These guidelines are based upon medical literature review and expert opinion and are intended to provide recommendations for Pain, Agitation-Sedation, and Delirium in the care of critically ill patients. **In general, the following guidelines should be followed in a stepwise progression. Pain should be adequately addressed before adding additional non-analgesic sedatives. Refer to graphical flow-sheet on page three of these guidelines.**

**Best Practice Guidelines**

1. **Management of Pain**
   
   1. Assess for pain frequently. Non-surgical and mechanically ventilated patients may also have pain due to bedside procedures, immobilization and the endotracheal tube.
   
   2. Non-opioids such as acetaminophen (Tylenol™) should be strongly considered to decrease overall opioid use and side effects. Opioid analgesics (fentanyl, hydromorphone or morphine) should then be considered for the management of non-neuropathic pain.
   
   3. Consider gabapentin for neuropathic pain.
   
   4. Many patients may achieve their sedation target via an analgesia based approach and may not need an additional sedative.

2. **Management of Agitation and Sedation (when mechanically ventilated)**
   
   1. Assess for level of agitation-sedation with the Richmond Agitation-Sedation Scale (RASS) at least every 4 hours.
   
   2. Reassess and establish RASS target level at least once every 12 hours.
   
   3. If analgesia is adequate and the patient remains agitated, preference should be given to non-benzodiazepine sedatives (e.g. propofol or dexmedetomidine). From a health economics standpoint, propofol should be used as the first line sedative medication for patients not expected to be extubated within 24 hours.
   
   4. Midazolam should be considered for patients who do not tolerate propofol/dexmedetomidine, those with active seizures, and those with alcohol withdrawal symptoms.
   
   5. Screen patients daily for readiness for spontaneous awakening trials and perform coupled awakening and spontaneous breathing trials on patients that pass the respective safety screens.

3. **Management of Delirium**
   
   1. Assess for delirium at least every 12 hours with the Confusion Assessment Method for the ICU (CAM-ICU).
   
   2. Try **non-pharmacological methods** first for treating delirium:
      
      a. Encourage early mobilization.
      
      b. Reduce exposure to deliriogenic medications such as benzodiazepines, anticholinergic medications (e.g. diphenhydramine), and steroids when applicable.
c. The following have limited evidence but should be considered due to ease and limited risk:
   i. Reorient patient.
   ii. Provide reading glasses, hearing aids if applicable.
   iii. Encourage family involvement and cognitive stimulation at bedside.
   iv. Remove restraints, Foley catheters, and other medical devices if possible.
   v. Improve sleep architecture (note that there is no evidence for melatonin or quetiapine in this regard) via focusing on keeping in-patient room lights on during the day and off at night, reducing night-time sleep interruption through reduction in ICU noise levels, and batched lab work, radiology, and procedures.

3. **Pharmacological approach:**
   a. There is very little evidence for prophylactic treatment of delirium, and this is limited to the cardiac surgical population where risperidone has been found effective in a small studies.  
   b. For severe hyperactive delirium (CAM-ICU positive and RASS +3 or +4): consider bolus propofol (if mechanically ventilated) or intravenous haloperidol to control delirium that would endanger the patient.
   c. For hyperactive delirium (CAM-ICU positive and RASS +1 or +2): consider scheduled or as needed (PRN) atypical antipsychotics. Except risperidone as mentioned above, there is insufficient evidence to recommend any particular medication within the class. There is no evidence that haloperidol decreases delirium in critically ill patients but may reduce hyperactive symptomology.
   d. For hypoactive delirium (CAM-ICU positive and RASS 0 to -3): consider reducing sedatives and other deliriogenic medications.
   e. Dexmedetomidine should be considered for patients requiring sedation in whom weaning from mechanical ventilation is hampered by delirium. Dexmedetomidine may also reduce duration of delirium in mechanically ventilated patients with delirium as compared to benzodiazepines.

