



JOHNS HOPKINS
M E D I C I N E

Prevention & Treatment of Delirium

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Disclosures



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- No conflicts of interest for this talk
- No financial relationships in past 3 years
- **Use of non-FDA approved pharmacologic agents** will be referenced
- Chair: **Johns Hopkins Delirium Consortium**
- Past President: **American Delirium Society (ADS)**

Overview & Objectives “Getting our Ducks in a Row”

After this lecture, attendees will be able to describe:

- 3 important harms associated with delirium
- Evidence for pharmacologic interventions in treatment and prevention
- 3 prevention/treatment non-pharmacologic strategies

Look for the baby duck slides!



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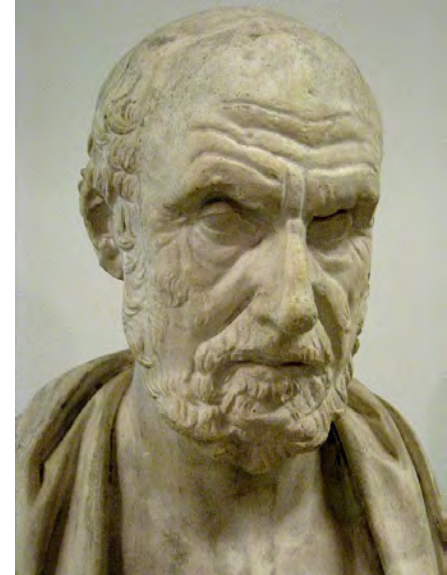


History of the Syndrome of Delirium

“The Top-Down View”

Hippocrates 460 - 370 BC

- ~ 2500 years ago
- Described: phrenitis (& lethargus)
- An acute disorder
- Associated with fever
- Problems with cognition, behavior
- Disrupted sleep & unstable moods



Remarkably consistent clinical description of the syndrome

Definition of Delirium: DSM-5

- Key feature is disturbance in attention/awareness
- Of relatively abrupt onset and symptoms that fluctuate
- New cognitive deficits eg., poor memory, disorientation, perceptual disturbances
- Not due to other neuropsychiatric disturbance (i.e. dementia)
- Due to underlying physiological disturbance
 - Other features often include but are not necessary for the diagnosis:
 - Sleep-wake cycle disturbance or reversal in majority of cases
 - Emotional lability or irritability
 - Hallucinations (onieroid = dream-like), illusions and delusions
 - Motor changes: agitation/or lethargy

Why do we Care?

- Common and commonly missed
- Delirium is associated with BAD outcomes
- Very distressing for patients and their loved ones
- You can watch the following interview with a patient at the following website:

<https://www.youtube.com/watch?v=Xs1MNBcTL9I>

You can see other videos

At the OACIS website:

<https://www.hopkinsmedicine.org/pulmonary/research/outcomes-after-critical-illness/oacis-videos-news.html#videos>



Why do we Care?

Delirium: Short Term Outcomes



- Associated with increased healthcare utilization
 - Increased mechanical ventilation duration (9 vs. 4 days)
 - Increased ICU length of stay (8 vs.5 days)
 - Increased hospital length of stay (21 vs. 11 days)
- Higher ICU costs (\$22,000 vs. \$13, 000)
- Estimated national annual costs \$4 to \$16 Billion
- Patient and caregiver suffering

Outcome of delirium in critically ill patients: systematic review and meta-analysis

BMJ 2015;350:h2538

Jorge I F Salluh,¹ Han Wang,² Eric B Schneider,² Neeraja Nagaraja,² Gayane Yenokyan,³ Abdulla Damluji,⁴ Rodrigo B Serafim,^{1,5} Robert D Stevens⁶

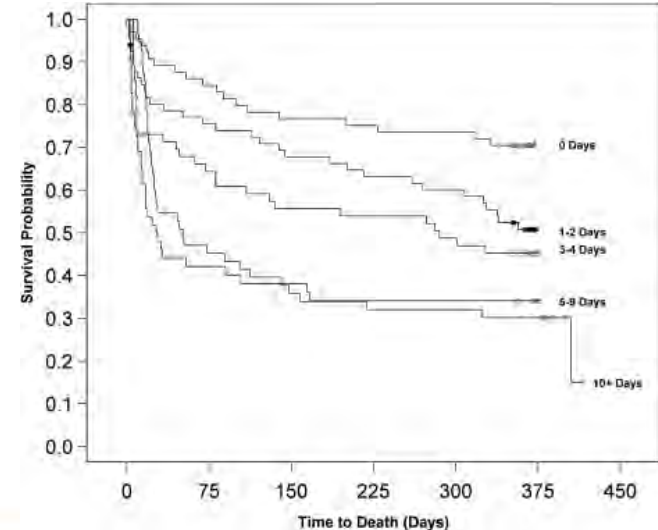


Delirious patients have a higher risk of death in the ICU...

