# **ORIGINAL RESEARCH**

# **ABCDE, but in That Order?** A Cross-Sectional Survey of Michigan Intensive Care Unit Sedation, Delirium, and Early Mobility Practices

Melissa A. Miller<sup>1</sup>, Sushant Govindan<sup>1</sup>, Sam R. Watson<sup>2</sup>, Robert C. Hyzy<sup>1</sup>, and Theodore J. Iwashyna<sup>1,3</sup>

<sup>1</sup>Department of Internal Medicine, University of Michigan, Ann Arbor; <sup>2</sup>Michigan Health and Hospital Association Keystone Center, Lansing, Michigan; and <sup>3</sup>Center for Clinical Management Research, Ann Arbor Veterans Affairs Healthcare System, Ann Arbor, Michigan

# Abstract

**Rationale:** A bundled approach to intensive care unit (ICU) care known as "Awakening and Breathing Coordination, Delirium monitoring/management, and Early exercise/mobility" (ABCDE) has been proposed, with evidence supporting individual interventions as well as the bundle as a whole. Few data exist on the bundle's implementation and efficacy in community practice.

**Objectives:** To evaluate self-reported rates of implementation of ABCDE components and their association with outcomes in a state-wide quality improvement collaborative.

**Methods:** A written survey was administered to representatives attending the 2012 annual meeting of the Michigan Health and Hospital Association's Keystone ICU collaborative. Respondents reported on their practices regarding spontaneous awakening trials, delirium assessments, and early mobility.

**Measurements and Main Results:** There were 212 respondents, a 76% response rate. Wide variation in focus was noted across the assessed components of ABCDE. Only 12% reported having

implemented routine spontaneous awakening trials and delirium assessments as well as early mobility, 36% reported not having early mobility as an active goal in their units (nonmovers), and 52% reported attempts at early mobility without both routine sedation interruption and delirium screening implementation. In adjusted models, those who implemented exercise with sedation interruption and delirium screening were 3.5 (95% confidence interval, 1.4–8.6) times more likely to achieve higher levels of exercise in ventilated patients than those who implemented exercise without both sedation interruption and delirium screening.

**Conclusions:** There is incomplete penetrance of aspects of ABCDE across ICUs in this highly motivated statewide quality improvement collaborative. Yet, implementation of exercise in the context of both sedation interruption and delirium screening was associated with improved self-reported mobility outcomes. Effective knowledge translation and implementation strategies may offer substantial benefits to ICU patients.

Keywords: delirium; critical care; mobility limitation

(Received in original form January 30, 2015; accepted in final form May 12, 2015)

Supported by the U.S. National Institutes of Health: K08, HL091249 (T.J.I.) and VA HSR&D IIR-11-109 (T.J.I.), and NIH/NHLBI, T32 HL07749-17 (M.A.M.). The views expressed here are the authors' own and do not necessarily represent the view of the U.S. government or the Department of Veterans Affairs.

Author Contributions: M.A.M., R.C.H., and T.J.I. were involved in concept and design of the work. M.A.M., R.C.H., and S.R.W. were involved in acquisition of data. M.A.M., S.G., and T.J.I. were involved in analysis and interpretation of the data. All authors were involved in drafting or revision of the manuscript, critical revision, and are accountable for the accuracy and integrity of the work.

Correspondence and requests for reprints should be addressed to Melissa A. Miller, B.S.N., M.D., M.S., 3916 Taubman Center, 1500 E. Medical Center Drive, SPC 5360, Ann Arbor, MI 48109-5360. E-mail: melissa.miller.pccm@gmail.com

This article has an online supplement, which is accessible from this issue's table of contents online at www.atsjournals.org

Ann Am Thorac Soc Vol 12, No 7, pp 1066–1071, Jul 2015 Copyright © 2015 by the American Thoracic Society DOI: 10.1513/AnnalsATS.201501-066OC Internet address: www.atsjournals.org

Intensive care unit (ICU)–acquired delirium and weakness have devastating consequences for survivors of critical illness (1–3). Iatrogenic factors such as mechanical ventilation, sedation, and immobilization are risk factors for acquiring delirium and weakness in the ICU (4–9). With sequelae ranging from increased mortality to longer ICU length of stay to persistent functional and cognitive dysfunction (10–13), there is an increasing need to target delirium and weakness with evidence-based interventions (14).