**Background Information and Literature Review**

Critically ill mechanically ventilated patients require analgesia, and frequently sedation, to tolerate mechanical ventilation, medical procedures, reduce stress response, decrease risk of self-injury, and decrease oxygen consumption. Unfortunately continuous sedative use is also associated with worsened patient outcomes including longer duration of mechanical ventilation, ICU length of stay, and higher rates of delirium. Delirium is a manifestation of brain organ dysfunction and is associated with worse clinical outcomes including risk of death and cognitive impairment.

The 2013 update of the Society of Critical Care Medicine guidelines for management describes a stepwise process that begins with pain assessment and analgesia. Only if pain is adequately treated and the patient is still agitated should a sedative be added. Benzodiazepines are discouraged in favor of either propofol or dexmedetomidine. Ultimately, sedation should be minimized whenever possible to improve patient outcomes via targeting light levels of sedation or performing daily awakening trials.
Delirium treatment remains somewhat controversial. The role of nonpharmacologic therapies has not been firmly established but should be considered given their generally safe and inexpensive nature. Early mobility is an important exception and should be strongly encouraged.\textsuperscript{4} Atypical antipsychotics are believed to decrease the duration of delirium although there is no evidence that one is better than the other.\textsuperscript{9,10} There is no evidence that haloperidol decreases delirium duration though may help in acute agitation to reduce hyperactive delirium symptoms. It is extremely important to screen all intensive care patients daily for both pain, level of agitation or sedation and delirium. Pain may be unrecognized or under-reported by patients – especially those who are mechanically ventilated or unable to speak. Similarly, a high percentage of delirium may be hypoactive and thus unappreciated or ignored.\textsuperscript{11} Recommendations for particular drug therapies is severely limited due to the lack of large, well-designed studies on the specific population of critically ill adults. Additionally, there is sparse data on treatment of different subsets of critically ill patients such as cardiac, general surgical, and neurology/neurosurgical.\textsuperscript{12,13} Because of this the general principles in this document should apply to those patients as well though specific extrapolations are obviously arguable. Sleep aids, such as quetiapine and melatonin, have similarly limited data and thus no recommendations can be made.\textsuperscript{14}

Authors:

Chris Cropsey, Wayne Babcock, Pratik Pandharipande

Approval Date:
**Analgesia/Sedation Protocol for Mechanically Ventilated Patients**

1. **In pain?**
   - Yes: Bolus dosing prn with either:
     - Fentanyl 50-100 mcg
     - Hydromorphone 0.1-0.3 mg
     - Morphine 2-5 mg
   - No: Controlled or anticipated control with < 3 bolus doses/hr

2. **At RASS target?**
   - Yes: Reassess often
   - No: Under-sedated

   *Propofol 5-30 mcg/kg/min*
   *Dexmed 0.2-1.5 mcg/kg/hr (if delirious\(^*/\) /weaning)*
   *Midazolam 1-3 mg prn\(^*\)*
   *(ETOH withdrawal or propofol intolerance\(^*\)).*

3. **CAM-ICU negative**
   - Reassess q 6-12 hrs

4. **CAM-ICU positive**
   - Non pharm management
   - Pharm management

**Over-sedated**
- Hold sedative/analgesics to achieve RASS target. Restart at 50% if clinically indicated

**SAT+SBT daily Physical therapy**

---

\(^*\) Midazolam 1-3 mg/hr gtt rarely if > 2 midaz boluses/hr and propofol intolerance
\(^*\) Propofol intolerance refers to propofol infusion syndrome, hemodynamic instability, increasing CPK >5000 IU/L, triglycerides >500 mg/dl or use >96 hrs
\(^*\) Start analgesics and sedatives at lowest dose and titrate in increments of 50% to achieve target pain and sedation goals respectively.
References:

