**Supplemental Table 42. Evidence Summaries and Evidence-To-Decision-Tables for Sleep Group Actionable Questions**

Question: Sleep monitoring compared to no sleep monitoring for critically ill patients in ICU

| **Quality assessment** | **Impact**  | **Quality** | **Importance** |
| --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** |
| Identification of Sleep Disordered Breathing |
| 2  | observational studies  | not serious  | not serious  | serious a | serious b | none  | Prospective, observational studies of patients with acute coronary syndromes and the presence/absence of sleep disordered breathing. Saito et al studied 49 patients and 17 healthy controls and found a higher number of apneic episodes per hour in the patients some of which were accompanied by oxygen desaturation. 11/49 patients had > 30 apneas/hr, 21/49 had oxygen saturation associated with the apneas and 16 of these 21 had accompanying arrhythmias (the majority were PAC’s). Full PSG was NOT performed; just respiratory polygraphy and hemodynamic monitoring. Van den Broecke et al. studied 27 patients with complete PSG early after admission as a screen for sleep disordered breathing. 82% had AHI > 15/hr. The majority of SDB was central. They also found that respiratory monitoring alone (“respiratory polygraphy”) underestimated AHI for central sleep disordered and periodic breathing but not obstructive sleep disordered breathing. Comment: In neither study was an outcome directly associated with the diagnosis.  | ⨁◯◯◯VERY LOW  | CRITICAL  |
| Need for Sedation |
| 1  | observational studies  | not serious  | not serious  | not serious  | very serious c | none  | Mistraletti et al. used actigraphy in 13 mechanically ventilated patients in a preliminary, prospective, observational trial to determine if motor activity could be used to monitor neurologic status and potentially contribute to sedation management. Actigraphically recorded movements were related to other measures of neurologic status such as sleep hours, RASS score, pain and anxiety. Comment: This was a preliminary study that suggested that such monitoring could be used to prevent too much/too little sedation.  | ⨁◯◯◯VERY LOW  | CRITICAL  |
| Neuro-prognostication |
| 2  | observational studies  | not serious  | not serious  | not serious  | not serious  | none  | Two studies that found a relationship between electroencephalographic characteristics of sleep and prognosis according to the Glasgow Outcome Scale. Valente et al. [1] studied 24 patients with traumatic brain injury with PSG for 24 hours at the subacute stage (at least 24 hr after sedative and neuroprotective drugs were withdrawn). PSG sleep pattern organization outperformed both Glasgow Coma Score and neuroimaging as a predictor of prognosis. Sutter et al. [2] performed an observational study of 142 patients with encephalopathy to determine if the finding of sleep elements on EEG are associated with a favorable outcome. The main finding was that only the presence of K-complexes was independently and significantly associated with a good outcome. Comment: interesting, plausible, and somewhat consistent findings suggest that features of the EEG in brain injured patients can contribute to prognosis.  | ⨁⨁◯◯LOW  | CRITICAL  |
| Need for intubation |
| 3  | observational studies  | not serious  | not serious  | serious d | serious b | none  | Bahammam et al. [3] studied 11 subject suspected of having SDB on the basis of clinical and historical features (from family members) who were admitted with acute hypercapneic respiratory failure. All had cor pulmonale. All but one was confirmed to have OSA and all but two had sleep hypoventilation syndrome. The authors believe that early diagnosis and appropriate treatment of the underlying problem may have helped avoid intubation for most patients (only 3/11 patients were intubated). They additionally followed patients months later and found mostly good compliance and improvements in daytime oxygen and CO2. Roche Campo et al. [4] studied 27 patients admitted to ICU with hypercapneic respiratory failure treated with non-invasive ventilation to see if late failure (need for invasive ventilation) could be predicted. They did PSG for 17 hr from day 2-4 after initiation of NPPV. Patients who failed NPPV had more abnormal EEG (absence of typical sign of wakefulness or sleep), circadian disruption, and less REM sleep. Interestingly the late NPPV failure patients also had a higher rate of delirium. Buckle et al. [5] studied 9 patients in hypercapneic and hypoxic respiratory failure prior to intubation. 7/9 had cor pulmonale. None had known SDB but 2 had severe OSA, 3 had CSA, 4 had hypoventilation with or without obstructive apneas. PSG was only for up to 3 hr during the day. 4/9 were intubated prior to PSG. This was mostly a feasibility study to determine if safe to study acutely ill patients in RF. But they ask the question of whether early diagnosis could lead to avoidance of intubation; however, they cannot make that conclusion based on their study. Comment: plausible but not feasible/generalizable to do PSG early in patients with acute respiratory failure to try to avoid intubation. No conclusion on the success of such a strategy can be made from these studies anyway.  | ⨁◯◯◯VERY LOW  | CRITICAL  |

**CI:** Confidence interval

**Explanations**

a. All patients studied had acute coronary syndrome. Also unclear that sleep disordered breathing was clinically significant.

b. Small number of patients leading to imprecise conclusions.

c. Very small number of patients, only a feasibility study or proof of concept.

d. Various sleep monitoring algorithms and techniques employed. All patients studied across 3 studies had underlying respiratory disease.

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| --- | --- |
| **Question** |  |
| Should sleep monitoring vs. no sleep monitoring be used for critically ill patients in ICU?  |
| Population:  | critically ill patients in ICU  | Background:  |  |
| Intervention:  | sleep monitoring  |  |
| Comparison:  | no sleep monitoring  |  |
| Main outcomes:  | * Identification of Sleep Disordered Breathing
* Need for Sedation
* Neuro-prognostication
* Need for intubation
 |  |
| **Assessment** |
|  | **Criteria**  | **Judgements**  | **Research evidence**  | **Additional considerations**  |
| Problem | **Is there a problem priority?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  |  |
| Benefits & harms of the options | **What is the overall certainty of this evidence?**  | ○ No included studies ● Very low ○ Low ○ Moderate ○ High  | **The relative importance or values of the main outcomes of interest:**

| **Outcome** | **Relative importance**  | **Certainty of the evidence (GRADE)**  |
| --- | --- | --- |
| Identification of Sleep Disordered Breathing | CRITICAL | ⨁◯◯◯VERY LOW |
| Need for Sedation | CRITICAL | ⨁◯◯◯VERY LOW |
| Neuro-prognostication | CRITICAL | ⨁⨁◯◯LOW |
| Need for intubation | CRITICAL | ⨁◯◯◯VERY LOW |

 |  |
| **Is there important uncertainty about how much people value the main outcomes?**  | ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability ○ No known undesirable outcomes  |
| **Are the desirable anticipated effects large?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  |
| **Are the undesirable anticipated effects small?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  |
| **Are the desirable effects large relative to undesirable effects?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  |
| Resource use | **Are the resources required small?**  | ○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |  |  |
| **Is the incremental cost small relative to the net benefits?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  |  |  |
| Equity | **What would be the impact on health inequities?**  | ○ Increased ● Probably increased ○ Uncertain ○ Probably reduced ○ Reduced ○ Varies  | Resource-poor centers would be less able to provide monitoring. |  |
| Acceptability | **Is the option acceptable to key stakeholders?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  |  |  |
| Feasibility | **Is the option feasible to implement?**  | ○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |  |  |

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| **Recommendation** **Should sleep monitoring vs. no sleep monitoring be used for critically ill patients in ICU?** |
| **Balance of consequences**  | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
|  | ○ | ○ | ○ | ○ | ○ |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Type of recommendation**  | We recommend against offering this option | We suggest not offering this option | We suggest offering this option | We recommend offering this option |
|  | ○ | ● | ○ | ○ |
| **Recommendation**  | We suggest against the use of routine physiologic monitoring for sleep in critically ill patients in the ICU. |
| **Justification**  | Gold standard for sleep monitoring in critically ill patients is unknown but may be very costly and labor-intensive with uncertain benefit in broad ICU population.  |
| **Subgroup considerations**  | In patients with acute coronary syndromes, sleep disordered breathing may be identified, often central, but outcomes were not demonstrably improved. Identification of sleep elements of EEG, ie REM and/or NREM and K complexes, has favorable prognostic significance for patients with neurologic injury or encephalopathy.Monitoring patients who present with hypercapneic respiratory failure may help identify those patients likely to fail NIV. |
| **Implementation considerations**  | Requires at least EEG and sometimes the ability to determine sleep stages which may not be readily accessible. |
| **Monitoring and evaluation**  |  |
| **Research possibilities**  | If it were feasible to monitor a broad population of ICU patients, it might identify those patients for whom more aggressive measures to facilitate sleep, pharmacologic or non-pharmacologic measures, might improve outcomes. Monitoring with PSG, however, is costly and cumbersome. Increased monitoring (i.e. with pt questionnaires…. ) should be studied to see if it would raise provider awareness and potentially improve pt satisfaction. |
| **Comments during electronic voting by entire panel** | Crucial to explain in there is simply not enough evidence to justify the cost in labor, equipment, etc. & equally important to reinforce the importance of asking patients and nurses about sleep even just as an ICU quality of life issue for which there is ample data. We are not recommending "against" monitoring; just not routine, physiologic monitoring. Agree with conditional not using routine physiologic sleep monitoring, not to be confused with subjective assessment of sleep quality |

