ADULT ICU DELIRIUM UPDATE

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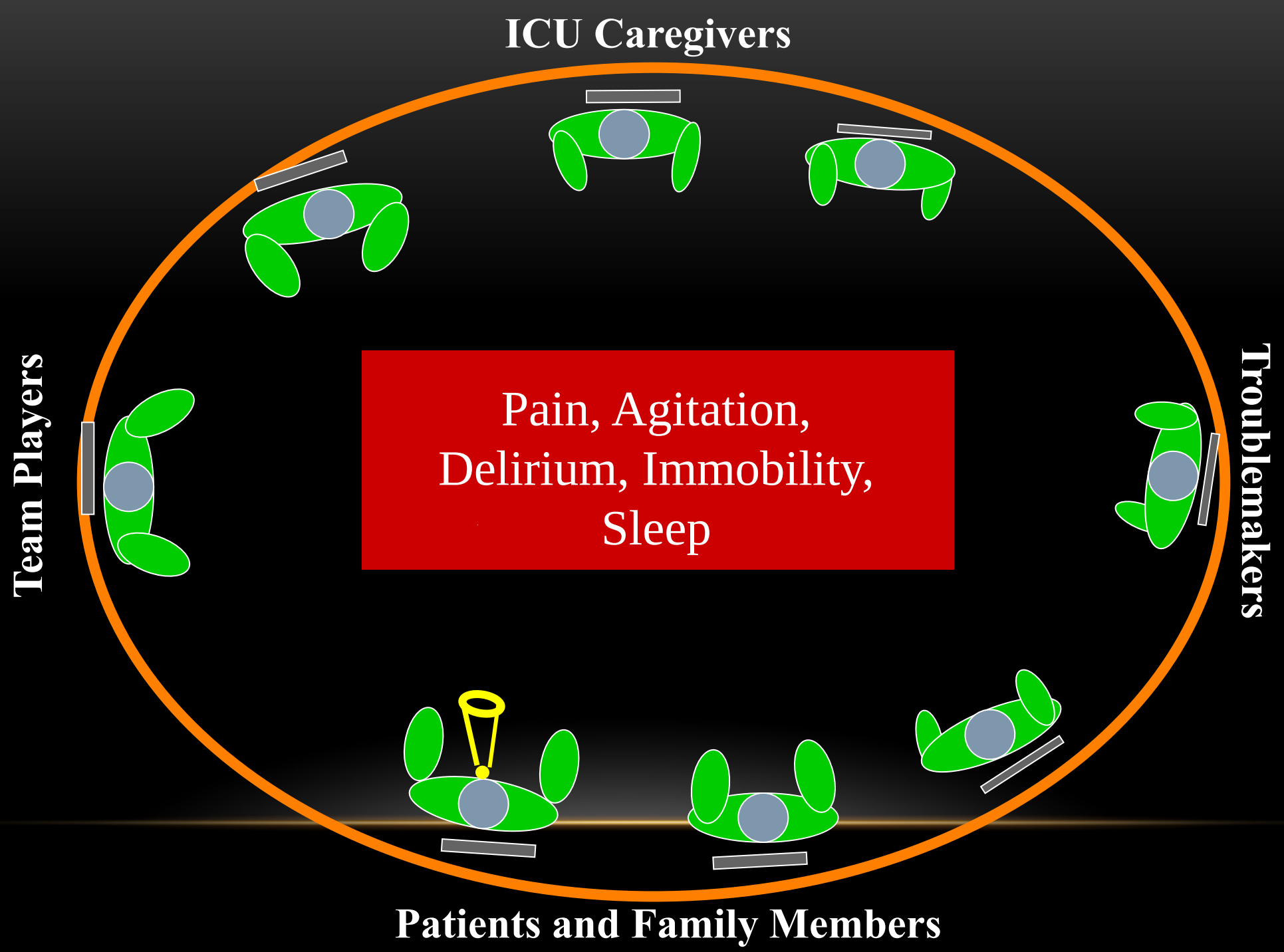
I HAVE NO FINANCIAL NOR INTELLECTUAL CONFLICTS OF INTEREST TO DISCLOSE


ICU Caregivers
Team Players
Troublemakers
Pain, Agitation, Delirium, Immobility, Sleep
Patients and Family Members

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

Devlin, John W., PharmD, FCCM (Chair)[1,2]; Skrobik, Yoanna, MD, FRCP(c), MSc, FCCM (Vice-Chair)[3,4]; Gélinas, Céline, RN, PhD[5]; Needham, Dale M., MD, PhD[6]; Slooter, Arjen J. C., MD, PhD[7]; Pandharipande, Pratik P., MD, MSCI, FCCM[8]; Watson, Paula L., MD[9]; Weinhouse, Gerald L., MD[10]; Nunnally, Mark E., MD, FCCM[11,12,13,14]; Rochwerg, Bram, MD, MSc[15,16]; Balas, Michele C., RN, PhD, FCCM, FAAN[17,18]; van den Boogaard, Mark, RN, PhD[19]; Bosma, Karen J., MD[20,21]; Brummel, Nathaniel E., MD, MSCI[22,23]; Chanques, Gerald, MD, PhD[24,25]; Denehy, Linda, PT, PhD[26]; Drouot, Xavier, MD, PhD[27,28]; Fraser, Gilles L., PharmD, MCCM[29]; Harris, Jocelyn E., OT, PhD[30]; Joffe, Aaron M., DO, FCCM[31]; Kho, Michelle E., PT, PhD[30]; Kress, John P., MD[32]; Lanphere, Julie A., DO[33]; McKinley, Sharon, RN, PhD[34]; Neufeld, Karin J., MD, MPH[35]; Pisani, Margaret A., MD, MPH[36]; Payen, Jean-Francois, MD, PhD[37]; Pun, Brenda T., RN, DNP[23]; Puntillo, Kathleen A., RN, PhD, FCCM[38]; Riker, Richard R., MD, FCCM[29]; Robinson, Bryce R. H., MD, MS, FACS, FCCM[39]; Shehabi, Yahya, MD, PhD, FCICM[40]; Szumita, Paul M., PharmD, FCCM[41]; Winkelman, Chris, RN, PhD, FCCM[42]; Centofanti, John E., MD, MSc[43]; Price, Carrie, MLS[44]; Nikayin, Sina, MD[45]; Misak, Cheryl J., PhD[46]; Flood, Pamela D., MD[47]; Kiedrowski, Ken, MA[48]; Alhazzani, Waleed, MD, MSc (Methodology Chair)[16,49]