Multiple initiatives have emerged as best practice in mechanically ventilated

patients: spontaneous awakening trials (15-17), spontaneous breathing trials (18-20), and early mobilization (21). However, most studies have tested these interventions as single-pronged interventions. Limited recent data suggest that a bundled approach is more effective; this has been coined "Awakening and Breathing Coordination, Delirium monitoring/management, and Early exercise/mobility," or ABCDE (22-26). The existing randomized controlled trial evidence base is rooted in protocolized practice, performed in single centers, and where each additional step of ABCDE was tested on a foundation of care that involved near uniform implementation of the previous steps.

There is a logical argument that one should only attempt to implement in sequence. For example, D (delirium screening) and E (early exercise) may be more effective after first limiting sedation, A (awakening patients)-this might be termed sequential implementation of ABCDE. There are few data on community practice regarding selection among these practices and the extent to which sequential or nonsequential implementation is common. It is also unclear whether complete implementation regarding components of ABCDE leads to improved outcomes versus incomplete methods. Therefore, we performed a cross-sectional survey study to assess the level of selfreported implementation of aspects of ABCDE. We hypothesized that there would be a wide variety of implementation practices, and that implementation of A, D, and E would be associated with increased self-reported levels of achieved patient mobility. Some of the results of these studies have been previously reported in the form of an abstract (27).

## Methods

#### Design

A written survey was administered to 278 representatives of 51 hospitals attending the January 2012 annual meeting of the Michigan Health and Hospital Association Keystone ICU initiative, a qualityimprovement collaborative focused on improving outcomes in Michigan ICUs. Respondents included staff nurses, nurse managers, physicians, hospital administrators, respiratory therapists, and pharmacists. The 2012 survey was part of

the Michigan Health and Hospital Association Keystone's ongoing quality improvement efforts to understand its members' practices along with self-reported outcomes. At the time, Keystone strongly advocated the use of the ABCDE bundle, which had been introduced sequentially. Spontaneous awakening trials had been introduced and emphasized from 2004, while delirium screenings had been advocated from the January 2009 workshop, and data collection regarding delirium screenings performed within the collaborative beginning in 2010. Early mobility initiatives had been strongly encouraged from 2011 through presentations at the January ICU workshop and during coaching calls throughout the year.

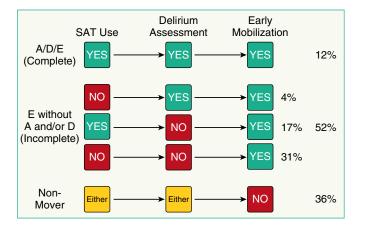
At the time of this survey, Keystone actively encouraged submission of data regarding frequency of spontaneous awakening trial and delirium assessment performance from collaborative members; however, this was an area the leadership also recognized as needing improvement. The survey contained multiple items assessing attitudes toward spontaneous awakening trial performance, delirium assessment, and data collection. Because of the sensitive nature of these attitudinal questions, the investigators and Keystone leadership believed that keeping surveys anonymous would encourage more honest feedback. This decision was reinforced in feedback from extensive preadministration testing of the survey instrument in members of multiple professional disciplines. Analysis of the data was approved by the University of Michigan Medical Center Institutional Review Board (HUM00065602).

#### Measures

*Outcome variables.* Respondents were asked if they routinely try to have patients actively engaged in exercise within 48–72 hours of mechanical ventilation. Respondents were also asked how many of their patients receiving physical therapy reach weight bearing (standing), marching in place, or walking before extubation. This outcome was considered met if respondents reported more than 10% of patients meeting one of these levels of exercise.

*Institutional and individual variables.* Respondents were asked if their unit or hospital had an association with a medical school, residency or house officers, critical care fellows, or other academic affiliation. Institutions were classified as academic if any of these criteria were met. Respondents were also asked about unit size (i.e., number of beds), whether the unit model was closed (in which only intensivist-led critical care teams write orders), frequency of data collection, and whether intensivists made primary decisions in their units.