	Relative Risk (95% CI)
ICU Mortality (95% CI)	2.19 (1.78 – 2.70)
adjusted for age, sex and APACHE	2.72 (1.75 – 3.69)

...and in the year after discharge.

Pisani MA, et al. Am J Respir Crit Care Med. 2009;180:1092-7.

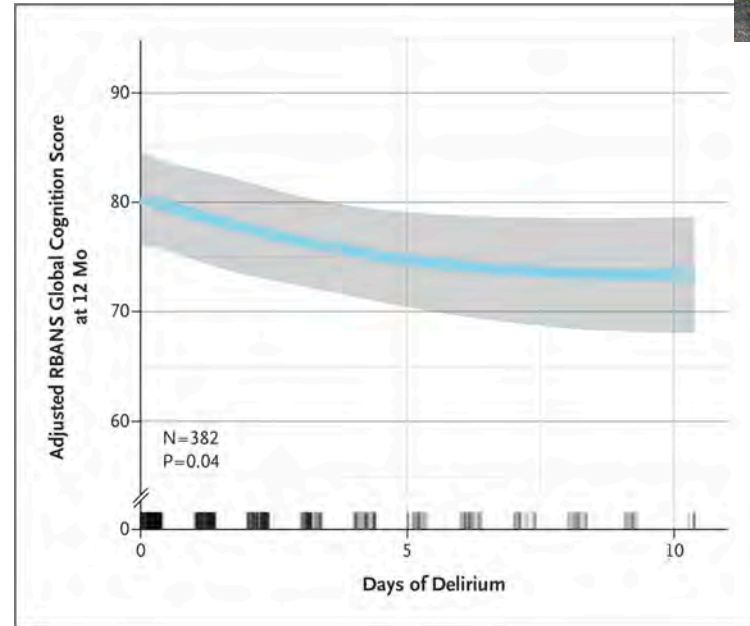


Why do we Care?

Delirium: Long Term Outcomes



- Functional decline
- New nursing home placement
- Persistent cognitive decline:
 - Those developing delirium have cognitive dysfunction up to 6-12 months after discharge and longer



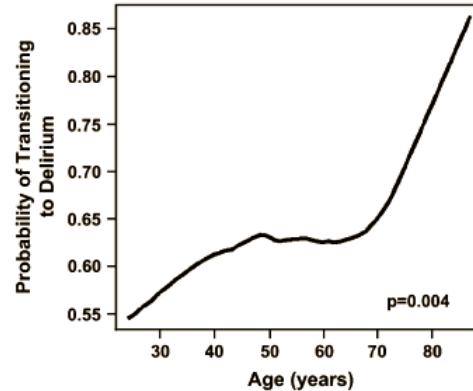
Epidemiology: Where Do We Find Delirium?

Prevalence

- Critically Ill Mechanically Ventilated Population
 - 60 – 85%
- General Medical Inpatient Units
 - 10 - 40%
- Medical Oncology Units
 - 20 – 70%
- Orthopedic Surgery: Hip fracture repair
 - 20 – 40%
- Why the variability?

As a Rule... More Delirium with:

