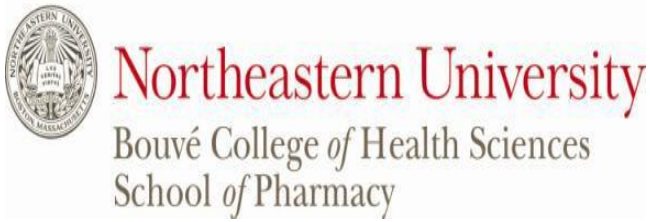
Interpretation and Implementation of the 2018 SCCM PADIS Guidelines

John W. Devlin. PharmD, BCCCP, FCCP, FCCM
Professor of Pharmacy, Northeastern University
Scientific Staff and Critical Care Pharmacist,
Division of Pulmonary, Critical Care and Sleep Medicine, Tufts Medical Center, Boston, MA



Disclosures

Research Funding

- NIA
- NHLBI
- AstraZeneca Pharmaceuticals
- American College of Clinical Pharmacy

Consultant/Speaker

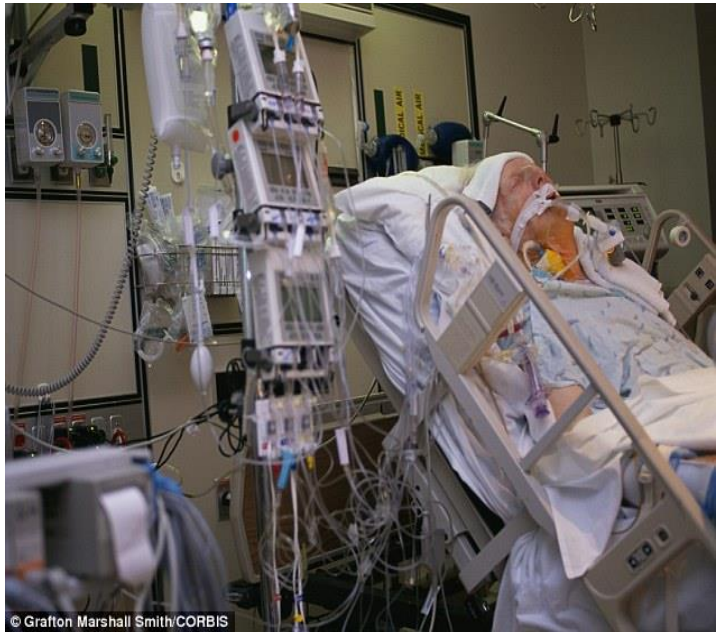
- LaJolla Pharmaceuticals

Objectives

- Summarize the methods and key recommendations from the 2018 SCCM PADIS guidelines
- Identify current evidence gaps surrounding PADIS optimization in the ICU
- Formulate an inter-professional plan to apply the ABCDEF bundle to daily ICU patient care

Pain

Agitation



COMA

Delirium

Disrupted Sleep

Fear

ICU memories

Mobilization and Rehab

Chronic Pain

Depression

Return to Independence

Persistent Cognitive Defects

Reduced Functionality

Family stress

Mortality

Increased healthcare costs

Quality of Life

METHODS & INTERPRETATION

Introduction

2018 **P**ain, **A**gitation/sedation, **D**elirium, **I**mmobility, and **S**leep disruption (**PADIS**) guideline

- Updating **2013** PAD guidelines by:
  - Adding 2 new topics: rehab/mobilization & sleep disruption
  - > 70% of questions new from 2013
  - Including patients as collaborators and co-authors
  - Adding experts from Europe & Australia
  - Focus on post-ICU, patient-centric outcomes
- 37 recommendations & 2 ungraded good practice statements
  - 2 of 37 recommendations, rated as “strong”
- 32 ungraded statements (*non-actionable* descriptive questions)

PICO and Descriptive Questions for PADIS CPG

Pain	Agitation/Sedation	Delirium	Immobility (Rehab/Mobility)	Sleep (Disruption)
Factors that influence pain	Light vs. deep sedation	Delirium prediction	Rehab or mobilization (performed in or our of bed) vs different rehab/mobilization intervention, placebo or sham	Comparison of sleep in critically ill adults vs: • Healthy adults • Delirium (vs no delirium) • MV (vs. no MV) Prevalence unusual sleep
Assessment • Patient self-report • Behavioral • Proxy reporters • Physiologic measures	Prevalence, rationale and outcomes of physical restraint use	• Risk factors • Influence of level of arousal on delirium assessment • Outcomes of delirium		
Protocol-based assessment and management: • Analgesia-first • Analgosedation	Daily sedation interruption vs. nurse-protocolized sedation	Delirium assessment using valid tool (vs. no assessment)	Harm associated with rehab/mobilization (either in or out of bed)	Use of physiologic/non-physiologic sleep monitoring
Multimodal analgesia to reduce opioid use: • Acetaminophen • Nefopam • Ketamine • Neuropathic analgesia • IV lidocaine • NSAID	MV patients after cardiac surgery: • Propofol vs benzodiazepines	Pharmacologic prevention: • Haloperidol • Atypical antipsychotic • Statin • Dexmedetomidine • Ketamine	Clinical indicators to safely initiate rehab/mobilization (either in or our of bed)	Risk factors affecting ICU sleep quality: • Prior to critical illness • ICU-acquired Disrupted sleep outcomes: • During ICU admission • After ICU discharge
Procedural analgesia • Opioid vs. none • High vs. low dose opioid • Local analgesia • Nitrous oxide • Isoflurane • NSAID (systemic/gel)	MV critically ill adults • Propofol vs benzodiazepines • Dexmedetomidine vs benzodiazepines • Propofol vs dexmedetomidine	Pharmacologic treatment: • Haloperidol • Atypical antipsychotic • Statin • Dexmedetomidine • Ketamine	Clinical indicators to stop rehab/mobilization (either in or out of bed)	Pharmacologic treatment: • Melatonin • Dexmedetomidine • Propofol
Non-pharmacologic analgesic strategies • Cybertherapy/Hypnosis • Massage • Music • Cold therapy • Relaxation techniques	Objective sedation monitoring tools	Non-pharmacologic delirium reduction interventions: • Single: Bright light therapy • Multi-component: ABCDEF bundle		Non-pharmacologic treatment: • AV vs PS mode • Adaptive vs PS mode • Aromatherapy • Music • Noise/Light reduction • Multimodal protocol

PADIS Guideline Authors

[1]John Devlin, PharmD **(Chair for Overall CPG)**
[2]Yoanna Skrobik, MD, MSc **(Vice-Chair)**

[3]Céline Gélinas, RN, PhD **(Chair, Pain)**
[4]Aaron Joffe, DO
[5]Kathleen Puntillo RN, PhD
[6]Gerald Chanques, MD, PhD
[7]Jean-Francois Payen, MD, PhD
[8]Paul Szumita, PharmD

[9]Pratik Pandharipande, MD, MSCI **(Chair, Sedation)**
[10]Richard Riker, MD
[11]Michele Balas, RN, PhD
[12]Yahya Shehabi, MD, PhD
[13]John Kress, MD
[14]Bryce Robinson MD, MS

[15]Arjen Slooter, MD, PhD **(Chair, Delirium)**
[16]Brenda Pun, RN, DNP
[17]Gilles Fraser, PharmD, MCCM
[18]Margaret Pisani, MD, MPH
[19]Karin Neufeld, MD, MPH
[20]Mark van den Boogaard, RN, PhD

[21]**Dale Needham, MD, PhD (Chair, Immobility)**
[22]Linda Denehy, PT, PhD
[23]Michelle Kho, PT, PhD
[24]Chris Winkelman, RN, PhD
[25]Nathaniel Brummel, MD, MSCI
[26]Jocelyn Harris, OT, PhD
[27]Julie Lanphere, DO
[28]Sina Nikayin, MD (research staff)

[29]Paula Watson, MD, MPH **(Co-Chair, Sleep)**
[30]Gerald Weinhouse, MD **(Co-Chair, Sleep)**
[31]Xavier Drouot, MD, PhD
[32]Karen Bosma, MD
[33]Sharon McKinley, RN, PhD

[34]Waleed Alhazzani, MD, MSc (**Chair, Methods**)
[35]Mark Nunnally, MD
[36]Bram Rochwerg, MD, MSc
[37]John Centofani, MD, MSc

[38]Carrie Price, MLS (medical librarian)
[39]Cheryl Misak, PhD (patient rep)
[40]Ken Kiedrowski, MA (patient rep)
[40]Pamela Flood, MD (patient rep)

Methods

- **G**rading of **R**ecommendations **A**ssessment, **D**evelopment and **E**valuation (**GRADE**) methodology
- Chairs, section heads, panel members, ICU survivors, librarian
- Topics selected/prioritized with input from ICU survivors, then:
  - Literature review: 5 electronic data-bases,1990 to October 2015
  - Evaluation of methodological rigor with GRADE guidance
  - Formulating & then voting on preliminary recommendations
  - In-person discussion among the full panel (SCCM 2017 Congress)
  - Anonymous Voting (>80% agreement with >70% response rate)
    - 100% of panel voted (with reminders/prompts)
- ICU survivors participated in every step

Devlin JW, et al. PADIS Method Innovations Paper. Crit Care Med 2018; 46:1457-1463

Strong vs. Conditional Recommendations

	Strong	Conditional
Patients	Applies to almost all patients	Applies to most patients (significant exceptions based on patient condition, values & preferences)
Supporting evidence	Moderate to high quality across broad populations	Conflicting, low quality, insufficient, and/or limited populations
Benefits versus burdens	Benefits clearly outweigh burdens	May be close balance between benefits and burdens
Influence of future research	Limited potential to change recommendation	Possible/probable potential to change recommendation
Performance or quality indicators	Can be readily adapted in most health-care systems	Requires significant deliberation at the local level based on practice patterns, patients served, and resource availability

Balas MC, et al. PADIS Interpretation and Implementation Paper. Crit Care Med 2018;46:1464-1470.

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

Michele C. Balas, PhD, RN, CCRN-K, FCCM, FAAN[1,2]; Gerald L. Weinhouse, MD[3,4]; Linda Denehy, PT, PhD[5]; Gerald Chanques, MD, PhD[6]; Bram Rochwerg, MD, MSc[7]; Cheryl J. Misak, DPhil[8]; Yoanna Skrobik, MD, FRCP(c), MSc, FCCM[9]; John W. Devlin, PharmD, FCCM[10,11]; Gilles L. Fraser, PharmD, MCCM[12,13]

three actionable and three descriptive questions. (A prioritized topic list is in **Supplemental Table 10** [Supplemental Digital Content 13, http://links.lww.com/CCM/D771], and voting results appear in **Supplemental Table 11** [Supplemental Digital Content 14, http://links.lww.com/CCM/D772].) The evidence summaries and evidence-to-decision tables used to develop recommendations for the agitation (sedation) group are available in **Supplemental Table 12** (Supplemental Digital Content 15, http://links.lww.com/CCM/D773), and the forest plots for all completed meta-analyses are available in **Supplemental Figure 3** (Supplemental Digital Content 16, http://links.lww.com/CCM/D774).

Topic list with prioritized scores

Recommendation voting results

Evidence summaries

Evidence to Decision tables

Forest plots for all meta-analyses

Balas MC, et al. PADIS Interpretation and Implementation Paper. Crit Care Med 2018;46:1464-1470.

PAIN

Protocol-Based Pain Assessment/Management

PICO Question	
P	Critically ill adult patients in an ICU
I	Protocol-based (analgesia/analgosedation) pain assessment and management program
C	Usual care
O	• Pain intensity • Medication exposure (opioids and sedatives) • Adverse events • Duration of mechanical ventilation • ICU Length of stay

Good practice statement:

Management of pain for adult ICU patients should be guided by routine pain assessment and pain should be treated before a sedative agent is considered

- Analgesia-first sedation:

  - An analgesic (usually an opioid) is used before a sedative to reach the sedative goal

- Analgesia-based sedation:

  - An analgesic (usually an opioid) is used instead of a sedative to reach the sedative goal.

Key Concepts with Analgesia-Based Sedation

- **Takes advantage of certain opioid properties**
  - Reduces/eliminates sedative requirements and their associated ADRs
  - Improves sedation-agitation scores
  - Dyspnea & respiratory depressant properties
- **May accentuate opioid-related ADR's**
  - Gastric dysmotilty, delirium, hypotension, myoclonus, chest wall rigidity
- **May not be appropriate for patients with GABA agonist/sedative needs:**
  - Alcohol/drug withdrawal & drug intoxication
  - Neuromuscular blockade
  - Elevated intracranial pressure & status epilepticus

Park G, et al. *Br J Anaesth.* 2007;98:76-82.
Rozendaal FW, et al. *Intensive Care Med.* 2009;35:291-298.
Devabhakthuni S,et al. *Ann Pharmacother*. 2012 Apr;46(4):530-40.

Key factors leading to a conditional (versus a strong) recommendation:

- Only 3 of 5 RCTs have consistent results for critical outcomes
- Most RCTs focused ICU subgroups (e.g. medical)
- Behavior pain scales not consistently used
- Safety outcomes not well described
- Choice of opioid varied
- All studies conducted in Europe
- None of the studies blinded
- Control group managed differently across studies

Recommendation:

We **suggest** using an assessment-driven, protocol-based (analgesia/analgosedation), stepwise approach for pain and sedation management in critically ill adults (*Conditional recommendation*, moderate quality of evidence)

Multimodal Analgesia

- Definition
  - *Combining different analgesics that act by different mechanisms and at different sites in the nervous system, resulting in additive or synergistic analgesia with lowered adverse effects compared to sole administration of individual analgesics*
- Also known as “balanced analgesia”
- Established 1993
- Recommended by perioperative practice guidelines
- Limited ICU literature

Kehlet H. *Anesth Analg*. 1993 Nov;77(5):1048-56.
Young A, et al. *Anesthesiol Clin*. 2012 Mar;30(1):91-100.
American Society of Anesthesiologists. *Anesthesiology*. 2012 Feb;116(2):248-73.
Buvanendran A, et al. *Curr Opin Anaesthesiol*. 2009 Oct;22(5):588-93.

