

Interpreting and Implementing the 2018 Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption Clinical Practice Guideline

Michele C. Balas, PhD, RN, CCRN-K, FCCM, FAAN^{1,2}; Gerald L. Weinhouse, MD^{3,4}; Linda Denehy, PT, PhD⁵; Gerald Chanques, MD, PhD⁶; Bram Rochweg, MD, MSc⁷; Cheryl J. Misak, DPhil⁸; Yoanna Skrobik, MD, FRCP(c), MSc, FCCM⁹; John W. Devlin, PharmD, FCCM^{10,11}; Gilles L. Fraser, PharmD, MCCM^{12,13}

¹Center of Excellence in Critical and Complex Care, College of Nursing, The Ohio State University, Columbus, OH.

²The Ohio State University Wexner Medical Center, Columbus, OH.

³Harvard Medical School, Boston, MA.

⁴Division of Pulmonary and Critical Care, Brigham and Women's Hospital, Boston, MA.

⁵Melbourne School of Health Sciences, University of Melbourne, Melbourne, VIC, Australia.

⁶Department of Anesthesia and Intensive Care, Montpellier University Saint Eloi Hospital, PhyMedExp, University of Montpellier, Montpellier, France.

⁷Department of Medicine, McMaster University, Hamilton, ON, Canada.

⁸Department of Philosophy, University of Toronto, Toronto, ON, Canada.

⁹Faculty of Medicine, McGill University, Montreal, QC, Canada.

¹⁰School of Pharmacy, Northeastern University, Boston, MA.

¹¹Division of Pulmonary, Critical Care and Sleep Medicine, Tufts Medical Center, Boston, MA.

¹²School of Medicine, Tufts University, Boston, MA.

¹³Department of Critical Care, Maine Medical Center, Portland, ME.

Although the authors of this article are members of the guideline committee, the views expressed in this article are from a personal perspective and do not represent the collective viewpoint of the guideline committee.

Dr. Balas received funding from Select Medical (primary investigator on research study exploring Assess, Prevent, and Manage Pain, Both Spontaneous Awakening Trials and Spontaneous Breathing Trials, Choice of analgesia and sedation, Delirium: Assess, Prevent, and Manage, Early mobility and Exercise, and Family engagement and empowerment bundle adoption). Dr. Denehy participates in the Australian Physiotherapy Association. Dr. Chanques participates in other healthcare professional organization activities. Dr. Rochweg participates as a guideline methodologist for other organizations (i.e., American Thoracic Society [ATS] and Canadian Blood Service) in addition to Society of Critical Care Medicine. Dr. Skrobik participates in the ATS and the American College of Chest Physicians, and she is on the editorial board for *Intensive Care Medicine* and *Chest*. Dr. Devlin has received research funding from the National Institute of Aging, National Heart, Lung and Blood Institute, and AstraZeneca Pharmaceuticals; is on the editorial board of *Critical Care Medicine*; and is the president of the American Delirium Society. The remaining authors have disclosed that they do not have any potential conflicts of interest.

For information regarding this article, E-mail: fraseg@mmc.org

Copyright © 2018 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc. All Rights Reserved.

DOI: 10.1097/CCM.0000000000003307

(*Crit Care Med* 2018; 46:1464–1470)

Key Words: agitation; delirium; immobility; implementation science; intensive care; pain; practice guideline; sleep

The 2018 Clinical Practice Guideline for the Prevention and Management of Pain, Agitation (Sedation), Delirium, Immobility, and Sleep (Disruption) (PADIS) in adult patients in the ICU addresses new management challenges related to pain, agitation, and delirium and offers guidance on two additional topics—rehabilitation/mobility and sleep (1, 2). The PADIS guidelines build on the 2013 Society of Critical Care Medicine (SCCM) PAD guidelines (3) and incorporate a number of methodological innovations, including critical illness survivor input from start to finish (4–6). The PADIS methods, with an emphasis on those approaches that are novel, are outlined in a separate methods article (7).

If guideline recommendations and statements are to improve ICU clinical practice, effective knowledge translation and implementation science efforts are critical. Although our goal was to provide specific recommendations for each question, we suspect some guideline readers may be discouraged by the conditional nature of many recommendations and daunted by the breadth of topics discussed. The goals of this accompanying article are to stimulate clinician dialogue, guide the interpretation of the PADIS 2018 recommendations and statements, facilitate implementation and quality improvement (QI) efforts, share strategies for effective bedside application, and provide patient scenarios where application of PADIS recommendations and statements may pose challenges.