- Increased Severity of Illness
- Older Age
- Cognitive Impairment

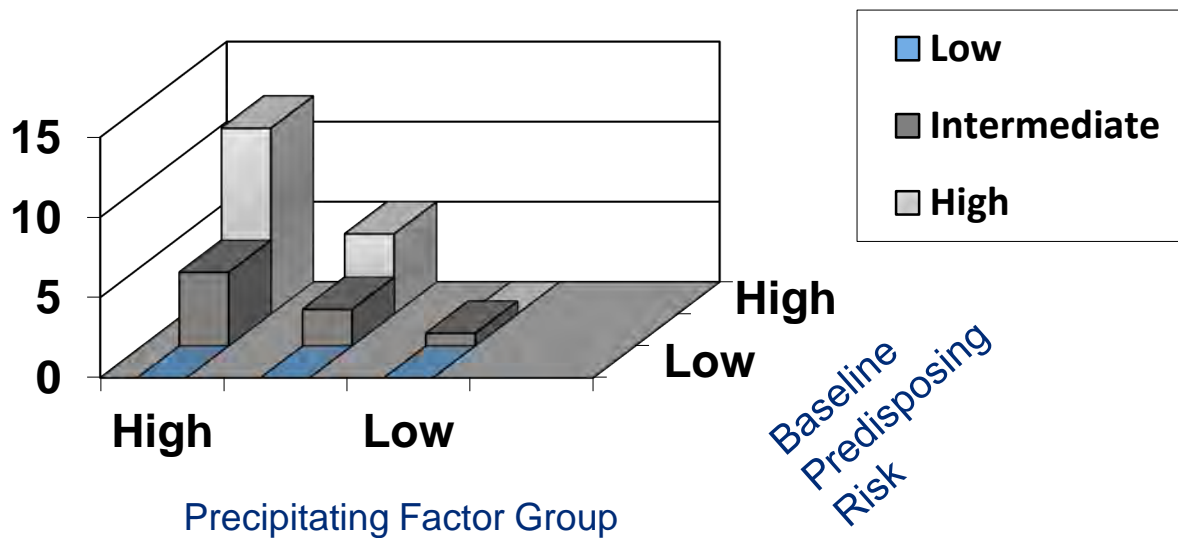


Probability of transitioning to delirium ↻ dramatically (by 2%) for each year of life after age 65.

The more ill the patient, the greater the likelihood of delirium.

Delirium Risk Model

Incidence of Delirium (per day)



Predisposing Factors - Vulnerability

- Baseline cognitive impairment
 - 2.5 X↑ risk if Demented
 - 25-31% of delirious patients have underlying dementia
- Chronic medical conditions:
 - Any medical illness
- Visual impairment
- Hearing impairment
- Functional impairment
- History of ETOH or other drug abuse

**The more predisposing risk factors ...
The more likely delirium will develop.
Therefore - target high-risk patients for prevention.**

Precipitating Risk Factors - Insults

- Medications
- New medical illnesses
- Infections
- ETOH/drug withdrawal
- Fluid/electrolyte abnormalities
- Urinary retention
- Fecal impaction
- Immobility
- Environmental influences
- Physical restraints
- Indwelling catheters
- Uncontrolled pain
- Sleep deprivation

Identification

33-95% of in hospital cases of delirium

- Missed - especially the hypoactive presentation
- Misdiagnosed as depression, psychosis or dementia
- Delirium trumps all other psychiatric dx
 - Can't make a diagnosis about depression or psychosis until delirium clears
- Often missed because cognition not tested actively
 - “ How are your feeling today Mrs. Smith?”
- May co-occur with dementia



Identification of Delirium

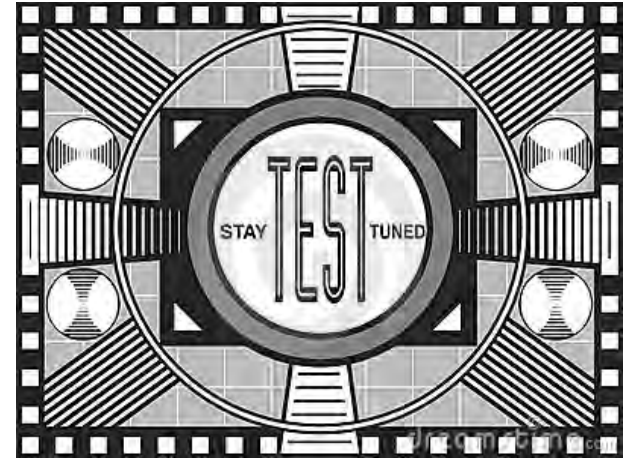
- History
 - Acute change from a previous baseline (collateral information)
- Mental State Exam
 - Changes in level of arousal (fluctuating level of consciousness)
 - Cognitive disturbances: Disorientation, ability to recall
 - Difficulty sustaining attention (days of the week backwards, serial 7's or “world” backwards)
 - Difficulty learning new information (decreased short term recall)
- Laboratory Investigations
 - EEG - Slowing of background rhythm “generalized dysfunction” but not 100% sensitive or specific
- Further history, physical exam and investigation
 - To identify etiology of the delirium

Identification of Delirium

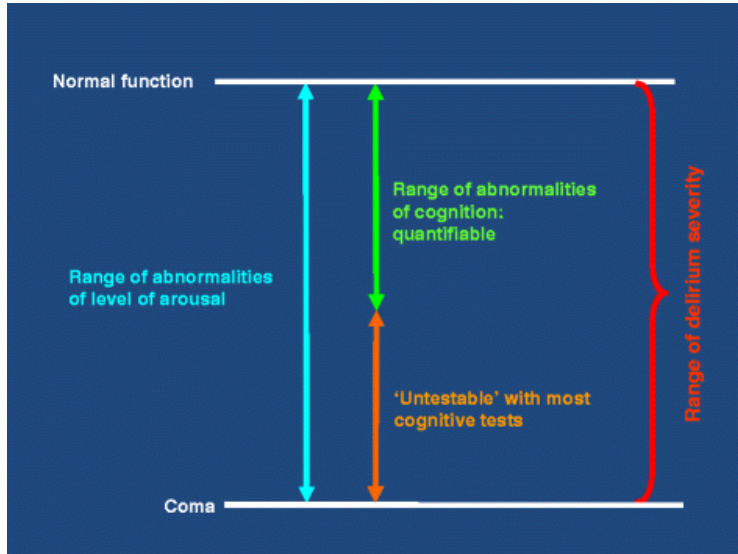
- Tips for eliciting history from family:
 - “This isn’t my granny!”
 - When did this change occur? In relation to what?
 - May help aide differential diagnosis
 - Medicine changes including new over-the-counter preps.
 - Other symptoms such as cough and fever

