



Brigham and Women's Hospital
Founding Member, Mass General Brigham

Optimizing the ABCDEF Bundle

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- Clinical Focus: Critical care pharmacy
- Research Focus:
 - Recognition, Prevention, and Treatment of Delirium in the ICU
 - Sedative Choice, Cost and Safety
 - Recognition, Prevention and Treatment of Disrupted Sleep in the ICU
 - Pharmacoepidemiology of Delirium in Critical Illness.

Disclosures

Research Funding:

NIA

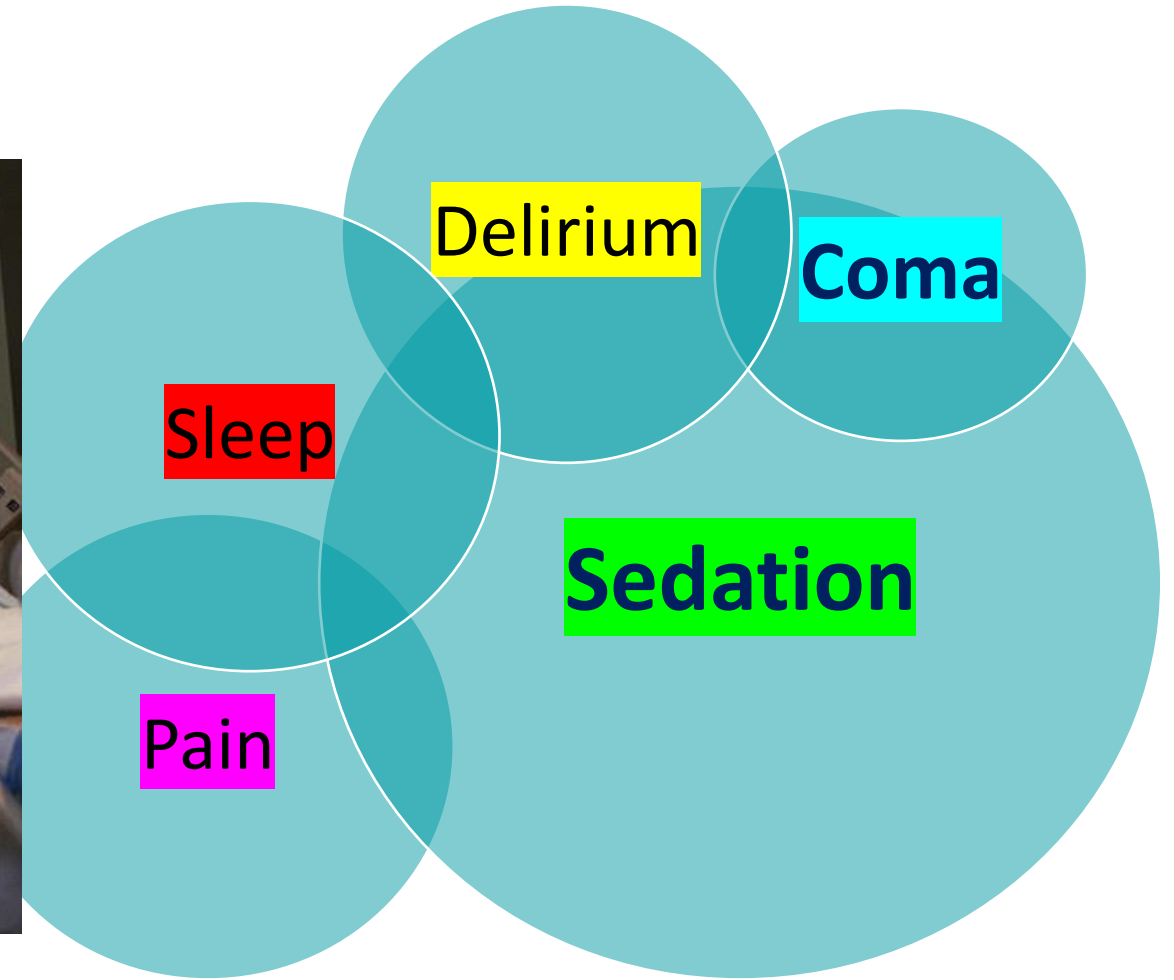
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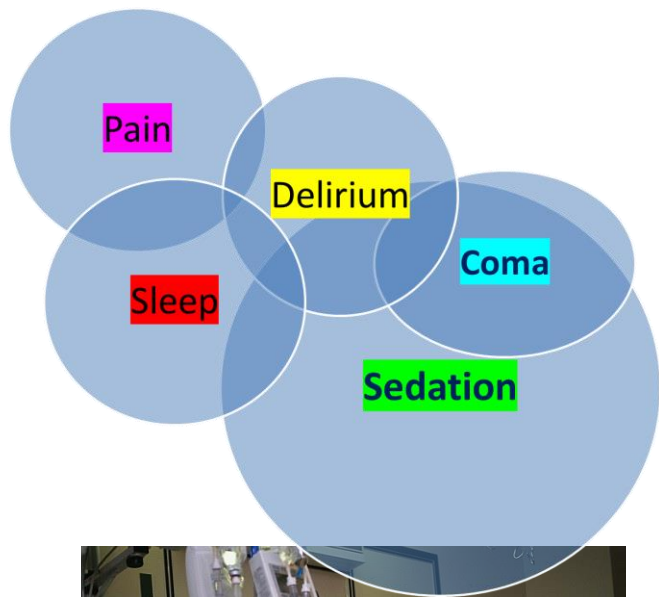
Consultant:

Ceribell Inc.

Noven Pharmaceuticals

Optimize patient comfort and safety & facilitate mechanical ventilation





ICU
Survivorship



Post-intensive care syndrome (PICS)

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graph TD; PICS[Post-intensive care syndrome (PICS)] --> PS[Psychological Symptoms]; PICS --> CS[Cognitive Symptoms]; PICS --> PH[Physical Symptoms];
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Psychological Symptoms

- Anxiety
- Depression
- PTSD
- Sleep problems

Cognitive Symptoms

- Executive function
- Memory
- Attention
- Visual-spatial
- Mental processing speed

Physical Symptoms

- Breathing difficulties
- Weakness and balance problems
- Neuromuscular impairment
- Pain or numbness

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Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU

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43 recommendations

Overwhelming!