**Question: Assist control mode ventilation compared to pressure support ventilation for improving sleep in critically ill adults**

| **Quality assessment** | **№ of patients** | **Effect** | **Quality** | **Importance** |
| --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **assist control mode ventilation** | **pressure support ventilation** | **Relative(95% CI)** | **Absolute(95% CI)** |
| Sleep Efficiency |
| 3  | randomised trials  | serious a | not serious  | not serious  | not serious  | none  | 61  | 61  | -  | MD **18.33 higher**(7.89 higher to 28.76 higher)  | ⨁⨁⨁◯MODERATE  | IMPORTANT  |
| Stage 1 Sleep |
| 2  | randomised trials  | serious a | not serious  | not serious  | serious b | none  | 41  | 41  | -  | MD **0.31 higher**(5.17 lower to 5.79 higher)  | ⨁⨁◯◯LOW  | IMPORTANT  |
| Stage 2 Sleep |
| 2  | randomised trials  | serious a | serious c | not serious  | serious b | none  | 41  | 41  | -  | MD **5.29 higher**(4.38 lower to 14.97 higher)  | ⨁◯◯◯VERY LOW  | IMPORTANT  |
| Stage 3 and 4 Sleep |
| 1  | randomised trials  | serious a | not serious  | not serious  | very serious d | none  | 15  | 15  | -  | MD **11 higher**(22.49 lower to 44.49 higher)  | ⨁◯◯◯VERY LOW  | IMPORTANT  |
| REM Sleep |
| 2  | randomised trials  | serious a | not serious  | not serious  | serious e | none  | 41  | 41  | -  | MD **2.79 higher**(0.53 higher to 5.05 higher)  | ⨁⨁◯◯LOW  | IMPORTANT  |

**CI:** Confidence interval; **MD:** Mean difference

#### Explanations

a. Both studies were unblinded with intervention. Other ROB domains not always reported.

b. Wide confidence intervals.

c. High Isquared with point estimates and confidence intervals on either side of unity.

d. Wide confidence intervals and small number of patients.

e. Despite confidence intervals that do not cross 1, a very small number of patients.

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| **Question** |  |
| Should assist control mode ventilation vs. pressure support ventilation be used for improving sleep in critically ill adults?  |
| Population:  | improving sleep in critically ill adults  | Background:  |  |
| Intervention:  | assist control mode ventilation  |  |
| Comparison:  | pressure support ventilation  |  |
| Main outcomes:  | * Sleep Efficiency
* Stage 1 Sleep
* Stage 2 Sleep
* Stage 3 Sleep
* REM Sleep
 |  |
| **Assessment** |
|  | **Criteria**  | **Judgements**  | **Research evidence**  | **Additional considerations**  |
| Problem | **Is there a problem priority?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  |  |
| Benefits & harms of the options | **What is the overall certainty of this evidence?**  | ○ No included studies ○ Very low ○ Low ● Moderate ○ High  | **The relative importance or values of the main outcomes of interest:**

| **Outcome** | **Relative importance**  | **Certainty of the evidence (GRADE)**  |
| --- | --- | --- |
| Sleep Efficiency | IMPORTANT | ⨁⨁⨁◯MODERATE |
| Stage 1 Sleep | IMPORTANT | ⨁⨁◯◯LOW |
| Stage 2 Sleep | IMPORTANT | ⨁◯◯◯VERY LOW |
| REM Sleep | IMPORTANT | ⨁⨁◯◯LOW |

 | Serious imprecision (wide CIs) for most outcomes. Desirable effects on sleep efficiency. |
| **Is there important uncertainty about how much people value the main outcomes?**  | ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability ○ No known undesirable outcomes  |
| **Are the desirable anticipated effects large?**  | ○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |
| **Are the undesirable anticipated effects small?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |
| **Are the desirable effects large relative to undesirable effects?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |
| Resource use | **Are the resources required small?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies |  | All ventilators capable of assist control and PSV modes. |
| **Is the incremental cost small relative to the net benefits?**  | ○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |  | Little or no net benefit |
| Equity | **What would be the impact on health inequities?**  | ○ Increased ○ Probably increased ● Uncertain ○ Probably reduced ○ Reduced ○ Varies  |  | Assist vent modes probably always an available alternative. |
| Acceptability | **Is the option acceptable to key stakeholders?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |  |  |
| Feasibility | **Is the option feasible to implement?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  |  |

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| --- |
| **Recommendation** **Should assist control mode ventilation vs. pressure support ventilation be used for improving sleep in critically ill adults?** |
| **Balance of consequences**  | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
|  | ○ | ○ | ○ | ● | ○ |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Type of recommendation**  | We recommend against offering this option | We suggest not offering this option | We suggest offering this option | We recommend offering this option |
|  | ○ | ○ | ● | ○ |
| **Recommendation**  | Assist control may improve sleep.we suggest offering assist control over pressure support ventilation for improving sleep in the critically ill patient |
| **Justification**  | Sleep efficiency and REM sleep were improved on assist control over psvmore studies needed -  small amount of imprecise evidence. |
| **Comments during electronic voting by entire panel** | I support the recommendation based solely on the data, and am certain that sleep will not always be enhanced by Assist control vs PSV and that it will be individual. The ultimate rationale will have to highlight that it should be a case-by-case decision and that a reference to the cohorts in the included studies might be considered. In the Tobin paper, for example, it was only the patients with CHF who benefited from ACV. 2.This recommendation seems to be heavily weighed based on sleep efficiency since that is only outcome that is impacted by AC. I am also concerned about practioners sedating patients to achieve AC when they may not have needed it on PS3.Asynchrony would be an interesting dimension to bring up with AC (and contrast to PSV in asynchrony propability as well as the effect of mode itself)4.I think that the text should indicate if this recommendation is suggesting that ventilator modes be changed at night. What are the implications....is it simply for decision making for daytime mode that will be best for night or (For example if you are choosing b/t two then AC is better for nighttime sleep.) or is it suggesting change be made at night if pt is on anything but AC (If you are on PS during the day, you should change to AC at night.)? Text should help focus interpret this. 5.Can the team members be more specific about when to offer AC - is this for all patients who are weaning from MV? RE: considerations in text - what evidence supports the suggestion to sedate patients on AC and what type of agents? It appears that this recommendation is mainly based on sleep efficiency outcome with one small and high risk-of-bias randomized controlled trial supporting it. I am not sure of the clinical importance of the sleep efficiency outcome or the strength of this RCT, especially when use of AC (vs PS) may require additional sedation that may cause harm. I am concerned that the evidence is not strong enough and the outcome is not important enough especially relative to this potential harm 2. Not convinced one is better than the other based on the data. Would favor a no recommendation, future studies 3. This recommendation implies that PSV is harmful. Based on 3 very small studies with total of 60 patients in each group. Thousand of patients are treated with PSV every day and night and we should not even suggest that this is wrong without reasonable evidence.It appears that this recommendation is mainly based on sleep efficiency outcome with one small and high risk-of-bias randomized controlled trial supporting it. I am not sure of the clinical importance of the sleep efficiency outcome or the strength of this RCT, especially when use of AC (vs PS) may require additional sedation that may cause harm. I am concerned that the evidence is not strong enough and the outcome is not important enough especially relative to this potential harm 2. Not convinced one is better than the other based on the data. Would favor a no recommendation, future studies 3. This recommendation implies that PSV is harmful. Based on 3 very small studies with total of 60 patients in each group. Thousand of patients are treated with PSV every day and night and we should not even suggest that this is wrong without reasonable evidence.Might be dangerous, text should detail that ACV shoul be considered after having improved PSV setting (no overassistance and associated alkalosis, no underassistance and associated fatigue, dyspnea, anxiety). Switching to ACV in an awake patient (by definition if it's for promoting sleep) would need to assess possible assynchrony and optimize vent setting to avoid any resedation... |

Question: Adaptive ventilation strategy compared to no such strategy for improving sleep in critically ill adults

| **Quality assessment** | **№ of patients** | **Effect** | **Quality** | **Importance** |
| --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **adaptive ventilation strategy** | **no such strategy**  | **Relative(95% CI)** | **Absolute(95% CI)** |
| Sleep Efficiency |
| 6  | randomised trials  | serious a | serious b | not serious  | not serious  | none  | 76  | 76  | -  | MD **6.73 higher**(1.49 higher to 11.96 higher)  | ⨁⨁◯◯LOW  | IMPORTANT  |
| Sleep Fragmentation |
| 5  | randomised trials  | serious a | serious b | not serious  | serious c | none  | 62  | 62  | -  | MD **1.73 lower**(4.79 lower to 1.33 higher)  | ⨁◯◯◯VERY LOW  | IMPORTANT  |
| Stage I Sleep |
| 6  | randomised trials  | serious a | not serious  | not serious  | serious d | none  | 62  | 62  | -  | MD **0.23 lower**(0.55 lower to 0.09 higher)  | ⨁⨁◯◯LOW  | IMPORTANT  |
| Stage 2 Sleep |
| 6  | randomised trials  | serious a | not serious e | not serious  | not serious  | none  | 62  | 62  | -  | MD **12.97 lower**(16.76 lower to 9.18 lower)  | ⨁⨁⨁◯MODERATE  | IMPORTANT  |
| Stage 3 and 4 Sleep |
| 1  | randomised trials  | serious a | not serious  | not serious  | very serious d | none  | 15  | 15  | -  | MD **2 lower**(33.85 lower to 29.85 higher)  | ⨁◯◯◯VERY LOW  | IMPORTANT  |
| REM Sleep |
| 6  | randomised trials  | serious a | serious b | not serious  | serious d | none  | 62  | 62  | -  | MD **0.16 higher**(0.2 lower to 0.51 higher)  | ⨁◯◯◯VERY LOW  | IMPORTANT  |
| Apneas (assessed with: # apneas/hr) |
| 3  | randomised trials  | serious a | not serious  | not serious  | very serious f | none  | 42  | 42  | -  | MD **2 fewer**(8.34 fewer to 4.34 more)  | ⨁◯◯◯VERY LOW  | IMPORTANT  |