HOW TO READ THE GUIDELINE

The PADIS guideline represents a wasted effort unless its recommendations can be easily interpreted, understood, and implemented by practicing ICU clinicians. Although the use

of GRADE methodology ensures a systematic and transparent approach (8), the basis for determining the strength and quality of evidence inserts uncertainty since the language used is not typically included in our critical care lexicon. Furthermore, critics justifiably express concerns about involving professionals whose very expertise potentially introduces bias, including intellectual conflicts of interest, in the guideline development effort (9).

So, where does a GRADE-naïve ICU clinician begin? The recommendations themselves (see PADIS executive summary) (2) are a good starting point. Each actionable question uses a PICO format (i.e., addresses which patients, intervention, comparator, and outcome are being assessed) and is then answered by a recommendation. These recommendations are intentionally brief and direct. (e.g., “We suggest using propofol as compared to benzodiazepines in mechanically ventilated cardiovascular surgery patients.”) They are meant for clinicians looking simply for bottom-line guidance. Although a strong recommendation is more valuable to clinicians than a conditional recommendation, practice guidelines, including PADIS, generally contain far more conditional than strong recommendations. The characteristics of conditional and strong recommendations are compared in **Table 1** (10).

After reading the recommendations, clinicians may have many important questions. For example, what factors did the panelists consider when generating the specific recommendation? Why was a conditional recommendation issued rather than a strong one? Why does the recommendation only address a specific population? The answer to some of these questions may be found in the “rationale” section which immediately follows each actionable recommendation (1). Relevant factors are described including a brief review of the evidence and strength, the balance of desirable and undesirable outcomes, and any relevant decision-making factors such as costs/resources, feasibility, subgroup considerations, etc. For most clinicians, the recommendation and rationale, taken together, should provide adequate insight and clarity to allow clinical application. The evidence gap sections describe why a question could not be answered unequivocally (i.e., uncertainty remains) and may be especially helpful for those interested in conducting future research. Finally, supplemental materials (1) (e.g., forest plots, evidence summaries, evidence-to-decision frameworks, and voting results) provide all the data that were considered by the guideline writing committee during its deliberations.

POTENTIAL BARRIERS TO INTERPRETING AND IMPLEMENTING PADIS RECOMMENDATIONS

The successful integration of the PADIS guideline into clinical practice will be heavily dependent on the methods used to disseminate (spread) and implement (effectively integrate) the recommendations (11, 12). Unfortunately, although guidelines often tell us “what” the right things to do are, they do not often describe “how” to integrate them effectively into everyday practice (13). This is particularly true in the critical care setting where well-designed dissemination and implementation science research remains in its infancy (14). Barriers to PADIS adoption can be identified across each of the five domains of the consolidated framework for implementation research (CFIR) (**Table 2**) (15–20).

To these CFIR items, we added three others chosen after reflecting on the discordances in local practices reflected by our regional, national, and international guideline expert members. These potential barriers should be proactively discussed at both the hospital/health system and ICU level prior to the initiation of formal implementation efforts. These often difficult and impassioned conversations should involve all key stakeholders (**Table 3**) and may be enhanced by using a variety of information gathering techniques (one-on-one meetings, anonymous surveys, and facilitated group discussions) (19).

The priority outcomes chosen for each question, many of which occur after ICU discharge (e.g., longer term cognitive dysfunction), may not immediately resonate with ICU clinicians who focus on more traditional outcomes like duration of mechanical ventilation and ICU mortality. In this situation, it may be helpful for those involved in PADIS implementation efforts to initially focus their teaching on the prevalence and consequences of postintensive care syndrome and the importance of family-centered care both during and after the ICU stay (21–23). Institutional buy-in is also important to establish performance metrics and provide needed resources and training to reach and maintain QI goals (including those involving clinical outcomes after discharge) (24, 25).