Actively Test Cognition

- Attention
 - Months of the year backwards
 - Days of the week backwards
 - Spell “world” backwards; serial 7’s
- Orientation
 - Time: Day, date, month, season, year
 - Place: Hospital, floor, building, street, city, state
- Recall – immediate and short term
- Use standardized screening tool:
 - 4AT [http:// 4AT.com](http://4AT.com) or CAM-ICU in nonverbal patients
 - MMSE: Mini-mental State Exam
 - MOCA: Montreal Cognitive Assessment



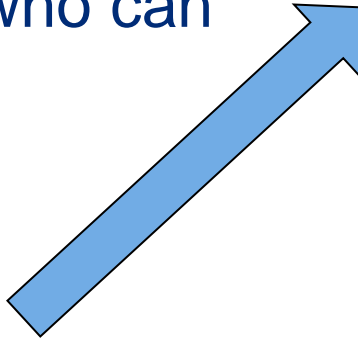
Attention and Arousal: Beware of the “Sleepy” Patient



Overlap between hypoactive delirium and reduced arousal states (hyperactive delirium not included).

European Delirium Association and American Delirium Society *BMC Medicine* 2014 **12**:141 doi:10.1186/s12916-014-0141-2

This test is used in the Johns Hopkins Medical system in patients who can speak.



Assessment tool for delirium & cognitive impairment

(AUSA)

Patient name: _____
 Date of birth: _____
 Patient number: _____
 Date: _____ Time: _____
 Tester: _____

CIRCLE

[1] ALERTNESS

This includes patients who may be markedly drowsy (eg, difficult to rouse and/or obviously sleepy during assessment) or agitated/irritable. Observe the patient. If asleep, attempt to wake with speech or gentle touch on shoulder. Ask the patient to state their name and address to assist rating.

Normal (fully alert, but not agitated, throughout assessment)	0
Mild sleepiness for <10 seconds after waking, then normal	0
Clearly abnormal	4

[2] AMT4

Age, date of birth, place (name of the hospital or building), current year.

No mistakes	0
1 mistake	1
2 or more: mistake estimateable	2

[3] ATTENTION

Ask the patient: "Please tell me the months of the year in backwards order, starting at December." To assist initial understanding one prompt of "what is the month before December?" is permitted.

Months of the year backwards	Achieves 7 months or more correctly	0
	Shuts but scores <7 months / refuses to start	1
	Unstable (cannot start because unusual, drowsy, inattentive)	2

[4] ACUTE CHANGE OR FLUCTUATING COURSE

Evidence of significant change or fluctuation in alertness, attention, other mental function (eg, paranoia, hallucinations) arising over the last 2 weeks and still evident in last 24hrs

No	0
Yes	4

4 or above: possible delirium +/- cognitive impairment
 1-3: possible cognitive impairment
 0: delirium or severe cognitive impairment unlikely (but delirium still possible if [4] information incomplete)

4AT SCORE

GUIDANCE NOTES

Version 1.2. Information and download: www.4AT.com
 The 4AT is a screening instrument designed for rapid initial assessment of delirium and cognitive impairment. A score of 4 or more suggests delirium but is not diagnostic; more detailed assessment of mental status may be required to reach a diagnosis. A score of 1-3 suggests cognitive impairment and more detailed cognitive testing and informal history-taking are required. A score of 0 does not definitely exclude delirium or cognitive impairment; more detailed testing may be required depending on the clinical context. Items 1-3 are rated solely on observation of the patient at the time of assessment. Item 4 requires information from one or more source(s), eg, your own knowledge of the patient, other staff who know the patient (eg, ward nurses), GP letters, case notes, charts. The tester should take account of communication difficulties (hearing impairment, dysphasia, lack of common language) when carrying out the test and interpreting the score.