**CI:** Confidence interval; **MD:** Mean difference

#### Explanations

a. Unblinded intervention in most studies. Unclear reporting of other ROB domains in many included studies.

b. High Isquared (>75%) with non overlapping confidence intervals.

c. Wide confidence intervals do not exclude harm.

d. Wide confidence intervals and small number of patients.

e. Isquared 60% however confidence intervals all found on same side of no effect.

f. Very small number of patients. Weight for meta-analysis all from a single study.

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| --- | --- |
| **Question** |  |
| Should adaptive ventilation strategy vs. no such strategy be used for improving sleep in critically ill adults?  |
| Population:  | improving sleep in critically ill adults  | Background:  |  |
| Intervention:  | adaptive ventilation strategy  |  |
| Comparison:  | no such strategy  |  |
| Main outcomes:  | * Sleep Efficiency
* Sleep Fragmentation
* Stage I Sleep
* Stage 2 Sleep
* REM Sleep
* Apneas
* Duration of Sleep
* Circadian Rhythmicity
* Delirium Occurrence
* Duration of Mechanical Ventilation
* Duration of ICU Stay
* ICU Mortality
 |  |
| **Assessment** |
|  | **Criteria**  | **Judgements**  | **Research evidence**  | **Additional considerations**  |
| Problem | **Is there a problem priority?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  | test |
| Benefits & harms of the options | **What is the overall certainty of this evidence?**  | ○ No included studies ○ Very low ● Low ○ Moderate ○ High  | **The relative importance or values of the main outcomes of interest:**

| **Outcome** | **Relative importance**  | **Certainty of the evidence (GRADE)**  |
| --- | --- | --- |
| Sleep Efficiency | IMPORTANT | ⨁⨁◯◯LOW |
| Sleep Fragmentation | IMPORTANT | ⨁◯◯◯VERY LOW |
| Stage I Sleep | IMPORTANT | ⨁⨁◯◯LOW |
| Stage 2 Sleep | IMPORTANT | ⨁⨁⨁◯MODERATE |
| REM Sleep | IMPORTANT | ⨁◯◯◯VERY LOW |
| Apneas | IMPORTANT | ⨁◯◯◯VERY LOW |
| Duration of Sleep | CRITICAL | - |

 | Values outcomes - subjective patient expressions more global assessment - don't consider these outcomes at this level of detail (eg REM, stage I, stage II)Sleep is an important outcome overall with limited variability in values however these outcomes have uncertainty.No data around certain sleep stages and patient perception. Patient (Ken) input suggests that patients may value these individual sleep outcomes more than thought if they understand them properly. Patient questionnaire correlation with sleep indices.Desirable effects - element of uncertainty given lack of many critical outcomes in reported literature. Perhaps uncertain vs probably no. more data may show more benefit but unable to say based on this evidence.Undesirable effects - probably small or small even without stage 3 and stage 4 data.Balance - not large desirable but compared to very small undesirable we think the balance is for net benefit however associated with large degree of uncertainty. |
| **Is there important uncertainty about how much people value the main outcomes?**  | ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability ○ No known undesirable outcomes  |
| **Are the desirable anticipated effects large?**  | ○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |
| **Are the undesirable anticipated effects small?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |
| **Are the desirable effects large relative to undesirable effects?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |
| Resource use | **Are the resources required small?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ● Varies  |  | Very ICU dependent - some ICUs the ventilators are already PAV compatible however if you don't have an adaptive ventilation mode then resources higher as would have to purchase these.Personnel resources are limited. |
| **Is the incremental cost small relative to the net benefits?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ● Varies  |  |  |
| Equity | **What would be the impact on health inequities?**  | ○ Increased ○ Probably increased ○ Uncertain ○ Probably reduced ○ Reduced ○ Varies  |  |  |
| Acceptability | **Is the option acceptable to key stakeholders?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  | Cost is the main variable to consider. |
| Feasibility | **Is the option feasible to implement?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |  | Again dependent on resources.Not a lot of staff training. |

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| --- |
| **Recommendation** **Should adaptive ventilation strategy vs. no such strategy be used for improving sleep in critically ill adults?** |
| **Balance of consequences**  | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
|  | ○ | ○ | ● | ○ | ○ |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Type of recommendation**  | We recommend against offering this option | We suggest not offering this option | We suggest offering this option | We recommend offering this option |
|  | ○ | ○ | ○ | ○ |
| **Recommendation**  | The panel did not make a recommendation regarding adaptive ventilation for sleep in critically ill. |
| **Justification**  | For centers with ventilators capable of providing adaptive ventiliation it is possible the benefits outweigh the harms and clinicians could consider using this ventilator mode to improve sleep.We could not recommend more widespread use pending further research. |
| **Subgroup considerations**  | not possible to make separate recommendations based on patients or ventilation mode due to low number of patients studied. |
| **Comments during electronic voting by entire panel** | This recommendation listed several outcomes, including ICU LOS and mortality in the EtoT profile, not reported in the GDT profile.What types of harm occurs with adaptive ventilation? |

**Question: NIV dedicated ventilator compared to NIV on an ICU ventilator for improving sleep in critically ill adults needing NIV**

| **Quality assessment** | **№ of patients** | **Effect** | **Quality** | **Importance** |
| --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **NIV dedicated ventilator** | **NIV on an ICU ventilator** | **Relative(95% CI)** | **Absolute(95% CI)** |
| Sleep Efficiency |
| 1  | randomised trials  | serious a | not serious  | not serious  | very serious b | none  | 12  | 12  | -  | MD **5 higher**(0.61 lower to 10.61 higher)  | ⨁◯◯◯VERY LOW  | IMPORTANT  |
| Stage 1 Sleep |
| 1  | randomised trials  | serious a | not serious  | not serious  | very serious b | none  | 12  | 12  | -  | MD **3.9 lower**(10.04 lower to 2.24 higher)  | ⨁◯◯◯VERY LOW  | IMPORTANT  |
| Stage 2 Sleep |
| 1  | randomised trials  | serious a | not serious  | not serious  | very serious b | none  | 12  | 12  | -  | MD **2 lower**(17.82 lower to 13.82 higher)  | ⨁◯◯◯VERY LOW  | IMPORTANT  |
| REM Sleep |
| 1  | randomised trials  | serious a | not serious  | not serious  | very serious b | none  | 12  | 12  | -  | MD **5 higher**(5.3 lower to 15.3 higher)  | ⨁◯◯◯VERY LOW  | IMPORTANT  |
| Sleep Fragmentation |
| 1  | randomised trials  | serious a | not serious  | not serious  | very serious b | none  | 12  | 12  | -  | MD **4 lower**(16.19 lower to 8.19 higher)  | ⨁◯◯◯VERY LOW  | IMPORTANT  |

**CI:** Confidence interval; **MD:** Mean difference

**Explanations**: a. Unblinded intervention. b. Confidence intervals wide. Very small number of patients and single trial.