A Focused Update to the Clinical Practice Guidelines for the Prevention and Management of Pain, Anxiety, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU

RATIONALE: Critically ill adults are at risk for a variety of distressing and consequential symptoms both during and after an ICU stay. Management of these symptoms can directly influence outcomes.

OBJECTIVES: The objective was to update and expand the Society of Critical Care Medicine's 2018 Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU.

The guidelines task force was composed of physicians, pharmacists, physiotherapists, and nurses. The task force developed evidence-based recommendations using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach. Conflict-of-interest policies were strictly followed in all phases of the guidelines, including task force selection and voting.

METHODS: The task force focused on five main content areas as they pertain to adult ICU patients: anxiety (new topic), agitation/sedation, delirium, immobility, and sleep disruption. We conducted a rigorous search of the literature, performed a critical appraisal of the evidence, and summarized the evidence.

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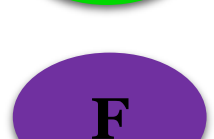
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ABCDEF Bundle Elements

-  Assess, Prevent and manage Pain
-  Both SAT and SBT
-  Choice of Analgesia and Sedation
-  Delirium: Assess, Prevent and Manage
-  Early Mobility and Exercise
-  Family Engagement and Empowerment



Assess, Prevent and Manage Pain

1. Assessment

- Use a valid assessment tool every 4 hours
- VAS-10 (vs. CPOT) preferred if patient can self-report

2. Prevention

- Anticipate pain/discomfort (e.g., mobility, procedures)

3. Management

- Treat pain before using a sedative
- Optimize non-pharmacologic analgesic strategies to reduce opioid use:
 - positioning, cold therapy, massage, music, relaxation strategies
- Use a multimodal analgesic approach i.e., non-opioid analgesics ± as needed opioids vs. scheduled IV opioids alone

Opioid Use Increases the Risk of Delirium in Critically Ill Adults Independently of Pain

Matthew S. Duprey¹, Sandra M. A. Dijkstra-Kersten^{2,3}, Irene J. Zaal^{2,3}, Becky A. Briesacher¹, Jane S. Saczynski¹, John L. Griffith⁴, John W. Devlin^{1,5}, and Arjen J. C. Slooter^{2,3,6}

Multinomial model on transitions of daily mental status conditional on opioid exposure

Mental Status		Opioid Exposure	Adjusted Odds ratio*^		P value
Day t	Day t+1				
Awake without delirium	Awake without delirium	No	reference		
Awake without delirium	Delirium	Yes	1.45	(1.24-1.69)	< 0.001
Awake without delirium	Delirium	10mg MEQ#	1.24	(1.15-1.39)	< 0.001

*adjusted for time-fixed covariables: admission category (medical, surgical, trauma), age, gender, Acute Physiology and Chronic Health Evaluation (APACHE) IV Score, body mass index, Charlson Comorbidity Index

^adjusted for time-varying covariables on day t: day of ICU admission, modified Sequential Organ Failure Assessment score (without neurologic component), use of mechanical ventilation, use of a benzodiazepine, presence of severe pain

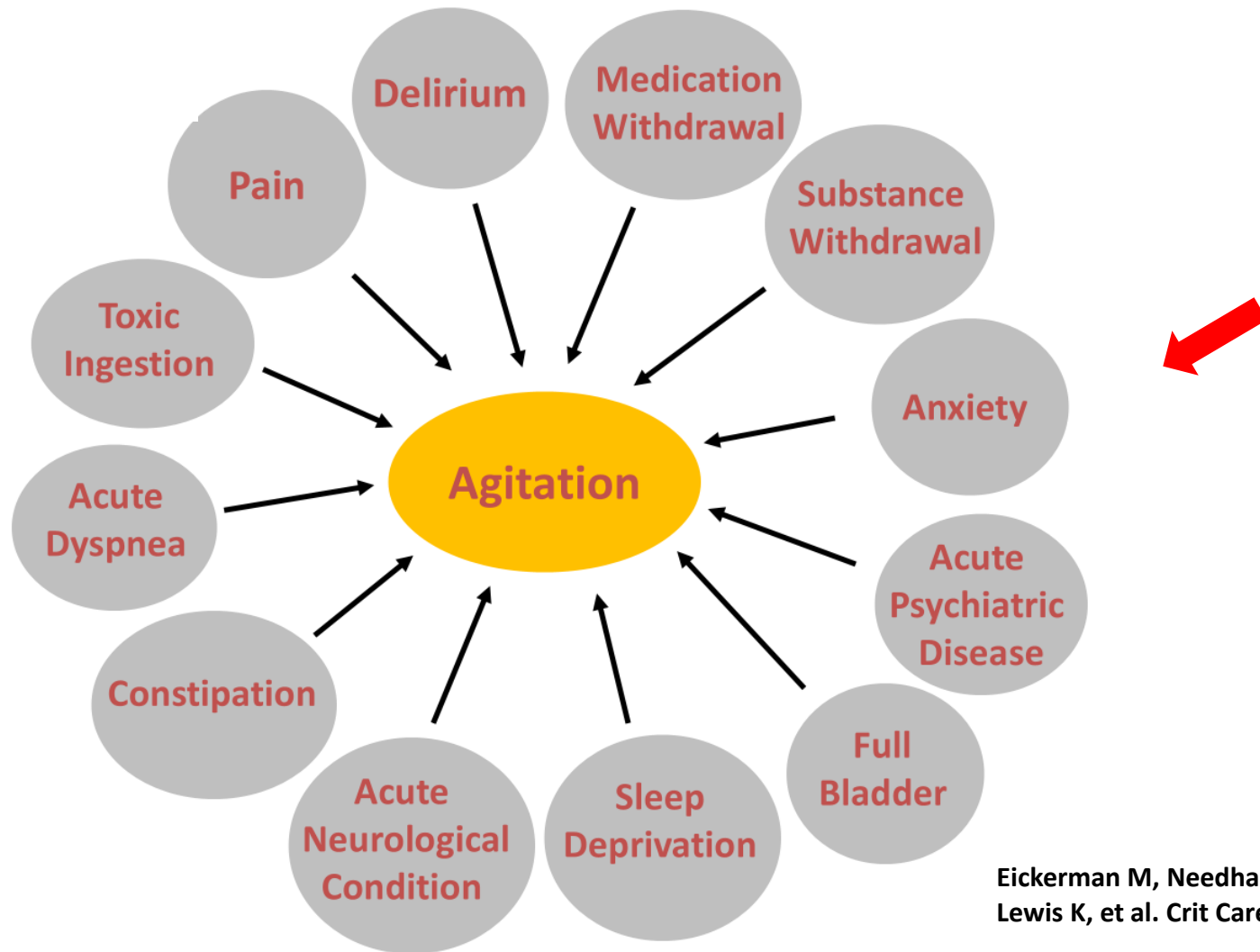
#adjusted odds ratio represents the odds for a 1 log-fold increase in morphine equivalent dose

Odds for delirium remained stable across study years and age groups, was observed in both medical and surgical patients, and was not dependent on the degree of pain present on the day preceding a transition to delirium.