Alertness: Altered level of alertness is very likely to be delirium in general hospital settings. If the patient shows significant altered alertness during the bedside assessment, score 4 for this item. **AMT4 (Abbreviated Mental Test - 4):** This score can be calculated from items in the AMT10 if the latter is done immediately before. **Acute Change or Fluctuating Course:** Fluctuation can occur without delirium in some cases of dementia, but marked fluctuation usually indicates delirium. To help elicit any hallucinations and/or paranoid thoughts ask the patient questions such as, "Are you concerned about anything going on here?", "Do you feel frightened by anything or anyone?", "Have you been seeing or hearing anything unusual?"

Unique screening tool as it rates the sleepy patient as "Positive"

www.4AT.com

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Look for the baby duck slides!



Treatment

- Delirium
- A psychiatric presentation
- Underlying medical problem
- Find and correct the cause
- Often more than one cause
- Use the following: “THINK” delirium

What to THINK about when delirium is present

T

Too Many Medications – polypharmacy (anticholinergics)

Too Little Water – dehydration

Toxicity from Organ Failure - heart, liver, kidney

Tremens - alcohol and benzodiazepine withdrawal

Thiamine or other nutritional deficiency

H

Hypoxemia – pulmonary embolus, pneumonia

I

Infection/sepsis

Immobilization

N

Nonpharmacological interventions – hearing aids, glasses, reorientation, music, noise control, ambulation – up and out of bed throughout the day, sleep protocols for night, family rooming-in

K

K⁺ or Electrolyte problems including hypo-Mg⁺²

** Adapted with permission from: Marta Render, MD –
Veteran Affairs In-patient Evaluation Center (IPEC)*

Pharmacologic Strategies

First principle:

- Do No Harm
- Minimize drugs associated with delirium
- Can we prevent or treat delirium with medicine?



Pharmacologic prevention and treatment of delirium in intensive care patients: A systematic review[☆], *Journal of Critical Care* 30 (2015) 799–807

Rodrigo B. Serafim, MD, MSc^{a,b,c}, Fernando A. Bozza, MD, PhD^{a,d}, Marcio Soares, MD, PhD^{a,e}, Pedro Emanuel A.A. do Brasil, MD, PhD^a, Bernardo R. Tura, MD, PhD^a, E. Wesley Ely, MD^{f,g}, Jorge I.F. Salluh, MD, PhD^{a,e,*}



- 15 studies on delirium prevention
- 7 studies on delirium treatment (time to delirium resolution)
- Therapies evaluated included:
 - Dexmedetomidine
 - Rivastigmine
 - Haloperidol and atypical antipsychotics
 - Statins
 - Dexamethasone
- **No agent could consistently prevent or treat delirium**



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Topic Timeline

Antipsychotics for the Prevention and Treatment of Delirium

SYSTEMATIC REVIEW | September 3, 2019

Download Main Document PDF 6.2 MB



<https://effectivehealthcare.ahrq.gov/products/antipsychotics/research>

Prevention of Delirium Using Antipsychotics?