Multimodal Analgesia

PICO Question

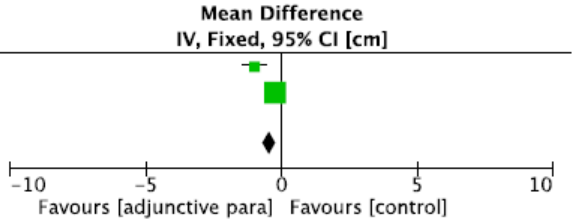
P	Critically ill adult patients in an ICU
I	Adjunctive: • Acetaminophen (IV/PO/PR) • Nefopam • Ketamine • Neuropathic analgesia • IV lidocaine • NSAID (IV/PO)
C	No use of the adjunctive intervention
O	• VAS score at 24 hours postoperatively (in cm) • Mean BPS pain scores until patient extubated • Pain score at extubation • Time to extubation (minutes) • Rescue opioid doses • Opioid consumption (in morphine equivalents)

Adjuvant Treatment -Acetaminophen

VAS Pain Score at 24 hours (postoperatively)

Study or Subgroup	Adjunctive paracetamol Mean [cm]	SD [cm]	Total	Placebo Mean [cm]	SD [cm]	Total	Weight	Mean Difference IV, Fixed, 95% CI [cm]
Cattabriga 2007	1	0.74	56	2	1.48	57	28.9%	−1.00 [−1.43, −0.57]
Memis 2010	2.4	0.55	20	2.64	0.3	20	71.1%	−0.24 [−0.51, 0.03]
Total (95% CI)			**76**			**77**	**100.0%**	**−0.46 [−0.69, −0.23]**

Heterogeneity: $Chi^2 = 8.52$, df = 1 (P = 0.004); $I^2 = 88\%$
Test for overall effect: Z = 3.89 (P < 0.0001)

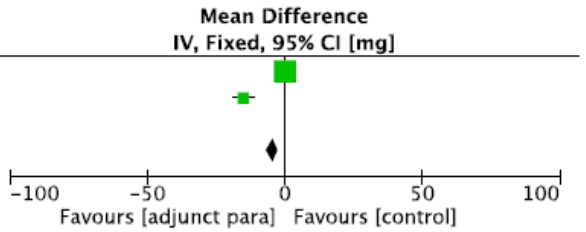


Adjuvant Treatment -Acetaminophen

Opoid Consumption (Morphine Equivalents)

Study or Subgroup	Adjunctive paracetamol Mean [mg]	SD [mg]	Total	Placebo Mean [mg]	SD [mg]	Total	Weight	Mean Difference IV, Fixed, 95% CI [mg]
Cattabriga 2007	5	5.9	56	5	7.4	57	70.1%	0.00 [−2.47, 2.47]
Memis 2010	9.59	2.275	20	24.75	8.3	20	29.9%	−15.16 [−18.93, −11.39]
Total (95% CI)			**76**			**77**	**100.0%**	**−4.54 [−6.60, −2.47]**

Heterogeneity: $Chi^2 = 43.48$, df = 1 (P < 0.00001); $I^2 = 98\%$
Test for overall effect: Z = 4.31 (P < 0.0001)



Considerations:

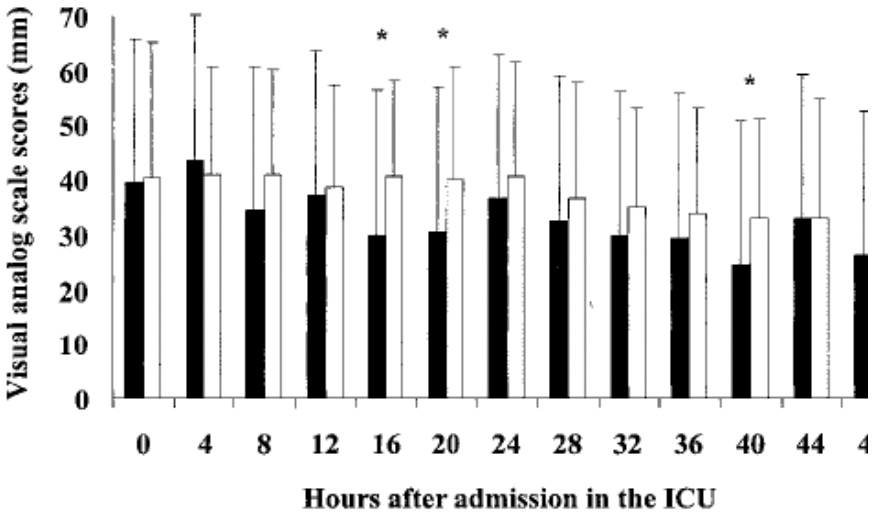
- Data limited to cardiac/abdominal surgery patients only
- Both RCTs single center; one very low quality
- Analgesia side effects not well evaluated
- Risk for hypotension in more unstable ICU patients?
- Availability and cost of IV acetaminophen varies widely around the world

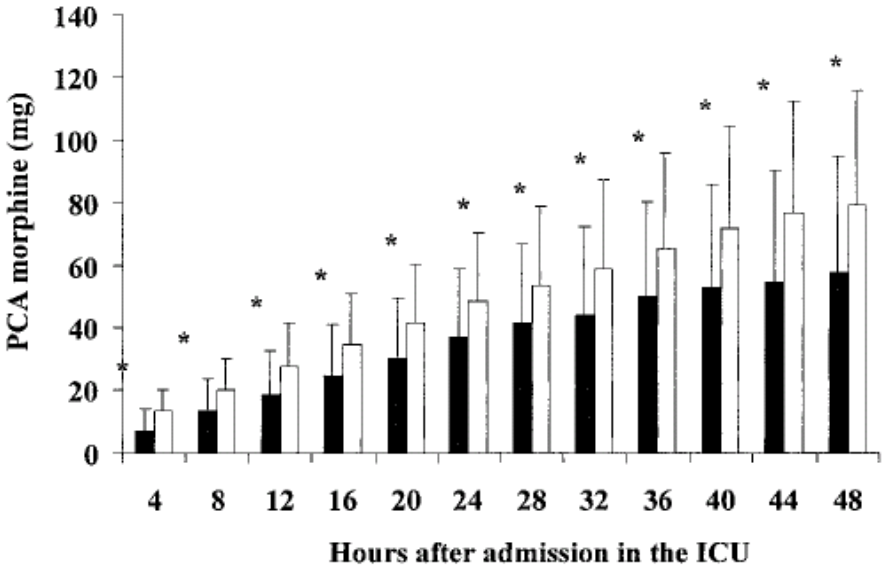
Adjunctive Acetaminophen (IV/PO/PR)

Recommendation:

We **suggest** using acetaminophen as an adjunct to an opioid to decrease pain intensity and opioid consumption for pain management in critically ill adults (conditional recommendation, very low quality of evidence)

Adjunctive Low-dose Ketamine in Surgical ICU Patients





Single center, prospective, randomized, double blind trial including 93 patients scheduled to have major abdominal surgery and post-op management and ventilation in the SICU. Patients were randomized to receive morphine PCA with either placebo or ketamine (for 48 hours). Both groups were allowed as needed morphine boluses.

Considerations:

- Only one RCT available (with a very high risk of bias)
- Data limited to abdominal surgery patients only
- Safety (particularly delirium) not reported
- Role of sedation on effect unclear
- Builds on considerable observational data in non-ICU post operative populations

Guillou N, et al. Anesth Analg 2003; 97:843-847

Adjunctive Low-dose Ketamine

Recommendation:

We **suggest** using low-dose ketamine (0.5 mg/kg IVP x 1; 1 -2 mcg/kg/min) as an adjunct to opioid therapy when seeking to reduce opioid consumption in post-surgical adults admitted to the ICU (Conditional recommendation, Very low quality of evidence)

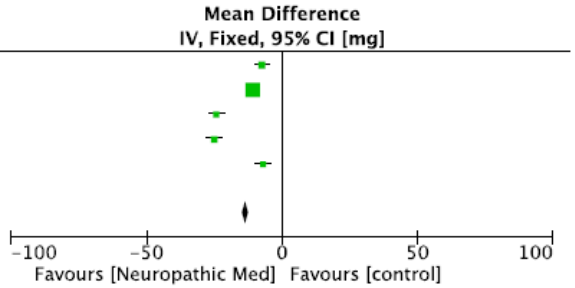
Adjunctive Neuropathic Pain Medications

Adjuvant Treatment – Neuropathic medication

Opioid Consumption in first 24 hours

Study or Subgroup	Neuropathic Pain Agent Mean [mg]	SD [mg]	Total	Control Mean [mg]	SD [mg]	Total	Weight	Mean Difference IV, Fixed, 95% CI [mg]
Joshi 2013	5.08	4.52	20	12.53	3.91	20	15.6%	−7.45 [−10.07, −4.83]
Pandey 2002	21.11	2.138	18	31.944	2.508	18	46.3%	−10.83 [−12.36, −9.31]
Pandey 2005	34.75	3.8	12	59.04	3.5	12	12.6%	−24.29 [−27.21, −21.37]
Pandey 2005	34.01	3.43	12	59.04	3.5	12	14.0%	−25.03 [−27.80, −22.26]
Pesonen 2011	9	6	35	16	7	35	11.5%	−7.00 [−10.05, −3.95]
Total (95% CI)			**97**			**97**	**100.0%**	**−13.54 [−14.57, −12.50]**

Heterogeneity: $Chi^2 = 168.44$, df = 4 ($P < 0.00001$); $I^2 = 98\%$
Test for overall effect: $Z = 25.61$ ($P < 0.00001$)



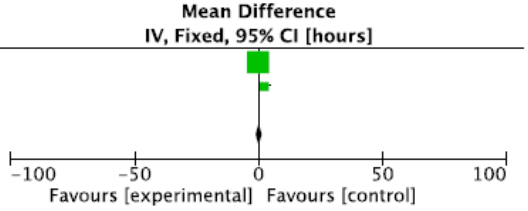
Significantly reduced in favor of neuropathic medication

Adjuvant Treatment – Neuropathic medication

Time to Extubation (hours)

Study or Subgroup	Neuropathic Pain Agent Mean [hours]	SD [hours]	Total	Control Mean [hours]	SD [hours]	Total	Weight	Mean Difference IV, Fixed, 95% CI [hours]
Joshi 2013	7.45	1.95	20	7.68	1.98	20	76.6%	−0.23 [−1.45, 0.99]
Pesonen 2011	10.63	4.75	29	8.33	3.88	31	23.4%	2.30 [0.10, 4.50]
Total (95% CI)			**49**			**51**	**100.0%**	**0.36 [−0.70, 1.43]**

Heterogeneity: $Chi^2 = 3.88$, df = 1 ($P = 0.05$); $I^2 = 74\%$
Test for overall effect: $Z = 0.67$ ($P = 0.51$)



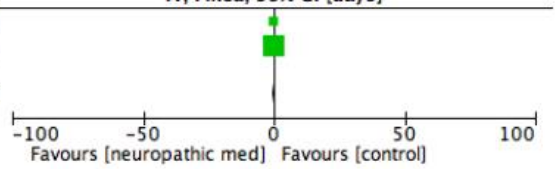
No difference

Adjuvant Treatment – Neuropathic medication

ICU Length of Stay (Days)

Study or Subgroup	Neuropathic Pain Agent Mean [days]	SD [days]	Total	Control Mean [days]	SD [days]	Total	Weight	Mean Difference IV, Fixed, 95% CI [days]
Joshi 2013	3.05	0.68	20	3.2	1.77	20	25.4%	−0.15 [−0.98, 0.68]
Pesonen 2011	1.5	0.8	29	1.5	1.1	31	74.6%	0.00 [−0.48, 0.48]
Total (95% CI)			**49**			**51**	**100.0%**	**−0.04 [−0.46, 0.38]**

Heterogeneity: $Chi^2 = 0.09$, df = 1 ($P = 0.76$); $I^2 = 0\%$
Test for overall effect: $Z = 0.18$ ($P = 0.86$)



No difference

Recommendations:

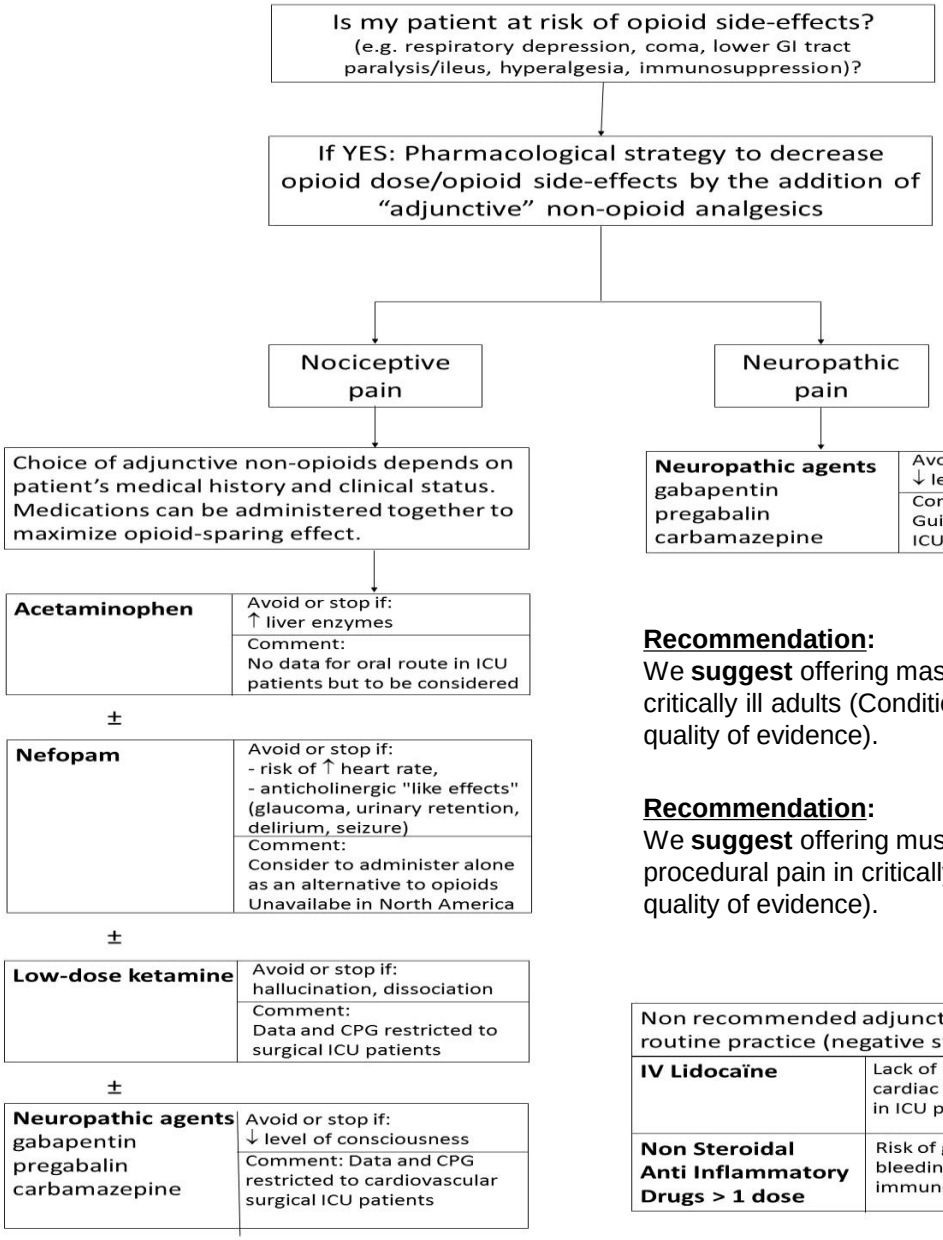
We **suggest** using a neuropathic pain medication (e.g., gabapentin, carbamazepine, and pregabalin) with opioids for pain management in ICU adults after cardiovascular surgery (Conditional recommendation, Low quality of evidence)

Multimodal Analgesia

Evidence Gaps:

- Each adjunctive non-opioid analgesic requires larger studies in critically ill adults to clearly evaluate their opioid-sparing properties and their ability to reduce opioid-associated adverse effects
- Little data in medical ICU patients
- Safety concerns related to specific non-opioid analgesics need to be evaluated in critically ill adults
- Optimal dose and route of administration unclear
- Efficacy and safety data of combination non-opioid analgesic required.

PADIS Algorithm for Use of Adjuvant Analgesics in Critically Ill Adults



<u>Recommendation</u>:
We **suggest** offering massage for pain management in critically ill adults (Conditional recommendation, Low quality of evidence).

<u>Recommendation</u>:
We **suggest** offering music therapy to relieve both non-procedural and procedural pain in critically ill adults (Conditional recommendation, Low quality of evidence).