Description of practice. Respondents were asked to report on their practices regarding the use of spontaneous awakening trials, delirium assessments, and early mobility, and the frequency with which they collected data regarding these practices. (Relevant questionnaire items are presented in the online supplement.) We did not assess the rate of spontaneous breathing trials as respiratory therapists were underrepresented in the group attending the meeting and we therefore had concerns about the reliability of the representative respondents' self-report regarding this particular intervention. Respondents were then grouped into one of several categories based on responses. Those who did not endorse early mobility as an active goal in their unit were deemed "nonmovers." Respondents who reported that early mobility (E) was an active goal were then determined to be complete, or A/D/E, implementers if they also reported routine spontaneous awakening trial use (>75% of mechanically ventilated patients undergo spontaneous awakening trials each day—A) and routine delirium assessment (>75% of mechanically ventilated patients undergo delirium assessments each day-D). All other respondents who endorsed early mobility as an active goal, but did not report either routine spontaneous awakening trial use or delirium assessment (or both), were classified as incomplete, or E without A or D implementers (Figure 1). We also created a score regarding frequency of self-reported data collection based on answers to the following questions: "On how many patient days do you collect data on delirium assessments?" and "On how many patient days do you collect data on spontaneous awakening trials (SATs)?" For each question, there were six levels of increasing frequency to choose from, with more than 90% representing the highest level. A data collection frequency score was created on the basis of the level of response to both questions, with 12 being the highest frequency of data collection and 2 being the



**Figure 1.** Groupings of respondents. ABCDE = Awakening and Breathing Coordination, Delirium monitoring/management, and Early exercise/mobility; SAT = spontaneous awakening trial.

lowest. Questionnaire items, details of score construction, and the distribution of responses are shown in the online data supplement.

#### **Statistical Analysis**

We employed descriptive univariate analysis for the variables of interest. We then used bivariable analysis to compare cultural and organizational variables with our outcome variables and with type of implementation. Chi-square testing assessed associations with categorical variables; the Student t test was employed for continuous variables. Multivariable logistic regression modeling evaluated the aforementioned groups for differences in their organizational characteristics and approach to early mobility and in reported outcomes. The emphasis on anonymity precluded the ability to analyze data on the basis of unit or institution, and therefore the data were analyzed in aggregate. The variables used to evaluate differences between groups and in outcomes were a priori determined by the investigators and included academic affiliation, intensivist-led management (either closed unit or mandatory intensivist consultation), and frequency of reported data collection.

We also evaluated characteristics of high-level data collectors by multivariable regression including the *a priori* determined variables of academic affiliation, intensivistled model, and reporting having sufficient resources to devote to research. We then used logistic regression to study the primary outcomes. We compared groups in their reported outcomes in early exercise and higher levels of exercise. As a sensitivity analysis, we also performed multivariable regressions controlling for academic affiliation, intensivist-led model, and highlevel data collection. These additional variables did not have significant associations with the primary outcomes in multivariable regression, and their removal from the models did not significantly change the associations of the groups with the primary outcomes. Therefore ultimately, these additional variables were not included in final models. SAS 9.3 was used for statistical analysis (SAS Institute, Cary, NC).

# Results

Of the 278 in attendance, we received 212 responses to our survey, a response rate of 76%. Median unit size was 16 beds, with an interquartile range of 21. Thirty-six percent reported being from intensivist-led units, either traditionally closed or with mandatory intensivist consultation. Seventy-six percent reported some academic affiliation. Demographic information concerning the respondents and represented units can be seen in Table 1.

#### **Components of ABCDE**

Incomplete compliance was noted across the assessed components of the bundle (Table 2). With respect to spontaneous awakening trials, 88% of those surveyed had a protocol in place, with only 45% reporting that more than three-quarters of their patients undergo spontaneous awakening trials every day. Only 31% of respondents reported performance of daily delirium assessments in at least threequarters of their ventilated patients.

Early mobility was reported as a specific goal for 65% of respondents, and 39% claimed to have their mechanically ventilated patients routinely engaged in active exercises within the first 48–72 hours. Twenty-three percent of respondents reported that at least one-tenth of their ventilated patients reach weight bearing, marching in place, or walking before extubation.

In addition, there was wide variation in data collection. Of the respondents, 32% reported collecting data for both spontaneous awakening trials and delirium assessments on more than 90% of days, representing those with the highest data collection scores. Almost 20% reported collecting data on less than 10% of days.

#### **Practice Patterns**

Respondents were then aggregated into three categories: A/D/E implementers; E without either A or D; and nonmovers, that is, those not attempting E (Figure 1). In total, 12% of those surveyed were A/D/E implementers, 52% were E without A or D implementers, and 36% were nonmovers.