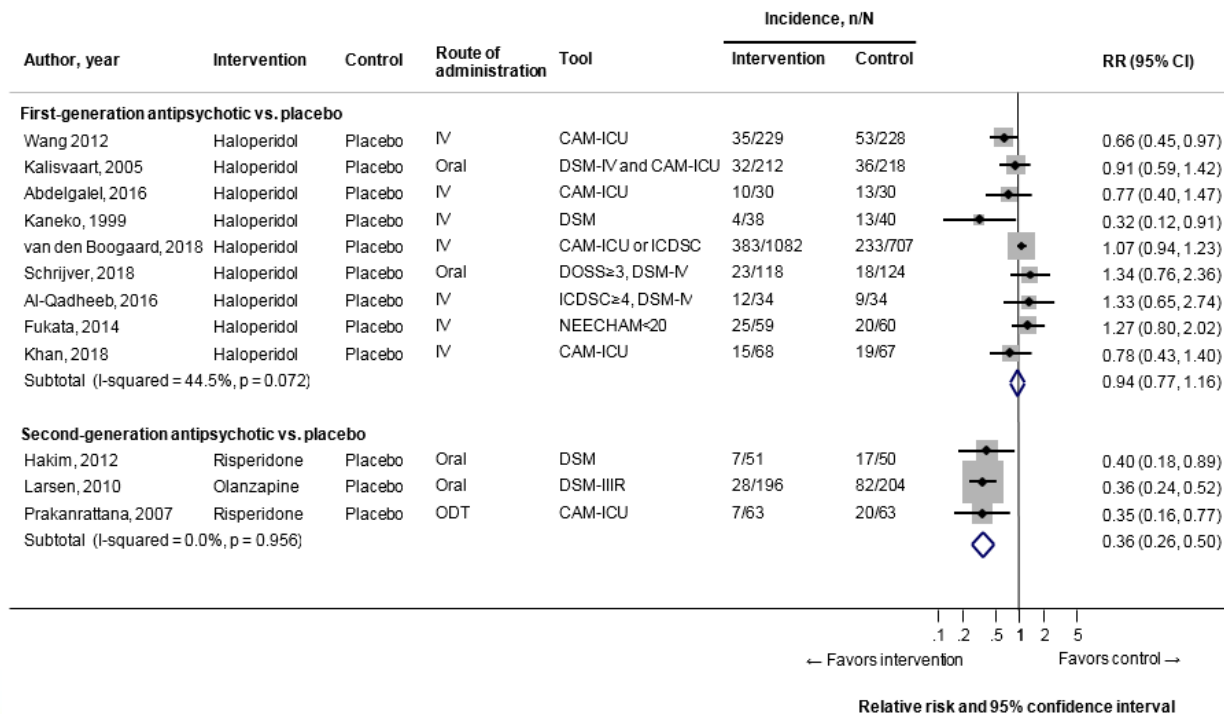


Figure 4. Meta-analysis of delirium incidence in trials comparing either haloperidol or second-generation antipsychotics with placebo among patients at risk for delirium



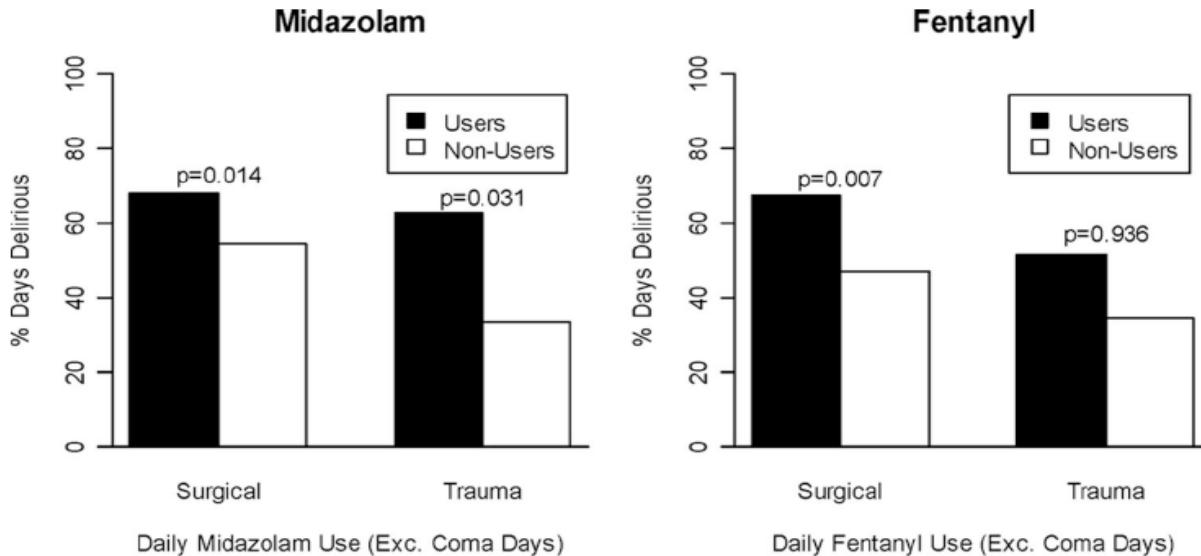
Key Findings: AHRQ Review

When using haloperidol/SGA's to prevent or treat delirium:

- ✓ No difference in the hospital LOS
- ✓ Little or no evidence to determine the effect of antipsychotics on many outcomes
- ✓ SGA's may ↓ delirium in postoperative pts
- ✓ Haloperidol/SGA's: little or no difference in sedation or EPS
- ✓ Heart-related SE's (QT prolongation) occurred more frequently with antipsychotics (note: but not statistically significantly so)
- ✓ Future studies needed to assess effects on:
 - ❖ Agitation and distress, Subsequent memories of delirium, Caregiver burden and distress, Inappropriate continuation of antipsychotic therapy, and long- term cognitive and functional outcomes.

