

Clinical practice guidelines for pain, agitation, delirium, sedation and mobilisation in the intensive care unit: A Rapid Review

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Executive Summary

Background

The Program Medical Director for Critical Care has requested a review of clinical practice guidelines for pain, agitation, delirium, sedation and mobilisation in the intensive care unit (ICU) to inform future implementation of a new clinical practice guideline in the ICU.

Objectives

The objective of this review was to review and summarise current clinical practice guidelines for pain, agitation, delirium, sedation and mobilisation in the intensive care unit (ICU).

Findings

A total of 4432 results were screened, of which 1 clinical practice guideline was included in this review¹. This guideline had a working group that was based in the United States, and produced on behalf of The American College of Critical Care Medicine¹. It is worthwhile pointing this out as recommendations in this guideline were assessed for strength via a consensus process taking the evidence and risk/benefits into account. Therefore, any consensus decision is likely to reflect the clinical context of the individuals (e.g. U.S. setting only).

			Guideline focus						Quality	
Author	Date	Country	Endorsed	Pain	Sedation	Agitation	Delirium	Mobilisation	Item 7	Item 12
Barr et al. ¹	2013	U.S.	✓*	✓	✓	✓	✓	✗	✓	✓

*This guideline was reviewed and endorsed by American College of Chest Physicians and the American Association for Respiratory Care; are supported by the American Association for Respiratory Care; and have been reviewed by the New Zealand Intensive Care Society.

Background

The Program Medical Director for Critical Care has requested a review of clinical practice guidelines for pain, agitation, delirium, sedation and mobilisation in the intensive care unit (ICU) to inform future implementation of a new clinical practice guideline in the ICU.

Objectives

The objective of this review was to review and summarise current clinical practice guidelines for pain, agitation, delirium, sedation and mobilisation in the intensive care unit (ICU).

Search strategy

The TRIP database and Google were searched by one author (CJ). In addition, a suite of other clinical practice guideline sources were also searched. Search terms can be found in Tables 1 & 2, and inclusion/exclusion criteria in Table 3. Papers identified were screened using inclusion and exclusion criteria established a priori. Searches of the TRIP database and the internet (using Google) were screened by one reviewer in consultation with colleagues as necessary.

NOTE: The evidence product is a Rapid Review, and as a result, all searches are restricted to only include the most recent evidence, which is defined as being that produced in the last five years.

Table 1. Topic search terms and relevant resource

Topic	TRIP database search terms	Google search terms
Pain	<u>Assessment</u> ICU AND assessment AND pain <u>Management</u> ICU AND treatment OR management AND pain	<u>Assessment</u> Guideline AND pain AND assessment "clinical practice guideline" -palliat -paed -ped -children -cancer <u>Management</u> Guideline AND pain AND treatment OR management AND "clinical practice guideline" -palliat -paed -ped -children -cancer
Agitation	<u>Assessment</u> ICU AND assessment AND agitation <u>Management</u> ICU AND treatment OR management AND agitation	<u>Assessment</u> Guideline AND agitation AND assessment "clinical practice guideline" -palliat* -paed -ped -children -cancer <u>Management</u> Guideline AND agitation AND treatment OR management AND "clinical practice guideline" -palliat -paed -ped -children -cancer
Sedation	<u>Assessment</u> ICU AND assessment AND sedation <u>Management</u> ICU AND treatment OR management AND sedation	<u>Assessment</u> Guideline AND sedation AND assessment "clinical practice guideline" -palliat -paed -ped -children <u>Management</u> Guideline AND sedation AND treatment OR management "clinical practice guideline" -palliat -paed -ped -children -cancer

Delirium	<u>Assessment</u> ICU AND assessment AND delirium <u>Management</u> ICU AND treatment OR management AND delirium	<u>Assessment</u> Guideline AND delirium AND treatment OR management "clinical practice guideline" -palliat -paed -ped -children -cancer <u>Management</u> Guideline AND delirium AND assessment "clinical practice guideline" -palliat -paed -ped -children -cancer
Mobilisation	<u>Assessment</u> ICU AND assessment AND mobilisation OR mobilization <u>Management</u> ICU AND treatment OR management AND mobilisation OR mobilization	<u>Assessment</u> Guideline AND mobilisation OR mobilization AND treatment OR management "clinical practice guideline" -palliat -paed -ped -children -cancer <u>Management</u> Guideline AND mobilisation OR mobilization AND treatment OR management "clinical practice guideline" -palliat -paed -ped -children -cancer