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- **37 recommendations (2 strong, 33 conditional)**
- **2 good practice statements**
- **32 ungraded, non-actionable statements**

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 • Dexmedetomidine • Ketamine • Statin	Clinical indicators to stop rehab/mobilization (either in or out of bed)	Pharmacologic sleep improvement: • 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 sleep improvement: • AV vs PS mode • Adaptive vs PS mode • Aromatherapy • Music • Noise/Light reduction • Multimodal protocol

GOALS FOR TODAY

- Describe advances in the understanding of risk factors and outcomes associated with delirium
- Apply key concepts for effective delirium management
- Argue against the use of antipsychotic agents to treat or prevent delirium in most patients

INTEGRATED PAIN, AGITATION, DELIRIUM MANAGEMENT

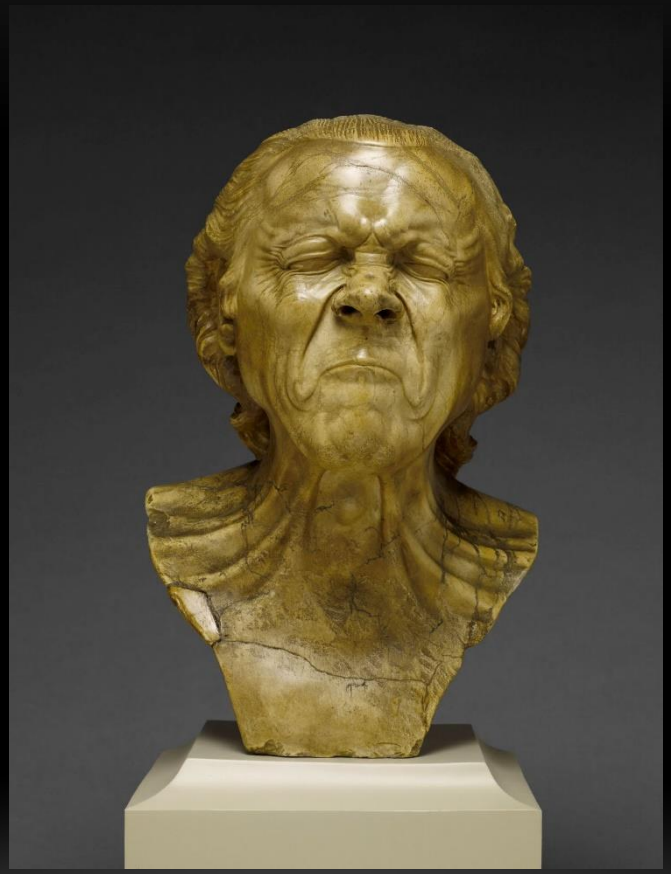
Courtesy J Barr, MD

MY DELIRIUM JOURNEY

If you hold a cat by the tail, you learn things that you cannot learn any other way.

Mark Twain

SKEPTICS



“It doesn't take a chef to know the milk is spoiled.” G Fraser 2013

DIFFERING POINTS OF VIEW CAN OFFER INSIGHT

"Science drives and informs our work,
yet there is unquestionably an element
of mass psychology impacting our practice."

May TL. CCM 2018; 46:1864

Hodge Podge Lodge

START WITH WHAT IS INDISPUTABLE

- Delirium is distressful to patients, families and caregivers
- Unfortunately scant data guide management of this distress
- Best review = 12 studies on delirium recall

  (Fuller. J Clin Nursing 2016 doi: 10.1111/jocn.13155)

  - Patients remembered incomprehensible experiences, strong emotional feelings and fear.
  - Included only 1 study of 41 ICU patients
- “significant gap in ICU delirium outcomes data includes the psychological toll that delirium exerts in real time on patients, families, and caregivers.” (Devlin. CCM 2018)

ICU DELIRIUM
THE UPDATED VERSION

- Frequency: probably <50% of ICU patients
  - Impressive range; 20-80% (1)
- Three-fold increase in 6-month mortality?
  - Newer data suggest very little direct influence (2,3)
  - Inserting delirium status into APACHE does not influence predicted mortality (4)
- Extra days on mechanical ventilation and in the hospital = $15K
- 50% have cognitive impairment at hospital discharge (5)
  - Long-term in 1/3
    - Difficult to establish causality. Also seen with ARDS and sepsis (6-7)

Old data
Ely JAMA 2004;291-1753-1762
Milbrandt CCM 2004;32:955-962
Dubois ICM 2001; 27:1297
Jones. ICU 2007; 33:978

Newer data
1) Rood. Aust Crit Care 2018, 2) Klein Klouwenberg BMJ 2014: G6652, 3) Al-Qadheeeb CCM 2014; 42:1442, 4) Van den Boogaard. Crit Care 2010, 14:R146, 5) Girard. Lancet Respir Med 2018;6:213, 6) Herridge. ICM 2016; 42:725, 7) Tate. CCM 2014; 42:1037