Non recommended adjunctive analgesics for routine practice (negative studies ± harms)	
IV Lidocaïne	Lack of data regarding cardiac and neurotoxicity in ICU patients
Non Steroidal Anti Inflammatory Drugs > 1 dose	Risk of gastric ulcer, bleeding, renal injury, immunosuppression

*Role of nerve blocks not evaluated in PADIS but likely important

AGITATION/SEDATION

Agitation/Sedation

- Sedatives may predispose pts to increased morbidity
  - Must determine specific indication for use (is pain present?)
  - Assess sedation status frequently using valid/reliable scales
  - Critically ill patients are prone to ↑ adverse events given:
    - reduced drug clearance; unpredictable response, baseline hemodynamic instability

2013 Guidelines

- Improving pts short-term outcome by:
  - Targeting light levels of sedation OR daily awakening trials
  - Minimizing benzodiazepines

2018 Guidelines

- Improving post-ICU outcomes by:
  - Sedation delivery paradigm & specific sedative medication choice
- **3 actionable (PICO) questions + 3 descriptive questions**

Light vs. Deep Sedation

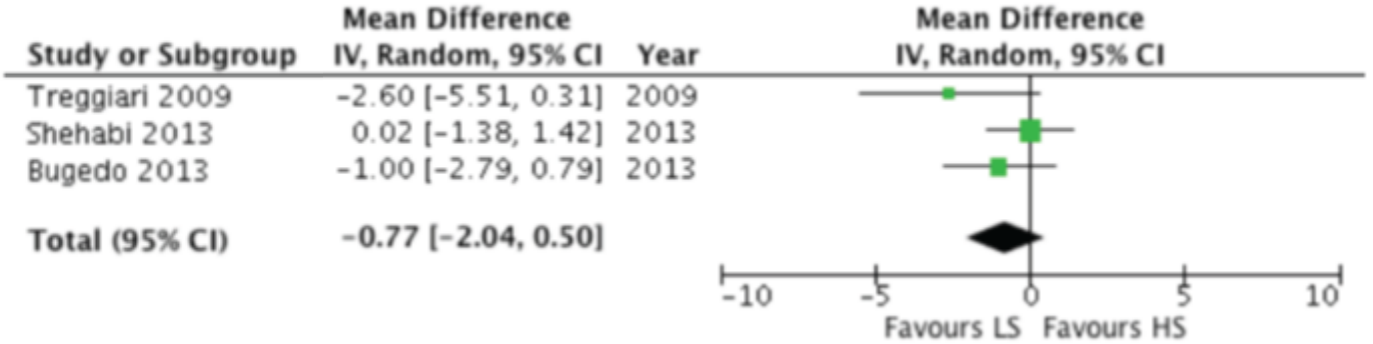
PICO Question			
P	Critically ill adults		
I	Lightly sedated (RASS = -2 to +1 or equivalent) (*DSI/SAT studies not included)		
C	Deeply sedated		
O	• 90-day mortality	• Time to extubation	• Delirium
	• Tracheostomy	• *Cognitive & physical function decline**	
	• Depression	• Post-traumatic stress disorder (PTSD)	

- **Rationale:** 8 RCTs, 3 observational studies

  **No RCTs evaluated post-ICU cognitive or physical functioning*

Light vs. Deep Sedation

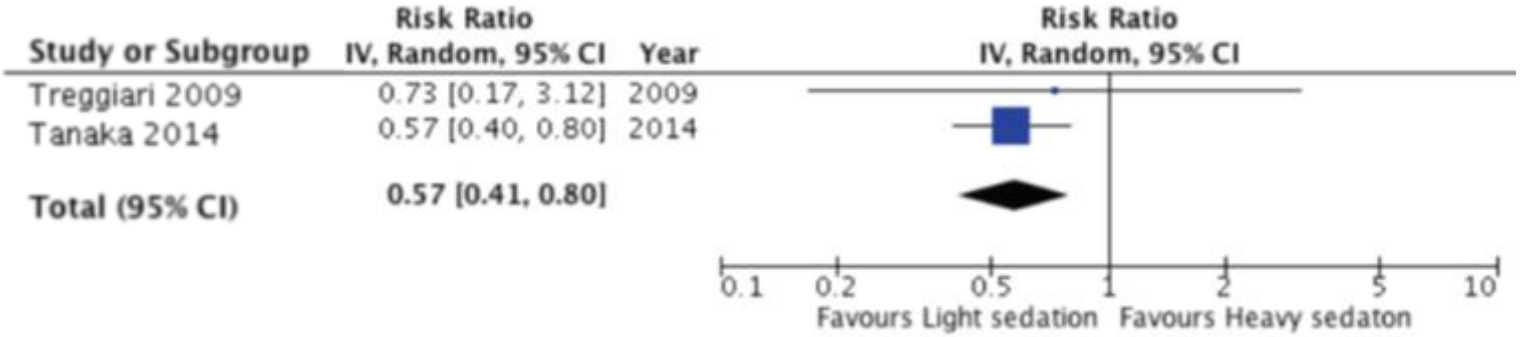
- **Time to extubation** (3 RCTs, 453 pts; low quality)
  - Associated w/ shorter time, MD -0.77 days (95% CI, -2.04 to 0.50)



- **Time to extubation** (3 observational, 1524 pts; low quality)
  - Associated w/ shorter time, MD -3.46 days (95% CI, -5.70 to -1.23)

Light vs. Deep Sedation

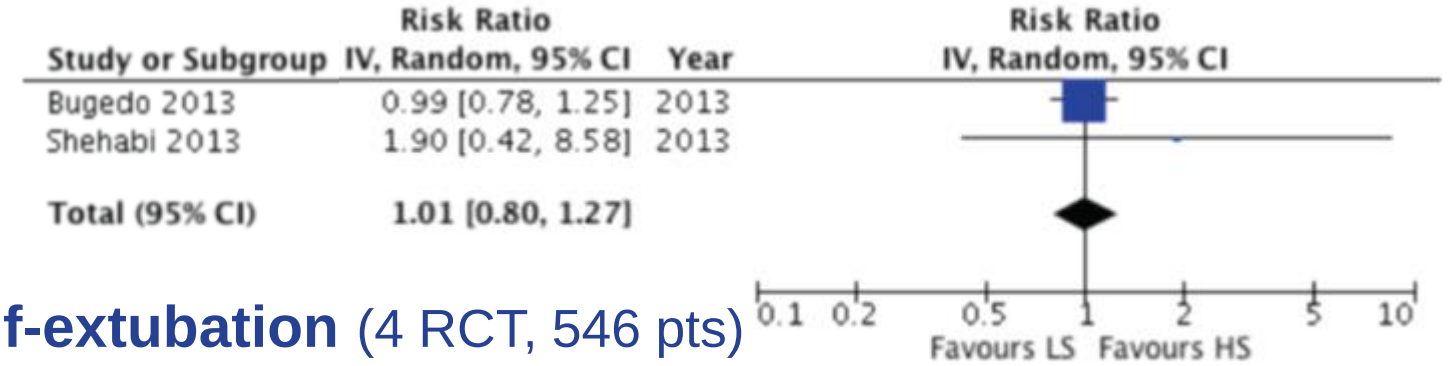
- **Tracheostomy rate** (1 RCT & 1 observational, 452 pts)
  - Reduced, RR 0.57 (95% CI, 0.41 to 0.80)



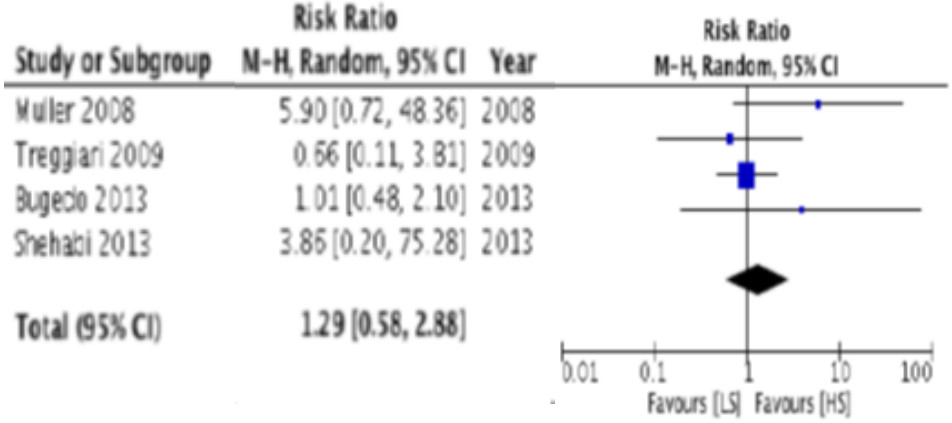
- Light sedation was NOT associated with reduction in:
  - Delirium (2 RCTs, 140 pts), RR 0.96 (95% CI, 0.80 to 1.16)
  - PTSD (2 RCTs, 62 pts), RR 0.67 (95% CI, 0.12 to 3.79)
  - Depression (2 RCTs, 128 pts), RR 0.76 (95% CI, 0.10 to 5.58)

Light vs. Deep Sedation

- **90 days mortality** (2 RCTs, 324 pts)
  - NOT significant, RR 1.01 (95% CI, 0.80 to 1.27; low quality)



- **Self-extubation** (4 RCT, 546 pts)
  - Not significant, RR 1.29 (95% CI, 0.58 to 2.88; low quality)



Light vs. Deep Sedation

Recommendation:

We ***suggest*** using light (vs. deep) sedation in critically ill, mech-ventilated adults (**conditional recommendation**, low quality of evidence).

Evidence gaps:

- No consensus on definition of light, moderate & deep sedation
- Relationship between changing sedation levels over time & clinical outcomes remain unclear
- The effect of light sedation on post-ICU, patient-specific factors need be evaluated in RCTs
- Dearth of info re: interactions between sedative choice, depth & patient-specific factors

Daily Sedative Interruption/Nurse Protocalized Sedation

- **Data:** 5 unblinded RCTs compared DSI to either usual or NP care (739 pts, usually benzodiazepine ± opioid)
  - While differences exist between individual RCTs re: the ability of DSI (vs. its comparator) to maintain light sedation, the overall ability for DSI and NP to achieve light sedation is similar
  - Both DSI & NP are safe

Ungraded statement:

Daily sedative interruption protocols and nursing protocolized targeted sedation can achieve & maintain a light level of sedation

Evidence gaps:

- Variability in nursing sedation assessment frequency & reporting
- Variability in sedative administrative routes among institutions
- Pt & family preference/education should be considered

Recommendation:

We ***suggest*** using ***either*** propofol or dexmedetomidine over benzodiazepines for sedation in critically ill, mechanically ventilated adults (***conditional recommendation***, low quality of evidence).

Evidence Gaps:

- Effect of sedative choice on longer-term, patient-centered, outcomes needs to be investigated; a reliance on evaluating faster extubation no longer suffices
- Patient perceptions, including their ability to communicate, while on different sedatives, needs to be evaluated
- Pharmacology of sedatives and their delivery methods needs to be considered
- Cost considerations are important and often vary between different countries
- Sedative choice in the context of analgosedation requires further evaluation
- Choice of sedative in certain patient subgroups needs further evaluation
  - Neurologically injured, hemodynamically unstable, needing deep sedation

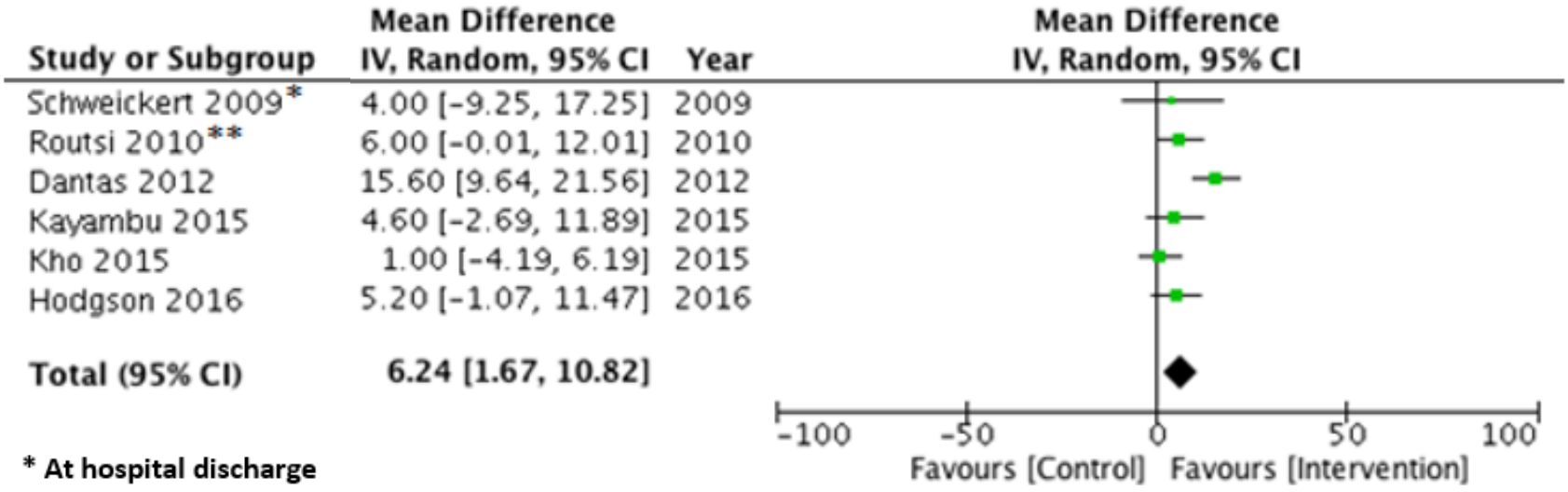
IMMOBILTY

Use of Rehabiltation/Mobility

PICO Question	
P	Critically ill adults
I	Rehab or mobilization (performed in-bed or out-of-bed)
C	Usual care, different rehab/mobility intervention, or placebo,
O	patient, family, or health system outcomes

Efficacy and Benefit

1. **Muscle strength at ICU discharge** (6 RCTs, 304 pt)
   - Improved by 6.2 points (95% CI, 1.7 to 10.8; scale is 0 to 60)
     - low quality (statistical heterogeneity, CI includes MCID)