|  |  |
| --- | --- |
| **Question** |  |
| Should NIV dedicated ventilator vs. NIV on an ICU ventilator be used for improving sleep in critically ill adults needing NIV?  |
| Population:  | improving sleep in critically ill adults needing NIV  | Background:  |  |
| Intervention:  | NIV dedicated ventilator  |  |
| Comparison:  | NIV on an ICU ventilator  |  |
| Main outcomes:  | * Sleep Efficiency
* Stage 1 Sleep
* Stage 2 Sleep
* REM Sleep
* Sleep Fragmentation
 |  |
| **Assessment** |
|  | **Criteria**  | **Judgements**  | **Research evidence**  | **Additional considerations**  |
| Problem | **Is there a problem priority?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  | NIV-dedicated vent availability is the main considertion, but most ICUs and/or resp med departments have these.. |
| Benefits & harms of the options | **What is the overall certainty of this evidence?**  | ○ No included studies ○ Very low ● Low ○ Moderate ○ High  | **The relative importance or values of the main outcomes of interest:**

| **Outcome** | **Relative importance**  | **Certainty of the evidence (GRADE)**  |
| --- | --- | --- |
| Sleep Efficiency | IMPORTANT | ⨁◯◯◯VERY LOW |
| Stage 1 Sleep | IMPORTANT | ⨁◯◯◯VERY LOW |
| Stage 2 Sleep | IMPORTANT | ⨁◯◯◯VERY LOW |
| REM Sleep | IMPORTANT | ⨁◯◯◯VERY LOW |
| Sleep Fragmentation | IMPORTANT | ⨁◯◯◯VERY LOW |

 | Single small study. Stage 1 and 2 were lower and REM was higher, sleep efficiency was higher and fragmentation lower. However CIs were large, ROB serious and quality low.Fragmentation related to asynchrony lower in ICU ventilator group - 14% v 28% in NIV-dedicated vent group.Little evidence of desirable effectLittle evidence of undesirable effects |
| **Is there important uncertainty about how much people value the main outcomes?**  | ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability ○ No known undesirable outcomes  |
| **Are the desirable anticipated effects large?**  | ● No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |
| **Are the undesirable anticipated effects small?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |
| **Are the desirable effects large relative to undesirable effects?**  | ○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |
| Resource use | **Are the resources required small?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |  | If purchase of NIV dedicated ventilators is required. |
| **Is the incremental cost small relative to the net benefits?**  | ○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |  |  |
| Equity | **What would be the impact on health inequities?**  | ○ Increased ○ Probably increased ● Uncertain ○ Probably reduced ○ Reduced ○ Varies  |  |  |
| Acceptability | **Is the option acceptable to key stakeholders?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  |  |  |
| Feasibility | **Is the option feasible to implement?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |  | With availability of a NIV-dedicated ventilator. |

|  |
| --- |
| **Recommendation** **Should NIV dedicated ventilator vs. NIV on an ICU ventilator be used for improving sleep in critically ill adults needing NIV?** |
| **Balance of consequences**  | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
|  | ○ | ○ | ● | ○ | ○ |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Type of recommendation**  | We recommend against offering this option | We suggest not offering this option | We suggest offering this option | We recommend offering this option |
|  | ○ | ● | ○ | ○ |
| **Recommendation**  | One study, 12 patients, if NIV dedicated vent not available it would not compromise patients' sleepWe make no recommendation regarding which ventilator type (NIV versus other) to use for improving sleep in the critically ill. |
| **Justification**  | No apparent sleep benefit of NIV dedicated ventilatorsEither ventilator performed suitably in the one included study. |
| **Comments during electronic voting by entire panel** | Neither technically 'improve' sleep and the semantics are confusing. Might triggering mechanisms may play a role also?Rec. based on one 24-pt study of 24 patien; do all ICU's (%? of ICU's) have these NIV options?The EtoD profile suggests that an NIV-dedicated ventilator should not be offered. |

**Question: Aromatherapy compared to no aromatherapy for improving sleep in critically ill adults**

| **Quality assessment** | **№ of patients** | **Effect** | **Quality** | **Importance** |
| --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **aromatherapy** | **no aromatherapy** | **Relative(95% CI)** | **Absolute(95% CI)** |
| Self reported Sleep |
| 2  | randomised trials  | serious a | not serious  | not serious  | serious b | none  | 53  | 53  | -  | SMD **0.02 SD higher**(0.36 lower to 0.41 higher)  | ⨁⨁◯◯LOW  | CRITICAL  |

**CI:** Confidence interval; **SMD:** Standardised mean difference

#### Explanations

a. Unblinded intervention. Some other domains had unclear ROB.

b. Wide confidence intervals do not exclude harm or benefit.

|  |  |
| --- | --- |
| **Question** |  |
| Should aromatherapy vs. no aromatherapy be used for improving sleep in critically ill adults?  |
| Population:  | improving sleep in critically ill adults  | Background:  |  |
| Intervention:  | aromatherapy  |  |
| Comparison:  | no aromatherapy  |  |
| Main outcomes:  | * Self reported Sleep
 |  |
| **Assessment** |
|  | **Criteria**  | **Judgements**  | **Research evidence**  | **Additional considerations**  |
| Problem | **Is there a problem priority?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  |  |
| Benefits & harms of the options | **What is the overall certainty of this evidence?**  | ○ No included studies ○ Very low ● Low ○ Moderate ○ High  | **The relative importance or values of the main outcomes of interest:**

| **Outcome** | **Relative importance**  | **Certainty of the evidence (GRADE)**  |
| --- | --- | --- |
| Self reported Sleep | CRITICAL | ⨁⨁◯◯LOW |

 | 2 small studies, total n=53, MD small and CIs wide |
| **Is there important uncertainty about how much people value the main outcomes?**  | ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability ○ No known undesirable outcomes  |
| **Are the desirable anticipated effects large?**  | ● No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |
| **Are the undesirable anticipated effects small?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |
| **Are the desirable effects large relative to undesirable effects?**  | ○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |
| Resource use | **Are the resources required small?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |  |  |
| **Is the incremental cost small relative to the net benefits?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  | No benefits so uncertain. |  |
| Acceptability | **Is the option acceptable to key stakeholders?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  | Low cost. Not much resources or trouble if you did it. Although no demonstratable benefit. |  |
| Feasibility | **Is the option feasible to implement?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |  |  |

|  |
| --- |
| **Recommendation** **Should aromatherapy vs. no aromatherapy be used for improving sleep in critically ill adults?** |
| **Balance of consequences**  | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
|  | ○ | ○ | ● | ○ | ○ |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Type of recommendation**  | We recommend against offering this option | We suggest not offering this option | We suggest offering this option | We recommend offering this option |
|  | ○ | ● | ○ | ○ |
| **Recommendation**  | We suggest not offering aromatherapy for improving sleep in critically ill adults. The results do not suggest this as a line of research worth pursuing. |
| **Justification**  | No clear benefit - no effect on sleep. Minimal harms or undesirables - if patients or practitioner felt strongly about it wouldn't be unreasonable. The only harm mentioned was triggered reactive airway disease or sensitivities.  |
| **Subgroup considerations**  | This data is in less severely ill patients. Really even more uncertain in more ill but hard to believe the effect would be stronger in sedated or more ill patients. |
| **Comments during electronic voting by entire panel** | recommendation was based on only one outcome. |

**Question: Acupressure compared to no acupressure for improving sleep in critically ill adults**

| **Quality assessment** | **№ of patients** | **Effect** | **Quality** | **Importance** |
| --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Acupressure** | **no acupressure** | **Relative(95% CI)** | **Absolute(95% CI)** |
| Duration of Sleep (assessed with: RN Observed) |
| 1  | randomised trials  | serious a | not serious  | not serious  | serious b | none  | 41  | 41  | -  | MD **1.1 hours higher**(0.39 higher to 1.81 higher)  | ⨁⨁◯◯LOW  | CRITICAL  |
| Duration of Sleep (assessed with: Actigraphy) |
| 1  | randomised trials  | serious a | not serious  | not serious  | serious b | none  | 41  | 41  | -  | MD **0.5 hours higher**(0.09 higher to 0.91 higher)  | ⨁⨁◯◯LOW  | CRITICAL  |
| Sleepiness (assessed with: Stanford scale) |
| 1  | randomised trials  | serious a | not serious  | not serious  | serious b | none  | 41  | 41  | -  | MD **0.4 lower**(0.66 lower to 0.14 lower)  | ⨁⨁◯◯LOW  | CRITICAL  |

**CI:** Confidence interval; **MD:** Mean difference

#### Explanations

a. Unclear allocation or randomization procedure. No blinding.

b. Confidence intervals exclude no effect however small number of patients and single study.

|  |  |
| --- | --- |
| **Question** |  |
| Should Acupressure vs. no acupressure be used for improving sleep in critically ill adults?  |
| Population:  | improving sleep in critically ill adults  | Background:  |  |
| Intervention:  | Acupressure  |  |
| Comparison:  | no acupressure  |  |
| Main outcomes:  | * Duration of Sleep
* Duration of Sleep
* Sleepiness
 |  |
| **Assessment** |
|  | **Criteria**  | **Judgements**  | **Research evidence**  | **Additional considerations**  |
| Problem | **Is there a problem priority?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  |  |
| Benefits & harms of the options | **What is the overall certainty of this evidence?**  | ○ No included studies ○ Very low ● Low ○ Moderate ○ High  | **The relative importance or values of the main outcomes of interest:**

| **Outcome** | **Relative importance**  | **Certainty of the evidence (GRADE)**  |
| --- | --- | --- |
| Duration of Sleep | CRITICAL | ⨁⨁◯◯LOW |
| Duration of Sleep | CRITICAL | ⨁⨁◯◯LOW |
| Sleepiness | IMPORTANT | ⨁⨁◯◯LOW |