OPTIMIZING IMPLEMENTATION SCIENCE STRATEGIES TO MAKE PRACTICE CHANGE

The release of the PADIS guideline will catalyze the integration of the recommendations into clinical practice in many ICUs

TABLE 1. Implications of Strength of Recommendation^a

Construct	Strong Recommendation	Conditional Recommendation
Patients	Applies to almost all patients	Applies to most patients with significant exceptions based on patient condition, values, and preferences
Supporting evidence	Moderate to high-quality data across broad patient populations	Data that are conflicting, low quality, insufficient, and/or involve limited patient populations
Benefits vs burdens	Benefits clearly outweigh burdens	There may be a close balance between benefits and burdens
Influence of future research	Limited potential to change recommendation	Possible/probable potential to change recommendation
Performance or quality indicators	Can be readily adapted in most healthcare systems	Requires significant deliberation at the local level based on practice patterns, patients served, resource availability

^aSpecific patient context should guide clinical decisions.

TABLE 2. Common Potential Barriers to Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption Adoption (17–20)

Construct	Potential Barrier to PADIS Adoption
Strength of evidence	Limitations due to available literature vs relevant clinical practice (1). Limitations as to how the strength of evidence is established. Do key stakeholders (particularly physicians) perceive the evidence supporting the PADIS guideline strong enough to support practice change?
Implementation complexity	Do providers perceive the recommendations will be difficult to apply?
Administrative support	Do senior administrators fully support PADIS implementation efforts? Do ICU team members feel that they are essential, valued, and knowledgeable partners in the change process?
Resource availability	Will the ICU have the staff and equipment (e.g., walkers, portable ventilators) required to implement recommendations? Will additional personnel be allocated to monitor progress, provide feedback, and make the necessary changes to the electronic health record?
Clinician time	Will the recommendations disrupt workflow? Will current practices be abandoned to facilitate new ones? Will documentation burden increase?
ICU team knowledge, beliefs, and skills	Do physicians or other ICU team members perceive the recommendations limit their autonomy? Does the ICU team have the necessary knowledge and skills to perform the recommended PADIS interventions? Does the ICU team have prior experience with quality/performance improvement projects that they could build upon?
Education support	Is PADIS educational material easily accessible? Is the education provided in multimodal way to facilitate knowledge transfer for persons with different learning styles? When and how will the training be provided?
Financial barriers/cost	Will the potential cost of recommendation adoption (e.g., need for a physical/occupational therapist, increased nursing hours) be offset by potential cost reductions (e.g., shorter ICU length of stay, decreased ICU readmissions, improved patient/family satisfaction)? How will cost-effectiveness be monitored?
ICU team communication and cooperation	How will changes be communicated to the ICU team? How will team members who refuse to change be handled? Are ICU team members equipped with effective interprofessional communication skills?
ICU culture	Does the team believe the recommendations are already being fully used in their ICU? Do they feel what they are presently doing is better than the recommendations? What are the perceived benefits to adopting the recommendations?
Priority in the ICU	Is the ICU team already taking part in multiple quality improvement projects? What other efforts take precedent over PADIS adoption?
Guideline adaptability	Can the PADIS guideline be adapted, tailored, refined, or reinvented to meet local needs?
Organizational incentives and rewards	Will PADIS implementation efforts result in extrinsic incentives such as goal-sharing awards, performance reviews, promotions, and/or raises in salary? Will internal and external benchmarking be used to monitor progress?
Self-efficacy	Do ICU team members believe in their own capabilities to execute courses of action to achieve PADIS implementation goals?
Local, district, and regional comparators	Are “cooperation” opportunities available as incentives to drive performance by comparing individual ICU granular anonymized data (effective analgesia, “within-target” sedation, etc.) for sustainable performance?
Learning healthcare systems framework	Are patient-centered value-driven healthcare deliverables captured to permit reflexive, scientifically sound, and ethical improvement initiatives?
International comparators	Are there platforms to facilitate access to information describing practice and cost to disseminate knowledge and align public health policy with individualized patient care to accelerate improvement initiatives?

PADIS = Pain, Agitation (Sedation), Delirium, Immobility, and Sleep (Disruption).

with different resources, patient populations, and otherwise varied local characteristics. Although many different implementation science strategies can support better recognition of PADIS-related symptoms, clinical bundle development, care reorganization, improved educational efforts, and new financial incentives (26, 27), none have been shown to be effective for a

“holistic” PADIS approach. The Plan-Do-Study-Act model (20) has been successful in delirium and may help accelerate PADIS recommendation adoption (16). Prior large-scale QI efforts (28, 29) have also found engagement (i.e., attracting and involving appropriate individuals in the implementation process) (17) to be one of the most important predictors of success. Whether

TABLE 3. Potential Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption Implementation Leaders

Nurses (staff, advanced practice, administration, aides, education/quality improvement departments)
Physicians (intensivists, house staff, administration)
Pharmacists
Respiratory therapists
Physical therapist
Occupational therapists
Speech therapists
Specialty consultants (e.g., palliative care, ethics, psychiatrists/psychologists), sleep medicine, rehabilitation
Pastoral care
Information technology staff
ICU patients and family members

comparators of granular data across ICUs to drive and maintain “quality competition” (30), learning frameworks (31), or international knowledge sharing platforms (32) help deliver better quality PADIS-related care remains to be tested.