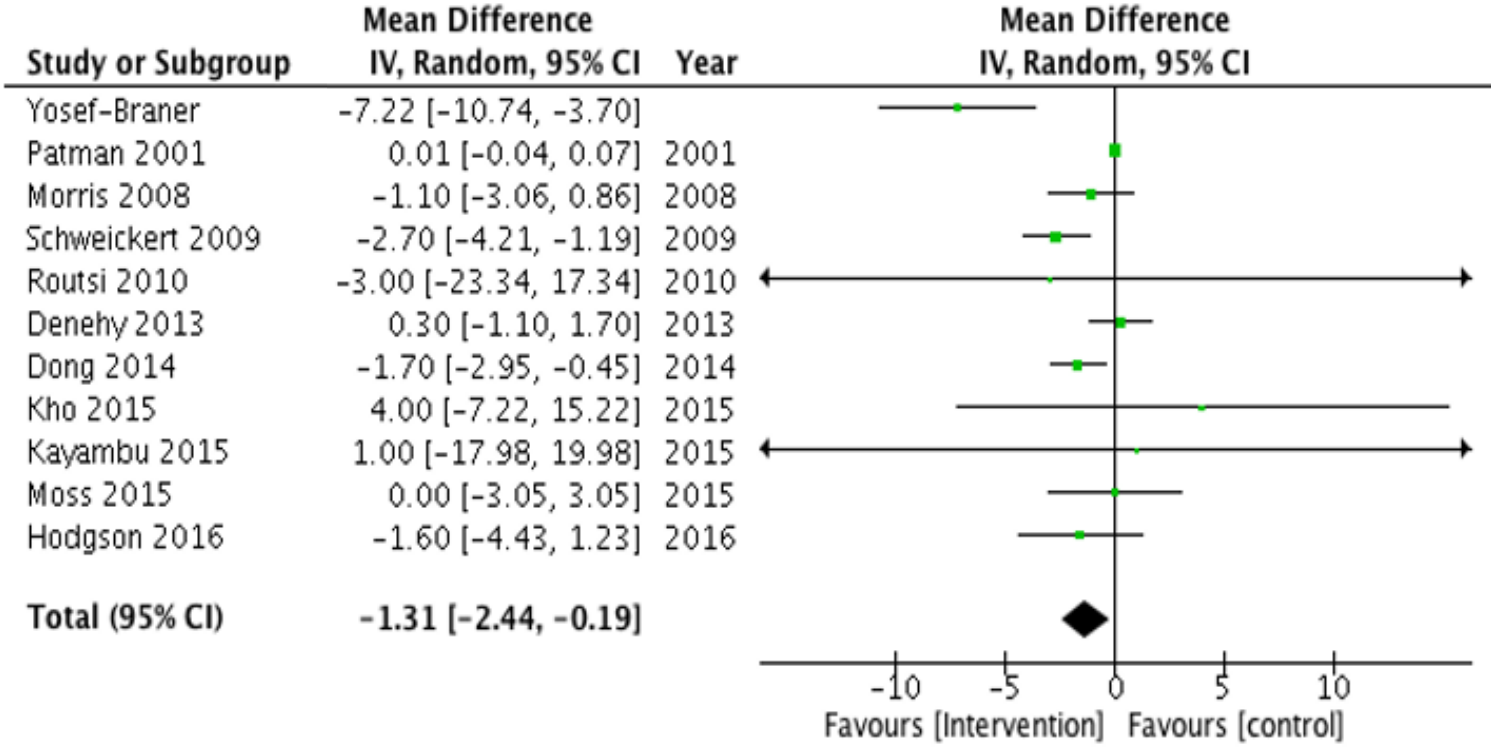
* At hospital discharge

** At ICU awakening

Efficacy and Benefit

2. Duration of mech. ventilation (11 RCTs, 1128 pt)

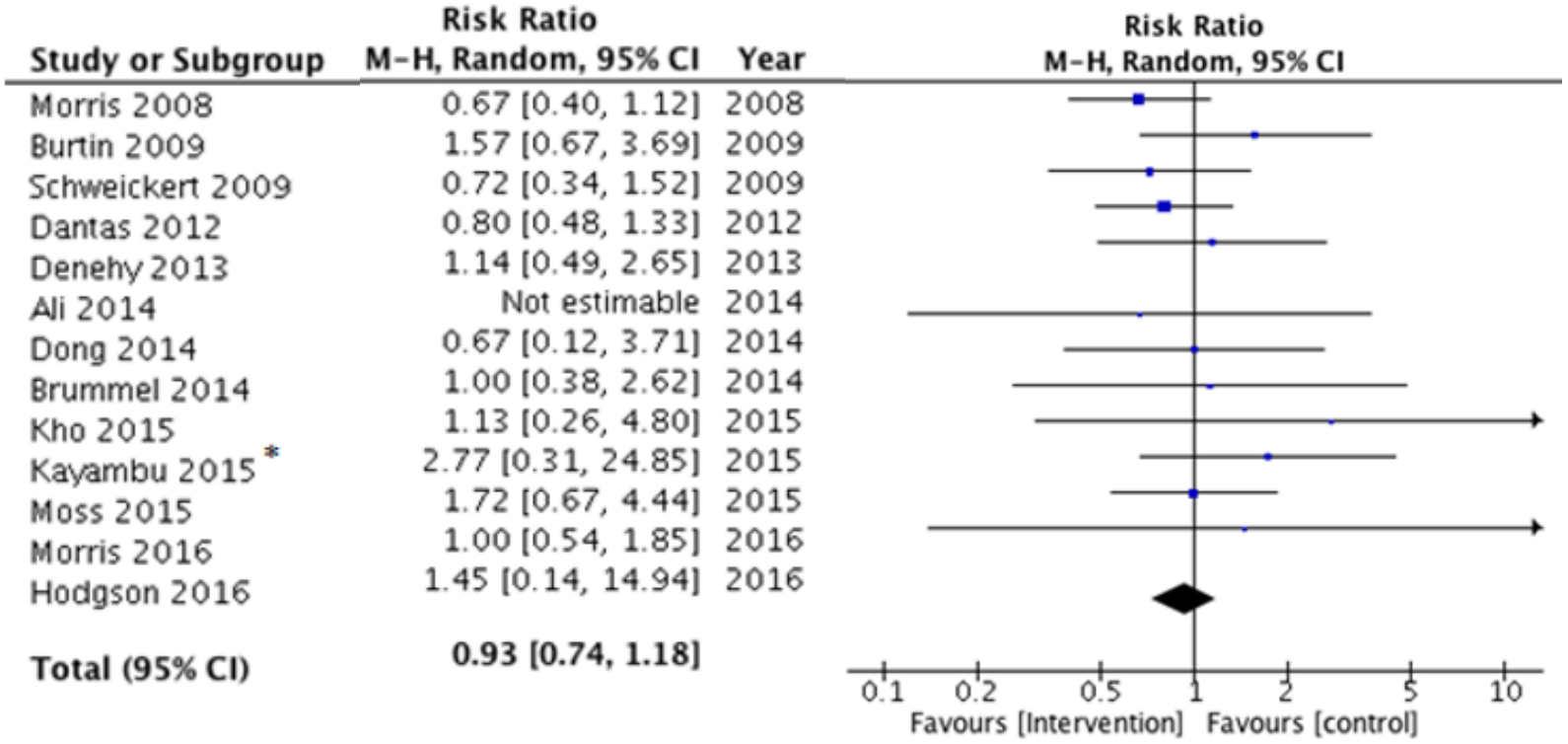
- Reduced by 1.3 days (95% CI, 2.4 to 0.2 days)
  - low quality (2 large RCT high ROB, competing risk, heterogeneity)



Efficacy and Benefit

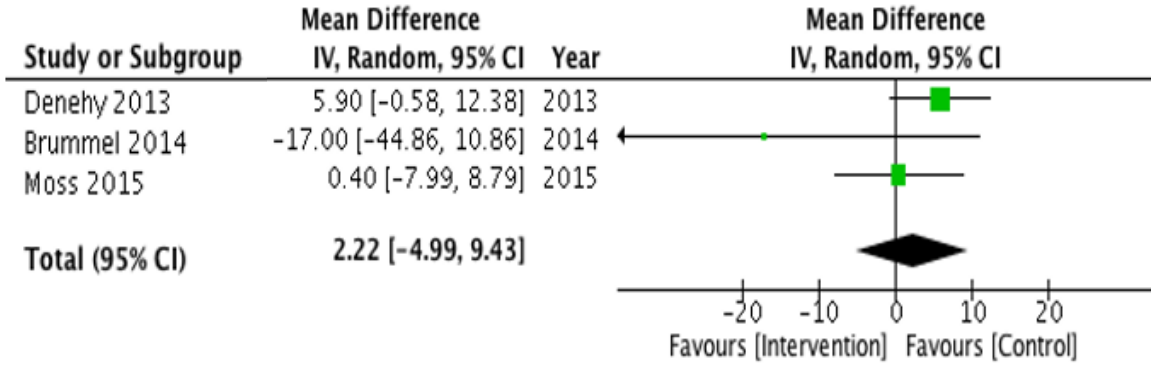
4. Hospital mortality (13 RCTs, 1421 pt)

– No effect, RR=0.93 (95% CI, 0.74 to 1.18) – moderate quality (CI includes harm)

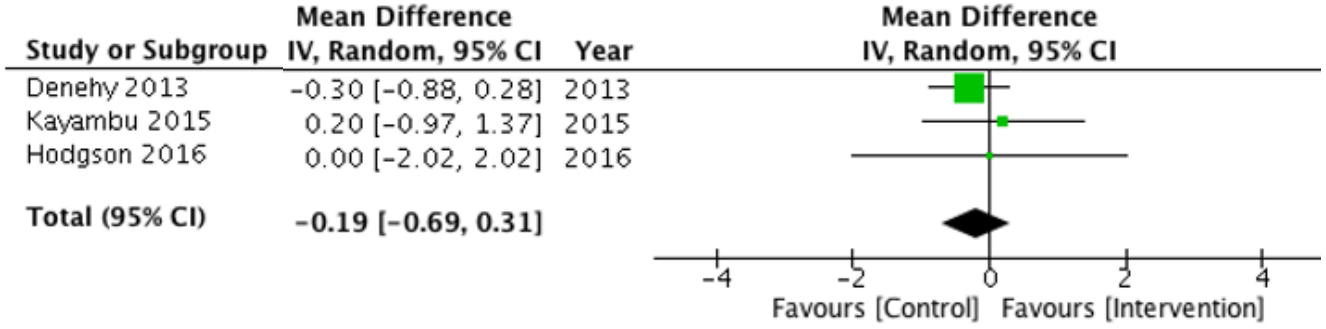


Efficacy and Benefit

5. **Physical func**: small N d/t heterogeneity in measures; NOT significant
   - Timed Up & Go test, mean dif 2.22 (95% CI, -4.99 to 9.43; 3 RCT, 172 pt)



   - Phys Func. in ICU (PFIT) test, mean dif -0.19 (95% CI, -0.69 to 0.31; 3 RCT, 209 pt)



Recommendation …

- Given a small benefit and the low overall quality of evidence, panel members agreed:
  - desirable consequences ***probably*** outweigh undesirable consequences

Formal Recommendation:

We ***suggest*** performing rehabilitation or mobilization in critically ill adults (***conditional recommendation***, low quality evidence).

- supports performing rehab/mobility over usual care or similar interventions with a reduced duration, frequency, or later onset
- **Implementation influenced by feasibility, staffing & resources across ICUs**

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	Start when **ALL** of the following are present:	Stop when **ANY** of the following are present:
Cardiovascular	● Heart rate between 60 - 130 bpm ● Systolic B/P between 90 - 180 mmHg, or ● Mean arterial pressure between 60-100	● Heart rate decreases <60 or increases >130 ● Systolic decreases <90 or increases >180 ● MAP decreases <60 or increases >100
Respiratory	● Respiratory rate between 5 - 40 bpm ● SpO_2 >=88% ● FiO_2 <0.6 & PEEP <10 cmH_2O ● Airway (ETT or trach) adequately secured	● Resp. rate decreases <5 or increases >40 ● SpO_2 decreases <88% ● Concerns re: securement of ETT or trach
Neurologic	● Able to open eyes to voice	● Change in LOC
Other	The following should be **absent:** ● New or symptomatic arrhythmia ● Chest pain with concern for ischemia ● Unstable spinal injury or lesion ● Unstable fracture ● Active or uncontrolled GI bleed **Mobility may be performed with** ● Femoral VAD, except sheath, in which hip mobilization is generally avoided ● Continuous renal replacement therapy ● Vasoactive medication infusion	If following develop & clinically relevant: ● New/symptomatic arrhythmia ● Chest pain with concern for ischemia ● Ventilator asynchrony ● Fall ● Bleeding ● Medical device removal or malfunction ● Distress reported by patient or clinician

Sleep

Non-Pharmacologic Interventions to Improve Sleep

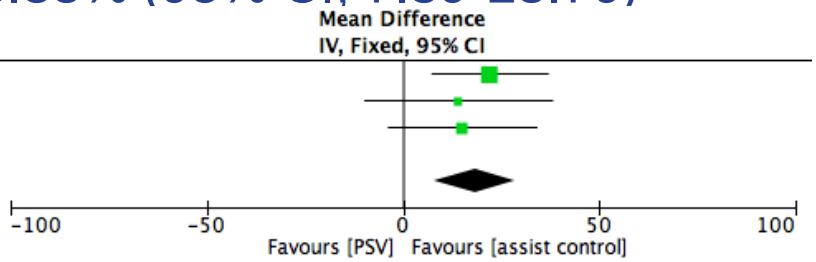
PICO Question		
P	Critically ill adult patients in an ICU	
I	• Assist control mode at night	• Acupressure
	• Adaptive ventilation at night	• Music
	• NIV-specific ventilator	• Noise Reduction
	• Aromatherapy	• Light Reduction
C	No use of the intervention	
O	• Time spent at each sleep stage • Sleep duration • Sleep fragmentation • Circadian rhythm	• Delirium occurrence • Duration of mechanical-ventilation • ICU mortality • Patient experience

Assist Control (vs. PS) ventilator mode at night

- **Sleep Efficiency** (3 RCTs, 61 pts)
  - Increased by mean difference of 18.33% (95% CI, 7.89-28.76)

Study or Subgroup	Control Ventilation Mean	SD	Total	PSV Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Andrejak 2013	61	25	26	39	29	26	50.3%	22.00 [7.28, 36.72]
Cabello 2008	58	28.2	15	44	37.8	15	19.1%	14.00 [-9.87, 37.87]
Toublanc 2007	65	25	20	50	35	20	30.6%	15.00 [-3.85, 33.85]
Total (95% CI)			61			61	100.0%	18.33 [7.89, 28.76]

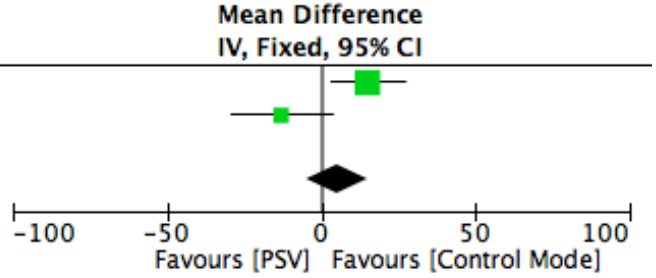
Heterogeneity: Chi² = 0.49, df = 2 (P = 0.78); I² = 0%
Test for overall effect: Z = 3.44 (P = 0.0006)



- **% of sleep time spent in REM sleep** (2 RCTs, 42 pts)
  - Increased by mean difference of 2.79% (95% CI, 0.53-5.05)

Study or Subgroup	Control Mode Mean	SD	Total	PSV Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Andrejak 2013	35	23	26	20	21	26	65.3%	15.00 [3.03, 26.97]
Cabello 2008	54	23.7	15	67	22.2	15	34.7%	-13.00 [-29.43, 3.43]
Total (95% CI)			41			41	100.0%	5.29 [-4.38, 14.97]

Heterogeneity: Chi² = 7.29, df = 1 (P = 0.007); I² = 86%
Test for overall effect: Z = 1.07 (P = 0.28)



- **% of sleep time in Stage 1 sleep** (2 RCTs, 42 pts)
  - NOT significant, increased by 0.31% (95% CI, -5.17 to 5.79)
- **% of sleep time in Stage 2 sleep** (2 RCTs, 42 pts)
  - NOT significant, increased by 5.29% (95% CI, -4.38 to 14.97)

Assist Control (vs. PS) ventilator mode at night

Rationale (cont'd):

- Other critical outcomes
  - Neither delirium, duration of MV, ICU LOS or patient preference evaluated in the 3 RCTs
- Although evidence quality low, risk of change to AC is low and all ventilators have an AC mode.
- For patients who are dyssynchronous on an AC mode (at night), particularly if sedation (with a BZ or Propofol) is required, a switch back to a PS mode may be required

Recommendation:

We suggest using assist control ventilation at night (vs. pressure support ventilation) to improve sleep in critically ill adults (conditional recommendation, low quality of evidence)

Use of Noise and Light Reduction Strategies to Improve Sleep

Rationale:

- Two RCTs and two observational studies evaluated the night time use of earplugs (with/without eye shades) in non-sedated ICU pts
  - Improved patient-reported sleep quality
  - Reduced delirium
  - Pooled analysis from 2 observational studies associated earplug use with a 20% increased chance of achieving 4 hrs sleep
- Studies not blinded, some patients refused earplugs and sicker patients not evaluated.
- Earplugs/eyeshades little risk and low cost

Recommendation:

We suggest using noise and light reduction strategies to improve sleep in critically ill adults (conditional recommendation, low quality of evidence).