 | Actigraphy and nurse observations known to be unreliable; MD lower with intervention for daytime sleepiness.  CIs wide and serious ROB.Desirable effects - uncertainty given small numbers however all 3 captured outcomes trended towards benefit of acupressure. |
| **Is there important uncertainty about how much people value the main outcomes?**  | ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability ○ No known undesirable outcomes  |
| **Are the desirable anticipated effects large?**  | ○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |
| **Are the undesirable anticipated effects small?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |
| **Are the desirable effects large relative to undesirable effects?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  |
| Resource use | **Are the resources required small?**  | ○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |  | Depends on health care setting -- availability of practitioner of acupressure.For example in US - not readily available and might require additional personnel. Similar in AUS. |
| **Is the incremental cost small relative to the net benefits?**  | ○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |  | Unless a country that already has staff capable of providing this intervention. |
| Equity | **What would be the impact on health inequities?**  | ○ Increased ○ Probably increased ● Uncertain ○ Probably reduced ○ Reduced ○ Varies  |  |  |
| Acceptability | **Is the option acceptable to key stakeholders?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |  | Comes back to cost again given minimal benefit.  |
| Feasibility | **Is the option feasible to implement?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |  | If a skilled acupressure practitioner is available only. |

|  |
| --- |
| **Recommendation** **Should Acupressure vs. no acupressure be used for improving sleep in critically ill adults?** |
| **Balance of consequences**  | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
|  | ○ | ○ | ● | ○ | ○ |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Type of recommendation**  | We recommend against offering this option | We suggest not offering this option | We suggest offering this option | We recommend offering this option |
|  | ○ | ● | ○ | ○ |
| **Recommendation**  | We suggest not offering acupressure to improve sleep in critically ill adults.  |
| **Justification**  | This recommendation is based on lack of evidence highlighting benefit and the resources required. In some cultures acupressure is more prevalent and accepted and this may be more useful.Also may be more beneficial in resource-rich setting with expertise and available practitioners. |
| **Subgroup considerations**  | Important to keep in mind the data we have is from less sick patients (APS <15). We are even less certain in the sicker and more sedated ICU patients. |
| **Implementation considerations**  | If we were to implement see comments above re: trained practitioners. |
| **Monitoring and evaluation**  |  |
| **Research possibilities**  | Further RCTs examining this intervention and the effect on ICU sleep.Better outcome measures to be included in these studies (eg self report, potentially polysomnography or Richard Campbell self reporting). |

**Question: Music compared to no music for improving sleep in critically ill adults**

| **Quality assessment** | **№ of patients** | **Effect** | **Quality** | **Importance** |
| --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **music** | **no music** | **Relative(95% CI)** | **Absolute(95% CI)** |
| Sleep Quality (assessed with: VSH Sleep Scale) |
| 1  | randomised trials  | serious a | not serious  | not serious  | very serious b | none  | 14  | 14  | -  | MD **48 higher**(34.52 lower to 130.52 higher)  | ⨁◯◯◯VERY LOW  | CRITICAL  |
| Sleep Efficiency |
| 1  | randomised trials  | serious a | not serious  | not serious  | very serious b | none  | 14  | 14  | -  | MD **2.3 higher**(27.36 lower to 31.96 higher)  | ⨁◯◯◯VERY LOW  | CRITICAL  |

**CI:** Confidence interval; **MD:** Mean difference

#### Explanations

a. Lack of blinding of intervention.

b. Small number of patients and wide confidence intervals.

|  |  |
| --- | --- |
| **Question** |  |
| Should music vs. no music be used for improving sleep in critically ill adults?  |
| Population:  | improving sleep in critically ill adults  | Background:  |  |
| Intervention:  | music  |  |
| Comparison:  | no music  |  |
| Main outcomes:  | * Sleep Quality
* Sleep Efficiency
 |  |
| Setting:  |  |  |
| Perspective:  |  |  |
| **Assessment** |
|  | **Criteria**  | **Judgements**  | **Research evidence**  | **Additional considerations**  |
| Problem | **Is there a problem priority?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  | 14/group and wide CIs |
| Benefits & harms of the options | **What is the overall certainty of this evidence?**  | ○ No included studies ● Very low ○ Low ○ Moderate ○ High  | **The relative importance or values of the main outcomes of interest:**

| **Outcome** | **Relative importance**  | **Certainty of the evidence (GRADE)**  |
| --- | --- | --- |
| Sleep Quality | CRITICAL | ⨁◯◯◯VERY LOW |
| Sleep Efficiency | CRITICAL | ⨁◯◯◯VERY LOW |

 | Self-reported sleep quality (VSH) and 2 h PSG (nocturnal) |
| **Is there important uncertainty about how much people value the main outcomes?**  | ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability ○ No known undesirable outcomes  |
| **Are the desirable anticipated effects large?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  |
| **Are the undesirable anticipated effects small?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |
| **Are the desirable effects large relative to undesirable effects?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  |
| Resource use | **Are the resources required small?**  | ○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |  | Patients were in single rooms only, music played on CD player"Relaxiing music" composed especially for the study |
| **Is the incremental cost small relative to the net benefits?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  |  |  |
| Acceptability | **Is the option acceptable to key stakeholders?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  |  | If especially composed music, single rooms and CD players required |
| Feasibility | **Is the option feasible to implement?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  |  | Depends on source of music and means of music delivery |

|  |
| --- |
| **Recommendation** **Should music vs. no music be used for improving sleep in critically ill adults?** |
| **Balance of consequences**  | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
|  | ○ | ○ | ● | ○ | ○ |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Type of recommendation**  | We recommend against offering this option | We suggest not offering this option | We suggest offering this option | We recommend offering this option |
|  | ○ | ● | ○ | ○ |
| **Recommendation**  | Intervention tested may not be feasible in many ICUs |
| **Justification**  | Too little evidence but worth investigating further. |
| **Comments during electronic voting by entire panel** | too little data for a recommendation for or against; single RCT with 28 patients. I vote for "no recommendation".Music needs to be defined. Music was provided in the room & against the recommendation of decreasing noise intensity at night. Short session of musictherapy using specific scores with decreasing music intensity and tempo to get patients relaxed were not tested except for pain and anxiety… would suggest either rephrazing (systematically providing music in the room at night) or no recommendation for promoting sleep in absence of pain or anxiety.caveats as to baseline habits, alternative relaxation techniques for those who do (and don't) find music useful, and identifying gaps and heterogeneity on the topic; perhaps add - "routine use" according to patient preference or request? |

**Question: A noise or light reduction strategy compared to no such strategy for improving sleep in critically ill adults**

| **Quality assessment** | **№ of patients** | **Effect** | **Quality** | **Importance** |
| --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **a noise or light reduction strategy** | **no such strategy** | **Relative(95% CI)** | **Absolute(95% CI)** |
| Quantity of Sleep (assessed with: Achieving >4hrs of sleep) |
| 2  | observational studies  | not serious  | not serious  | not serious  | serious a | none  | 39/84 (46.4%)  | 33/78 (42.3%)  | **RR 1.20**(0.64 to 2.24)  | **85 more per 1,000**(from 152 fewer to 525 more)  | ⨁◯◯◯VERY LOW  | CRITICAL  |
| Self Reported Sleep |
| 1 b | randomised trials  | serious c | not serious  | not serious  | serious d | none  | 20  | 20  | -  | MD **5 higher**(2.19 higher to 7.81 higher)  | ⨁⨁◯◯LOW  | CRITICAL  |
| Delirium (assessed with: NEECHAM Score (higher better)) |
| 1  | randomised trials  | not serious  | not serious  | not serious  | serious e | none  | 69  | 67  | -  | MD **2 higher**(0.11 higher to 3.89 higher)  | ⨁⨁⨁◯MODERATE  | CRITICAL  |
| Sleep Efficiency |
| 1  | randomised trials  | serious c | not serious  | not serious  | very serious a | none  | 20  | 20  | -  | MD **2 lower**(6.26 lower to 2.26 higher)  | ⨁◯◯◯VERY LOW  | IMPORTANT  |
| Sleep Fragmentation |
| 1  | randomised trials  | serious c | not serious  | not serious  | serious e | none  | 20  | 20  | -  | MD **2 higher**(10.4 lower to 14.4 higher)  | ⨁⨁◯◯LOW  | IMPORTANT  |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. Wide confidence intervals and small number of patients.

b. Based on single study (Le Guen 2014). Van Rompaey 2012 also showed significant benefit in patient reported sleep in those wearing ear plugs but did not present numbers with SD or SE and therefore could not be pooled.

c. Lack of blinding may have influenced subjective outcome.

d. Confidence intervals exclude no effect however small number of patients from single centre.

e. Small number of events or patients.