Implementation leaders may want to begin their efforts by using adoption strategies highlighted in the prior PAD guideline (3) by assessing current practice through walking rounds, case reviews, and staff interviews; reviewing existing PADIS-related policies and procedures; identifying those committees that should be involved in change; performing a gap analysis (what should be done vs what is already being done); evaluating the electronic health record to see what PADIS-related documentation is already in place; and exploring the ICU’s culture to identify why current practice is the way it is (18, 33). They may also want to consider contacting external change agents such as experts in the field of PADIS, including guideline authors, and the SCCM ICU liberation committee (<http://www.iculiberation.org/Pages/default.aspx>) with questions they have regarding interpretation or application of the guideline.

Next, both ICU “opinion leaders” (i.e., individuals in the organization who have formal or informal influence on the attitudes and beliefs of their colleagues) and potential PADIS “champions” (individuals who dedicate themselves to supporting, marketing, and leading implementation and overcoming indifference or resistance that the PADIS adoption may provoke in an organization) (17) should be identified and asked if they are willing to take part in the process. If institutional protocols and care bundles exist, these too can be updated and/or built upon to accommodate the new guideline recommendations. It is important to note that there really is no need to “reinvent the wheel.” Many organizations and healthcare systems can provide protocols that address many of the PADIS recommendations. Finally, an implementation plan and methods to monitor progress should be developed. This plan should include the planning, implementation, and evaluation strategies that heighten the likelihood that guideline

TABLE 4. Key Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption Planning, Implementation and Evaluation Strategies

Planning
Assess for readiness and identify barriers and facilitators to adoption
Identify early adopters, opinion leaders, and champions
Perform a local needs assessment
Provide ongoing granular metrics for tracking
Change record systems
Develop disincentives
Involve and inform executives
Visit other sites
Develop academic partnerships
Consider creating or participating in a collaborative
Implementation
Develop a formal implementation plan
Provide ongoing educational meetings and outreach sessions/distribute educational materials
Mandate change
Model and stimulate change
Promote adaptability
Use reminders
Evaluation
Use data experts
Conduct cyclical small test of change
Audit and provide feedback on both process and outcome measures
Tailor strategies
Broaden comparators

implementation efforts will be successful (Table 4) (34). Sustaining practice changes over time can be challenging. Benchmark data, continuously collected and publicly posted in the ICU, can be effective (35). The use of daily rounding checklists, goal setting, and clinician prompting should also be considered (36).

APPLICATION OF PADIS RECOMMENDATIONS COMMON ICU PATIENT SCENARIOS NOT EXPLICITLY ADDRESSED IN THE GUIDELINE

Clinical practice guidelines are often criticized because they do not clearly offer management options for common clinical conditions, and if they do, those suggestions are usually vague and lack unequivocal direction. From a guideline development point of view, this is entirely appropriate for topics that are not well studied or have conflicting data reported in the

literature. As a result, many clinical scenarios have no proven or even preferred choices to guide management decisions. This section identifies clinical questions specific to each of the five components of the PADIS guideline; they are not meant to be exhaustive in nature. Rather, they are examples of pedagogical problem-solving (37) and should be used by critical care clinicians as examples to further discussion, debate, and application of the guideline recommendations to real-life clinical scenarios.

Pain Section Clinical Questions

How do we evaluate pain when all the components of Behavioral Pain Scales (Critical Care Pain Observation Tool [CPOT] and Behavioral Pain Score [BPS]) are not available for assessment? What guides the choice of pharmacologic and nonpharmacologic pain management interventions in a patient who may not tolerate opioid therapy?