RISK FACTORS FOR DELIRIUM UNGRADED STATEMENTS

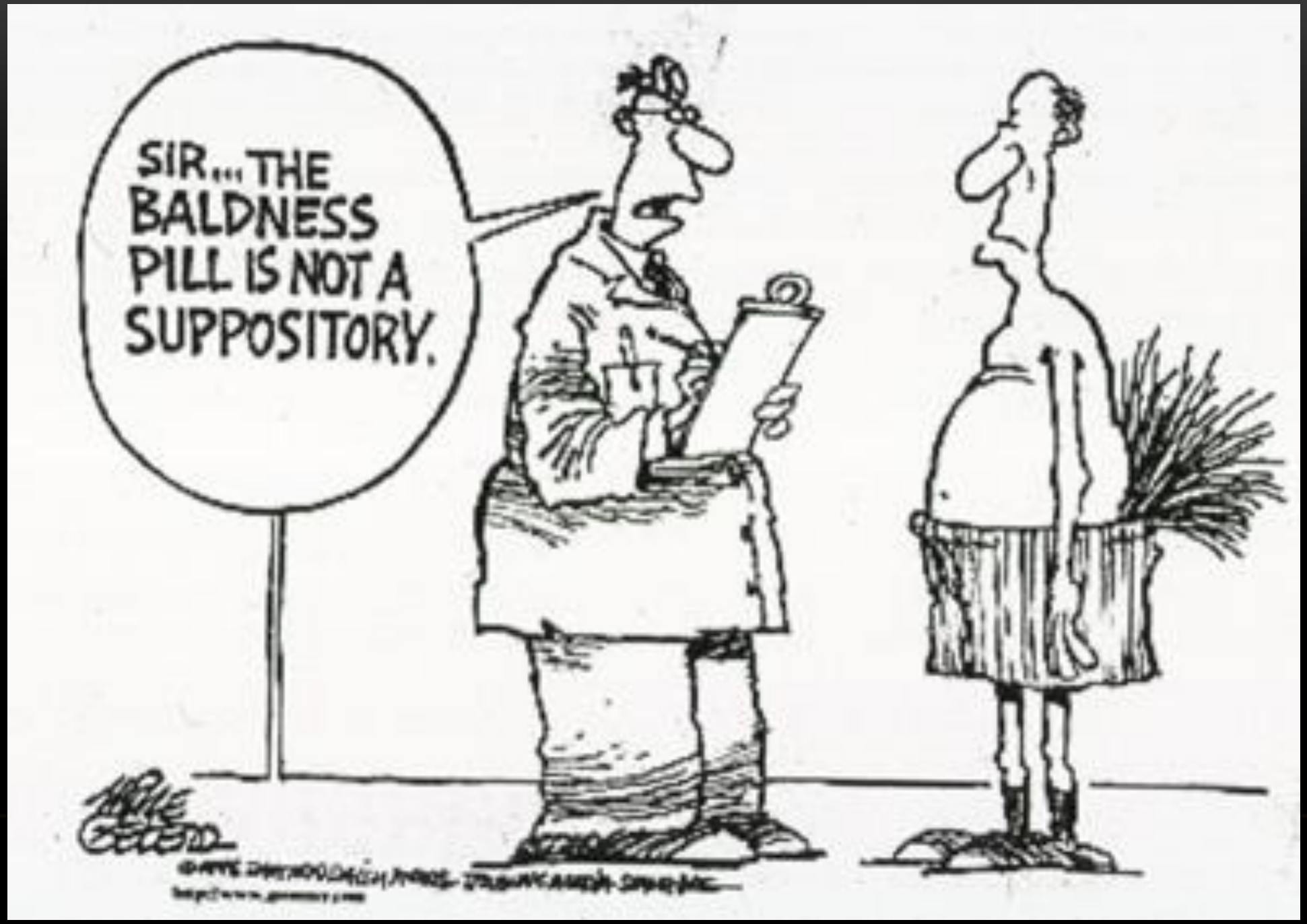
2013 Guidelines

- Dementia
- Severity of illness
- Coma
- Benzodiazepines (maybe)
- Hypertension
- Alcoholism

2018 Guidelines

- Dementia
- Severity of illness
- Coma
- Benzodiazepines
- Age
- Blood transfusions
- Pre-ICU emergency surgery/trauma

What about infections, metabolic derangements, CNS diseases, toxins, substance withdrawal?


SIR... THE BALDNESS PILL IS NOT A SUPPOSITORY.

BENZODIAZEPINES ARE NOT ALWAYS THE DEVIL'S HANDIWORK

- Benzodiazepines are GOOD for patients…
  - With anxiety related to ventilator weaning
    - Prn midazolam
    - Low dose clonazepam
      - Goal is anxiolysis without blunting respiratory drive or inducing coma
  - Recovering from or in the throes of hemodynamic instability
  - At risk for GABA agonist withdrawal
- No randomized data suggest any negative effect on survival

SHORT AND LONG-TERM OUTCOMES OF DELIRIUM
(USING DELIRIUM SCREENING TOOLS)

UNGRADED STATEMENT

- **Strong** Association: Cognitive impairment at 3 and 12 months and longer hospital stay
- **NO** Association: PTSD and post-ICU distress
- **Inconsistent** Association: ICU LOS, discharge disposition other than home, depression, functionality/dependence and mortality

POP QUIZ: TRUE OR FALSE ABOUT ADULT ICU DELIRIUM

- Systematic evaluations of delirium are recommended by the 2013 and the 2018 PAD guidelines and are associated with improved outcomes

POP QUIZ: TRUE OR FALSE ABOUT ADULT ICU DELIRIUM

- Nonpharmacologic-based preventative strategies for delirium can decrease its frequency