|  |  |
| --- | --- |
| **Question** |  |
| Should a noise or light reduction strategy vs. no such strategy be used for improving sleep in critically ill adults?  |
| Population:  | improving sleep in critically ill adults  | Background:  |  |
| Intervention:  | a noise or light reduction strategy  |  |
| Comparison:  | no such strategy  |  |
| Main outcomes:  | * Quantity of Sleep
* Self Reported Sleep
* Sleep Efficiency
* Sleep Fragmentation
* REM Sleep
 |  |
| **Assessment** |
|  | **Criteria**  | **Judgements**  | **Research evidence**  | **Additional considerations**  |
| Problem | **Is there a problem priority?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  | Quality of sleep, self-reported sleep, sleep efficiency, REM improved.- Nonvent PACU patients- HDU patients, 73% extubated, 25% trachs.all studies used eye shades and ear plugs |
| Benefits & harms of the options | **What is the overall certainty of this evidence?**  | ○ No included studies ○ Very low ● Low ○ Moderate ○ High  | **The relative importance or values of the main outcomes of interest:**

| **Outcome** | **Relative importance**  | **Certainty of the evidence (GRADE)**  |
| --- | --- | --- |
| Quantity of Sleep | CRITICAL | ⨁⨁◯◯LOW |
| Self Reported Sleep | CRITICAL | ⨁⨁◯◯LOW |
| Sleep Efficiency | IMPORTANT | ⨁⨁◯◯LOW |
| Sleep Fragmentation | IMPORTANT | ⨁⨁◯◯LOW |
| REM Sleep | IMPORTANT | ⨁⨁◯◯LOW |

 | Wide CIsEspecially for quality of sleep and probably delirium. |
| **Is there important uncertainty about how much people value the main outcomes?**  | ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability ○ No known undesirable outcomes  |
| **Are the desirable anticipated effects large?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |
| **Are the undesirable anticipated effects small?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |
| **Are the desirable effects large relative to undesirable effects?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |
| Resource use | **Are the resources required small?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  |  |
| **Is the incremental cost small relative to the net benefits?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |  |  |
| Equity | **What would be the impact on health inequities?**  | ○ Increased ○ Probably increased ● Uncertain ○ Probably reduced ○ Reduced ○ Varies  |  |  |
| Acceptability | **Is the option acceptable to key stakeholders?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |  | Patients had to be able to apply/remove earplugs and eye shades themselves. |
| Feasibility | **Is the option feasible to implement?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |  | In willing patients. |

|  |
| --- |
| **Recommendation** **Should a noise or light reduction strategy vs. no such strategy be used for improving sleep in critically ill adults?** |
| **Balance of consequences**  | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
|  | ○ | ○ | ● | ○ | ○ |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Type of recommendation**  | We recommend against offering this option | We suggest not offering this option | We suggest offering this option | We recommend offering this option |
|  | ○ | ○ | ● | ○ |
| **Recommendation**  | Apparent benefit in self-reported sleep quality, not costly |
| **Justification**  | May be able to be implemented in most crit care settings and many patients. |
| **Comments during electronic voting by entire panel** | Low evidence, low harmThe questions differ; the evidence profiles report noise OR light reduction strategies. Can we be more specific about the recommendation based on the evidence? Is it a light or noise reduction strategy, or both? |

**Question: Melatonin compared to no such strategy for improving sleep in critically ill adults**

| **Quality assessment** | **№ of patients** | **Effect** | **Quality** | **Importance** |
| --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **melatonin** | **no such strategy**  | **Relative(95% CI)** | **Absolute(95% CI)** |
| Delirium |
| 1  | randomised trials  | serious a | not serious  | serious b | very serious c | none  | 4/12 (33.3%)  | 1/12 (8.3%)  | **RR 4.00**(0.52 to 30.76)  | **250 more per 1,000**(from 40 fewer to 1,000 more)  | ⨁◯◯◯VERY LOW  | CRITICAL  |
| Sleep Awakenings |
| 1  | randomised trials  | serious a | not serious  | not serious  | very serious c | none  | 8  | 6  | -  | MD **0.4 fewer**(6.06 fewer to 5.26 more)  | ⨁◯◯◯VERY LOW  | CRITICAL  |
| Sleep Duration |
| 1  | randomised trials  | not serious  | not serious  | not serious  | very serious c | none  | 16  | 16  | -  | MD **3.4 minutes fewer**(55.96 fewer to 49.16 more)  | ⨁⨁◯◯LOW  | CRITICAL  |
| Sleep Quality (assessed with: BIS SEI and RCSQ) |
| 1  | randomised trials  | serious a | not serious  | not serious  | serious d | none  | 12  | 12  | -  | MD **0.09 lower**(0.14 lower to 0.04 lower)  | ⨁⨁◯◯LOW  | CRITICAL  |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations a. Some missing outcome data with a small number of patients. b. No details regarding how delirium was diagnosed. c. Very wide confidence intervals, very small number of events. Difficult to make any conclusions.

d. Very small number of patients despite relatively tight confidence intervals.

|  |  |
| --- | --- |
| **Question** |  |
| Should melatonin vs. no such strategy be used for improving sleep in critically ill adults?  |
| Population:  | improving sleep in critically ill adults  | Background:  |  |
| Intervention:  | melatonin  |  |
| Comparison:  | no such strategy  |  |
| Main outcomes:  | * Delirium
* Sleep Awakenings
* Sleep Duration
* Sleep Quality
 |  |
| **Assessment** |
|  | **Criteria**  | **Judgements**  | **Research evidence**  | **Additional considerations**  |
| Problem | **Is there a problem priority?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  |  |
| Benefits & harms of the options | **What is the overall certainty of this evidence?**  | ○ No included studies ● Very low ○ Low ○ Moderate ○ High  | **The relative importance or values of the main outcomes of interest:**

| **Outcome** | **Relative importance**  | **Certainty of the evidence (GRADE)**  |
| --- | --- | --- |
| Delirium | CRITICAL | ⨁◯◯◯VERY LOW |
| Sleep Awakenings | CRITICAL | ⨁◯◯◯VERY LOW |
| Sleep Duration | CRITICAL | ⨁⨁◯◯LOW |
| Sleep Quality | CRITICAL | ⨁⨁◯◯LOW |

 |  |
| **Is there important uncertainty about how much people value the main outcomes?**  | ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability ○ No known undesirable outcomes  |
| **Are the desirable anticipated effects large?**  | ● No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |
| **Are the undesirable anticipated effects small?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |
| **Are the desirable effects large relative to undesirable effects?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |
| Resource use | **Are the resources required small?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  |  |
| **Is the incremental cost small relative to the net benefits?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  | Difficult to know without being sure of the benefits but the cost is low. |  |
| Equity | **What would be the impact on health inequities?**  | ○ Increased ○ Probably increased ○ Uncertain ● Probably reduced ○ Reduced ○ Varies  | Should be relatively accessible to most if not all.  So it should not contribute to inequity. |  |
| Acceptability | **Is the option acceptable to key stakeholders?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  | Some institutions may not offer melatonin (such as my own) because it is not an FDA-approved drug.  However, if there were compelling data in favor of its use, it would likely be made available. Ramelteon might be an FDA-alternative but is not tested for sleep in the ICU.  |  |
| Feasibility | **Is the option feasible to implement?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  |  |

|  |
| --- |
| **Recommendation** **Should melatonin vs. no such strategy be used for improving sleep in critically ill adults?** |
| **Balance of consequences**  | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
|  | ○ | ○ | ○ | ○ | ○ |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Type of recommendation**  | We recommend against offering this option | We suggest not offering this option | We suggest offering this option | We recommend offering this option |
|  | ○ | ○ | ○ | ○ |
| **Recommendation**  | Not enough data to justify a recommendation.To include in text below no recommendation or consider as a standalone recommendation? If one does choose to use pharmacologic agents for improving sleep in ICU, we suggest melatonin as an initial pharmacological agent to improve sleep in critically ill before trying other pharmacologic agents with potentially more troublesome side effect profiles. - based only on expert opinion and indirect data |
| **Justification**  | Three small studies, two of which suggest a benefit.  So benefits are uncertain; risks small (small cost, infrequent adverse effects) but not zero.Considered no recommendation however felt like although benefit is not clear the harm is most minimal compared to other agents.Indirect data suggests safety of melatonin (well tolerated in other populations such as elderly).  |
| **Research possibilities**  | Ramelteon is an FDA-approved melatonin receptor agonist which has had one large study in both ICU and ward patients suggest it reduced delirium; benefits with regard to sleep unknown.Need more comparative data for melatonin. Stratification of harm with different sleep agents in the ICU population. |
| **Comments during electronic voting by entire panel** | Can we add "and melatonin receptor agonists" to this? 24 patients in 1 RCT & no recommendation. Is this consistent across all recommendations?the evidence suggests some benefit without risk or excessive costs. If pharmacological agents for sleep are needed, we suggest melatonin as an initial agent before trying other molecules associated with more side effects |

**Question: Dexmedetomidine compared to no such strategy for improving sleep in critically ill adults**

| **Quality assessment** | **№ of patients** | **Effect** | **Quality** | **Importance** |
| --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **dexmedetomidine**  | **no such strategy**  | **Relative(95% CI)** | **Absolute(95% CI)** |
| Sleep Fragmentation |
| 2  | randomised trials  | not serious  | serious a | not serious  | serious b | none  | 41  | 39  | -  | SMD **0.2 SD lower**(0.65 lower to 0.25 higher)  | ⨁⨁◯◯LOW  | CRITICAL  |
| Stage 1 Sleep |
| 2  | randomised trials  | not serious  | not serious  | not serious  | serious b | none  | 41  | 39  | -  | MD **30.37 lower**(50.01 lower to 10.73 lower)  | ⨁⨁⨁◯MODERATE  | IMPORTANT  |
| Stage 2 Sleep |
| 2  | randomised trials  | not serious  | not serious  | not serious  | serious b | none  | 41  | 39  | -  | MD **47.85 higher**(24.05 higher to 71.64 higher)  | ⨁⨁⨁◯MODERATE  | IMPORTANT  |