Prevalence and Risk Factors for Development of Delirium in Surgical and Trauma Intensive Care Unit Patients

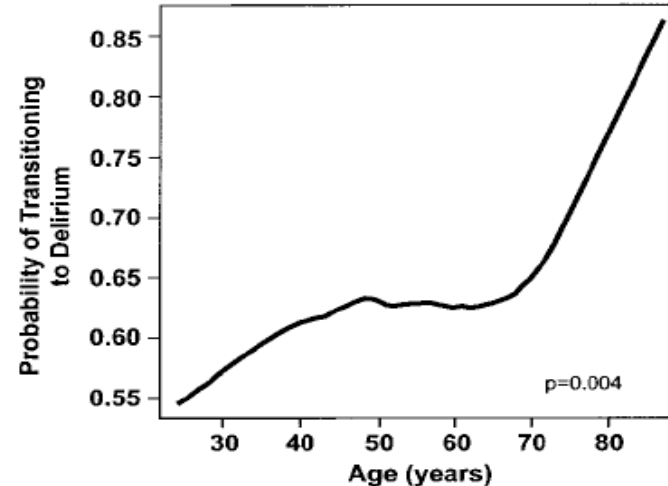
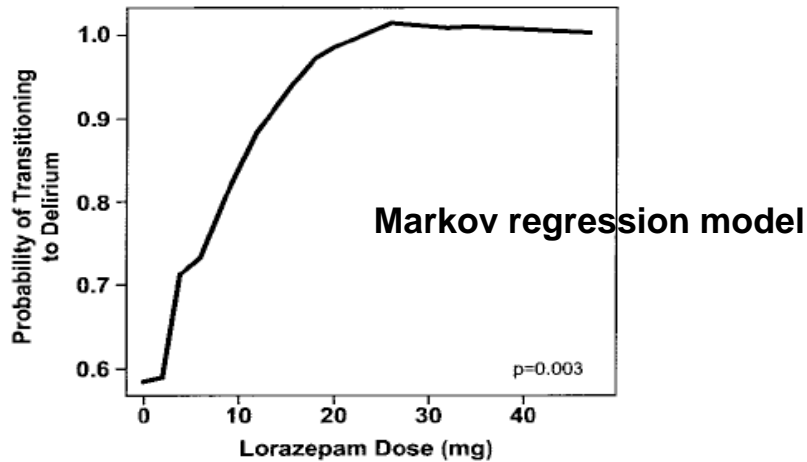
Pratik Pandharipande, MD, MSCI, Bryan A. Cotton, MD, FACS, Ayumi Shintani, PhD, MPH, Jennifer Thompson, MPH, Brenda Truman Pun, MSN, ACNP, John A. Morris, Jr., MD, FACS, Robert Dittus, MD, MPH, and E. Wesley Ely, MD, MPH



Pandharipande P et al., J Trauma 2008;65:34-41.

Lorazepam Is an Independent Risk Factor for Transitioning to Delirium in Intensive Care Unit Patients

Pratik Pandharipande, M.D., M.S.C.I.,* Ayumi Shintani, Ph.D., M.P.H.,† Josh Peterson, M.D., M.P.H.,‡
Brenda Truman Pun, R.N., M.S.N., A.C.N.P.,§ Grant R. Wilkinson, Ph.D., D.Sc.,|| Robert S. Dittus, M.D., M.P.H.,#
Gordon R. Bernard, M.D.,** E. Wesley Ely, M.D., M.P.H.††



Probability of transition to delirium increased with lorazepam dose given in prior 24 hrs

Risk of delirium increased dramatically for each year of life after 65 year of age

Pandharipande P et al., Anesthesiology 2006;104:21-26.

Sedation Protocols

Goal patient below...



- RASS goal: **0 = ALERT and AWAKE**
- Fentanyl & midazolam (A-1)
- Avoid infusions, use prn
 - Initially q 5 min (if needed)
 - Then q 1-2hr
- Daily stop of prn & infusion
- Anticipate agitation
 - Do not use benzo
 - Use IV haloperidol (check QTc)

Pharmacologic Interventions – Take-away



- Do no harm: minimize psychoactive meds and sedation
- Antipsychotics do not decrease delirium incidence or LOS
- If needed for symptomatically (distress and anxiety) – stop them with resolution of symptoms ASAP



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Management & Prevention of Delirium



Non-pharmacologic strategies:

- Early physical and cognitive rehabilitation
- Improved sleep
- Multi-faceted non-pharm protocols



Summary of ICU Mobility Outcomes

www.hopkinsmedicine.org/OACIS

- Improves delirium
- Improves physical function
- Decreases LOS
- Improves Physical Function QOL
- Timing of mobility matters – early
- Sedation practices matter
- Mobility matters, not who delivers it