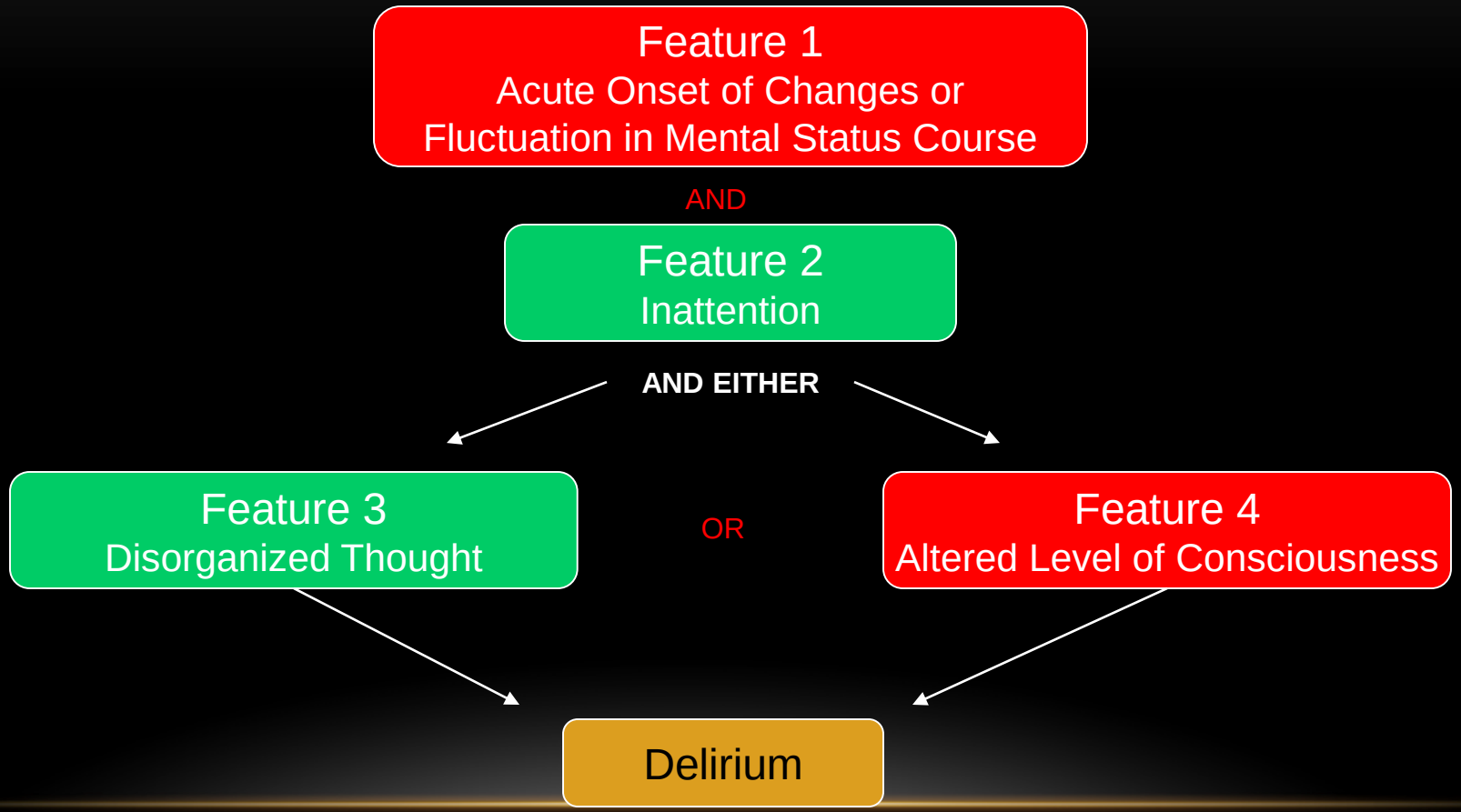
POP QUIZ: TRUE OR FALSE ABOUT ADULT ICU DELIRIUM

- Pharmacologic treatment of delirium limits its severity and duration

SHOULD **DELIRIUM** SYSTEMATICALLY BE **ASSESSED**?

- Good practice statement: Critically ill adults should be regularly assessed for delirium using a valid tool.

CONFUSION-ASSESSMENT METHOD FOR ICU (CAM-ICU)



Ely. JAMA 2001; 286:2703

THEORETICAL RATIONALE FOR SYSTEMATIC DELIRIUM ASSESSMENT

- Many cases (particularly the hypoactive variant) are missed
- Early delirium identification can facilitate correction of its inciting cause
- Assessments are easy to perform and are valid measures of delirium
- There is low probability of harm
- May reassure patients and families if distressful symptoms occur and open the conversation to include the post-intensive care syndrome (PICS)

IMPACT OF DELIRIUM ASSESSMENT

Study	Design	N	Outcomes Measured	Results
Bigatello. J Trauma Acute Care Surg 2013	Randomized prospective (notification)	283	Vent-free days, ICU LOS, time to Delirium tx	**No Diff**
Van den Boogaard. Crit Care 2009	Before/after (CAM use)	1153	Frequency and duration of Delirium	**More haloperidol**
Andrews. AJCC 2015	Before/after (CAM use)	229	Duration of restraints, ICU, and MV	**No Diff**
Park. Acute Crit Care 2018	Before/after (notification)	652	Duration of ICU and Delirium and mortality	**No Diff**
Reade Crit Care Resusc 2011	Before/after (CAM use)	288	RN documentation of Delirium	**Less Delirium identified!**
Luetz. J Crit Care 2016	Prospective adherence DDS/ CAM assessment	185	Mortality, ICU, hospital and MV duration	**All reduced if Delirium assessment >50%**

GAPS IN DELIRIUM ASSESSMENT DATA

- "The lack of high quality trials investigating the effect of delirium assessment underscores the gaps in understanding the relationship between delirium assessment and patient-centered outcomes, treatment decisions, patient and family satisfaction, and staff satisfaction." Devlin CCM 2018; 46:e825
- Contrast with….
  - Pain and agitation assessments ARE associated with improved outcomes Chanques. CCM 2006; 34:1691