**CI:** Confidence interval; **SMD:** Standardised mean difference; **MD:** Mean difference

#### Explanations

a. High Isquared.

b. Very small number of patients despite narrow confidence intervals.

|  |  |
| --- | --- |
| **Question** |  |
| Should dexmedetomidine vs. no such strategy be used for improving sleep in critically ill adults?  |
| Population:  | improving sleep in critically ill adults  | Background:  |  |
| Intervention:  | dexmedetomidine  |  |
| Comparison:  | no such strategy  |  |
| Main outcomes:  | * Sleep Fragmentation
* Stage 1 Sleep
* Stage 2 Sleep
 |  |
| **Assessment** |
|  | **Criteria**  | **Judgements**  | **Research evidence**  | **Additional considerations**  |
| Problem | **Is there a problem priority?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  |  |
| Benefits & harms of the options | **What is the overall certainty of this evidence?**  | ○ No included studies ○ Very low ○ Low ● Moderate ○ High  | **The relative importance or values of the main outcomes of interest:**

| **Outcome** | **Relative importance**  | **Certainty of the evidence (GRADE)**  |
| --- | --- | --- |
| Sleep Fragmentation | CRITICAL | ⨁⨁⨁◯MODERATE |
| Stage 1 Sleep | IMPORTANT | ⨁⨁⨁◯MODERATE |
| Stage 2 Sleep | IMPORTANT | ⨁⨁⨁◯MODERATE |

 |  |
| **Is there important uncertainty about how much people value the main outcomes?**  | ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability ○ No known undesirable outcomes  |
| **Are the desirable anticipated effects large?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |
| **Are the undesirable anticipated effects small?**  | ○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |
| **Are the desirable effects large relative to undesirable effects?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ● Varies  |
| Resource use | **Are the resources required small?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  | No more resources then with other infusions |  |
| **Is the incremental cost small relative to the net benefits?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  | Drug cost is not small.  Cost savings by improved sleep not quantified |  |
| Equity | **What would be the impact on health inequities?**  | ○ Increased ○ Probably increased ○ Uncertain ○ Probably reduced ○ Reduced ● Varies  | Low resource institution may not make dexmedetomidine available? |  |
| Acceptability | **Is the option acceptable to key stakeholders?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  |  |
| Feasibility | **Is the option feasible to implement?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  |  |

|  |
| --- |
| **Recommendation** **Should dexmedetomidine vs. no such strategy be used for improving sleep in critically ill adults?** |
| **Balance of consequences**  | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
|  | ○ | ○ | ● | ○ | ○ |
| **Type of recommendation**  | We recommend against offering this option | We suggest not offering this option | We suggest offering this option | We recommend offering this option |
|  | ○ | ● | ○ | ○ |
| **Recommendation**  | The panel cannot make a recommendation on the use of dexmedetomidine to improve sleep in critically ill adults |
| **Justification**  | Without dexmedetomidine, sleep was evenly distributed between day and night which may interfere with other, evidence-based strategies such as early mobilization. Sleep architecture (less stage I, more stage II, no significant amount SWS and REM) while on infusion of dexmedetomidine is consistent with finding of other, non randomized study (Oto et al). Studies are limited to two studies of patients mechanically ventilated for at least 48 hr and hemodynamically stable and one study of patients immediately post-op from non-cardiac surgery who were not mechanically ventilated. |
| **Subgroup considerations**  | Unknown if these results apply to those with atypical sleep patterns, delirious patients, or patients on other sedatives; they were excluded from study.In a very recent study (Wu et al), non-intubated elderly patients after non-cardiac surgery slept better subjectively if dexmedetomidine was infused prophylactically on the first post-operative night. |
| **Implementation considerations**  | Cost may be what most limits implementation. |
| **Monitoring and evaluation**  | Hemodynamic monitoring necessary given the adverse effects of the drug. |
| **Research possibilities**  | More study of use of dexmedetomidine for broader ICU patient population.  Other, patient-centered outcomes could be measured, ie delirium, length of mechanical ventilation, patient satisfaction. |
| **Comments during electronic voting by entire panel** | Pros/ cons should figure in rationale for guidance for when it might be appropriate to use.Stage 1 sleep was lower/ stage 2 higher in 2 RCTs: small sample; is that beneficial to ICU patients? Is no recommendation based on costs, availability, and resources (e.g., monitoring)? Should Dex be suggested when other interventions failed to improve sleep? Why were outcomes such as delirium, ICU LOS, or mortality not included? |

**Question: Propofol compared to no propofol for improving sleep in critically ill adults**

| **Quality assessment** | **№ of patients** | **Effect** | **Quality** | **Importance** |
| --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **propofol** | **no propofol** | **Relative(95% CI)** | **Absolute(95% CI)** |
| Sleep Fragmentation |
| 1  | randomised trials  | serious a | not serious  | not serious  | serious b | none  | 12  | 12  | -  | MD **3.3 lower**(11.19 lower to 4.59 higher)  | ⨁⨁◯◯LOW  | CRITICAL  |
| Sleep Duration |
| 1  | randomised trials  | serious a | not serious  | not serious  | serious b | none  | 12  | 12  | -  | MD **46 minutes higher**(8.94 lower to 100.94 higher)  | ⨁⨁◯◯LOW  | CRITICAL  |
| Stage 1 Sleep |
| 1  | randomised trials  | serious a | not serious  | not serious  | serious c | none  | 12  | 12  | -  | MD **9.9 lower**(23.69 lower to 3.89 higher)  | ⨁⨁◯◯LOW  | IMPORTANT  |
| Stage 2 Sleep |
| 1  | randomised trials  | serious a | not serious  | not serious  | very serious d | none  | 12  | 12  | -  | MD **2.8 higher**(13.28 lower to 18.88 higher)  | ⨁◯◯◯VERY LOW  | IMPORTANT  |

#### Explanations a. Lack of blinding of intervention. Unclear allocation concealment. b. Wide confidence intervals do not exclude harm.

c. Wide confidence intervals. d. Very wide confidence intervals and low number of patients.

|  |  |
| --- | --- |
| **Question** |  |
| Should propofol vs. no propofol be used for improving sleep in critically ill adults?  |
| Population:  | improving sleep in critically ill adults  | Background:  |  |
| Intervention:  | propofol  |  |
| Comparison:  | no propofol  |  |
| Main outcomes:  | * Sleep Fragmentation
* Sleep Duration
* Stage 1 Sleep
* Stage 2 Sleep
 |  |
| **Assessment** |
|  | **Criteria**  | **Judgements**  | **Research evidence**  | **Additional considerations**  |
| Problem | **Is there a problem priority?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  |  |
| Benefits & harms of the options | **What is the overall certainty of this evidence?**  | ○ No included studies ○ Very low ● Low ○ Moderate ○ High  | **The relative importance or values of the main outcomes of interest:**

| **Outcome** | **Relative importance**  | **Certainty of the evidence (GRADE)**  |
| --- | --- | --- |
| Sleep Fragmentation | CRITICAL | ⨁⨁◯◯LOW |
| Sleep Duration | CRITICAL | ⨁⨁◯◯LOW |
| Stage 1 Sleep | IMPORTANT | ⨁⨁◯◯LOW |
| Stage 2 Sleep | IMPORTANT | ⨁◯◯◯VERY LOW |

 |  |
| **Is there important uncertainty about how much people value the main outcomes?**  | ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability ○ No known undesirable outcomes  |
| **Are the desirable anticipated effects large?**  | ● No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |
| **Are the undesirable anticipated effects small?**  | ● No ○ Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |
| **Are the desirable effects large relative to undesirable effects?**  | ○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  |
| Resource use | **Are the resources required small?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  |  |
| **Is the incremental cost small relative to the net benefits?**  | ○ No ● Probably no ○ Uncertain ○ Probably yes ○ Yes ○ Varies  | No clear benefit proven |  |
| Equity | **What would be the impact on health inequities?**  | ○ Increased ○ Probably increased ○ Uncertain ○ Probably reduced ○ Reduced ○ Varies  | probably no effect |  |
| Acceptability | **Is the option acceptable to key stakeholders?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |  |  |
| Feasibility | **Is the option feasible to implement?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  |  |  |

|  |
| --- |
| **Recommendation** **Should propofol vs. no propofol be used for improving sleep in critically ill adults?** |
| **Balance of consequences**  | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
|  | ○ | ○ | ● | ○ | ○ |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Type of recommendation**  | We recommend against offering this option | We suggest not offering this option | We suggest offering this option | We recommend offering this option |
|  | ○ | ● | ○ | ○ |
| **Recommendation**  | There is insufficient data to support the use of propofol versus no propofol to facilitate sleep in select mechanically ventilated patients.   |
| **Justification**  | Despite animal studies that suggest that sedation with propofol may mimic or at least not interfere with the restorative effects of sleep, data does not suggest improvement in sleep efficiency, duration, and stage 2 sleep.  Propofol is known to suppress both REM and SWS although its effects are dose-dependent.  |
| **Subgroup considerations**  | Studies have excluded patients with delirium, atypical sleep EEG findings, sepsis, APACHE scores >15, and use of other sedatives so its use in the general critical care population remains unknown.  |
| **Monitoring and evaluation**  | Hemodynamic and respiratory monitoring is required |
| **Research possibilities**  | Further study of critically ill patients varying the propofol dose and controlling for sleep during the day as well as looking at other, patient-centered outcomes. |
| **Comments during electronic voting by entire panel** | I would favor no reco as for DEX as ppf study (Kondili 2012) had a sedation protocol ppf ajustment based on a regular sedation assessment (Ramsay 3 = responsive!) with the risk the investigators regularly woke patients during the night... |