Logistic regression modeling revealed a variety of differences between the groups. A/D/E implementers were more likely to be high-level data collectors (score of 12) than the other groups (odds ratio [OR], 3.5; 95% confidence interval [CI], 1.5–8.2) whereas E

**Table 1.** Respondent and organizational characteristics

Variable	%
Unit beds, median (interquartile range)	16 (21)
Academic affiliation Intensivist-led staffing (closed unit	76 36
or mandatory intensivist consultation) Professional role	
Nurse manager Nurse educator/clinical nurse	18 13
specialist Staff nurse	36
Physical therapist/occupational therapist/speech therapist	8
Physician	6
Other (representatives of quality management $[n = 7]$ and infection control $[n = 5]$ , nursing leadership not included above [n = 8], and respiratory therapy [n = 1])	19

Component	Measure	Percentage of Respondents Self-
Component	include	Reporting Meeting Measure
A (BC)	>75% of ventilated patients undergo daily SAT	45
D	>75% of ventilated patients undergo daily delirium assessment	31
E	Early mobility is an active unit goal	65
Outcome	>10% of ventilated patients receiving physical therapy reach weight-bearing status before extubation (high levels of exercise)	23
Outcome	Routinely try to have patients engaged in active exercise within first 48–72 h of mechanical ventilation (early exercise)	39

*Definition of abbreviations*: ABCDE = Awakening and Breathing Coordination, Delirium monitoring/ management, and Early exercise/mobility; SAT = spontaneous awakening trial.

without A or D implementers were less likely to be high-level data collectors (OR, 0.28; CI, 0.15-0.55). In fact, for each point in the intensity of data collection score, respondents were 1.2 (CI, 1.1–1.4; *P* = 0.01) times more likely to be A/D/E implementers. In a multivariable analysis controlling for data collection, E without A or D implementers were more likely to report academic affiliation (OR, 2.9; CI, 1.4-5.7). Although in univariate analysis academic affiliation and the intensivist-led model were significantly associated with being a high-level data collector, none of the included variables were significantly associated with reported high-level data collection in multivariable analysis.

Although both A/D/E and E without A or D implementers were more likely to engage mechanically ventilated patients in early active exercise than nonmovers, A/D/E implementers were more likely to report getting patients to higher levels of exercise than E without A or D implementers (OR, 15.6 [CI 4.7–51.8] vs. OR, 4.5 [1.6–12.2]; P = 0.006). When directly comparing A/D/E implementers versus E without A or D implementers, A/D/E implementers were 3.5 (CI, 1.4–8.6) times more likely to report getting patients to higher levels of exercise (Table 3).

We also examined the role of delirium assessment in A/D/E implementation, to test the hypothesis that the spontaneous awakening trial alone is the key intervention leading to successful early mobility. We compared A/D/E implementers with those reporting that they were performing routine spontaneous awakening trials, but not routinely assessing for delirium (A/E no D

Table 3. Relative likelihood of reporting achievement of higher levels of exercise\*

Comparison	OR for High-Level Exercise <sup>†</sup> (95% CI)	P Value
A/D/E <sup><math>\ddagger</math></sup> vs. nonmovers <sup>§</sup>	15.6 (4.7–51.8)	<0.0001
A/D/E vs. E without A or D <sup>  </sup>	3.5 (1.4–8.6)	0.0063
E without A or D vs. nonmovers	4.5 (1.6–12.2)	0.004

Definition of abbreviations: ABCDE = Awakening and Breathing Coordination, Delirium monitoring/ management, and Early exercise/mobility; CI = confidence interval; OR = odds ratio; SAT = spontaneous awakening trial.

spontaneous awakening trial. \*Unadjusted regression results, as results were not significantly confounded by other tested

covariates (see text for description).

<sup>†</sup>High-level exercise: respondents who report getting more than 10% of patients to standing, marching in place, or walking before extubation.

<sup>‡</sup>A/D/E: Complete implementers—those reporting early mobility efforts (E) and routine implementation of SATs (A) and delirium assessments (D).

<sup>§</sup>Nonmovers: those who report no active early mobility efforts.

<sup>II</sup>E without A or D: incomplete implementers—those who report early mobility efforts (E) without routine implementation of SATs (A) and/or delirium assessments (D).

implementers). We also compared this group with others. We found that those who were performing routine spontaneous awakening trials but not routine delirium assessment were less likely than A/D/E implementers to achieve early exercise (OR, 0.33 [CI, 0.11-0.97]) or to achieve higher levels of exercise (OR, 0.15 [CI, 0.05–0.52]). When comparing A/E no D to other E with no A implementers, there was no significant difference in achieving early exercise or achieving higher levels of exercise (OR, 0.58 [CI, 0.25-1.31] and OR, 0.43 [CI, 0.15-1.25], respectively). In fact, point estimates suggest that A/E no D implementers performed worse than E no A implementers, although associations did not reach statistical significance.