Table 2. Clinical practice guideline source and search terms

Source	Search terms
National Institute for Health and Care Excellence (NICE) https://www.nice.org.uk/	pain OR delirium OR agitation OR sedation OR mobilisation AND ICU OR "intensive care unit"
National Guideline Clearinghouse https://www.guideline.gov/	pain OR delirium OR agitation OR sedation OR mobilisation AND ICU OR "intensive care unit"
BMJ Best Practice https://bestpractice.bmj.com/	pain OR delirium OR agitation OR sedation OR mobilisation AND ICU OR "intensive care unit"
Scottish Intercollegiate Guidelines Network (SIGN) http://www.sign.ac.uk/	pain OR delirium OR agitation OR sedation OR mobilisation AND ICU OR "intensive care unit"
College of Physicians and Surgeons of Ontario http://www.cpso.on.ca/Policies-Publications/CPGs-Other-Guidelines	pain OR delirium OR agitation OR sedation OR mobilisation AND ICU OR "intensive care unit"

Table 3. Inclusion/Exclusion criteria

Population	Include: Adults Exclude: Neonatal, paediatric, adolescent
Interventions	Include: Pain, agitation, delirium, sedation, mobilisation

Outcomes	Include: Assessment and management Exclude: All other outcomes
Context	Include: Patients in the intensive care unit Exclude:
Types of evidence	Include: Clinical practice guidelines Exclude: All other types of evidence
Limits	Date: Since 2013 (last 5 years) Language: Publications in English.

Quality Appraisal

An internationally recognised appraisal tool, AGREE II², was used to determine if each guideline was developed using an evidence-based approach. Two key criteria were used to appraise each guideline on their evidence-based process and content. The AGREE II criteria includes:

- Criterion 7: Were systematic methods used to search for evidence?
- Criterion 12: Is there an explicit link between the recommendations and the supporting evidence?

Each guideline was given one point for each criteria, with a possible total of 2 points. If the guideline did not meet the criteria, it was given a zero. If required, a full appraisal using all criteria can be conducted for the future.

NOTE: Where required, all guidelines and their background documentation were searched to determine if an evidence-based approach was used in the development process. It should also be noted that if the guideline did not meet Criteria 7 or 12, that does not necessarily mean that the recommendations in the guideline were not informed by evidence, but that, an explicit evidence-based method was not used or information explaining this process could not be explicitly determined.

Results

Search results

A total of 4432 results were screened (3358 results from TRIP & 1047 from Google). Of these, 18 results were explored, with 12 full-text items retrieved. A total of 1 clinical practice guidelines are included in this review¹. This guideline had a working group that was based in the United States, and produced on behalf of The American College of Critical Care Medicine¹. It is worthwhile pointing this out as recommendations in this guideline were assessed for strength via a consensus process taking the evidence and risk/benefits into account. Therefore, any consensus decision is likely to reflect the clinical context of the individuals (e.g. U.S. setting only).

Summary of findings

Table 4 provides a summary of the clinical practice guideline found in this report¹. In regards to the quality of evidence provided, high quality was based on the evidence being high quality randomised controlled trials; moderate quality was based on randomised controlled trials with significant limitations, or high-quality observational studies; and low quality refers to observational studies only.