This adapted slide originally from Carrie Goodson MD

JHH MICU Sleep QI

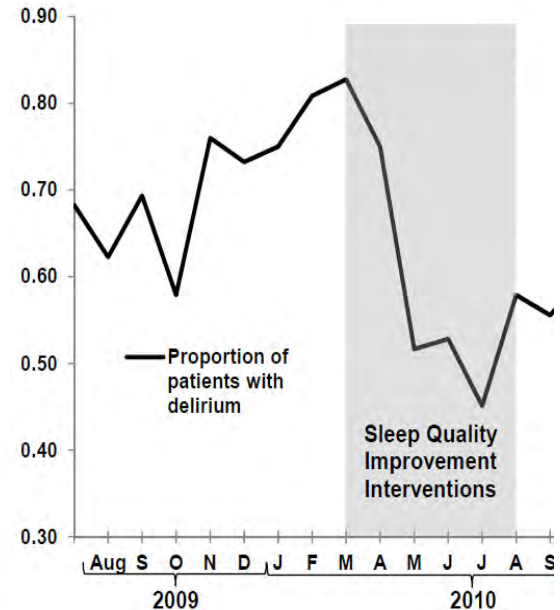
Crit Care Med 2013

The Effect of a Quality Improvement Intervention on Perceived Sleep Quality and Cognition in a Medical ICU*

Biren B. Kamdar, MD, MBA, MHS^{1,2}; Lauren M. King, RN, MSN^{1,3}; Nancy A. Collop, MD⁴;
 Sruthi Sakamuri, BS⁵; Elizabeth Colantuoni, PhD^{1,6}; Karin J. Neufeld, MD, MPH^{1,7};
 O. Joseph Bienvenu, MD, PhD^{1,7}; Annette M. Rowden, PharmD⁸; Pegah Touradji, PhD^{1,9,10};
 Roy G. Brower, MD²; Dale M. Needham, MD, PhD^{1,2,10}

Table 4. ICU cognitive and secondary outcomes

ICU outcome	Baseline N = 110 patients, 634 patient- days	Sleep QI N = 175 patients, 826 patient- days	QI vs. Baseline Adjusted Odds Ratio or Difference (95% CI)	P Value
Delirium outcomes				
Delirium/coma-free days in MICU, no. (%)	272 (43)	399 (48)	1.64 (1.04-2.58)	0.03 ^a
Patients without delirium/coma during ICU stay, no. (%)	34 (31)	89 (51)	2.20 (1.13-4.27)	0.02 ^a



Efficacy of Non-Pharmacological Interventions to Prevent and Treat Delirium in Older Patients: A Systematic Overview. The SENATOR project ONTOP Series

Iosief Abraha^{1*}, Fabiana Trotta¹, Joseph M. Rimland², Alfonso Cruz-Jentoft³, Isabel Lozano-Montoya³, Roy L. Soiza⁴, Valentina Pierini⁵, Paolo Dessì Fulgheri⁵, Fabrizia Lattanzio², Denis O'Mahony⁶, Antonio Cherubini¹



2015 Jun 10;10(6):e0123090.
doi: [10.1371/journal.pone.0123090](https://doi.org/10.1371/journal.pone.0123090).
eCollection 2015

31 primary studies in last 20 years from 26 systematic reviews

- Age \geq 60
- Surgical and Medical acute care setting
- Single and multi-component interventions
 - Staff Education
 - Multi-disciplinary team
 - Avoidance of Sensory Deprivation
 - Orientation Protocol
 - Sleep protocol
 - Early mobilization
 - Hydration
 - Nutrition
 - Oxygen delivery
 - Pain control
 - Drug list review – stop unneeded meds

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2015 Jun 10;10(6):e0123090.
doi: [10.1371/journal.pone.0123090](https://doi.org/10.1371/journal.pone.0123090).
eCollection 2015

Pooled Delirium Incidence Reduced by:

- 29% in surgical setting
- RR 0.71 (95% CI: 0.59 to 0.86)

- 35% in medical setting
- RR 0.65 (95% CI: 0.49 to 0.86)

What do these non-pharmacologic interventions look like in the ICU?

Reading the Newspaper



*Provided by: Satoru Hashimoto MD; Director of Intensive Care,
Kyoto Prefectural University of Medicine, Japan*

Enjoying Difficult Sudoku



*Provided by: Satoru Hashimoto MD; Director of Intensive Care,
Kyoto Prefectural University of Medicine, Japan*

Walking outside of the ICU



Walking outside for Sunshine Therapy



Early Mobility



Wii-hab



Hydrotherapy



Felten-Barentsz AJRCCM 2015;191(4):476-77
Wegner Austral Crit Care 2017 in press

Prevention and Treatment Summary



- Need to detect delirium
 - Test cognition (4AT or CAM-ICU)
- Correct the underlying causes
- Do no harm
 - Reduce deliriogenic meds
 - Reduce sedation
 - No clear evidence for pharmacologic agents to shorten the course
- Use non-pharmacologic bundled care for prevention & treatment
 - Increased mobility
 - Cognitive rehabilitation
 - Improved sleep

Thank you for your Time