**Question: A non-pharmacological protocol for sleep improvement compared to no such protocol in critically ill adults**

| **Quality assessment** | **№ of patients** | **Effect** | **Quality** | **Importance** |
| --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **a non-pharmacological protocol for sleep improvement** | **no such protocol** | **Relative(95% CI)** | **Absolute(95% CI)** |
| Mortality |
| 1  | randomised trials  | serious a | not serious  | not serious  | very serious b | none  | 0/20 (0.0%)  | 2/20 (10.0%)  | **RR 0.20**(0.01 to 3.92)  | **80 fewer per 1,000**(from 99 fewer to 292 more)  | ⨁◯◯◯VERY LOW  | CRITICAL  |
| ICU Length of Stay (assessed with: hours) |
| 1  | randomised trials  | serious a | not serious  | not serious  | very serious b | none  | 20  | 25  | -  | MD **5.9 hours fewer**(16.42 fewer to 4.62 more)  | ⨁◯◯◯VERY LOW  | CRITICAL  |
| Hospital Length of Stay (assessed with: days) |
| 1  | randomised trials  | serious a | not serious  | not serious  | very serious b | none  | 20  | 25  | -  | MD **1.9 days fewer**(6.91 fewer to 3.11 more)  | ⨁◯◯◯VERY LOW  | CRITICAL  |
| Duration Mechanical Ventilation (assessed with: hours) |
| 1  | randomised trials  | serious a | not serious  | not serious  | very serious b | none  | 20  | 25  | -  | MD **0.7 hours higher**(5.05 lower to 6.45 higher)  | ⨁◯◯◯VERY LOW  | CRITICAL  |
| Sleep Quality (assessed with: RSCQ (\*\*higher is worse here)) |
| 1  | randomised trials  | serious a | not serious  | not serious  | serious c | none  | 20  | 25  | -  | MD **32.7 lower**(45.56 lower to 19.84 lower)  | ⨁⨁◯◯LOW  | CRITICAL  |
| Delirium |
| 3  | observational studies  | not serious  | not serious d | not serious  | not serious  | none  | 116/359 (32.3%)  | 139/292 (47.6%)  | **RR 0.62**(0.42 to 0.91)  | **181 fewer per 1,000**(from 43 fewer to 276 fewer)  | ⨁⨁◯◯LOW  | CRITICAL  |
| Daytime Sleepiness |
| 3  | observational studies  | not serious  | not serious  | not serious  | serious e | none  | 79  | 76  | -  | MD **1.2 higher**(0.45 higher to 1.94 higher)  | ⨁◯◯◯VERY LOW  | CRITICAL  |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. Unclear allocation concealment and lacked blinding.

b. Very small number of patients and extremely wide confidence intervals.

c. Despite confidence intervals all on the side of benefit there are small number of enrolled patients.

d. High Isquared (60%) but all point estimates on the side of benefit for protocolized therapy.

e. Wide confidence intervals do not exclude benefit or harm.

|  |  |
| --- | --- |
| **Question** |  |
| Should a non-pharmacological protocol for sleep improvement vs. no such protocol be used in critically ill adults?  |
| Population:  | critically ill adults  | Background:  |  |
| Intervention:  | a non-pharmacological protocol for sleep improvement  |  |
| Comparison:  | no such protocol  |  |
| Main outcomes:  | * Mortality
* ICU Length of Stay
* Hospital Length of Stay
* Duration Mechanical Ventilation
* Sleep Quality
* Delirium
* Daytime Sleepiness
 |  |
| **Assessment** |
|  | **Criteria**  | **Judgements**  | **Research evidence**  | **Additional considerations**  |
| Problem | **Is there a problem priority?**  | ○ No ○ Probably no ○ Uncertain ○ Probably yes ● Yes ○ Varies  | Self-reported sleep quality improved.Delirium decreased. | Outcomes: mortality, ICU LOS, hosp LOS, MV duration, self-reported sleep quality (RCSQ, reverse scored), delirium, daytime sleepiness |
| Benefits & harms of the options | **What is the overall certainty of this evidence?**  | ○ No included studies ● Very low ○ Low ○ Moderate ○ High  | **The relative importance or values of the main outcomes of interest:**

| **Outcome** | **Relative importance**  | **Certainty of the evidence (GRADE)**  |
| --- | --- | --- |

MortalityICU LOSHospital LOSLength of MVDeliriumDaytime sleepiness | Very low from 1 RCT for sleep quality, in elective CABG patients in 1 center.Low for delirium from 3 observational studies (n=651) in a mixed critical care population in 3 centers.Wide CIs for sleep qualityHigh I squared for delirium, but all estimates on side of benefit.Sleep quality - 33/100 betterDelirium - RR 0.62, 181 fewer/1000 Depends on components of intervention. Some patients do not like ear plugs, eye shades and/or music and need to be able to decline them. Problem for a trial (dropouts) but OK for regular care. |
| **Is there important uncertainty about how much people value the main outcomes?**  | ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability ○ No known undesirable outcomes  |
| **Are the desirable anticipated effects large?**  | ○ No ○ Probably no ● Uncertain ○ Probably yes ○ Yes ○ Varies  |
| **Are the undesirable anticipated effects small?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |
| **Are the desirable effects large relative to undesirable effects?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  |
| Resource use | **Are the resources required small?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  | Equipment used inexpensive and easily obtained.Staff behavioral changes inexpensive to do, but require intensive effort to implement and sustain. | Equipment used inexpensive and easily obtained.Staff behavioral changes inexpensive to do, but require intensive effort to implement and sustain. |
| **Is the incremental cost small relative to the net benefits?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  | If improvements in sleep quality and delirium are generalizable to most critical care patients. |  |
| Equity | **What would be the impact on health inequities?**  | ○ Increased ○ Probably increased ○ Uncertain ● Probably reduced ○ Reduced ○ Varies  | No expensive equipment required so could be implemented widely in facilities with a range of resource availability. |  |
| Acceptability | **Is the option acceptable to key stakeholders?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  | If delirium reduced. |  |
| Feasibility | **Is the option feasible to implement?**  | ○ No ○ Probably no ○ Uncertain ● Probably yes ○ Yes ○ Varies  | But requires effort to implement and sustain. |  |

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| **Recommendation** **Should a non-pharmacological protocol for sleep improvement vs. no such protocol be used in critically ill adults?** |
| **Balance of consequences**  | Undesirable consequences *clearly outweigh* desirable consequences in most settings | Undesirable consequences *probably outweigh* desirable consequences in most settings | The balance between desirable and undesirable consequences *is closely balanced or uncertain* | Desirable consequences *probably outweigh* undesirable consequences in most settings | Desirable consequences *clearly outweigh* undesirable consequences in most settings |
|  | ○ | ○ | ○ | ○ | ○ |

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| **Type of recommendation**  | We recommend against offering this option | We suggest not offering this option | We suggest offering this option | We recommend offering this option |
|  | ○ | ○ | ● | ○ |
| **Recommendation**  | Consider using multicomponent interventions (guidelines, bundles, protocols) consisting of . . . aimed at improving sleep. |
| **Justification**  | The research evidence available suggests that such interventions reduce the incidence of delirium and may improve patients' perceptions of the quality of their sleep in critical care. |
| **Subgroup considerations**  | Interventions of earplugs, eye shades and music should not be used unless patients can decline their use or remove them. |
| **Implementation considerations**  | Staff behavioral components require effort to implement and sustain. As with all CPGs, continuing reinforcement and monitoring of adherence is required to sustain their use and potential benefits. |
| **Monitoring and evaluation**  | Monitoring of adherence - regular audits of staff adherence to components of the intervention, selected and randomly varied.Evaluation - routine assessment of sleep and delirium.  |
| **Research possibilities**  | Further evaluation of effects of interventions on sleep, with PSG if possible, and delirium.Identification of the effective components and combinations of these. |
| **Comments during electronic voting by entire panel** | We did not consider sleep as a risk factor for delirium, yet data within this recommendation suggest that the intervention reduced the risk of delirium by ~50%. Should reconcile sleep & delirium findings. There is no consensus about which elements of a bundle should be included; patient preference should be considered. The question is specific to a non-pharmacological protocol; the recommendation refers to a sleep promoting multicomponent protocol, not specific to non-pharmacological strategies. Suggestion: Sleep promoting non-pharmacological protocol? Ongoing research, QI reporting?Suggest recommendation include "non-pharmacological" and specify types of interventions in the evidence.What about the challenges in measuring adherence to the recommendation?Limited populations reported in the evidence, may consider being very specific about which population this recommendation applies to. |

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