RICHMOND AGITATION-SEDATION SCALE (RASS) TO ASSESS AROUSAL

[redacted]. RICHMOND AGITATION–SEDATION SCALE

Score	Term	Description
+4	Combative	Overtly combative or violent; immediate danger to staff
+3	Very agitation	Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff
+2	Agitated	Frequent nonpurposeful movement or patient–ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	
−1	Drowsy	Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice
−2	Light sedation	Briefly (less than 10 seconds) awakens with eye contact to voice
−3	Moderate sedation	Any movement (but no eye contact) to voice
−4	Deep sedation	No response to voice, but any movement to physical stimulation
−5	Unarousable	No response to voice or physical stimulation

Sessler. AJRCCM 2002; 166:1338

THE INFLUENCE OF AROUSAL ON DELIRIUM ASSESSMENTS

- 4 observational trials
- 12,264 paired CAM-ICU assessments at different levels of arousal (RASS 0 to -3)
- When data were not available, authors were contacted
- Most patients with RASS -3 were UTA (unable to assess)

- Compared frequency of positive CAM-ICU assessments when patients were sedated versus when they were wakeful

Svenningsen Acta Anaesthesiol 2013; 57:288
Haenggi. ICM 2013; 39:2171
Gusmao-Flores ICM 2014; 40:137
Patel AJRCCM 2014; 189:658

RASS AND POSITIVE CAM-ICU ASSESSMENTS
N = 12,264

Study	RASS -2 to -3			RASS 0 to -1		
	# Assessments	# CAM ICU positive	Frequency (%)	# Assessments	# CAM ICU positive	Frequency (%)
1	471	301	64	9441	2065	22
2	92	90	98	71	22	31
3	100	80	80	896	146	16
4	124	119	98	1019	259	25
Total	787	590	**75%**	11427	2492	**22%**

1. Svenningsen 2013, 2. Haenggi 2013, 3. Gusmao-Flores 2013, 4. Patel 2014.

BUT……

- Couldn’t this relationship be explained by the fact that delirium can present with a decreased arousal level independent of sedative use?

- Sure!
  - Data from sedation interruption trials limit that confounder since it only involves changes in arousal related to sedatives

PAIRED RASS AND POSITIVE CAM-ICU ASSESSMENTS (N = 1306) IN STUDIES WITH SEDATION INTERRUPTION

Study	RASS -2 to -3			RASS 0 to -1		
	# Assessments	# CAM ICU positive	Frequency (%)	# Assessments	# CAM ICU positive	Frequency (%)
1	471	301	64	9441	2065	22
2	**92**	**90**	**98**	**71**	**22**	**31**
3	100	80	80	896	146	16
4	**124**	**119**	**98**	**1019**	**259**	**25**
Total	216	209	**97%**	1090	281	**26%**

1. Svenningsen 2013, 2. Haenggi 2013, 3. Gusmao-Flores 2013, 4. Patel 2014

WHAT DOES THIS ALL MEAN?

- Available data are consistent and of great magnitude
- These data contribute to the argument that wakefulness is a desirable sedation titration goal for the majority of patients.
- Evaluating delirium when patients are wakeful limits artifact in the assessment

TIMING OF CAM-ICU VS SEDATION DEPTH

Should I do a CAM-ICU assessment before, during, or after a Spontaneous Awakening Trial (SAT)?

“The best picture of the patient’s mental status will come from assessing delirium serially throughout the day. Thus, we recommend that you assess patients for delirium both before and after daily sedative interruption (SAT).”

icudelirium.org accessed 8.15.16

RAPIDLY REVERSIBLE, SEDATION-RELATED DELIRIUM

PATEL. AJRCCM 2014; 189:658

N = 102 pts: Blinded paired CAM-ICU results before and after daily sedation interruption with one year follow-up

Sedation-related delirium = CAM POS → CAM NEG within 2h sedation interruption

10 = no delirium; 12 rapid reversible delirium; 51 persistent delirium; 24 mixed

OUTCOMES: NO DELIRIUM (ND), RAPIDLY REVERSIBLE DELIRIUM (RRD), PERSISTENT DELIRIUM (PD)

	ND	RRD	PD
ICU LOS (d)	4	4.5 →	13.1
Hosp LOS (d)	8.1	6.7 →	25.4
MV time (d)	2.4	2.5 →	6.2
D/C home (%)	80	100 →	27
Mortality % (1yr)	20	25 →	66

Sedation-related delirium may portend no long-term consequences other than those directly related to pharmacology (time on the ventilator and in the ICU)

Patel. AJRCCM 2014; 189:658

OTHER RAPIDLY REVERSIBLE DELIRIUM DATA

KENES PHARMACOTHERAPY 2017; 37:1357

- Post hoc subgroup analysis of a Quality Assurance study NOT designed to evaluate clinical outcomes (Stollings. Ann Pharmacotherapy 2015; 49:883)
- Possibly evaluated delirium before/after 4 hours of stopping sedatives
  - Unknown if all sedatives were actually held x 4 hours
- 20% had rapidly reversible delirium
  - Outcomes were the same as for those without delirium

PHARMACOLOGIC STRATEGIES TO **PREVENT** DELIRIUM

- Postoperative studies using haloperidol, risperidone, dexmedetomidine (1-3)
  - Reduced delirium incidence, but no difference in clinical outcomes
  - Data were from patients with low severity of illness
- **Newer data:** ICU patients at high risk for delirium using prophylactic haloperidol
  - Randomized 1 vs 2 mg IV haloperidol three times daily with placebo control
  - N = 1789
  - No difference: 28 day mortality, delirium incidence, delirium-free and coma-free days, duration of mechanical ventilation, ICU or hospital stay
    - Van den Boogaard. JAMA 2018; 319:680

1) WANG. CCM 2012; 40;731. 2) PRAKANRATTANA. ANAESTH INTENSIVE CARE 2007; 35:714. 3) SU. LANCET 2016; 388:1893.