## Discussion

In this cross-sectional survey, we found ongoing incomplete penetrance and variable implementation of components of ABCDE in Michigan ICUs, especially in the areas of delirium assessment and achievement of early mobility in ventilated patients. This is particularly notable given that the ICUs represented in the Keystone Collaborative are highly motivated units engaged in an effort to improve this practice. A clear majority of respondents reported attempting mobility without having implemented routine sedation interruption and delirium screening. Such incompleteor, perhaps, nonsequential-implementation was also associated with lower self-reported success in mobilization.

For several years, individual components of ABCDE have been shown to improve outcomes in critically ill patients. Single intervention studies dating to the mid-1990s on aspects of the bundle have demonstrated decreased ventilator days, sedative exposure, and ICU-related costs (15, 16, 18). In the late 2000s, early physical therapy in mechanically ventilated patients was shown to improve functional status and outcomes (21). However, only more recently has a bundle of these initiatives been proposed to target cognitive and functional decline in critically ill patients (25, 26). This bundling is purported to strengthen implementation. A logical progression in patient care can be seen with use of the bundle, each aspect has evidence in the literature to support its implementation, and all aspects of the

bundle need to be performed to maximize the benefit in patients (28). This rationale has been used in deploying bundles throughout other areas of medicine. In fact, a few studies have shown improved outcomes both from ABC and ABCDE bundles, although these have been in highly structured, controlled settings (20, 21, 23).

As has been noted extensively in the literature, practical implementation of bundles has its own challenges and needs to be assessed separately. In fact, Balas and colleagues identified facilitators and barriers to acceptance of the ABCDE bundle in a single center (22). Our study further provides data from multiple ICUs of varying sizes and demographics across an entire state to illustrate three important points: inadequate penetrance of ABCDE components, variable implementation methods, and potential consequences of variable implementation for levels of achieved patient mobility. Complete or sequential implementers who had the upstream components of ABCDE, spontaneous awakening trial performance and delirium assessment, in place reported achieving higher levels of self-reported patient activity than their peers. Further, those who reported routine spontaneous awakening trial performance but not delirium assessment were no more successful than other incomplete or nonsequential implementers in achieving self-reported exercise outcomes. In other words, this study preliminarily adds another layer of evidence to the notion that, with respect to ABCDE, the whole truly is greater than the sum of its individual parts.

With respect to group-specific associations, complete implementers were more likely to be high-level data collectors than their peers. In fact, each incremental increase in self-reported frequency of data collection supported the likelihood that a respondent would be a complete implementer. Causation is impossible to

establish with our present study design, and it is possible that those with more resources for data collection would also have more resources for early mobility initiatives. However, when controlling for responses that might reflect those increased resources, such as academic institution, intensivist-led units, or resources to devote to research, our findings did not change. Therefore, we suspect the act of data collection and analysis allows for improved quality assessments among health care teams, which then allows for feedback and improved performance of the interventions studied. This has been recognized as a priority in the medical realm (29), and it has even been shown to improve efficiency in other sectors of our society (30).

Our study has important limitations that must be addressed. First, the sample of respondents was drawn from the Michigan Health and Hospital Association Keystone ICU annual meeting. These attendees likely represent a motivated cohort of thought leaders, not a broad reflection of ICU practitioners from across the state or at a national level. However, this cohort is more likely to be aware of data collection efforts, and if anything is more likely be aware of appropriate ABCDE practice. Second, data and outcomes were selfreported and not directly observed; therefore, these represent how respondents think of their own practice. Third, the data for this analysis were obtained from a survey; thus, we must consider nonresponse bias in our interpretation, although our 76% response rate compares favorably with the published literature (31). Fourth, in this type of survey study, ideally we would analyze the data by taking into account clustering of representatives from units and hospitals. However, we chose to deemphasize identifying information to encourage honesty in responses, and therefore a stratified and weighted analysis was not

possible. The Michigan Health and Hospital Association has a policy of subsidizing attendance costs for three representatives from each unit, which decreases the effect of weighting of attendance of larger institutions. Attendance by several representatives of most units was confirmed in review of attendance records collected separately (not for research purposes). Fifth, we were unable to assess the spontaneous breathing trial component of ABCDE given the underrepresentation of respiratory therapists in our cohort. However, to our knowledge, this is still the largest, most complete assessment of bundle components in daily practice to date.