B

Both Spontaneous Breathing Trial/Spontaneous Breathing Trial

1. Consider (and treat) additional reasons for agitation.



B**Both Spontaneous Awakening Trial/Spontaneous Breathing Trial****1. Establish and communicate a new sedation goal every 24 hours**

- Conduct regular RASS assessments
- Is the documented RASS score accurate? (RN spot checking)
- What is the ICU culture re: oversedation if it delays SBTs/extubation?

2. Consider 24/7 q2h sedative titration protocol

- Preferred by RNs over spontaneous awakening trials (SATs)

3. Strategies to maintain a daytime wakeful patient

- Rely on PRN sedative use; avoid scheduled sedative use when possible
- Sedation ≠ good sleep

Choice of Analgesia and Sedation

1. Reevaluate opioid/analgesic and sedative choices daily

- Address potential concerns about opioid, dexmedetomidine or benzodiazepine withdrawal
- Change scheduled to PRN; if PRN order not used in 24 hours stop it

2. Change to enteral/oral analgesics/sedatives

- Avoid IV route unless acute pain/agitation or patients has a non-functioning gut

3. Avoid (or dose-reduce) medications proven to be delirium-causing:

- Benzodiazepines
- Opioids
- High-dose corticosteroids
- Antibiotics with high CNS penetration: cefepime, meropenem
- Keppra
- Metoclopramide

ORIGINAL ARTICLE

Dexmedetomidine or Propofol for Sedation in Mechanically Ventilated Adults with Sepsis

	Dexmedetomidine N=214	Propofol N=208	Difference
APACHE-II	27 [21, 32]	27 [22, 32]	
Medical	64%	65%	
Moderate-Severe ARDS	26%	29%	
<i>Outcomes</i>			
Days without delirium or coma at 14 d* median [95% CI]	10.7 [8.5, 12.5]	10.8 [8.7, 12.6]	NS
Ventilator-free days at 28 days* median [95% CI]	23.7 [20.5, 25.4]	24.0 [20.9, 25.4]	NS
Mortality at 90 days*	38%	39%	NS
Telephone Interview for Cognitive Status (TICS) at 6 mo.	40.9 [33.6, 47.1]	41.4 [34.0, 47.3]	NS
RASS score while receiving study sedation	-2 [-3 to -1]	- 1.9 [-3 to -0.9]	NS
Daily adherence to all ABCDE bundle elements	86%	85%	NS

*Multivariable adjustment for n=16 variables; % age-adjusted

Hughes CG, Mailloux PT, Devlin JW, et al. New Engl J Med (Feb 2 2021)