Melatonin to improve sleep

Rationale:

- 3 small RCT (n=60), 3-10 mg HS
- Only lower, acuity patients with chronic respiratory failure evaluated
- Each RCT reported different outcomes; pooling not possible
- Variable methods used to evaluate sleep (ie. BIS, RN observation, actigraphy)
- No clear improvements in sleep
- While relatively safe and low cost, not FDA regulated.

Recommendation:

We make no recommendation regarding the use of melatonin to improve sleep in critically ill adults (no recommendation, very low quality of evidence).

Dexmedetomidine to improve sleep

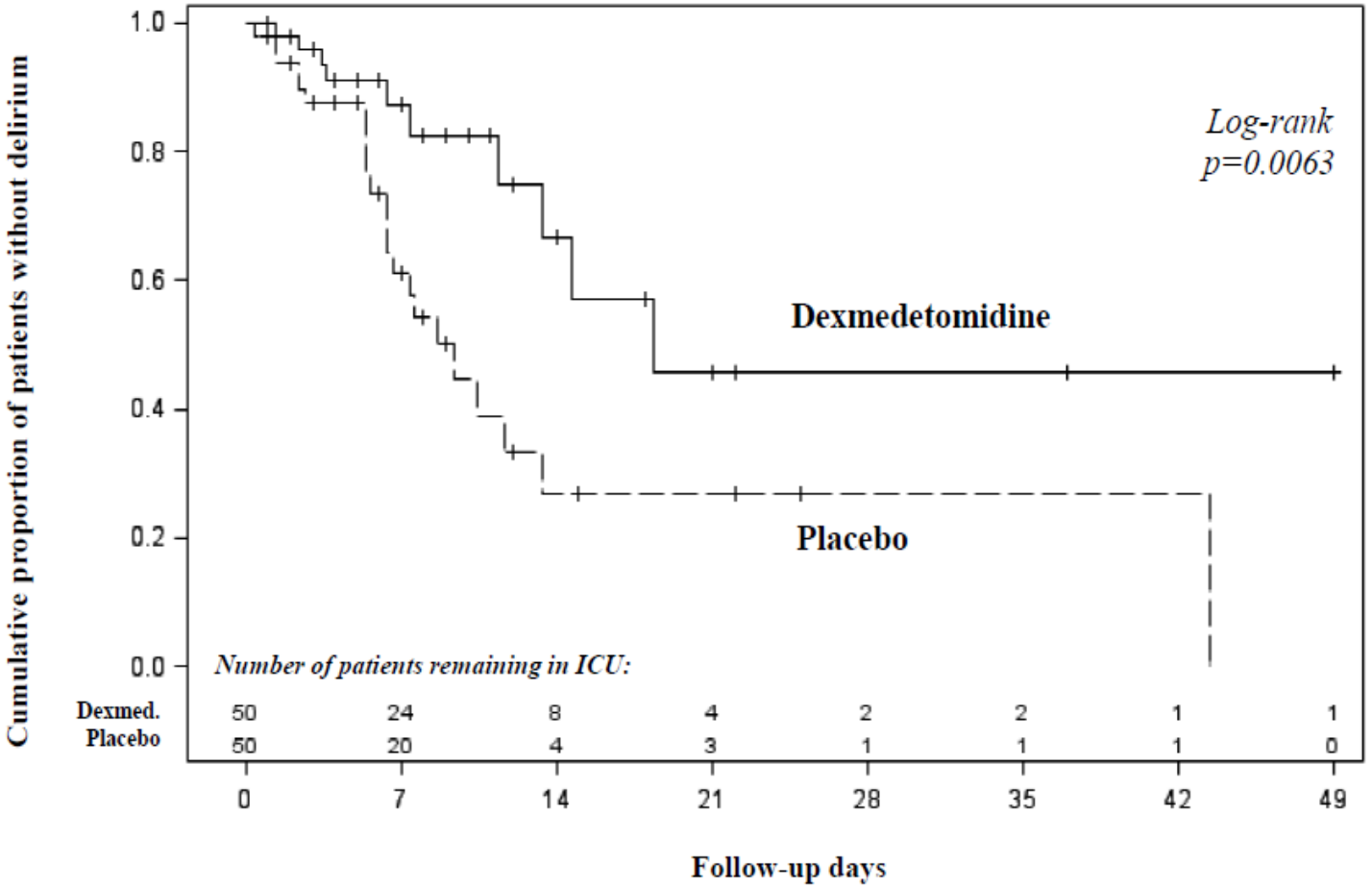
Rationale:

- 2 RCTs (n=74)
  - 1 RCT evaluated MV adults requiring sedation
  - 1 RCT in non-MV adults
- Significant increase in Stage 2 sleep
  - Mean difference = + 47.85% min (95% CI, 24.05-71.64)
- Significant decrease in Stage 1 sleep
  - Mean difference = - 30.37% min (95% CI, -50.01 to -10.73)
- No effect on sleep fragmentation or % time spent in REM sleep
- Neither delirium, duration of MV, ICU LOS or patient preference evaluated in either RCT
- Concerns about generalizability to all ICU adults, hemodynamic effects, and cost in terms of using dexmedetomidine to ONLY improve sleep (vs. when an IV sedative is needed)

Recommendation:

We make no recommendation regarding the use of dexmedetomidine to improve sleep in critically ill adults (no recommendation, very low quality of evidence).

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



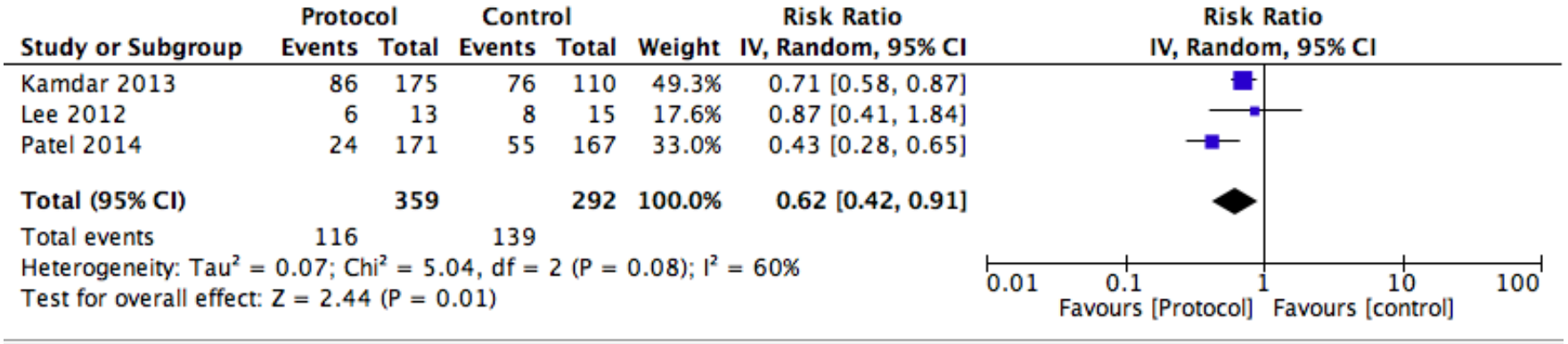
Skrobik Y, Duprey M, Hill NS, Devlin JW. AJRCCM 2018

Sleep Promoting Protocol

PICO Question		
P	Critically ill adult patients in an ICU	
I	Multicomponent sleep-promoting protocol	
C	No use of a protocol	
O	• Time spent at each sleep stage • Sleep duration • Sleep fragmentation • Circadian rhythm	• Delirium occurrence • Duration of mech-vent • ICU mortality • Patient experience

Study	Design	Population	Components	Patient-reported Sleep Quality
Hu RF 2010	RCT	Cardiac Surgery	Earplugs, eye shades, music	Better with protocol
Kamdar B 2013	Before-after	Medical	Ear plugs/eye shades/music Clustering of care, mobilization, Zolpidem (no delirium); Antipsychotic (delirium)	No difference with protocol
Li SJ 2014	Before - after	Medical	Earplugs, eye shades, music	No difference with protocol
Patel J 2014	Before-after	Mixed	Ear plugs/eye shades Removal of meds known to worsen sleep	Better with 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).

Sleep Evidence Gaps

- The influence of critical illness, delirium and mechanical ventilation on sleep quality remains poorly defined.
- A reliance on patient sleep quality reporting excludes many patients having the most disrupted sleep (delirium, sedated).
- The best method to sleep measurement, classification and how to measure individual sleep-related factors remain unclear.
- Non-pharmacologic sleep improvement strategies need to be rigorously evaluated in large RCTs and involve higher acuity patients
- Rigorous RCTs of medication(s) solely administered to improve sleep (vs. reduce agitation) need to be conducted
- The best interventions/combination of interventions to include in a sleep protocol remain uncertain

Delirium

Delirium Pharmacological Prevention

Question:
Should a pharmacologic agent (versus no use of this agent) be used to ***prevent*** delirium in ***all*** critically ill adults?

Rationale: 3 RCTs, 1283 pts

Significant reduction in delirium incidence favoring the pharmacologic agent:

- **Haloperidol*** (457 pts), RR 0.66; 95% CI, 0.45 to 0.97; low quality
  - *Update: REDUCE RCT (1789 pts): No effect on delirium or survival
- **Risperidone** (126 pts), RR 0.35; 95% CI, 0.16 to 0.77; low quality
- **Dexmed**** (700 pts), OR 0.35; 95% CI, 0.22 to 0.54; low quality

**Su et al Dexmed for prevention of delirium in elderly patients after non-cardiac surgery. *Lancet* 2016
low severity of illness; only surgical pts, assessing short-term outcomes; cost & side effects

Delirium Pharmacological Prevention

Recommendation:

We suggest **NOT** using haloperidol, an atypical antipsychotic, dexmedetomidine, statin, or ketamine to ***prevent*** delirium in **all** critically ill adults (Conditional recommendation, very low to low quality of evidence)

N=1789 patients randomized!

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Haloperidol on Survival Among Critically Ill Adults With a High Risk of Delirium

The REDUCE Randomized Clinical Trial

Mark van den Boogaard, PhD; Arjen J. C. Slooter, MD, PhD; Roger J. M. Brüggemann, PharmD, PhD; Lisette Schoonhoven, PhD; Albertus Beishuizen, MD, PhD; J. Wytze Vermeijden, MD, PhD; Danie Pretorius, MD; Jan de Koning, MD; Koen S. Simons, MD; Paul J. W. Dennesen, MD, PhD; Peter H. J. Van der Voort, MD, PhD; Saskia Houterman, PhD; J. G. van der Hoeven, MD, PhD; Peter Pickkers, MD, PhD; and the REDUCE Study Investigators

Baseline Characteristics Not Different

	Haloperidol 1mg IV q6h (n=350)	Haloperidol 2mg IV q6h (n=732)	Placebo (n=707
Age (years)	66.1	66.7	67.0
Mechanically Ventilated (%)	48.9	49.9	50.5
APACHE II score	20.1	19.2	19.0
Sepsis (%)	30.6	37.4	33.1
PRE-DELIRIC risk for delirium (%)	26.3	26.1	24.6
QTc, ms	440	447	443

Van den Boorgard M, et al. JAMA 2018; 319(7):680-691

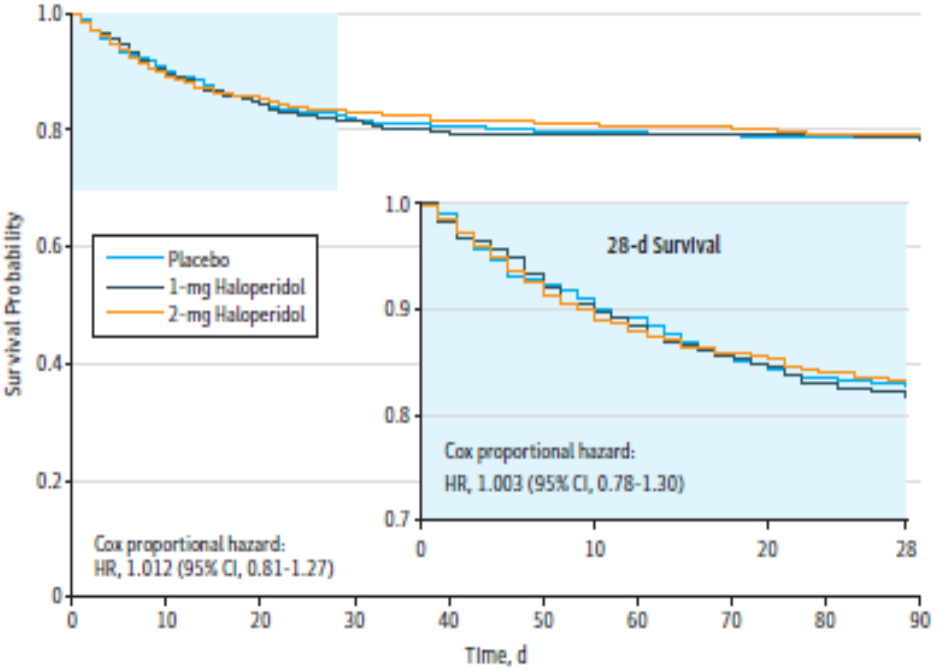
JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Haloperidol on Survival Among Critically Ill Adults With a High Risk of Delirium

The REDUCE Randomized Clinical Trial

Mark van den Boogaard, PhD; Arjen J. C. Slooter, MD, PhD; Roger J. M. Brüggemann, PharmD, PhD; Lisette Schoonhoven, PhD; Albertus Beishuizen, MD, PhD; J. Wytze Vermeijden, MD, PhD; Danie Pretorius, MD; Jan de Koning, MD; Koen S. Simons, MD; Paul J. W. Dennesen, MD, PhD; Peter H. J. Van der Voort, MD, PhD; Saskia Houterman, PhD; J. G. van der Hoeven, MD, PhD; Peter Pickkers, MD, PhD; and the REDUCE Study Investigators

Figure 2. Survival Analysis at 28 and 90 Days



No. at risk

Placebo	707	644	600	580	571	565	563	559	557	556
1-mg Haloperidol	350	317	297	285	279	278	278	278	277	276
2-mg Haloperidol	732	658	627	609	599	595	591	589	582	579

For the 28-day end point, follow-up for the 1-mg haloperidol group was a median of 28 days (interquartile range [IQR], 28-28 days); for the 2-mg group, 28 days (IQR, 28-28 days); and for the placebo group, 28 days (IQR, 28-28 days). For the 90-day end point, follow-up for the 1-mg haloperidol group was 90 days (IQR, 90-90 days), for the 2-mg haloperidol group, 90 days (IQR, 90-90 days); and for the placebo group, 90 days (IQR, 90-90 days).