Response

The PADIS guideline advocates that analgesia must take priority over sedation, both to control pain and to avoid sedative overuse. Use of validated behavioral pain tools is preferred to assess pain in ICU patients unable to communicate. Occasionally, patients may be unable to self-report pain and have conditions such as weakness or joint deformations that do not allow assessment of limb movement or muscle tension. As a result, validated tools (BPS or CPOT) cannot be “strictly” applied. In this situation, clinicians may still want to consider facial expression as an indicator of pain. Any changes in behavior or vital signs observed during painful procedures (e.g., suctioning, turning) should also be considered, even if they are not used in recommended tools. Furthermore, physical examinations should be diligently performed to detect and treat complications (e.g., peritonitis, compartment syndrome) before escalating analgesia or sedation.

Although opioids are regarded as the first-line management option for ICU pain in the PADIS guideline, some patients will never require them (38). Although the guidelines conditionally suggest the use of a multimodal approach with adjunctive nonopioids like acetaminophen, low-dose ketamine, or nefopam in an effort to limit opioid exposure and potential adverse events, the evidence to support these recommendations was generally weak, and many ICU subpopulations were not well represented in studies. Conversely, an agent for which there was also sparse evidence but that is part of clinical practice in some centers, IV lidocaine, received a recommendation against its use as safety concerns were highlighted. Choice of adjunctive analgesics will thus depend on availability/cost and the potential for individualized safety concerns: acetaminophen (e.g., hepatotoxicity), ketamine (e.g., hallucinations), nefopam (e.g., tachycardia). Nonpharmacologic interventions (e.g., massage, music therapy) can also be used in a “multimodal approach.” Cold therapy, conditionally recommended before chest tube removal, may also prove useful as a pain reduction strategy for other painful procedures.

Sedation Section Clinical Question

What guides the choice of pharmacotherapy when treating agitation in a patient who is hemodynamically unstable?

Response

Although the PADIS guidelines make specific recommendations regarding sedative approaches and choices, it does not distinguish between pharmacologic treatment options for agitation in hemodynamically stable versus hypotensive patients. Three potential options exist: 1) aggressive analgesation with synthetic opioids such as fentanyl relieves discomfort and facilitates ambivalence to the environment. Since fentanyl does not cause histamine release, hypotension, should it occur, is likely related to a diminished stress response. High-dose fentanyl carries the risk of serotonin syndrome especially if other serotonergic agents are administered (39); 2) if greater sedation is required, intermittently administered benzodiazepines on an “as needed” basis may suffice. It should be noted that the association between benzodiazepine use and delirium occurrence is strongest with continuous infusion administration when administered doses are usually greater (40); and 3) sometimes these strategies are not effective, and alternative approaches such as continuously infused propofol or dexmedetomidine may be necessary albeit with clear concern for their adverse effects. Newer use of older agents such as phenobarbital and valproate can be considered in select patients (41).

Delirium Section Clinical Question

What guides the choice of pharmacotherapy for the symptomatic treatment of agitated and nonagitated delirium and do these interventions affect delirium severity and duration?

Response

The PADIS guideline suggests that many critically ill adults screen positive for delirium, but does not provide guidance on pharmacologic treatment options other than haloperidol, an atypical antipsychotic, or a HMG-CoA reductase inhibitor (i.e., a statin) should not be routinely used. Among the sequelae of delirium (1), distress experienced by patients, families, and care providers is one of the most important. Unfortunately, there is a dearth of data on the topic, and as a result, the best pharmacologic intervention to reduce patient stress due to delirium remains unclear (42). In addition, no pharmacologic management option has demonstrated an effect on delirium-related outcomes such as long-term cognitive impairment prevalence, duration of ICU and hospital stay, discharge disposition, or physical and psychological functionality after hospital discharge.

The removal or reversal of inciting factors remains the mainstay of delirium management in the ICU. For example, benzodiazepines, if they are required, are associated with a dose-dependent increase in a positive delirium screening result; simply reducing exposure may be all that is needed (40). Some intensivists may choose to treat delirium with an antipsychotic, particularly when agitation, not related to pain, is present (43). Antipsychotic choice is guided by patient factors (e.g., gastrointestinal tract accessibility, side effects such as QTc prolongation, etc.). It should be emphasized that there are few supportive data on ICU antipsychotic use and that the initiation of psychoactive medications during critical illness often results their inappropriate continuation after ICU discharge (44, 45).