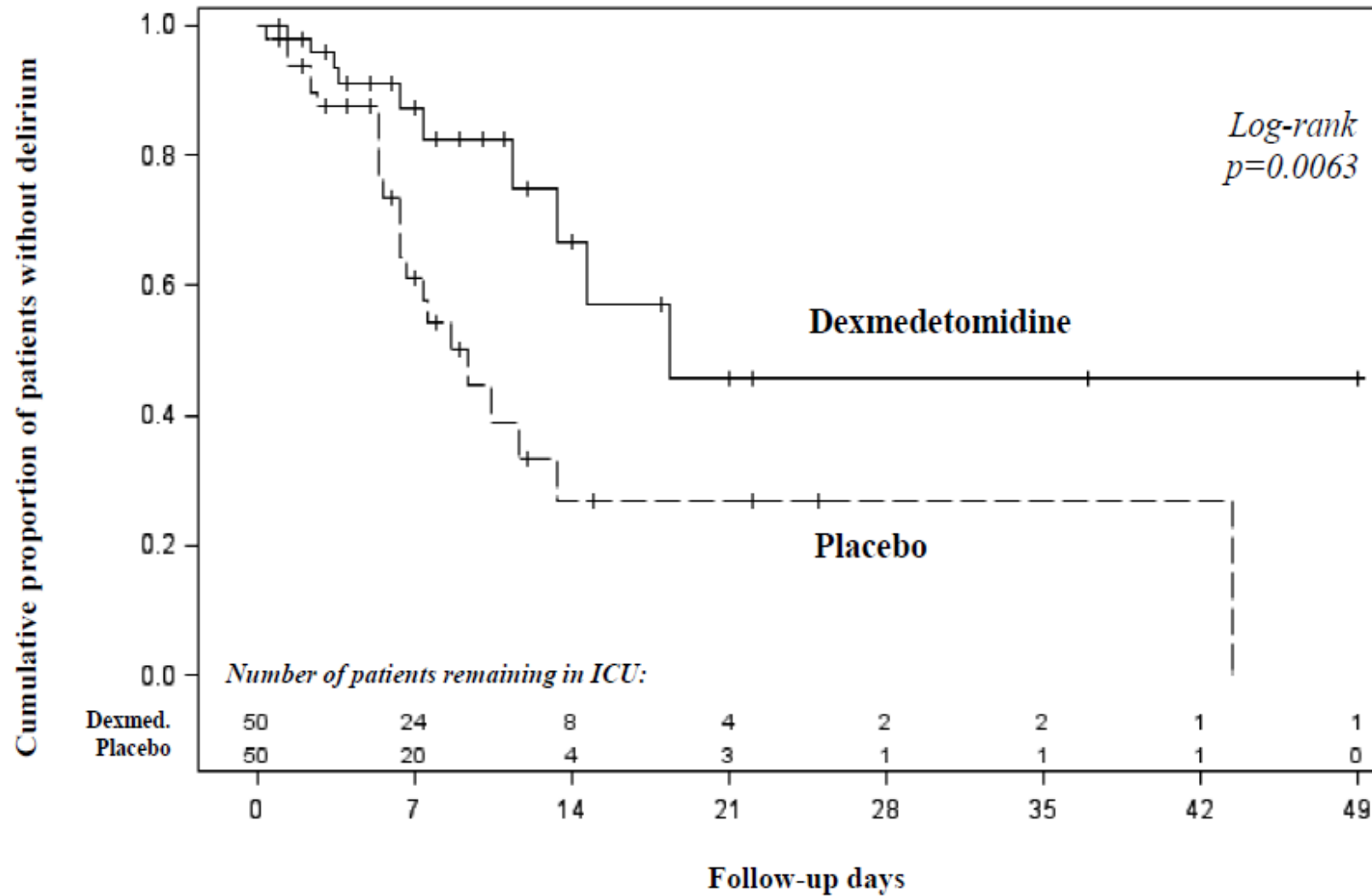
Delirium: Assess, Prevent and Manage

- 1. Assess for Delirium every RN shift with CAM-ICU (or ICDSC)**
 - Ensure patients are maximally awake before CAM-ICU screening
 - Delirium assessments should be documented/reported on rounds (including patient symptoms)
 - All ICU clinicians should be trained on proper CAM-ICU use
- 2. Evaluate patients for the presence of new delirium risk factors daily**

Dr. DRE:

<u>D</u> iseases	New onset sepsis/infection Worsening organ dysfunction Worsening hypoxemia Dehydration
<u>DR</u> ug Removal	Sedative de-escalation e.g., SATs Reduce benzodiazepines and opioids Stop/reduce psychoactive meds
<u>E</u> nvironment	Immobilization Sleep disruption Noise/light Hearing aids/glasses

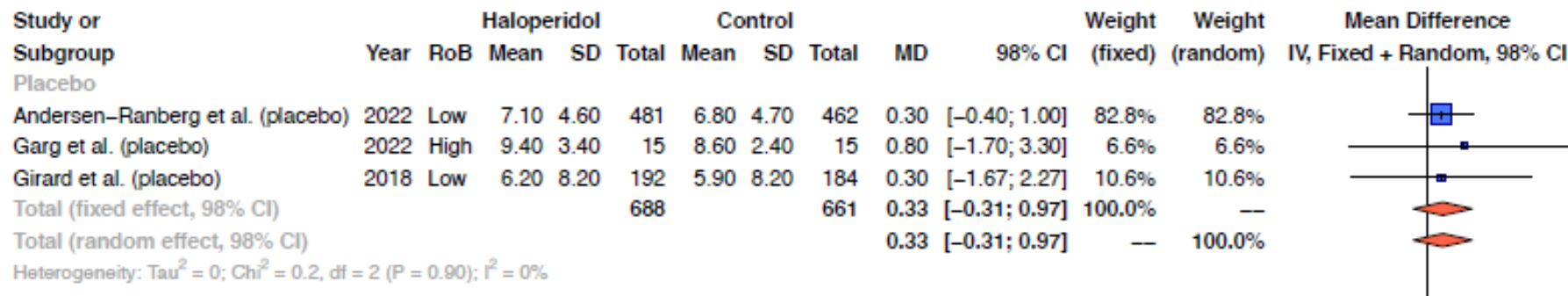
Low-dose Nocturnal Dexmedetomidine Prevents ICU Delirium: A Randomized, Placebo-Controlled trial



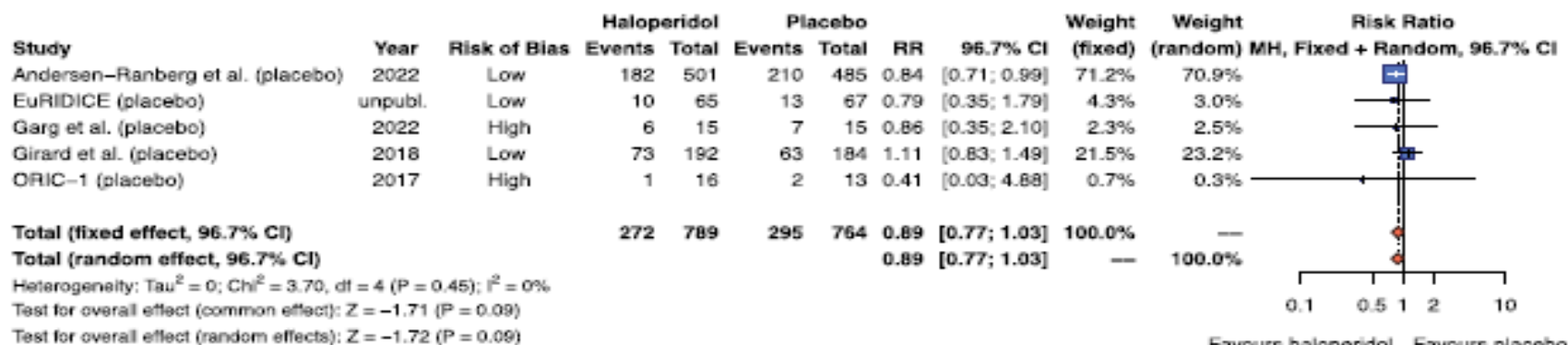
No difference in LEEDS Sleep Score between groups

Summary of IV Haloperidol (vs. Placebo) Delirium Treatment RCTs

Figure S20: Days alive without delirium or coma (14 days); haloperidol versus all comparators



All-cause mortality



All-cause mortality of placebo-controlled trials

Fig. 2 Forest plot of all-cause mortality in placebo-controlled trials. Forest plot of all-cause mortality in placebo-controlled trials. Three trials were at overall low risk of bias, and two trials were at overall high risk of bias. Size of the squares reflects the size of the trial (sample size). The horizontal bars represent 96.7% confidence intervals

Antipsychotic vs. None (Treatment)

Rationale, includes:

- No benefit for any critical outcomes
- **Not Routinely (vs. Never)** given that patients with fear, anxiety or agitation not-related to pain may still benefit from a short-course of antipsychotic therapy
- Unnecessary continuation causes significant morbidity & cost

Recommendation:

We **suggest NOT** routinely using haloperidol and atypical antipsychotic to treat delirium (conditional recommendation, low quality of evidence).