Van den Boorgard M, et al. JAMA 2018; 319(7):680-691

Delirium Pharmacological Treatment

PICO Question		
P	Critically ill adult patients in an ICU	
I	• Haloperidol	• Atypical antipsychotic
	• Statin	• Dexmedetomidine
C	No use of the medication	
O	• Delirium duration	• Duration of mech-vent
	• ICU LOS	• Mortality

Antipsychotic/statin vs. None (Treatment)

Rationale, includes:

- **Unnecessary continuation causes significant morbidity & cost**

Recommendation:

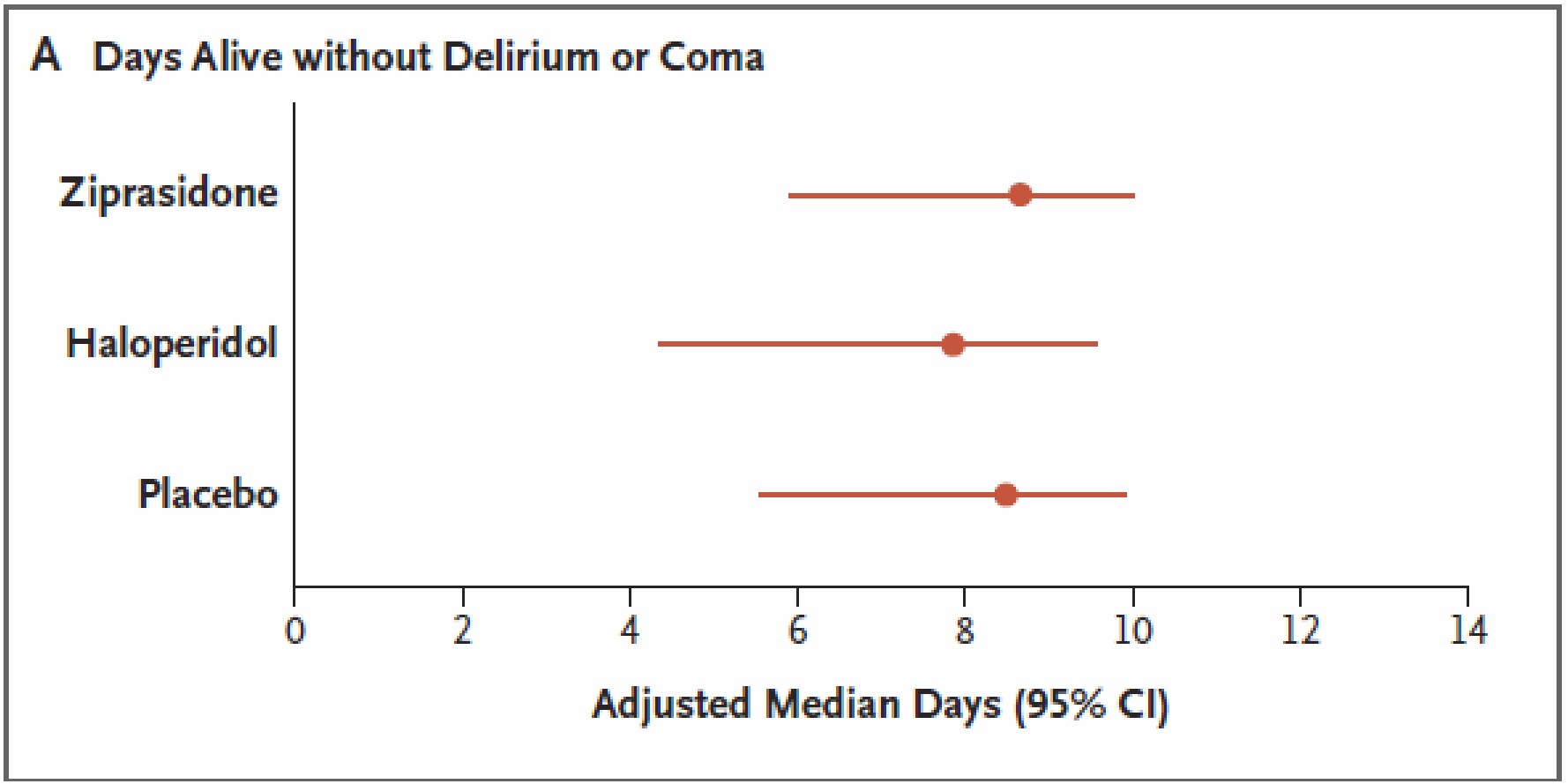
We *suggest NOT* ***routinely*** using haloperidol and atypical antipsychotic to treat delirium (conditional recommendation, low quality of evidence).

Although this recommendation discourages the "routine" use of antipsychotic agents in the treatment of delirium, patients who experience significant distress secondary to symptoms of a delirium such as anxiety, fearfulness, hallucinations, or delusions, or who are agitated and may be physically harmful to themselves or others, may benefit from short-term use of haloperidol or an atypical antipsychotic until these distressing symptoms resolve based on the panel's clinical experience. Patients who start with an antipsychotic for delirium in the ICU often remain on these medications unnecessarily after discharge (305–307).

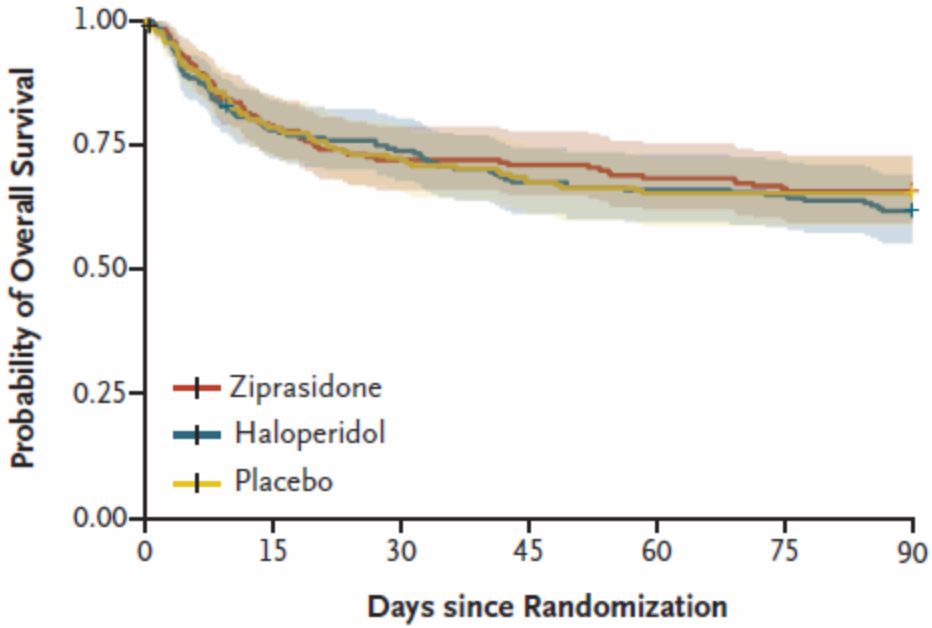
Haloperidol and Ziprasidone for Treatment of Delirium in Critical Illness

T.D. Girard, M.C. Exline, S.S. Carson, C.L. Hough, P. Rock, M.N. Gong, I.S. Douglas, A. Malhotra, R.L. Owens, D.J. Feinstein, B. Khan, M.A. Pisani, R.C. Hyzy, G.A. Schmidt, W.D. Schweickert, R.D. Hite, D.L. Bowton, A.L. Masica, J.L. Thompson, R. Chandrasekhar, B.T. Pun, C. Strength, L.M. Boehm, J.C. Jackson, P.P. Pandharipande, N.E. Brummel, C.G. Hughes, M.B. Patel, J.L. Stollings, G.R. Bernard, R.S. Dittus, and E.W. Ely, for the MIND-USA Investigators*

Girard TD et al. N Engl J Med 2018; 379:2506



Girard TD et al. N Engl J Med 2018; 379:2506



No. at Risk (cumulative no. of deaths)

Ziprasidone	190 (0)	150 (40)	137 (53)	135 (55)	130 (60)	126 (64)	125 (65)
Haloperidol	192 (0)	149 (42)	141 (50)	129 (62)	126 (65)	124 (67)	118 (73)
Placebo	184 (0)	143 (39)	132 (50)	123 (59)	119 (63)	119 (63)	119 (63)

Figure 3. Effects of Haloperidol, Ziprasidone, and Placebo on 90-Day Survival.

Girard TD et al. N Engl J Med 2018; 379:2506

Dexmedetomidine vs. Placebo (Treatment)

Rationale: 1 RCT (71 pts)

- Significant increase in ventilator-free hours
  - Mean Difference 17 hrs (95% CI, 4 to 33 hrs); very low quality
- NO effect on ICU/Hosp LOS or hospital discharge location

Recommendation:

We ***suggest*** using dexmedetomidine for delirium in mechanically ventilated adults where agitation is precluding weaning/extubation (conditional recommendation, low quality of evidence).

Multicomponent Delirium Reduction Bundle

*Not AF bundle *Only partially focused on improving sleep

Rationale: 5 studies (1 RCT*, 4 Before-after), 1318 pts

- Use of these strategies was associated with:
  - Reduced delirium significantly, OR=0.59 (95% CI, 0.39 to 0.88)
  - Decreased ICU duration of delirium, ICU LOS & Hospital mortality

Author (year)	Design/ Population	Intervention vs control
Colombo (2012)	Before-after Mixed ICU	**N=144 vs N=170 (Usual care)** Reorientation strategy, and environmental, acoustic and visual stimulation
Foster (2013)	Before-after Mixed ICU	**N=84 vs N=164 (Usual care)** MCI protocol (sedation, sleep-wake, sensory stimulation, mobility and music)
Moon (2015)	**RCT*** Mixed ICU	**N=60 vs N=63 (Usual care, no prevention program)** MCI prevention program: delirium risk monitoring, cognition and orientation, environment, early therapeutic intervention
Hanison (2015)	Before-after Mixed ICU	**N=127 vs N=23 (Usual care)** 2 cycle MCI program: 1st cycle: reducing delirogenic drugs, daily sedation breaks, environment changes, more light exposure, use of communication aid, 2nd cycle: natural light, use of clocks
Rivosecchi (2016)	Before-after Mixed ICU	**N=253 vs N=230 (Usual care)** MCI program: music, opening blinds, reorientation and cognitive stimulation, eye/ear protocol

Multicomponent Delirium Reduction Bundle:

The ABCDEF Bundle

*Generally not focused on improving sleep

ABCDE(F) multi-intervention approach					
A	**B**	**C**	**D**	**E**	**F**
Assessment, Prevention, Management of **Pain**	**B**oth SATs and SBTs	**C**hoice of Sedation and Analgesia	**D**elirium Assessment, Prevention and Management	**E**arly Mobility and Exercise	**F**amily Engagement and Empowerment

ABCDE bundle multi-intervention approach (1 Before-after), 296 pts

- Significantly associated with:
  - Less delirium, 49% vs. 62%, OR=0.55 (95% CI, 0.33 to 0.93)

ABCDEF bundle approach (1 Cohort study), 6064 pts

- Included a focus on “F”, Family engagement
- Improvement in bundle compliance significantly associated with:
  - Reduced mortality & more coma/delirium free ICU days

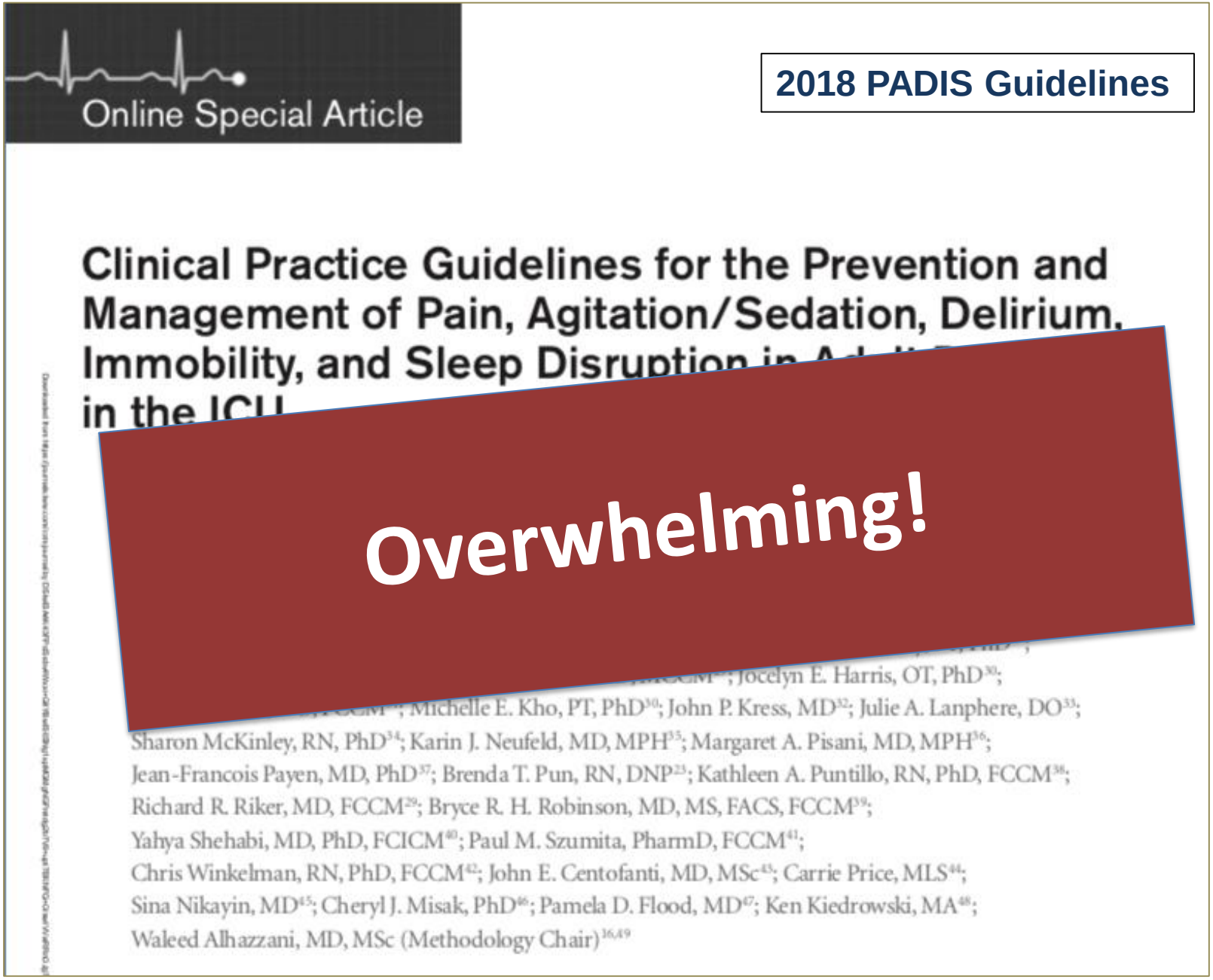
Multicomponent Delirium Reduction Bundle

Recommendation:
We ***suggest*** using a multicomponent, non-pharmacologic intervention that is focused on (but not limited to) **reducing modifiable risk factors** for delirium, improving cognition, and optimizing sleep, mobility, hearing, and vision in critically ill adults (conditional recommendation, low quality of evidence)

*also refer to sleep section recommendation to use a protocol focused solely on improving sleep

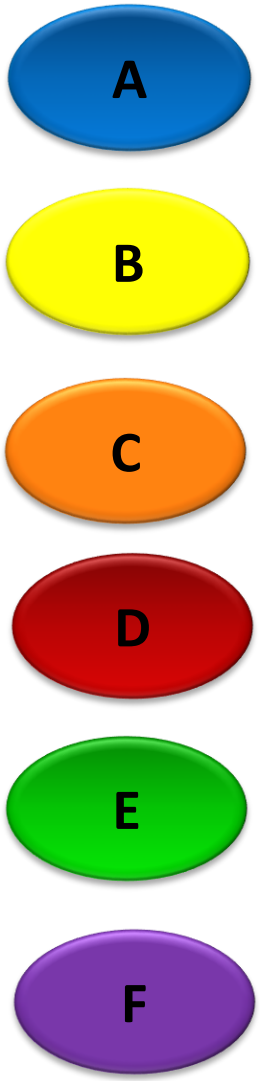
Evidence gaps:

- Understanding role of each intervention in a multicomponent intervention plan
- Role of families in reducing patient stress and facilitating non-pharmacologic delirium prevention and management
- Qualitatively evaluate the experience of patients with delirium
- Consistent definition of each intervention



Devlin, et al.. Crit Care Med. 2018 Sep;46(9):e825-e873.