Table 4. Summary of Barr et al., 2013¹

Topic and subheading	Recommendation	Quality
Pain and Analgesia		
Incidence of pain	i. Adult medical, surgical, and trauma ICU patients routinely experience pain, both at rest and with routine ICU care.	Moderate
	ii. Pain in adult cardiac surgery patients is common and poorly treated; women experience more pain than men after cardiac surgery.	Moderate
	iii. Procedural pain is common in adult ICU patients.	Moderate
Pain assessment	i. We recommend that pain be routinely monitored in all adult ICU patients.	Moderate
	ii. The Behavioral Pain Scale (BPS) and the Critical-Care Pain Observation Tool (CPOT) are the most valid and reliable behavioral pain scales for monitoring pain in medical, postoperative, or trauma (except for brain injury) adult ICU patients who are unable to self-report and in whom motor function is intact and behaviors are observable. Using these scales in other ICU patient populations and translating them into foreign languages other than French or English require further validation testing.	Moderate
	iii. We do not suggest that vital signs (or observational pain scales that include vital signs) be used alone for pain assessment in adult ICU patients.	Low
	iv. We suggest that vital signs may be used as a cue to begin further assessment of pain in these patients, however.	Low
Treatment of pain	i. We recommend that pre-emptive analgesia and/or non-pharmacologic interventions (e.g., relaxation) be administered to alleviate pain in adult ICU patients prior to chest tube removal.	Low
	ii. We suggest that for other types of invasive and potentially painful procedures in adult ICU patients, pre-emptive analgesic therapy and/or non-pharmacologic interventions may also be administered to alleviate pain.	Low

iii. We recommend that intravenous (IV) opioids be considered as the first-line drug class of choice to treat non-neuropathic pain in critically ill patients.	Low
iv. All available IV opioids, when titrated to similar pain intensity endpoints, are equally effective.	Low
v. We suggest that nonopioid analgesics be considered to decrease the amount of opioids administered (or to eliminate the need for IV opioids altogether) and to decrease opioid-related side effects.	Low
vi. We recommend that either enterally administered gabapentin or carbamazepine, in addition to IV opioids, be considered for treatment of neuropathic pain.	High
vii. We recommend that thoracic epidural anesthesia/ analgesia be considered for postoperative analgesia in patients undergoing abdominal aortic aneurysm surgery.	Moderate
viii. We provide no recommendation for using a lumbar epidural over parenteral opioids for postoperative analgesia in patients undergoing abdominal aortic aneurysm surgery, due to a lack of benefit of epidural over parenteral opioids in this patient population.	High
ix. We provide no recommendation for the use of thoracic epidural analgesia in patients undergoing either intrathoracic or nonvascular abdominal surgical procedures, due to insufficient and conflicting evidence for this mode of analgesic delivery in these patients.	Moderate
x. We suggest that thoracic epidural analgesia be considered for patients with traumatic rib fractures.	Moderate
xi. We provide no recommendation for neuraxial/ regional analgesia over systemic analgesia in medical ICU patients, due to lack of evidence in this patient population.	No evidence

Sedation & Agitation

Depth of sedation vs. clinical outcomes

i. Maintaining light levels of sedation in adult ICU patients is associated with improved clinical outcomes (e.g., shorter duration of mechanical ventilation and a shorter ICU length of stay [LOS]).	Moderate
ii. Maintaining light levels of sedation increases the physiologic stress response, but is not associated with an increased incidence of myocardial ischemia.	Moderate
iii. The association between depth of sedation and psychological stress in these patients remains unclear.	Low
iv. We recommend that sedative medications be titrated to maintain a light rather than a deep level of sedation in adult ICU patients, unless clinically contraindicated.	Moderate

Monitoring depth of sedation and brain function	<p>i. The Richmond Agitation-Sedation Scale (RASS) and Sedation-Agitation Scale (SAS) are the most valid and reliable sedation assessment tools for measuring quality and depth of sedation in adult ICU patients.</p> <p>ii. We do not recommend that objective measures of brain function (e.g., auditory evoked potentials [AEPs], Bispectral Index [BIS], Narcotrend Index [NI], Patient State Index [PSI], or state entropy [SE]) be used as the primary method to monitor depth of sedation in noncomatose, nonparalyzed critically ill adult patients, as these monitors are inadequate substitutes for subjective sedation scoring systems.</p> <p>iii. We suggest that objective measures of brain function (e.g., AEPs, BIS, NI, PSI, or SE) be used as an adjunct to subjective sedation assessments in adult ICU patients who are receiving neuromuscular blocking agents, as subjective sedation assessments may be unobtainable in these patients.</p> <p>iv. We recommend that EEG monitoring be used to monitor non-convulsive seizure activity in adult ICU patients with either known or suspected seizures, or to titrate electro suppressive medication to achieve burst suppression in adult ICU patients with elevated intracranial pressure.</p>	<p>Moderate</p> <p>Moderate</p> <p>Moderate</p> <p>High</p>
Choice of sedative	<p>i. We suggest that sedation strategies using non-benzodiazepine sedatives (either propofol or dexmedetomidine) may be preferred over sedation with benzodiazepines (either midazolam or lorazepam) to improve clinical outcomes in mechanically ventilated adult ICU patients.</p>	<p>Moderate</p>
Delirium		
Detecting and monitoring delirium	<p>i. We recommend routine monitoring of delirium in adult ICU patients.</p> <p>ii. The Confusion Assessment Method for the ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC) are the most valid and reliable delirium monitoring tools in adult ICU patients.</p> <p>iii. Routine monitoring of delirium in adult ICU patients is feasible in clinical practice.</p>	<p>Moderate</p> <p>High</p> <p>Moderate</p>
Delirium risk factors	<p>i. Four baseline risk factors are positively and significantly associated with the development of delirium in the ICU: pre-existing dementia, history of hypertension and/or alcoholism, and a high severity of illness at admission.</p> <p>ii. Coma is an independent risk factor for the development of delirium in ICU patients.</p> <p>iii. Conflicting data surround the relationship between opioid use and the development of delirium in adult ICU patients.</p>	<p>Moderate</p> <p>Moderate</p> <p>Moderate</p>