**PAIN, AGITATION-SEDATION, DELIRIUM**

**Assess and Treat**

<table>
<thead>
<tr>
<th>Statements and Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Pain assessment should be routinely performed in all ICU patients (1B).</td>
</tr>
<tr>
<td>• Self report is preferred over the use of behavioral pain scales to assess pain in ICU patients who are able to communicate (B).</td>
</tr>
<tr>
<td>• The BPS and CPOT are the most valid and reliable behavioral pain scales for use in ICU patients who cannot communicate (B).</td>
</tr>
<tr>
<td>• Vital signs should not be used alone to assess pain, but they may be used adjunctively for pain assessments (2C).</td>
</tr>
<tr>
<td>• Preemptively treat chest tube removal with either analgesics and/or non-pharmacologic therapy (1C).</td>
</tr>
<tr>
<td>• Suggest preemptively treating other types of procedural pain with analgesic and/or non-pharmacologic therapy (2C).</td>
</tr>
<tr>
<td>• Use opioids as first line therapy for treatment of non-neuropathic pain (1C).</td>
</tr>
<tr>
<td>• Suggest using non-opioid analgesics in conjunction with opioids to reduce opioid requirements and opioid-related side effects (2C).</td>
</tr>
<tr>
<td>• Use gabapentin or carbamazepine, in addition to intravenous opioids, for treatment of neuropathic pain (1A).</td>
</tr>
<tr>
<td>• Use thoracic epidural for postoperative analgesia in abdominal aortic surgery patients (1B).</td>
</tr>
<tr>
<td>• Suggest thoracic epidural analgesia be used for patients with traumatic rib fractures (2B).</td>
</tr>
</tbody>
</table>

---

**AGITATION**

<table>
<thead>
<tr>
<th>Statements and Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Depth and quality of sedation should be routinely assessed in all ICU patients (1B).</td>
</tr>
<tr>
<td>• The RASS and SAS are the most valid and reliable scales for assessing quality and depth of sedation in ICU patients (B).</td>
</tr>
<tr>
<td>• Suggest using objective measures of brain function to adjunctively monitor sedation in patients receiving neuromuscular blocking agents (2B).</td>
</tr>
<tr>
<td>• Use EEG monitoring either to monitor non-convulsive seizure activity in ICU patients at risk for seizures, or to titrate electrocorticographic medication to achieve burst suppression in ICU patients with elevated intracranial pressure (1A).</td>
</tr>
<tr>
<td>• Target the lightest possible level of sedation and/or use daily sedative interruption (1B).</td>
</tr>
<tr>
<td>• Use sedation protocols and checklists to facilitate ICU sedation management (1B).</td>
</tr>
<tr>
<td>• Suggest using analgesia-first sedation for intubated and mechanically ventilated ICU patients (2B).</td>
</tr>
<tr>
<td>• Suggest using non-benzodiazepines for sedation (either propofol or dexmedetomidine) rather than benzodiazepines (either midazolam or lorazepam) in mechanically ventilated adult ICU patients (2B).</td>
</tr>
</tbody>
</table>

---

**DELIRIUM**

<table>
<thead>
<tr>
<th>Statements and Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Delirium assessment should be routinely performed in all ICU patients (1B).</td>
</tr>
<tr>
<td>• The CAM-ICU and ICDSC delirium monitoring tools are the most valid and reliable scales to assess delirium in ICU patients (A).</td>
</tr>
<tr>
<td>• Mobilize ICU patients early when feasible to reduce the incidence and duration of delirium, and to improve functional outcomes (1B).</td>
</tr>
<tr>
<td>• Promote sleep in ICU patients by controlling light and noise, clustering patient care activities, and decreasing stimuli at night (1C).</td>
</tr>
<tr>
<td>• Avoid using rivastigmine to reduce the duration of delirium in ICU patients (1B).</td>
</tr>
<tr>
<td>• Suggest avoiding the use of antipsychotics in patients who are at risk for torsades de pointes (2B).</td>
</tr>
<tr>
<td>• Suggest not using benzodiazepines in ICU patients with delirium unrelated to ETOH/benzodiazepine withdrawal (2B).</td>
</tr>
</tbody>
</table>