ABCDEF Bundle Elements



A Assess, Prevent and manage Pain

B Both SAT and SBT

C Choice of analgesia and Sedation

D Delirium: Assess, Prevent and Manage

E Early Mobility and Exercise

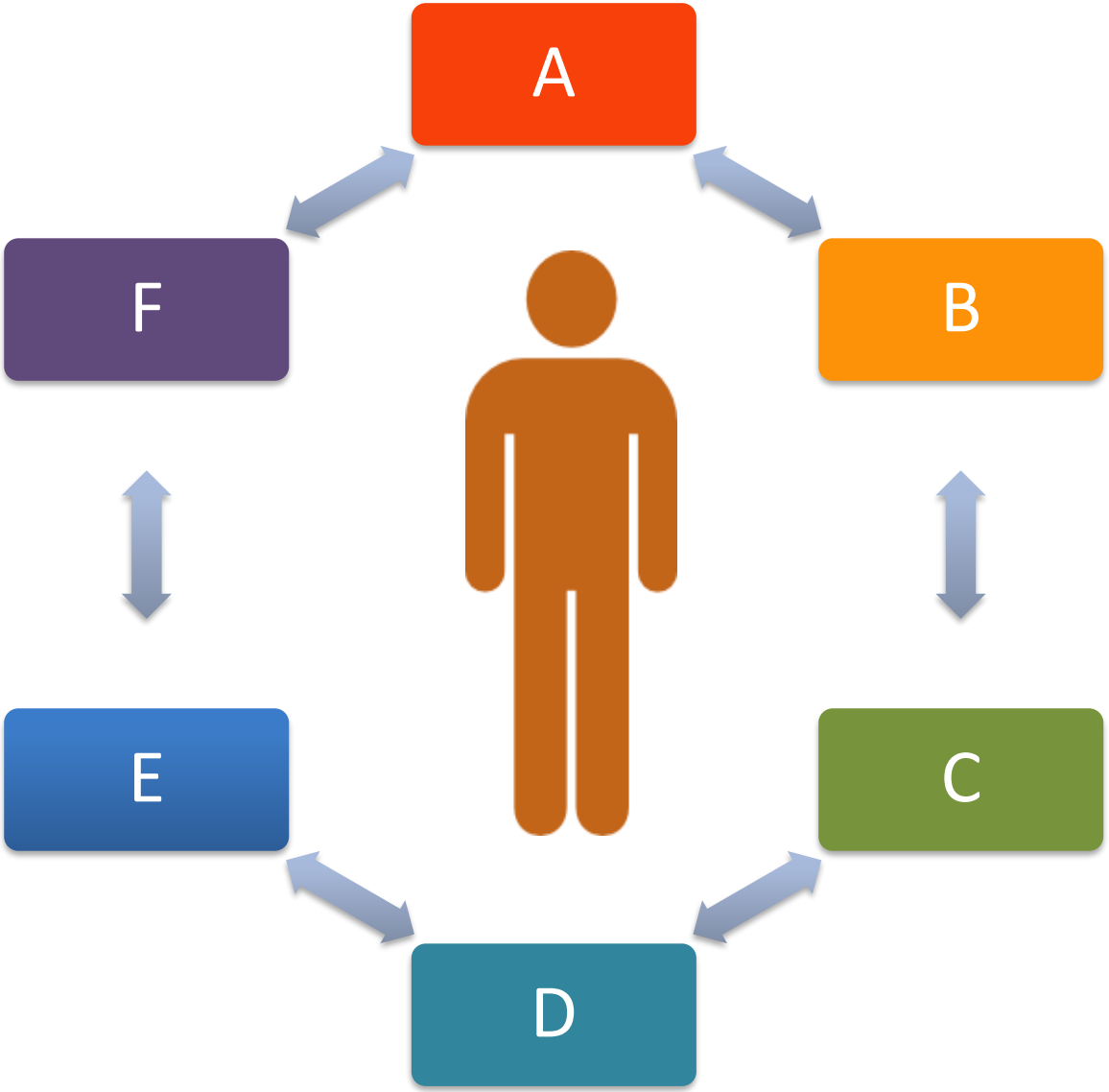
F Family Engagement and Empowerment

Vasilevskis EE, et al. *Chest*. 2010;138(5):1224-1233.
Davidson JE, et al. *Am Nurse Today*. 2013;8(5):32-38.

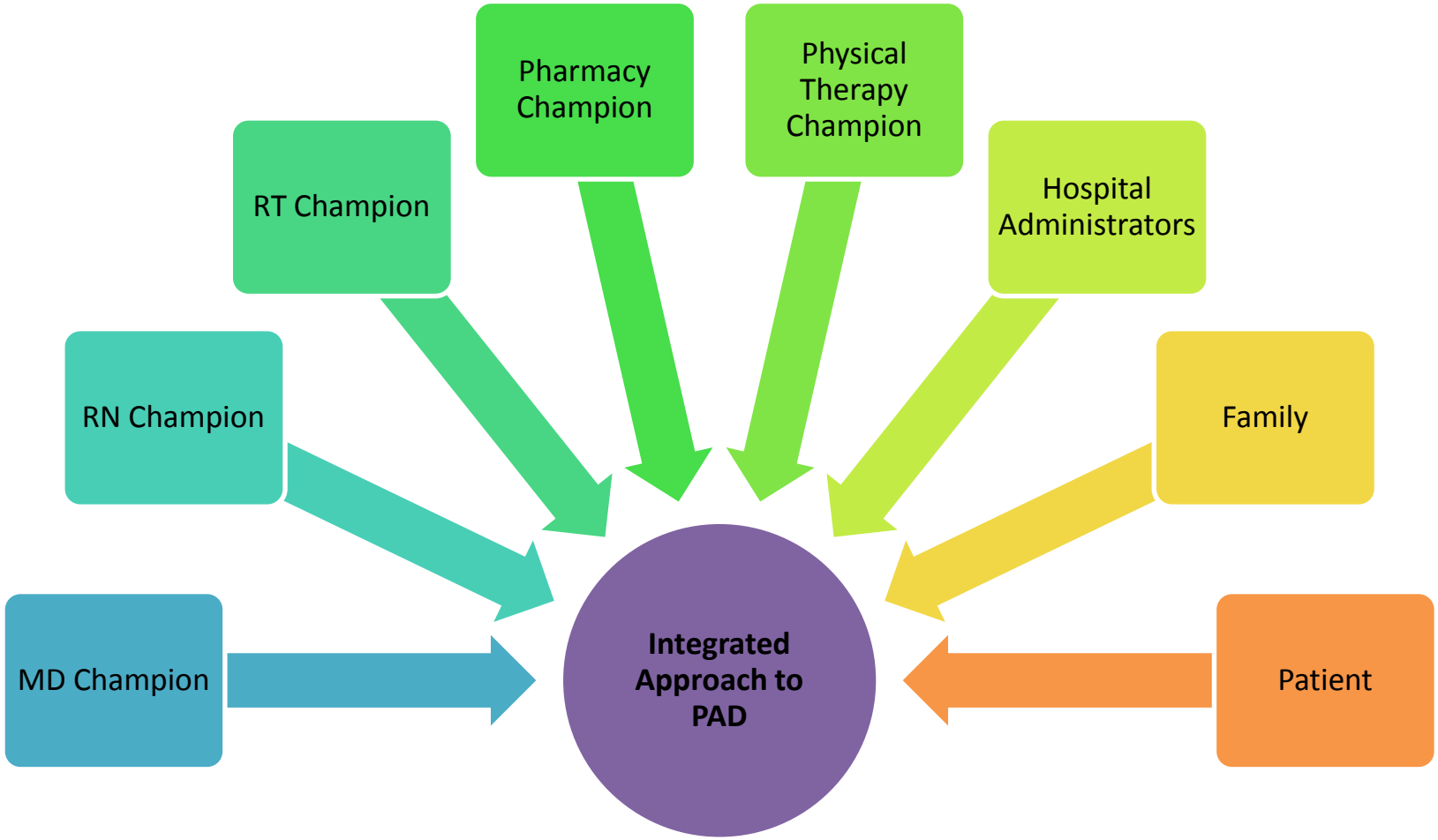
A Framework for Care

Patient (and family)- focused

Applies to Every ICU Patient



Interdisciplinary Team-Focused



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

Brenda T. Pun, DNP, RN, FCCM[1]; Michele C. Balas, PhD, RN, CCRN-K, FCCM, FAAN[2,3]; Mary Ann Barnes-Daly, MS, RN, CCRN-K, DC[4]; Jennifer L. Thompson, MPH[5]; J. Matthew Aldrich, MD[6]; Juliana Barr, MD, FCCM[7,8]; Diane Byrum MSN, RN, CCRN-K, CCNS, FCCM[9]; Shannon S. Carson, MD[10]; John W. Devlin, PharmD, FCCM[11]; Heidi J. Engel, PT, DPT[12]; Cheryl L. Esbrook, OTR/L, BCPR[13]; Ken D. Hargett, MHA, FAARC, FCCM[14]; Lori Harmon, RRT, MBA, CPHQ[15]; Christina Hielsberg, MA[15]; James C. Jackson, PsyD[1]; Tamra L. Kelly, BS, RRT, MHA[4]; Vishakha Kumar, MD, MBA[15]; Lawson Millner, RRT[16]; Alexandra Morse, PharmD[4]; Christiane S. Perme, PT, CCS, FCCM[14]; Patricia J. Posa, BSN, MSA, CCRN-K[17]; Kathleen A. Puntillo, PhD, RN, FCCM, FAAN[18]; William D. Schweickert, MD[19]; Joanna L. Stollings, PharmD, FCCM[20]; Alai Tan, PhD[2]; Lucy D'Agostino McGowan, PhD[21]; E. Wesley Ely, MD, MPH, FCCM[1,22]

Pun B, et al. *Crit Care Med.* 2019; 47:3-14

ICU Liberation Collaborative - Methods

- **Collaborative Overview**
  - 68 academic, community and VA ICUs
  - 20 months
  - Operationalized the bundle (with flexibility)
  - Operationalized the daily benchmarks for each element
  - Each Site: Interprofessional Executive Team
  - Education and Support Provided:
    - In Person Meetings
    - Coaching Calls
    - Peer Benchmarking
    - Online materials
    - Resource Sharing

Pun B, et al. *Crit Care Med.* 2019; 47:3-14

Bundle Performance

ABCDEF bundle performance (our main exposure) was evaluated in two ways:

1. Complete performance:
- patient received every eligible bundle element on any given day
2. Proportional performance
- percentage of eligible bundle elements performed on any given day

Pun B, et al. *Crit Care Med.* 2019; 47:3-14

Relationship Between Degree of Bundle Performance and Outcomes

We explored the association between complete and proportional ABCDEF bundle performance and patient, symptom and system outcomes

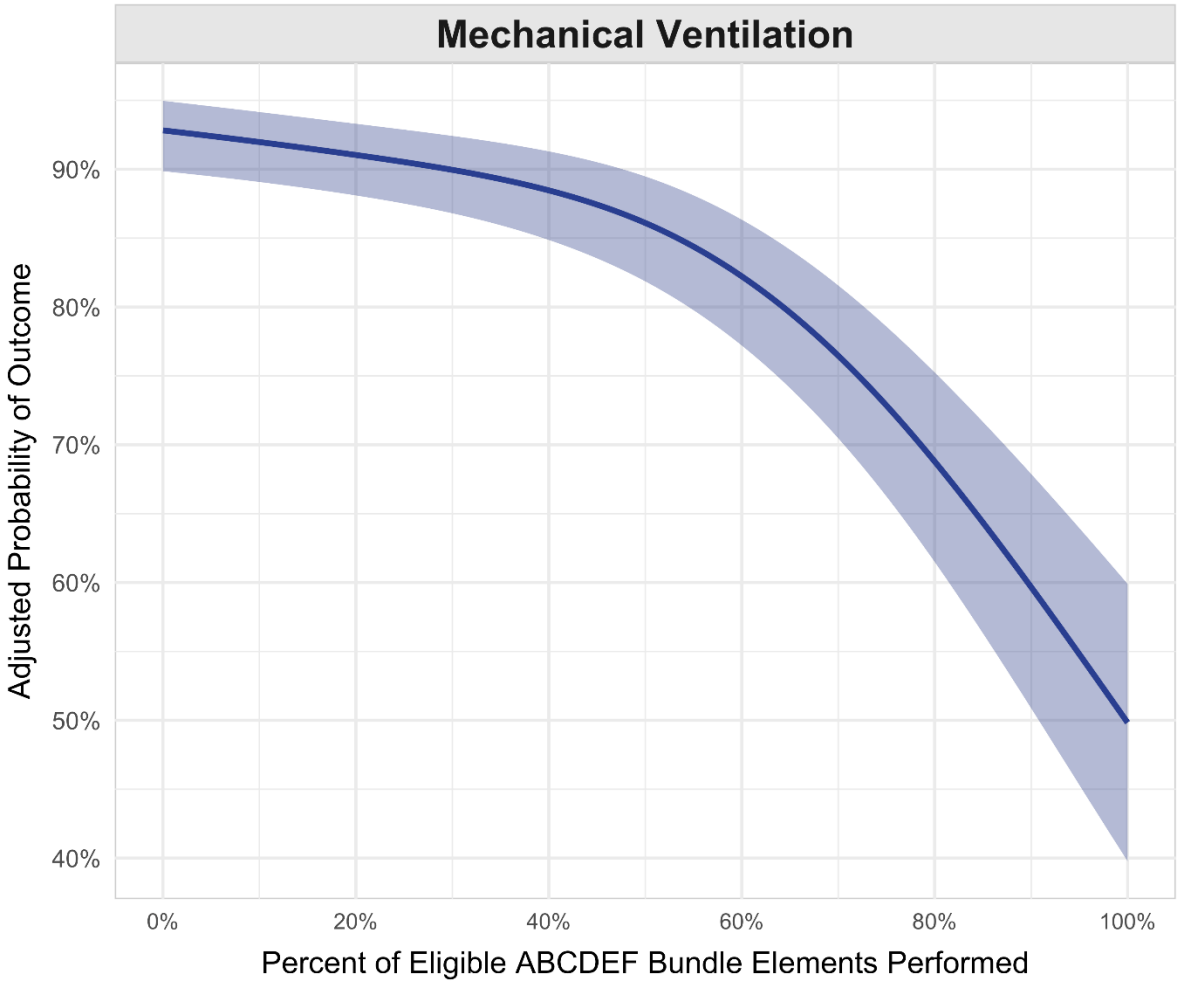
*All models were adjusted for a minimum of 18 a priori- determined potential confounders.