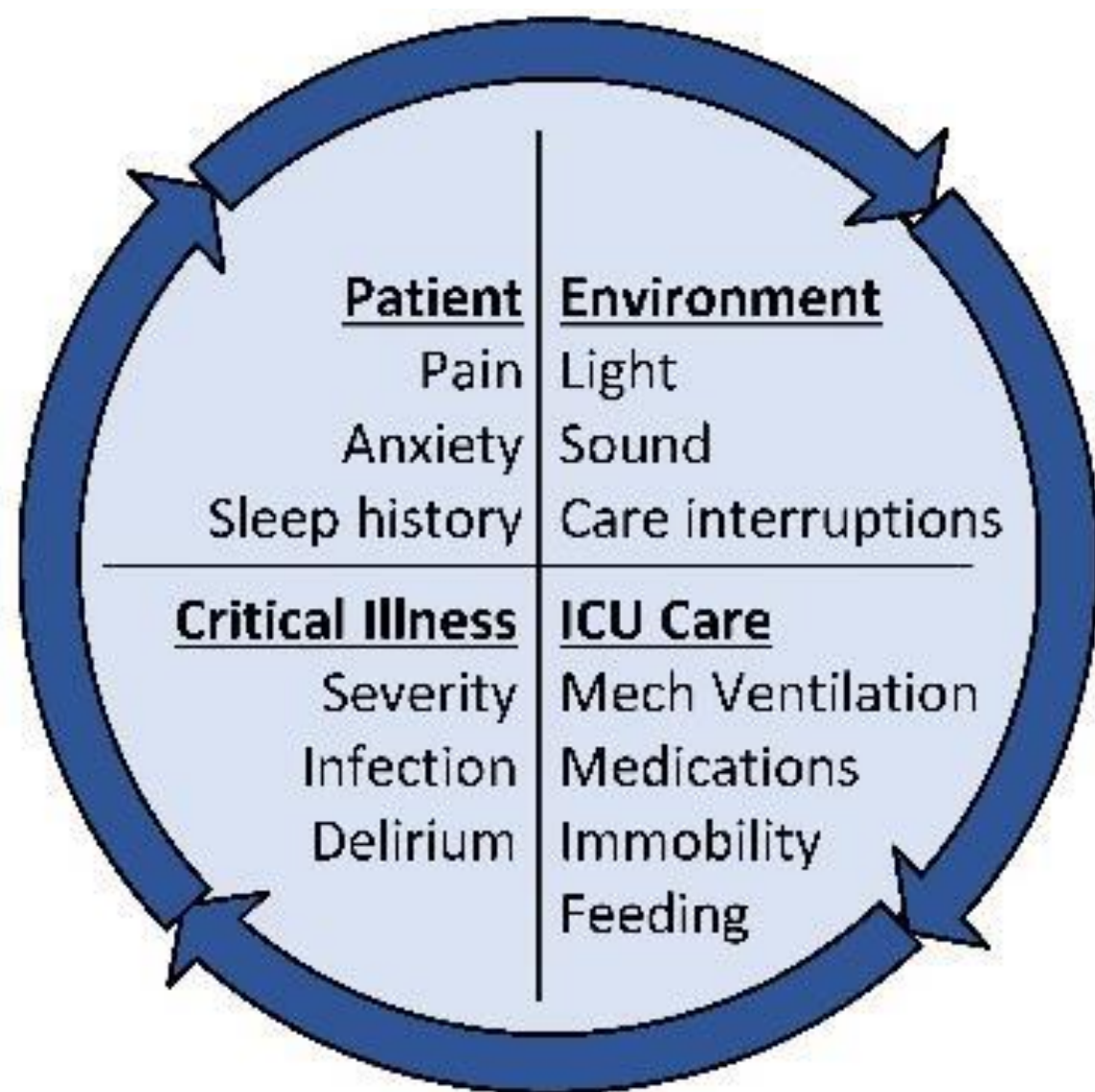
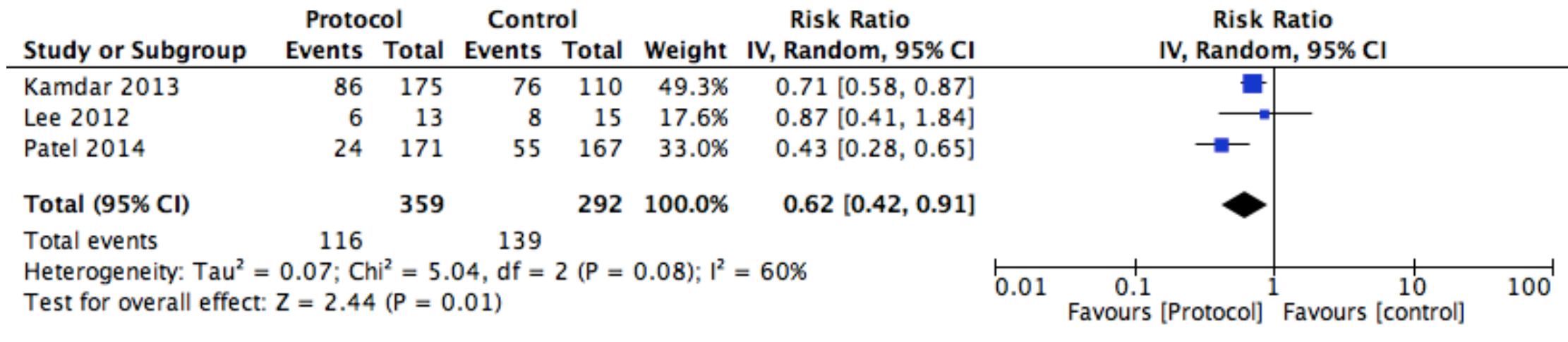


Fig 4: Causes of ICU sleep & circadian disruption

Evidence: Sleep Promoting Protocol



Delirium prevalence: RR: 0.62; 95% CI, 0.42 to 0.91 (for n=3 before-after studies)

Recommendation:

We suggest using a sleep-promoting, multicomponent protocol in critically ill adults (conditional recommendation, low quality evidence).