PHARMACOLOGIC STRATEGIES TO **PREVENT** DELIRIUM

- **Recommendation:**
- We suggest **not** using haloperidol, atypical antipsychotics, dexmedetomidine, statins, or ketamine to **prevent** delirium in **all** critically ill adults (conditional recommendation, very low to low quality of evidence).
- **Newer data: How about low-dose nocturnal dexmedetomidine?**
  - N = 100 (dex vs placebo begun 2130 until 0630)
  - 80% dex and 54% placebo patients were delirium-free in the ICU (p =0.006)
  - Average dex dose 0.5 mcg/kg/hr to achieve target RASS -1
  - No effect on time in the ICU, in the hospital or on the ventilator, nor on sleep and mortality. Skrobik AJRCCM 2018; 197:1147

POP QUIZ: PROVEN TREATMENT OPTIONS FOR DELIRIUM INCLUDE

- Intravenous haloperidol
- Enteral quetiapine for symptom control
- Enteral clonidine for symptom control
- None of the above

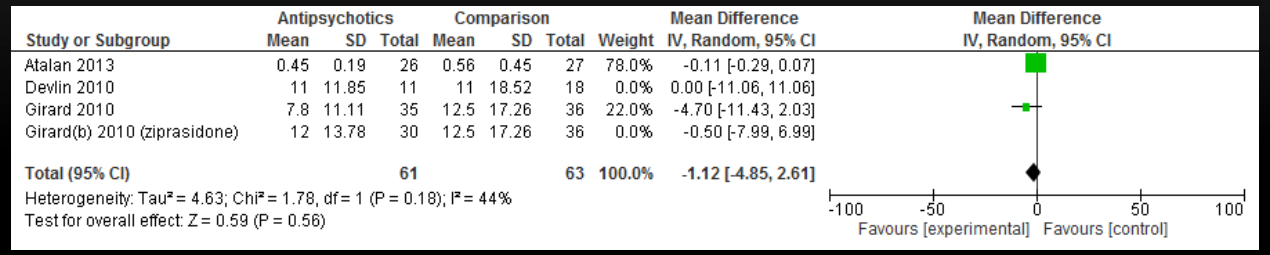
CLICK TO ADD TEXT

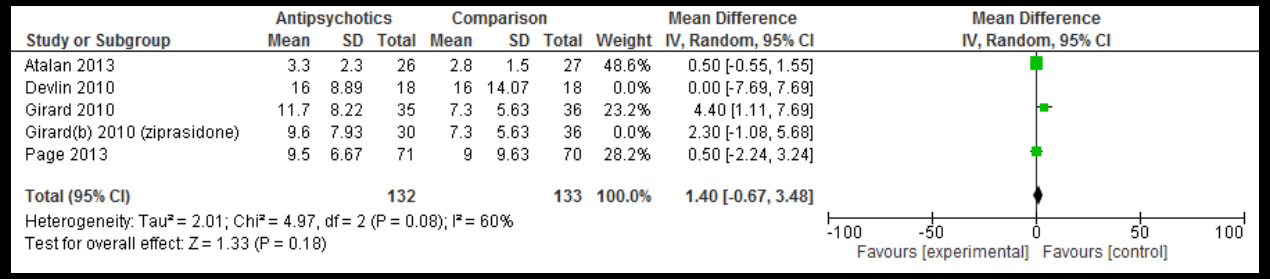
PHARMACOLOGIC **TREATMENT** OF DELIRIUM

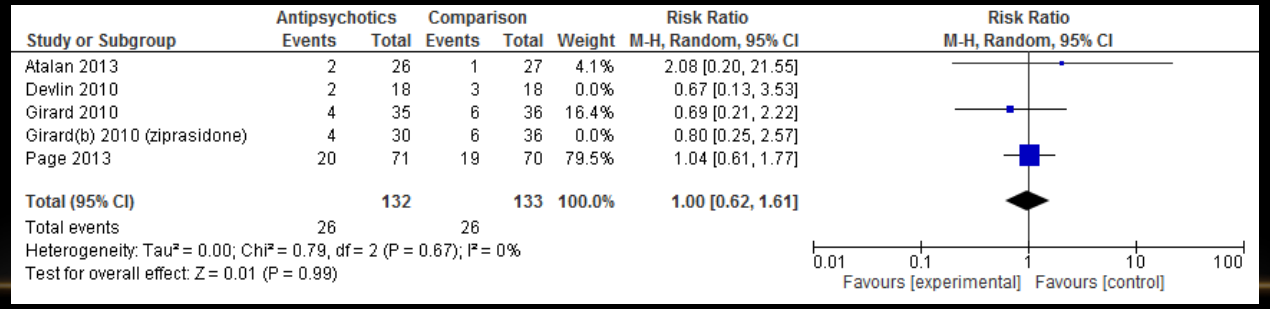
PICO Question	
P	Critically ill adult patients in an ICU
I	Haloperidol Atypical antipsychotic Statin Dexmedetomidine
C	No use of the medication
O	• Delirium duration • Duration of mechanical ventilation • ICU Length of stay • Mortality

Devlin JW, et al. CCM 2018

Influence of Haloperidol on the Duration of Delirium, Mechanical Ventilation, and ICU Stay = NONE







ATYPICAL ANTIPSYCHOTICS FOR ICU DELIRIUM TREATMENT?