Rehabilitation/Mobilization Section Clinical Question

What criteria exist for commencing rehabilitation/mobilization and how should this intervention be safely initiated in complicated critically ill patients who may be hemodynamically unstable and/or delirious?

Response

As conditionally recommended in the PADIS guidelines, rehabilitation/mobilization commenced within a few days of initiating mechanical ventilation (vs later) is safe, feasible, and beneficial (46–49). Mechanical ventilation via an oral endotracheal tube is not a contraindication to rehabilitation/mobilization; indeed, waiting for clinician judgment that the patient is “ready” delays mobilization for up to 5 days and may worsen recovery probability. Patients’ pain, agitation/sedation, and delirium status, as well as cardiovascular and pulmonary status, complete the assessment for rehabilitation/mobilization. Assessing the patient’s capability for in-bed movement after an evaluation of appropriate function, position, and securement of the medical devices such as the endotracheal tube, vascular access, and drains helps guide subsequent rehabilitation/mobilization goals. Communication within the clinical team is important in planning and conducting rehabilitation/mobilization interventions (50). After conducting the above assessments, it may be decided to sit patients on the edge of the bed for 10 minutes to demonstrate stability of their cardiovascular, respiratory, and neurologic systems. Thereafter, patients can be asked to stand next to the bed for around 6 minutes; if they tire, they can be transferred into a bedside chair. The duration of rehabilitation/mobilization interventions should be based upon ongoing patient monitoring given the lack of existing evidence regarding the optimal duration of rehabilitation/mobilization.

Sleep Section Clinical Question

What is the best strategy to encourage sleep in mechanically ventilated patients and is it appropriate to reinstate home sleeping medications in the ICU, particularly if delirium is present?

Response

As outlined in the guideline, patients who use sleep aids at home are known to be at risk for poor sleep in the ICU; however, many sleep aids such as the benzodiazepine-receptor agonists confer risk in critically ill patients and have not been tested for efficacy in this context (51). The relationship between delirium and poor sleep in the ICU is complex and remains poorly understood (52). All efforts should be made to minimize disruptive interruptions and to create a safe, quiet environment at night conducive to sleep. Delirium management should proceed according to the PADIS guideline. If a sedative infusion is necessary, dexmedetomidine may be preferred from the standpoint of sleep architecture, but evidence suggesting a corresponding improvement in sleep outcomes (e.g., patient-reported sleep quality) is lacking. As noted in the guideline, melatonin is an unproven, low-risk, low-cost option

for patients with accessible and functional gastrointestinal tracts. For other sleep disorders such as restless legs syndrome, treatment would have to be considered on a case-by-case basis since both the untreated syndrome and its medical management with dopamine agonists may contribute to agitation. As recommended in the PADIS guideline, nonpharmacologic sleep interventions should be instituted in all ICU patients.

CONCLUSIONS

The 2018 PADIS guideline provides the multiprofessional ICU team with important new guidance on how to manage pain, agitation, delirium, immobility, and disrupted sleep in critically ill adults from a patient-centric perspective. It should inspire clinicians to reflect on current practices, identify gaps, and use proven QI strategies to enhance care for critically ill patients. Although the guideline cannot provide definitive answers on all topics judged important by experts and patients/families, it can serve as a comprehensive foundation for discussions on clinical issues that have immediate relevance to patient care. Uncertainties inherent to individual care management should not interfere with QI initiatives that focus on all PADIS domains since they have the potential to enhance the care of the critically ill.