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|---|----------|
| iv. Benzodiazepine use may be a risk factor for the development of delirium in adult ICU patients. | Moderate |
| v. There are insufficient data to determine the relationship between propofol use and the development of delirium in adult ICU patients. | Low |
| vi. In mechanically ventilated adult ICU patients at risk of developing delirium, dexmedetomidine infusions administered for sedation may be associated with a lower prevalence of delirium compared to benzodiazepine infusions. | Moderate |

Delirium treatment

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| i. There is no published evidence that treatment with haloperidol reduces the duration of delirium in adult ICU patients. | No evidence |
| ii. Atypical antipsychotics may reduce the duration of delirium in adult ICU patients. | Low |
| iii. We do not recommend administering rivastigmine to reduce the duration of delirium in ICU patients. | Moderate |
| iv. We do not suggest using antipsychotics in patients at significant risk for torsades de pointes (i.e., patients with baseline prolongation of QTc interval, patients receiving concomitant medications known to prolong the QTc interval, or patients with a history of this arrhythmia). | Low |
| v. We suggest that in adult ICU patients with delirium unrelated to alcohol or benzodiazepine withdrawal, continuous IV infusions of dexmedetomidine rather than benzodiazepine infusions be administered for sedation to reduce the duration of delirium in these patients. | Moderate |

Strategies for Managing Pain, Agitation, and Delirium to Improve ICU Outcomes

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| a. We recommend either daily sedation interruption or a light target level of sedation be routinely used in mechanically ventilated adult ICU patients. | Moderate |
| b. We suggest that analgesia-first sedation be used in mechanically ventilated adult ICU patients. | Moderate |
| c. We recommend promoting sleep in adult ICU patients by optimizing patients' environments, using strategies to control light and noise, clustering patient care activities, and decreasing stimuli at night to protect patients' sleep cycles. | Low |
| d. We provide no recommendation for using specific modes of mechanical ventilation to promote sleep in mechanically ventilated adult ICU patients, as insufficient evidence exists for the efficacy of these interventions. | No Evidence |
| e. We recommend using an interdisciplinary ICU team approach that includes provider education, pre-printed and/or computerized protocols and order forms, and quality ICU rounds checklists to facilitate the use of pain, agitation, and delirium management guidelines or protocols in adult ICUs. | Moderate |

Quality appraisal

Overall, the quality of the guidelines included in this review was high (Table 5).

Table 5. Quality appraisal of included guidelines

Guideline	Evidence-based?	
	Item 7	Item 12
Barr et al., 2013	Yes	Yes

Conclusions

This review found one high quality clinical practice guidelines that addressed pain, agitation, sedation and delirium in adults in the ICU. No guidelines were found for mobilisation.

References

1. Barr J, Fraser GL, Puntillo K, Ely EW, Gélinas C, Dasta JF, Davidson JE, Devlin JW, Kress JP, Joffe AM, Coursin DB. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Critical Care Medicine*. 2013 Jan 1;41(1):263-306.
2. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. *The Canadian Medical Association Journal*. 2010 Dec 14;182(18):E8392. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20603348>