely EW. A screening, prevention, and restoration model for saving the injured brain in intensive care unit survivors. *Crit Care Med*. 2010;38(10 suppl):S683-S691.
57. Frimpong K, Stollings JL, Carlo ME, Ely EW. ICU delirium viewed through the lens of the PAD guidelines and the ABCDEF implementation bundle. 2014. [http://www.icudelirium.org/docs/ICULiberation\\_Frimpong\\_DeliriumABCDEF\\_d1\\_2015.pdf](http://www.icudelirium.org/docs/ICULiberation_Frimpong_DeliriumABCDEF_d1_2015.pdf). Accessed July 15, 2016.
58. Balas MC, Vasilevskis EE, Olsen KM, et al. Effectiveness and safety of the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle. *Crit Care Med*. 2014;42(5):1024-1036.
59. Kram SL, DiBartolo MC, Hinderer K, Jones RA. Implementation of the ABCDE bundle to improve patient outcomes in the intensive care unit in a rural community hospital. *Dimens Crit Care Nurs*. 2015;34(5):250-258.
60. Ullman AJ, Aitken LM, Rattray J, et al. Diaries for recovery from critical illness. *Cochrane Database Syst Rev*. 2014;12:CD010468.