REFERENCES

- Devlin JW, Skrobik Y, Gélinas C, et al: Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. *Crit Care Med* 2018; 46:e825–e873
- Devlin JW, Skrobik Y, Gélinas C, et al: Executive Summary: Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. *Crit Care Med* 2018; 46:1532–1548
- Barr J, Fraser GL, Puntillo K, et al; American College of Critical Care Medicine: Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med* 2013; 41:263–306
- Greene SM, Tuzzio L, Cherkin D: A framework for making patient-centered care front and center. *Perm J* 2012; 16:49–53
- Selva A, Sanabria AJ, Pequeño S, et al: Incorporating patients' views in guideline development: A systematic review of guidance documents. *J Clin Epidemiol* 2017; 88:102–112
- Clay AS, Misak C: Engaging survivors of critical illness in health care assessment and policy development. Ethical and practical complexities. *Ann Am Thorac Soc* 2016; 13:1871–1876
- Devlin JW, Skrobik Y, Rochweg B, et al: Methodological Innovation in Creating Clinical Practice Guidelines: Insights From the 2018 Society of Critical Care Medicine Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption Guideline Effort. *Crit Care Med* 2018; 46:1457–1463
- Guyatt GH, Oxman AD, Vist GE, et al: GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. *BMJ (Clinical Research Ed)* 2008; 336:924–926
- Committee on Conflict of Interest in Medical Research, Education, and Practice: Conflicts of interest and development of clinical practice guidelines. *In: Conflict of Interest in Medical Research, Education, and Practice*. Lo B, Field MJ (Eds). Washington, DC, National Academies Press, 2009
- Schünemann HJ, Wiercioch W, Brozek J, et al: GRADE Evidence to Decision (EtD) frameworks for adoption, adaptation, and de novo development of trustworthy recommendations: GRADE-ADOLEPMENT. *J Clin Epidemiol* 2017; 81:101–110
- Grimshaw JM, Russell IT: Effect of clinical guidelines on medical practice: A systematic review of rigorous evaluations. *Lancet* 1993; 342:1317–1322