- Two RCTs (quetiapine and ziprasidone) Devlin CCM 2010; 38:419, Girard CCM 2010; 38:428
- Total N 48 (intervention) and 54 (placebo)
    - Open label haloperidol in both studies for treatment of agitation
    - Outcomes evaluated (metaA)
        - Duration of delirium: No Diff
        - MV duration : No Diff
        - ICU LOS: No Diff
- Continuation of these agents inadvertently/inappropriately poses potential harm

ANTIPSYCHOTIC CONTINUATION

Study	Design	Patients Studied	ICU to Floor n (%)	Floor to Discharge n (%)*
Jasiak et al. J Pharm Pract. 2013;26(3):253	Single-center, retrospective	59	28/59 (47)	20/28 (71)
Rowe et al. J Crit Care. 2015;30:1283	Single-center, retrospective	341	n/a	82/341 (24)
Flurie et al. Am J Health-Syst Pharm. 2015;72(suppl 3):S133	Single-center, retrospective	87	23/87 (26)	9/23 (39)
Kram et al. J Crit Care. 2015;30:814	Single-center, retrospective	133	112/133 (84)	38/112 (34)
Gilbert et al. J Intensive Care Med. 2016. DOI: 10.1177/0885066615622424	Single-center, retrospective	161	85/161 (53)	54/85 (64)
Marshall et al. J Crit Care. 2016;33:119	Single-center, retrospective	3,119	n/a	642/3,119 (21)
			248/440 (56%)	**845/3,708 (23%)**

Courtesy of David Gagnon

NEWER DATA: RCT OF HALOPERIDOL, ZIPRASIDONE AND PLACEBO FOR ICU DELIRIUM GIRARD NEJM 2018; 379:2506

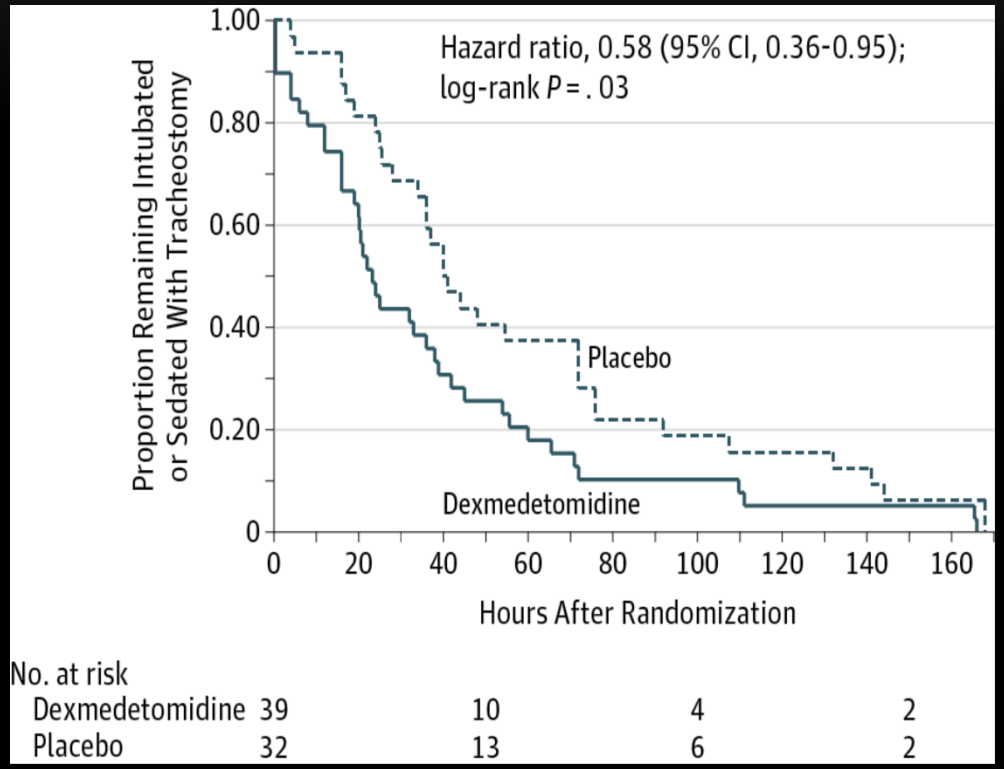
- ICU adults with acute respiratory failure or shock with hyper and hypoactive delirium; QTc <550 msec
- N = 566; APACHE II = 29, Delirium frequency 48%, hypoactive = 89% ("37% had hyperactive delirium" median duration = 0 days) NEJM 2019; 380; 1778
- Outcomes = days alive without delirium or coma for 14 days, delirium duration, 30 and 90 day survival, time on the ventilator, in the ICU, and in the hospital
- Results = Antipsychotic use did not affect any of the measured outcomes; no difference in use of ancillary medications (analgesics and sedatives)

CALL IT CURTAINS FOR ANTIPSYCHOTICS?

Not so fast!

While supportive data are lacking for the outcomes measured, it is unknown if delirium related distress can be relieved with antipsychotics

DEXMEDETOMIDINE FOR DELIRIUM TREATMENT?



Reade MC, et al JAMA 2016; 315:1416-1468

- Dex vs placebo in patients unable to wean because of agitated delirium
- Screened 21,500 intubated patients to enroll 71 study patients
- Study terminated early because lack of funding
- Dexmedetomidine resulted in more ventilator-free hours at 7 days
- No benefit: - ICU/hospital LOS
  - Discharge disposition

PHARMACOLOGIC TREATMENT OF DELIRIUM

- We suggest not routinely using haloperidol, an atypical antipsychotic, or a HMG-CoA reductase inhibitor (i.e., a statin) to treat delirium.