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 (037–0.79)	< 0.001
Discharge destination[f]	0.64 (0.51–0.80)	< 0.001

Pun B, et al. *Crit Care Med.* 2019; 47:3-14

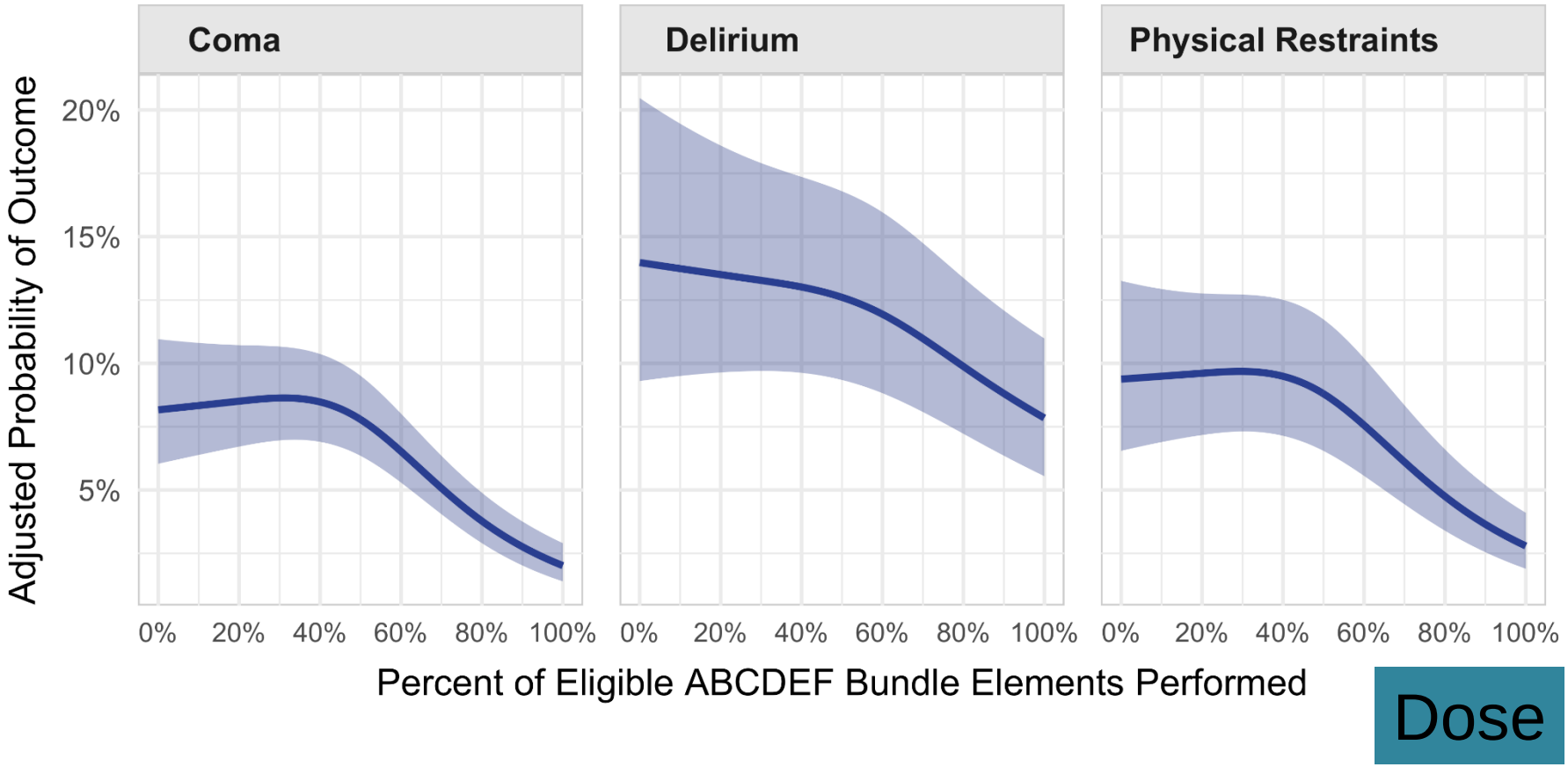
Results: Symptom-Related Outcomes



Dose

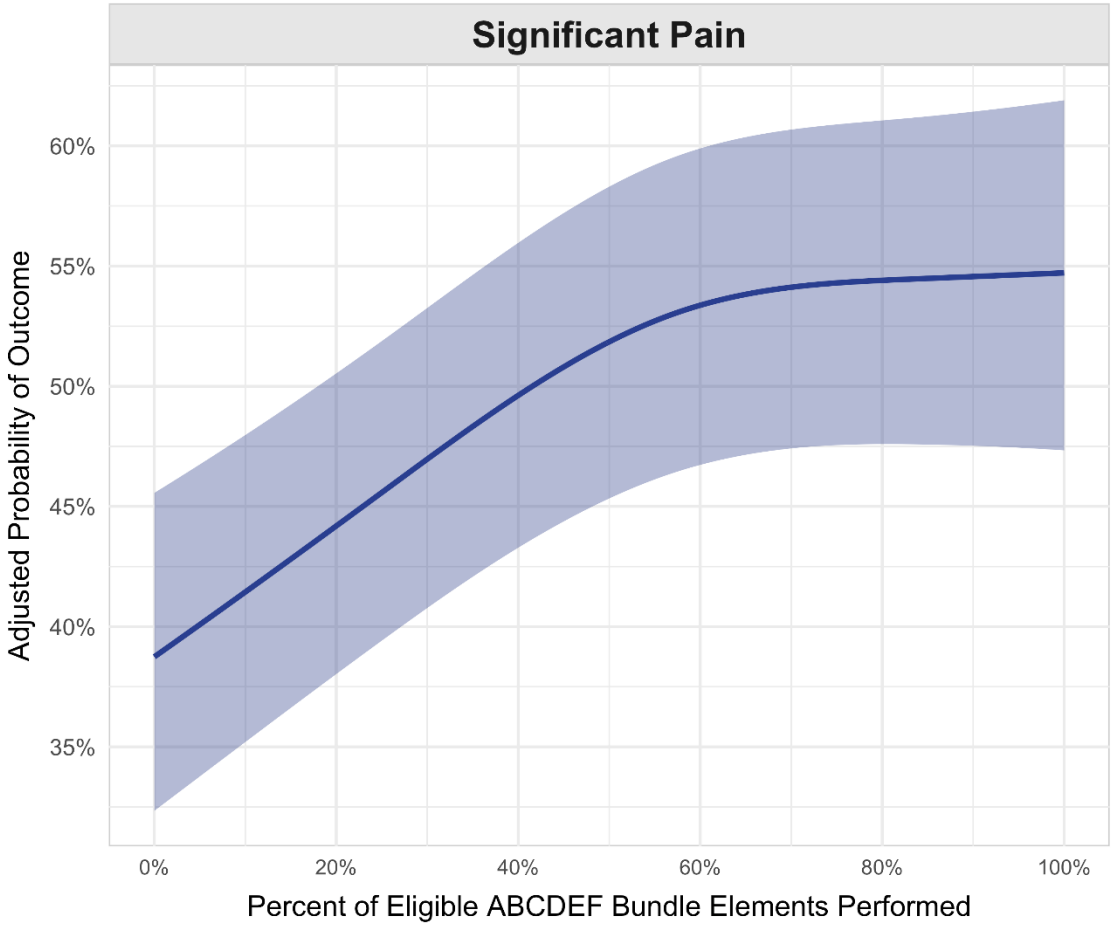
Pun B, et al. *Crit Care Med.* 2019; 47:3-14

Results:
Symptom-Related Outcomes



Pun B, et al. *Crit Care Med.* 2019; 47:3-14

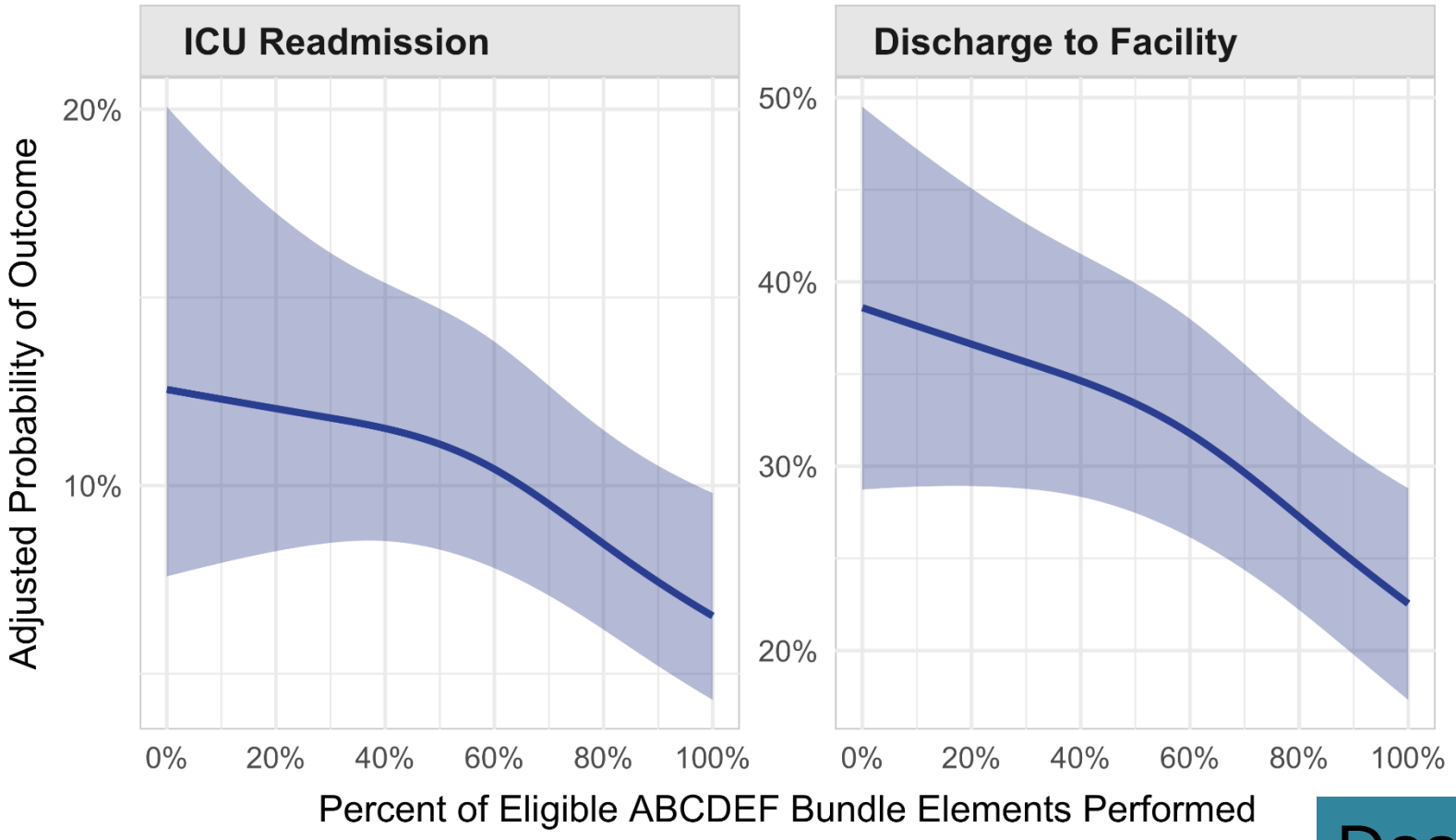
Results:
Symptom-Related Outcomes



Dose

Pun, et al. *Crit Care Med.* 2019; 47:3-14

Results:
System-Related Outcomes



Dose

Pun, et al. *Crit Care Med.* 2019; 47:3-14

A Assess, Prevent and Manage Pain

Summary

Assessment – Use a valid assessment tool
Prevention – Anticipate pain (risk factors; procedures)
Management of Pain – Treat pain before using a sedative

Metrics

- Every 4 hours
- Self Report:
  - 0–10 Numeric Rating Scale (NRS)
- Unable to Self Report
  - Critical-Care Pain Observation Tool (CPOT)

Role of Pharmacists

- Opioids
- Multimodal analgesia
- Education about range orders

B Both SAT and SBT

Summary

Spontaneous Breathing Trial and Extubation Decisions

Metric

- **Safety Criteria**
- **Failure Criteria**

Role of Pharmacists

- Maintaining patient wakefulness
- Daily reminders
- Change in sedative/opioid may be required
  - Non-opioid analgesic
  - Dexmedmedetomidine (vs propofol)

C Choice of Analgesia and Sedation

Summary

Assessment – Using a valid tool
Targeted sedation
Making best choice for sedation agent(s)

Metric

- **Every 4 hours**
- **Targets**
- **Sedation/Agitation Scale**
  - **RASS**
  - **SAS**

Role of Pharmacists

- Maintain most patients at a light level of sedation
- Reduce use of continuous IV sedatives
- Transition from IV to NGT/PO
- Daily reassessment of all psychoactive medication use

D Delirium: Assess, Prevent and Manage

Summary

Assessment – Use a valid tool

Prevention – Non-pharmacologic interventions

- think sleep improvement and better mobility

Management – Avoid antipsychotics in most patients

Metric

- **Once/shift assessment**
- **Assessment Tools:**
  - Confusion Assessment Method for the ICU (CAM-ICU) – when patient maximally awake
  - Intensive Care Delirium Screening Checklist (ICDSC)

Role of Pharmacists

- Educating teams about minimal antipsychotic role
- Daily medication review to remove unnecessary/ deliriogenic meds
- Sleep improvement
  - Focus on non-pharm

E Early Mobility and Exercise

Summary

Rehabilitation/Mobilization
Regular – early and often

Metric

- **Safety Criteria**
- **Failure Criteria**

Role of Pharmacists

- Earlier elements
  - Pain prevention
  - Light sedation level
  - Delirium prevention/ management

F Family Engagement and Empowerment

Summary

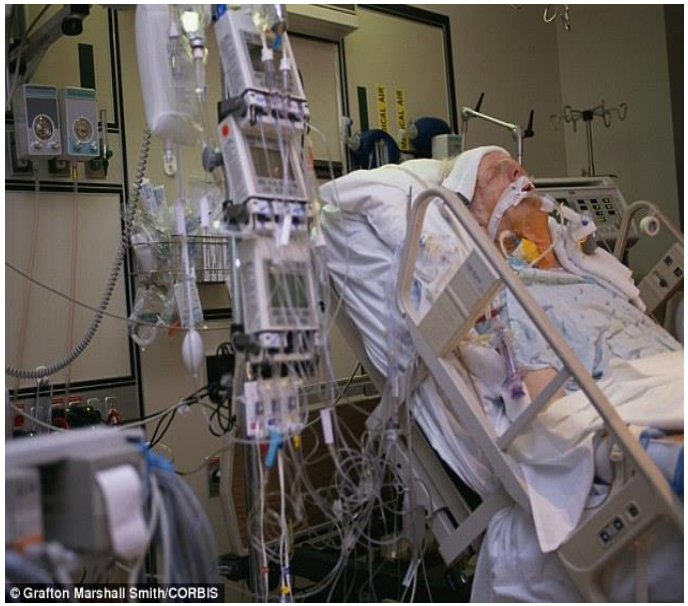
Involving, engaging and empowering patients and families to be active participants in care

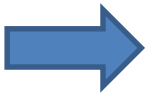
Metric

- **Every day**

Role of Pharmacists

- Availability for education
- Home medication reconciliation


© Grafton Marshall Smith/CORBIS




Questions?