12. Weiss CH: Why do we fail to deliver evidence-based practice in critical care medicine? *Curr Opin Crit Care* 2017; 23:400–405
13. Vander Schaaf EB, Seashore CJ, Randolph GD: Translating clinical guidelines into practice: Challenges and opportunities in a dynamic health care environment. *N Carolina Med J* 2015; 6:230–234
14. Mensah GA: Embracing dissemination and implementation research in cardiac critical care. *Glob Heart* 2014; 9:363–366
15. Damschroder LJ, Aron DC, Keith RE, et al: Fostering implementation of health services research findings into practice: A consolidated framework for advancing implementation science. *Implement Sci* 2009; 4:50
16. Kirk MA, Kelley C, Yankey N, et al: A systematic review of the use of the consolidated framework for implementation research. *Implement Sci* 2016; 11:72
17. Sadeghi-Bazargani H, Tabrizi JS, Azami-Aghdash S: Barriers to evidence-based medicine: A systematic review. *J Eval Clin Pract* 2014; 20:793–802
18. Balas MC, Burke WJ, Gannon D, et al: 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:S116–S127
19. Costa DK, White MR, Ginier E, et al: Identifying barriers to delivering the awakening and breathing coordination, delirium, and early exercise/mobility bundle to minimize adverse outcomes for mechanically ventilated patients: A systematic review. *Chest* 2017; 152:304–311
20. Needham DM, Davidson J, Cohen H, et al: Improving long-term outcomes after discharge from intensive care unit: Report from a stakeholders' conference. *Crit Care Med* 2012; 40:502–509
21. Boehm LM, Vasilevskis EE, Dietrich MS, et al: Organizational domains and variation in attitudes of intensive care providers toward the ABCDE bundle. *Am J Crit Care* 2017; 26:e18–e28
22. Elliott D, Davidson JE, Harvey MA, et al: Exploring the scope of post-intensive care syndrome therapy and care: Engagement of non-critical care providers and survivors in a second stakeholders meeting. *Crit Care Med* 2014; 42:2518–2526
23. Davidson JE, Aslakson RA, Long AC, et al: Guidelines for family-centered care in the neonatal, pediatric, and adult ICU. *Crit Care Med* 2017; 45:103–128
24. Wick EC, Galante DJ, Hobson DB, et al: Organizational culture changes result in improvement in patient-centered outcomes: Implementation of an integrated recovery pathway for surgical patients. *J Am Coll Surg* 2015; 221:669–677; quiz 785–786
25. Weled BJ, Adzhigirey LA, Hodgman TM, et al; Task Force on Models for Critical Care: Critical care delivery: The importance of process of care and ICU structure to improved outcomes: An update from the American College of Critical Care Medicine Task Force on Models of Critical Care. *Crit Care Med* 2015; 43:1520–1525
26. Kahn JM: Bringing implementation science to the intensive care unit. *Curr Opin Crit Care* 2017; 23:398–399
27. Weiss CH, Krishnan JA, Au DH, et al; ATS Ad Hoc Committee on Implementation Science: An official American Thoracic Society Research Statement: Implementation science in pulmonary, critical care, and sleep medicine. *Am J Respir Crit Care Med* 2016; 194:1015–1025
28. 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; 42:1024–1036
29. Barnes-Daly MA, Phillips G, Ely EW: Improving hospital survival and reducing brain dysfunction at seven California community hospitals: Implementing PAD guidelines via the ABCDEF bundle in 6,064 patients. *Crit Care Med* 2017; 45:171–178
30. Miller MR, Griswold M, Harris JM II, et al: Decreasing PICU catheter-associated bloodstream infections: NACHRI's quality transformation efforts. *Pediatrics* 2010; 125:206–213
31. Stein BD, Adams AS, Chambers DA: A learning behavioral health care system: Opportunities to enhance research. *Psychiatr Serv* 2016; 67:1019–1022
32. Najafizada SAM, Sivanandan T, Hogan K, et al: Ranked performance of Canada's health system on the international stage: A scoping review. *Health Policy* 2017; 13:59–73
33. Pun BT, Balas MC, Davidson J: Implementing the 2013 PAD guidelines: Top ten points to consider. *Semin Respir Crit Care Med* 2013; 34:223–235
34. Mukherjee V, Evans L: Implementation of the surviving sepsis campaign guidelines. *Curr Opin Crit Care* 2017; 23:412–416
35. Rawat N, Yang T, Ali KJ, et al: Two-state collaborative study of a multifaceted intervention to decrease ventilator-associated events. *Crit Care Med* 2017; 45:1208–1215
36. Cavalcanti AB, Bozza FA, Machado FR, et al: Effect of a quality improvement intervention with daily round checklists, goal setting, and clinician prompting on mortality of critically ill patients: A randomized clinical trial. *JAMA* 2016; 315:1480–1490
37. 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:R19
38. Skrobik Y, Ahern S, Leblanc M, et al: Protocolized intensive care unit management of analgesia, sedation, and delirium improves analgesia and subsyndromal delirium rates. *Anesth Analg* 2010; 111:451–463
39. van Ewijk CE, Jacobs GE, Girbes ARJ: Unsuspected serotonin toxicity in the ICU. *Ann Intensive Care* 2016; 6:85
40. Zaal IJ, Devlin JW, Hazelbag M, et al: Benzodiazepine-associated delirium in critically ill adults. *Intensive Care Med* 2015; 41:2130–2137
41. Gagnon DJ, Fontaine, GV, Riker, RR, et al: Repurposing valproate, enteral clonidine, and phenobarbital for comfort in adult ICU patients: A literature review with practical implications. *Pharmacotherapy* 2017; 37:1309–1321
42. Black P, Boore JR, Parahoo K: The effect of nurse-facilitated family participation in the psychological care of the critically ill patient. *J Adv Nurs* 2011; 67:1091–1101
43. Devlin JW, Smithburger P, Kane JM, et al: Intended and unintended consequences of constraining clinician prescribing: The case of antipsychotics. *Crit Care Med* 2016; 44:1805–1807
44. Tomichek JE, Stollings JL, Pandharipande PP, et al: Antipsychotic prescribing patterns during and after critical illness: A prospective cohort study. *Crit Care* 2016; 20:378
45. Marshall J, Herzig SJ, Howell MD, et al: Antipsychotic utilization in the intensive care unit and in transitions of care. *J Crit Care* 2016; 33:119–124
46. 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; 373:1874–1882
47. Schaller SJ, Anstey M, Blobner M, et al; International Early SOMS-guided Mobilization Research Initiative: Early, goal-directed mobilisation in the surgical intensive care unit: A randomised controlled trial. *Lancet* 2016; 388:1377–1388
48. Tipping CJ, Harrold M, Holland A, et al: The effects of active mobilisation and rehabilitation in ICU on mortality and function: A systematic review. *Intensive Care Med* 2017; 43:171–183
49. Denehy L, Lanphere J, Needham DM: Ten reasons why ICU patients should be mobilized early. *Intensive Care Med* 2017; 43:86–90
50. Parry SM, Nydahl P, Needham DM: Implementing early physical rehabilitation and mobilisation in the ICU: Institutional, clinician, and patient considerations. *Intensive Care Med* 2018; 44:470–473
51. Weinhouse GL: Delirium and sleep disturbances in the intensive care unit: Can we do better? *Curr Opin Anaesthesiol* 2014; 27:403–408
52. Pandharipande PP, Ely EW, Arora RC, et al: The intensive care delirium research agenda: A multinational, interprofessional perspective. *Intensive Care Med* 2017; 43:1329–1339