Causes, Consequences, and Treatments of Sleep and Circadian Disruption in the ICU

An Official American Thoracic Society Research Statement

✎ Melissa P. Knauert, Najib T. Ayas, Karen J. Bosma, Xavier Drouot, Mojdeh S. Heavner, Robert L. Owens, Paula L. Watson, M. Elizabeth Wilcox, Brian J. Anderson, Makayla L. Cordoza, John W. Devlin, Rosalind Elliott, Brian K. Gehlbach, Timothy D. Girard, Biren B. Kamdar, Amy S. Korwin, Elizabeth R. Luszczek, Sairam Parthasarathy, Claudia Spies, Jag Sunderram, Irene Telias, Gerald L. Weinhouse, and Phyllis C. Zee; on behalf of the American Thoracic Society Assembly on Sleep and Respiratory Neurobiology

- 1. Advance the development of new ICU sleep and circadian disruption measures.**
- 2. Develop automated methods which leverage patient and environmental variables available at the bedside to measure ICU sleep and circadian domains in real time.**
- 3. Leverage implementation science strategies to assure intervention fidelity and sustainability of multicomponent sleep and circadian interventions.**
- 4. Increase collaboration among inter-professional and clinical-translational investigators to harmonize research methods and promote multisite investigation.**
- 5. Maximize study results by embedding mechanistic outcomes within larger clinical trials focused on clinically important patient-centered outcomes.**
- 6. Characterize/identify the association between individual ICU sleep and circadian disruption domains and patient outcomes.**
- 7. Investigate the impact of including personalization in sleep promotion interventions.**

Sleep in Critical Illness

Physiology, Assessment, and
Its Importance to ICU Care

Gerald L. Weinhouse
John W. Devlin
Editors

 Springer



Early Mobilization and Rehabilitation

- 1. Screen Every ICU Patient Daily for Rehabilitation/Mobility**
 - PT ideal for screening
 - RN, RT, RN assistants (and family) can deliver the mobilization
 - In bed rehabilitation will benefit patient
 - Address orthostatic hypotension/dizziness (often med-related)
- 2. Ensure consensus re: Mobilization Start/Stop Criteria.**
- 3. Start mobilization efforts in 1-2 ICU beds and then slowly expand**
- 4. Mobility RCTs show early mobility is far more effective than late mobility**
- 5. Mobility will reduce delirium and long-term cognitive decline**

Table 1. Safety criteria for start/stop rehab/mobilization (in-bed or out-of-bed)

Safety criteria	Starting a Rehab/Mobility session	Stopping a Rehab/Mobility session
System	<u>Start</u> when ALL of the following are present:	<u>Stop</u> when ANY of the following are present:
Cardiovascular	<ul style="list-style-type: none"> ● Heart rate between 60 - 130 bpm ● Systolic B/P between 90 - 180 mmHg, or ● Mean arterial pressure between 60-100 	<ul style="list-style-type: none"> ● Heart rate decreases <60 or increases >130 ● Systolic decreases <90 or increases >180 ● MAP decreases <60 or increases >100
Respiratory	<ul style="list-style-type: none"> ● Respiratory rate between 5 - 40 bpm ● SpO₂ ≥88% ● FiO₂ <0.6 & PEEP <10 cmH₂O ● Airway (ETT or trach) adequately secured 	<ul style="list-style-type: none"> ● Resp. rate decreases <5 or increases >40 ● SpO₂ decreases <88% ● Concerns re: securement of ETT or trach
Neurologic	<ul style="list-style-type: none"> ● Able to open eyes to voice 	<ul style="list-style-type: none"> ● Change in LOC
Other	<p>The following should be absent:</p> <ul style="list-style-type: none"> ● New or symptomatic arrhythmia ● Chest pain with concern for ischemia ● Unstable spinal injury or lesion ● Unstable fracture ● Active or uncontrolled GI bleed <p>Mobility may be performed with:</p> <ul style="list-style-type: none"> ● Femoral VAD, except sheath, in which hip mobilization is generally avoided ● Continuous renal replacement therapy ● Vasoactive medication infusion 	<p>If following develop & clinically relevant:</p> <ul style="list-style-type: none"> ● New/symptomatic arrhythmia ● Chest pain with concern for ischemia ● Ventilator asynchrony ● Fall ● Bleeding ● Medical device removal or malfunction ● Distress reported by patient or clinician



Family Engagement and Empowerment

- 1. Attempt to involve, engage and empower patients and families to be active participants in daily rounds and care**
- 2. The best way for this to be done remains unclear**