The consequences of critical illness are far reaching and have implications well beyond the initial ICU stay. Moreover, lifesaving strategies employed on the "front end" of treating the critically ill are now known to have morbidity and mortality ramifications if left unchecked. ABCDE mitigates functional and cognitive decline in controlled settings acutely, and our study suggests the benefit of full sequential implementation of the bundle in a practical setting through a statewide survey of motivated critical care practitioners. We believe this lends credence to the claim that ABCDE is a crucial component in ICUlevel care to ensure that patients do not just survive, but are given the best opportunity to recover.

Author disclosures are available with the text of this article at www.atsjournals.org.

Acknowledgment: The authors thank Sarah L. Krein, Ph.D., R.N., in the design of the survey questions, and Laetitia Shapiro in the preparation of the data. The authors also thank Phyllis McLellan, R.N., M.S.N., C.N.O.R., and Christine T. George, M.S., R.N., of the Michigan Health and Hospitals Association for their assistance regarding Keystone data, assistance with survey items, and workshop attendance records.

#### References

- 1 Jackson JC, Girard TD, Gordon SM, Thompson JL, Shintani AK, Thomason JWW, Pun BT, Canonico AE, Dunn JG, Bernard GR, *et al.* Long-term cognitive and psychological outcomes in the Awakening and Breathing Controlled Trial. *Am J Respir Crit Care Med* 2010;182:183–191.
- 2 Jackson JC, Gordon SM, Hart RP, Hopkins RO, Ely EW. The association between delirium and cognitive decline: a review of the empirical literature. *Neuropsychol Rev* 2004;14:87–98.
- 3 Banerjee A, Girard TD, Pandharipande P. The complex interplay between delirium, sedation, and early mobility during critical illness:

applications in the trauma unit. *Curr Opin Anaesthesiol* 2011;24: 195–201.

- 4 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.
- 5 Riker RR, Shehabi Y, Bokesch PM, Ceraso D, Wisemandle W, Koura F, Whitten P, Margolis BD, Byrne DW, Ely EW, et al.; SEDCOM (Safety and Efficacy of Dexmedetomidine Compared with Midazolam) Study Group. Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial. *JAMA* 2009;301:489–499.

- 6 Herridge MS, Cheung AM, Tansey CM, Matte-Martyn A, Diaz-Granados N, Al-Saidi F, Cooper AB, Guest CB, Mazer CD, Mehta S, *et al.*; Canadian Critical Care Trials Group. One-year outcomes in survivors of the acute respiratory distress syndrome. *N Engl J Med* 2003;348:683–693.
- 7 Herridge MS, Tansey CM, Matté A, Tomlinson G, Diaz-Granados N, Cooper A, Guest CB, Mazer CD, Mehta S, Stewart TE, et al.; Canadian Critical Care Trials Group. Functional disability 5 years after acute respiratory distress syndrome. N Engl J Med 2011;364: 1293–1304.
- 8 Weinert CR, Calvin AD. Epidemiology of sedation and sedation adequacy for mechanically ventilated patients in a medical and surgical intensive care unit. *Crit Care Med* 2007;35:393–401.
- 9 Kollef MH, Levy NT, Ahrens TS, Schaiff R, Prentice D, Sherman G. The use of continuous i.v. sedation is associated with prolongation of mechanical ventilation. *Chest* 1998;114:541–548.
- 10 Ely EW, Shintani A, Truman B, Speroff T, Gordon SM, Harrell FE Jr, Inouye SK, Bernard GR, Dittus RS. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *JAMA* 2004;291:1753–1762.
- 11 Iwashyna TJ, Ely EW, Smith DM, Langa KM. Long-term cognitive impairment and functional disability among survivors of severe sepsis. JAMA 2010;304:1787–1794.
- 12 Pisani MA, Kong SY, Kasl SV, Murphy TE, Araujo KL, Van Ness PH. Days of delirium are associated with 1-year mortality in an older intensive care unit population. Am J Respir Crit Care Med 2009;180: 1092–1097.
- 13 Ely EW, Gautam S, Margolin R, Francis J, May L, Speroff T, Truman B, Dittus R, Bernard R, Inouye SK. The impact of delirium in the intensive care unit on hospital length of stay. *Intensive Care Med* 2001;27:1892–1900.
- 14 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;138:1224–1233.
- 15 Brook AD, Ahrens TS, Schaiff R, Prentice D, Sherman G, Shannon W, Kollef MH. Effect of a nursing-implemented sedation protocol on the duration of mechanical ventilation. *Crit Care Med* 1999;27: 2609–2615.
- 16 Kress JP, Pohlman AS, O'Connor MF, Hall JB. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med 2000;342:1471–1477.
- 17 Mehta S, Burry L, Cook D, Fergusson D, Steinberg M, Granton J, Herridge M, Ferguson N, Devlin J, Tanios M, *et al.*; SLEAP Investigators; Canadian Critical Care Trials Group. Daily sedation interruption in mechanically ventilated critically ill patients cared for with a sedation protocol: a randomized controlled trial. *JAMA* 2012; 308:1985–1992.
- 18 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.
- 19 Esteban A, Frutos F, Tobin MJ, Alía I, Solsona JF, Valverdú I, Fernández R, de la Cal MA, Benito S, Tomás R, *et al.*; Spanish Lung Failure