- conditional recommendation, very low to low quality of evidence

- We suggest using dexmedetomidine for delirium in mechanically ventilated adults where agitation is precluding weaning/extubation

- conditional recommendation, low quality of evidence

NON-PHARMACOLOGIC TREATMENT OF DELIRIUM

PICO Question	
P	Critically ill adult patients in an ICU
I	Multicomponent strategy including (but not limited to): - Strategies to reduce or shorten delirium (reorientation, cognitive stimulation) - Sleep improvement (minimize light/noise) - Improve wakefulness - Reduce immobility, offer hearing or visual aids
C	No use of this strategy
O	• Delirium duration • Duration of mechanical ventilation • ICU Length of stay • Mortality

MULTICOMPONENT NON-PHARM STRATEGIES = EFFICACY (YES)

Author (year)	Design	Intervention	Summary delirium related Results (intervention vs control)	Risk of bias
Colombo . Minerva Anestesiol 2012	Before-after	N=144 Reorientation, environmental, acoustic and visual stimulation (music, book reading)	- Delirium: 22% vs. 35%; p=0.02 - LOS-ICU: 5days vs 3.5days; p<0.001	High risk
Foster. Clin Nurs Spec 2013	Before-after	N=84 Sedation, sleep-wake, sensory stimulation, mobility and music	- Delirium: 31% vs. 28%; NS	High risk
Moon. Int J Nurs Stud 2015	RCT	N=60 Delirium risk monitoring, cognition and orientation, environment, early therapeutic intervention	- Delirium: 20% vs. 33.3%; p=0.10 - LOS-ICU: 10.8days vs. 10.0days; p=0.68 - In-hospital mortality: 6.7% vs. 20.6%; p=0.02 - 30-days in-hospital mortality: 6.7% vs. 17.5%; p=0.07	High risk
Hanison. BMJ Qual Improv Rep 2015	Before-after	N=127 2 cycle program: 1st cycle: reducing deliriogenic drugs, daily sedation breaks, environment changes, more light exposure, use of communication aid, 2nd cycle: natural light, clocks	- Delirium: 44% (1st cycle) 29% (2nd cycle). vs. usual care 65%; NS	High risk
Rivosecchi J Crit Care 2016	Before-after	N=253 music, opening blinds, reorientation and cognitive stimulation, eye/ear protocol	- Delirium: 9.4% vs 15.7%; p=0.04 - LOS-ICU: 2.8days vs. 2.4days; p=0.79 - ICU mortality: 11.1% vs 7.5%; p=0.21	High risk

MULTICOMPONENT NON-PHARM STRATEGIES = EFFICACY (NO)

Author (year)	Design	Intervention	Summary delirium related Results (intervention vs control)	Risk of bias
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Foster. Clin Nurs Spec 2013	Before-after	N=84 Sedation, sleep-wake, sensory stimulation, mobility and music	- Delirium: 31% vs. 28%; NS	High risk
Moon. Int J Nurs Stud 2015	RCT	N=60 Delirium risk monitoring, cognition and orientation, environment, early therapeutic intervention	- Delirium: 20% vs. 33.3%; p=0.10 - LOS-ICU: 10.8 days vs. 10 days; p=0.68 - In-hospital mortality: 6.7% vs. 20.6%; p=0.02 - 30-day in-hospital mortality: 6.7% vs. 17.5%; p=0.07	High risk
Hanison. BMJ Qual Improv Rep 2015	Before-after	N=127 2 cycle program: 1st cycle: reducing deliriogenic drugs, daily sedation breaks, environment changes, more light exposure, use of communication aid, 2nd cycle: natural light, clocks	- Delirium: 44% (1st cycle) 29% (2nd cycle). vs. usual care 65%; NS	High risk
Rivosecchi J Crit Care 2016	Before-after	N=253 music, opening blinds, reorientation and cognitive stimulation, eye/ear protocol	- Delirium: 9.4% vs 15.7%; p=0.04 - LOS-ICU: 2.8 days vs. 2.4 days; p=0.79 - ICU mortality: 11.1% vs 7.5%; p=0.21	High risk

THE ABCDEF BUNDLE (ICULIBERATION.ORG)

- **A**ssess, prevent, and manage pain
- **B**oth SAT and SBT
- **C**hoice of analgesia and sedation (including depth of sedation)
- **D**elirium: assess, prevent, and manage
- **E**arly mobility and exercise
- **F**amily engagement and empowerment (not specifically discussed in the guidelines)

ABCDEF BUNDLE IMPROVES OUTCOMES

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- Before and after study design using data from 15,000 patients
- Evaluated mortality, ICU and hospital discharge, time on the ventilator, coma, delirium, pain and restraint use, ICU readmission and discharge destination
  - All as a function of daily adherence to bundle components
- Corrected for 18 confounders (except for delirium and acuity of illness)
- Found a dose-related improvement in all outcomes except pain
  - Was this because bundle use facilitated identification of pain?

SUMMARY: NEWER DELIRIUM DATA DESCRIBE

- Different rates, risk factors, and outcomes
- A dearth of objective data supporting systematic assessments
- The significant influence of levels of arousal on delirium assessments
- Rapidly reversible delirium as a variant without significant impact on selected outcomes
- The ineffectiveness of pharmacologic management
- The possible effectiveness of nonpharmacologic management

TAKE HOME POINTS

- Avoid sedation confounding of delirium assessments
- Go beyond the CAM-ICU screening tests for delirium and work hard to establish its etiology
- For agitated patients with delirium, patient/staff safety is important. Dexmedetomidine has the most consistent support, but other agents may be helpful. Remember to treat pain!!
- Antipsychotics begun in the ICU for agitated delirium should be discontinued as soon as possible!
- No data support the use of antipsychotics for hypoactive delirium
- Nonpharmacologic interventions are the mainstay of delirium management in 2019
- We have much to learn about this condition!


“Cure sometimes, comfort always.”
Armstrong and Crisp