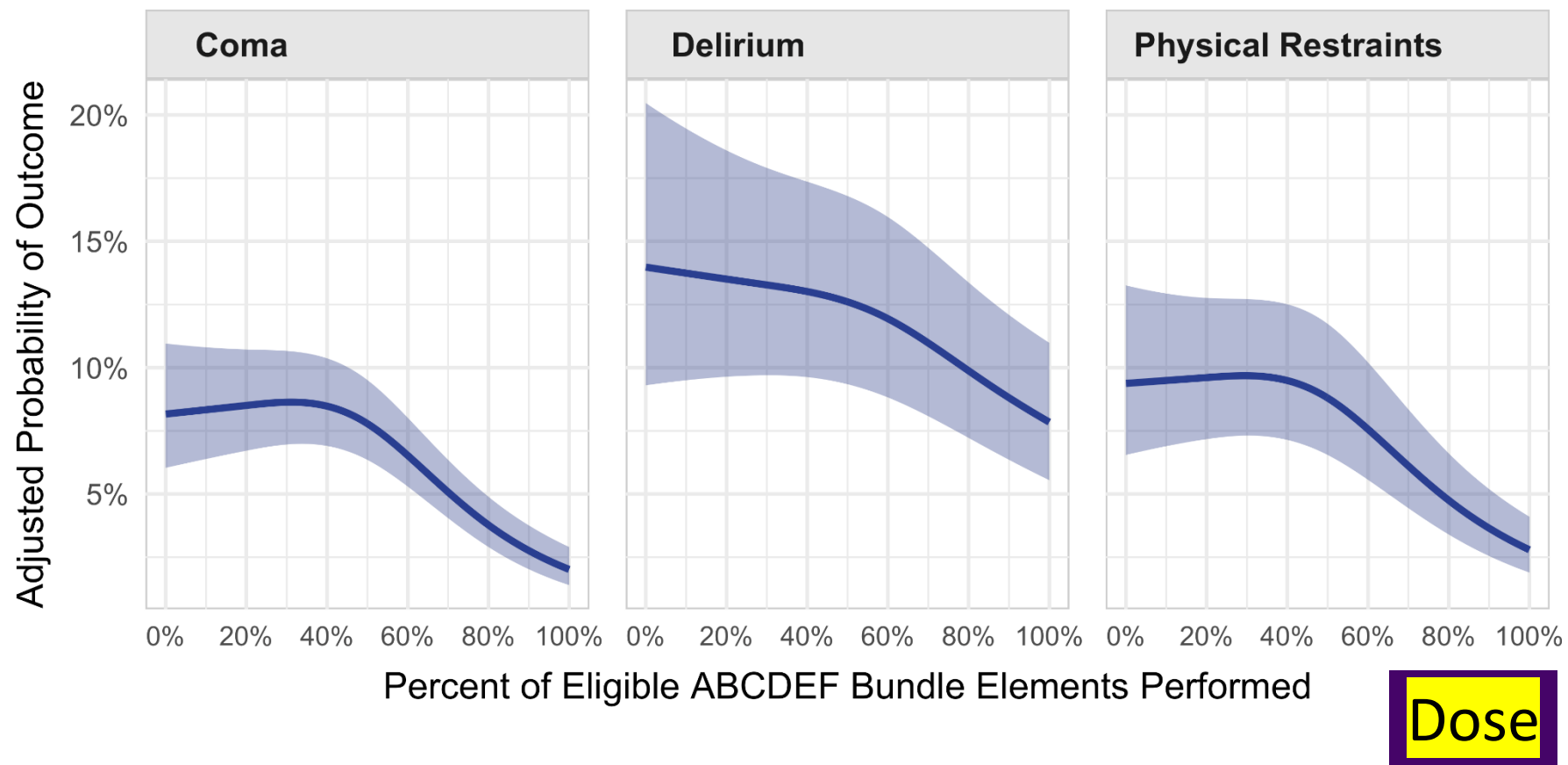
Caring for Critically Ill Patients with the ABCDEF Bundle: Results of the ICU Liberation Collaborative in Over 15,000 Adults

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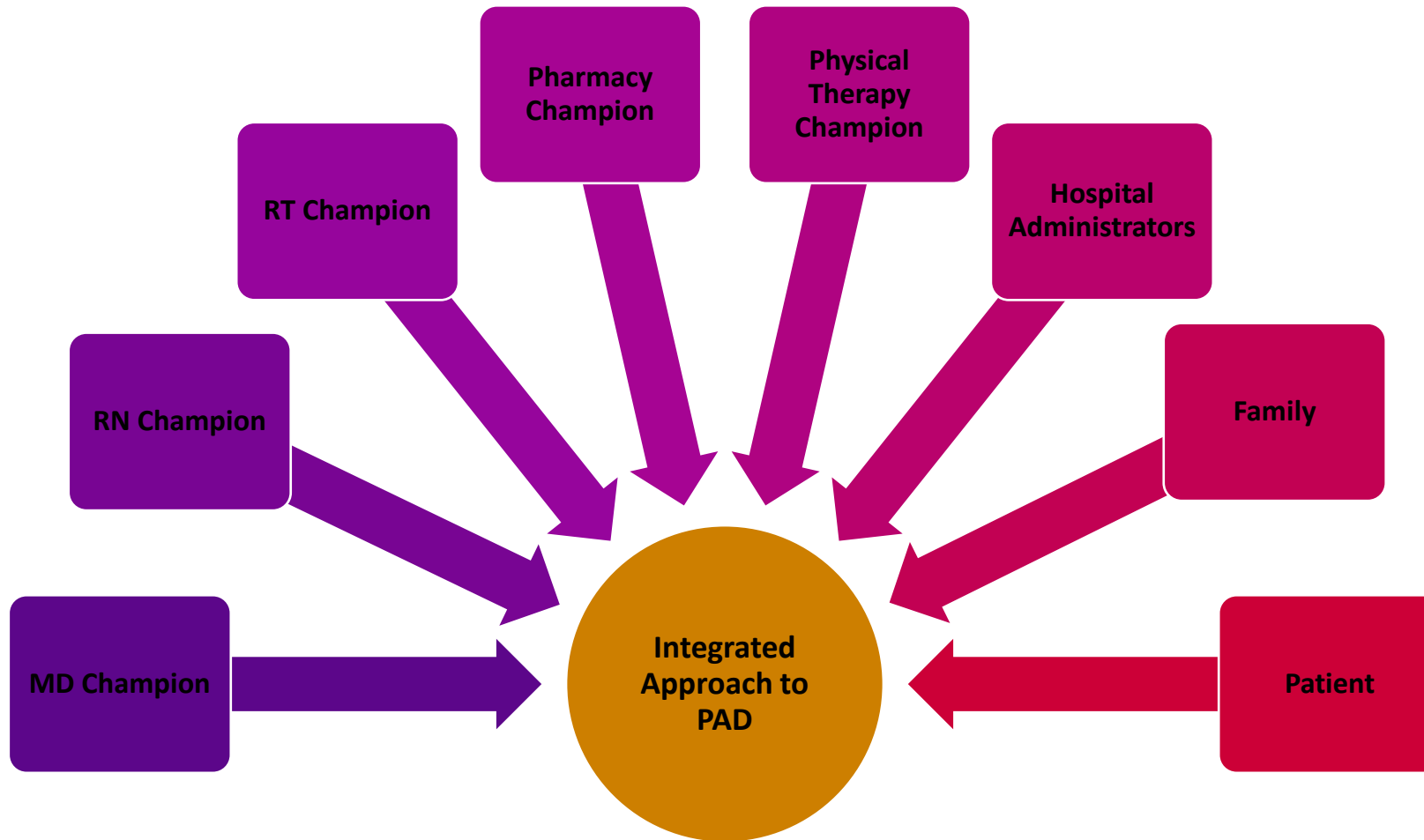
TABLE 2. Outcomes for Patients With Complete (vs Incomplete) ABCDEF Bundle Performance: Data are Adjusted Hazard Ratios (AHRs) and Adjusted Odds Ratios (AORs)