Collaborative Group. A comparison of four methods of weaning patients from mechanical ventilation. *N Engl J Med* 1995;332: 345–350.

- 20 Girard TD, Kress JP, Fuchs BD, Thomason JWW, Schweickert WD, Pun BT, Taichman DB, Dunn JG, Pohlman AS, Kinniry PA, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled Trial): a randomised controlled trial. *Lancet* 2008;371:126–134.
- 21 Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, Spears L, Miller M, Franczyk M, Deprizio D, *et al.* Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet* 2009;373: 1874–1882.
- 22 Balas MC, Burke WJ, Gannon D, Cohen MZ, Colburn L, Bevil C, Franz D, Olsen KM, Ely EW, Vasilevskis EE. Implementing the Awakening and Breathing Coordination, Delirium monitoring/management, and Early exercise/mobility bundle into everyday care: opportunities, challenges, and lessons learned for implementing the ICU Pain, Agitation, and Delirium Guidelines. *Crit Care Med* 2013;41(9, Suppl 1):S116–S127.
- 23 Balas MC, Vasilevskis EE, Olsen KM, Schmid KK, Shostrom V, Cohen MZ, Peitz G, Gannon DE, Sisson J, Sullivan J, et al. Effectiveness and safety of the Awakening and Breathing Coordination, Delirium monitoring/management, and Early exercise/mobility bundle. Crit Care Med 2014;42:1024–1036.
- 24 Carrothers KM, Barr J, Spurlock B, Ridgely MS, Damberg CL, Ely EW. Contextual issues influencing implementation and outcomes associated with an integrated approach to managing pain, agitation, and delirium in adult ICUs. *Crit Care Med* 2013;41:S128–S135.
- 25 Morandi A, Brummel NE, Ely EW. Sedation, delirium and mechanical ventilation: the "ABCDE" approach. *Curr Opin Crit Care* 2011;17: 43–49.
- 26 Pandharipande P, Banerjee A, McGrane S, Ely EW. Liberation and animation for ventilated ICU patients: the ABCDE bundle for the back-end of critical care. *Crit Care* 2010;14:157.
- 27 Miller MA, Krein SL, George CT, Watson SR, Hyzy R, Iwashyna TJ. ABCDE, but not in that order? Nonsequential implementation of a recommended bundle in a statewide quality improvement collaborative [abstract]. Am J Respir Crit Care Med 2013;276:A3896.
- 28 Institute for Healthcare Improvement. Raising the bar with bundles: treating patients with an all-or-nothing standard. *Jt Comm Perspect Pat Safe* 2006;6:5–6.
- 29 Curtis JR, Cook DJ, Wall RJ, Angus DC, Bion J, Kacmarek R, Kane-Gill SL, Kirchhoff KT, Levy M, Mitchell PH, *et al.* Intensive care unit quality improvement: a "how-to" guide for the interdisciplinary team. *Crit Care Med* 2006;34:211–218.
- 30 Brynjolfsson E, Hitt LM, Kim HH. Strength in numbers: how does datadriven decision making affect firm performance? [2011]. Available from: http://papers.srn.com/sol3/papers.cfm?abstract\_id=1819486
- 31 Asch DA, Jedrziewski MK, Christakis NA. Response rates to mail surveys published in medical journals. *J Clin Epidemiol* 1997;50: 1129–1136.