Outcomes	Complete Bundle Performance	p Value
Patient-Related Outcomes	AHR (95% CI)	
ICU discharge ^a	1.17 (1.05–1.30)	< 0.004
Hospital discharge ^b	1.19 (1.01–1.40)	< 0.033
Death ^c	0.32 (0.17–0.62)	< 0.001
Symptom-Related Outcomes^d	AOR (95%CI)	
Mechanical ventilation	0.28 (0.22–0.36)	< 0.0001
Coma	0.35 (0.22–0.56)	< 0.0001
Delirium	0.60 (0.49–0.72)	< 0.0001
Significant pain	1.03 (0.88–1.21)	0.7000
Physical restraints	0.37 (0.30–0.46)	< 0.0001
System-Related Outcomes	Adjusted OR (95%CI)	
ICU readmission ^e	0.54 (0.37–0.79)	< 0.001
Discharge destination ^f	0.64 (0.51–0.80)	< 0.001

Results: Symptom-Related Outcomes



Interprofessional Team Important



Use of Implementation Strategies Including a Formalized ICU Rounding Strategy and Important to ABCDEF Bundle Success



Best Practices for Conducting Interprofessional Team Rounds to Facilitate Performance of the ICU Liberation (ABCDEF) Bundle

Joanna L. Stollings, PharmD, FCCM, FCCP^{1,2}; John W. Devlin, PharmD, FCCM, FCCP^{3,4};
John C. Lin, MD⁵; Brenda T. Pun, DNP, RN, FCCM^{2,6}; Diane Byrum, MSN, RN, CCRN-K, CCNS, FCCM⁷;
Juliana Barr, MD, FCCM^{8,9}





Case of RS – ICU day #2 (8am)

RS is a 72 year old female who remains in the Surgical ICU POD #2 after emergent surgical repair of a leaking 3 inch abdominal aortic aneurysm.

HR =110, BP = 98/63, RR = 20; SaO2 =99%

CPOT= 2, RASS = -3, CAM-ICU = negative

Mechanically ventilated: SIMV =14, TV 500, FiO2 = 40%, PEEP=5

Tolerating tube feeds at 20 mL/hr

Receiving fentanyl 25-50 mcg IVP q4h prn pain, propofol @ 30 mcg/kg min, and haloperidol 1mg IV q6h

She has not left the bed since she arrived in the emergency department.

Prior to admission she enjoyed bridge and golfed weekly in a women's golf league.

What is the most important intervention to make in RS's care at this time?

- a. Increase haloperidol to 2mg IV q6h as this is the dose shown in the REDUCE RCT (JAMA 2018) to prevent delirium and reduce 28-d mortality.
- b. Hold her propofol to reach a RASS = 0 and conduct an SBT screen.
- c. Hold her propofol to reach a RASS = 0 and try to mobilize her out of bed.
- d. Given she is in pain, a known risk factor for delirium, start a continuous IV fentanyl infusion @ 50 mcg/hr.

What is the most important intervention to make in RS's care at this time?

- a. Increase haloperidol to 2mg IV q6h as this is the dose shown in the REDUCE RCT (JAMA 2018) to reduce delirium and 28-d mortality.
- b. Hold her propofol to reach a RASS = 0 and conduct an SBT screen.
- c. Hold her propofol to reach a RASS = 0 and try to mobilize her out of bed.
- d. Given she is in pain, a known risk factor for delirium, start a continuous IV fentanyl infusion @ 50 mcg/hr.

B. is correct. RS does require deep sedation; once RS is woken up to a RASS=0; a key priority is to work towards SBT and extubation. A. is wrong as the REDUCE RCT found haloperidol regardless of dosing arm (1 mg q6h or 2mg q6h) does not prevent delirium or reduce 30- or 90-day mortality. C. is wrong. While sedation should be lighted to RASS=0; the greater priority today is to try to extubate her (vs. keep her intubated and try to mobilize her). If RS fails SBT today, then early mobilization is a priority tomorrow. D is wrong as RS has low pain (CPOT =2) so current fentanyl IVP PRN is adequate; Duprey MS et al AJRCCM 2021 found that opioid use, in a dose-related, fashion increased delirium risk independent of pain.

Case of RS – ICU day #2 (6pm)

CPOT= 1, RASS = range -1 to +1, CAM-ICU = positive

HR =82, BP =114/72, RR =19; SaO2 =98%

Mechanically ventilated: SIMV =14, TV 500, FiO2 = 40%, PEEP=5

Receiving fentanyl 25-50 mcg IVP q4h prn pain

Propofol infusion on hold, haloperidol stopped

What is the most important intervention to make in RS's care at this time?

- a. Initiate a dexmedetomidine infusion; titrate to RASS=-2 to 0
- b. Conduct an SBT screen; initiate a SBT if screening criteria passed
- c. Attempt to mobilize her out of bed
- d. Initiate quetiapine 50mg po q8h via her feeding tube

What is the most important intervention to make in RS's care at this time?

- a. Initiate a dexmedetomidine infusion; titrate to RASS=-2 to 0
- b. Conduct an SBT screen; initiate a SBT if she passes screening criteria**
- c. Attempt to mobilize her out of bed
- d. Initiate quetiapine 50mg po q8h via her feeding tube

B is correct as RS is now wakeful and the most important priority is to get her on a SBT (if she passes SBT screen) with hopes of extubation. A is wrong as the only reason to initiate dexmedetomidine in a patient with delirium is to treat agitation but RS currently is calm. C. is wrong. While sedation should be lighted to RASS=0; the greater priority today is to try to extubate her (vs. keep her intubated and try to mobilize her). If RS fails SBT today, then early mobilization is a priority tomorrow. D. is wrong. RS does not have symptoms of delirium that currently warrant antipsychotic use. While one small RCT by Devlin et al Crit Care Med 2010 demonstrates delirium resolves faster with quetiapine (vs placebo) use; this study has many important methodological limitations.

MOC REFLECTIVE STATEMENT (BRIEF TAKE HOME NOTES FOR REFERENCE)

The ABCDEF bundle is a daily well-established, interprofessional quality improvement approach to deliver practice guidelines/best evidence focused on reducing pain, agitation, delirium, immobility and disrupted sleep to ICU adults

- Key strategies for ABCDEF bundle implementation success:
 - Identify the specific role of each ICU team member
 - Structure ICU interprofessional rounds to support ABCDEF bundle use
 - Incorporate existing EPIC/Cerner ABCDEF bundle builds
 - Start with 2 beds in your ICU and then expand

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