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# Rapid Clinical Updates: Delirium and Inpatient Psychotropics

## Speakers

**Jennifer Woodard, MD**

*Clinical Assistant Professor*

*Divisions of Hospital Medicine and Geriatrics at University of  
Wisconsin-Madison*

**Babar Ali Khan, MD**

*Professor of Medicine*

*Floyd and Reba Smith Chair of Respiratory Diseases*

Moderated by

**Joe Sweigart, MD, MPH, SFHM**

*Division of Hospital Medicine  
University of Kentucky*

# Dr. Joseph Sweigart, MD, FHM, SFHM

- **Associate Professor**
  - University of Kentucky, Division of Hospital Medicine
- **SHM Board of Directors**



# Dr. Jennifer Woodard, MD

- **Clinical Assistant Professor**
  - Divisions of Hospital Medicine and Geriatrics at University of Wisconsin-Madison
- **Associate Program Director**
  - Geriatrics Fellowship



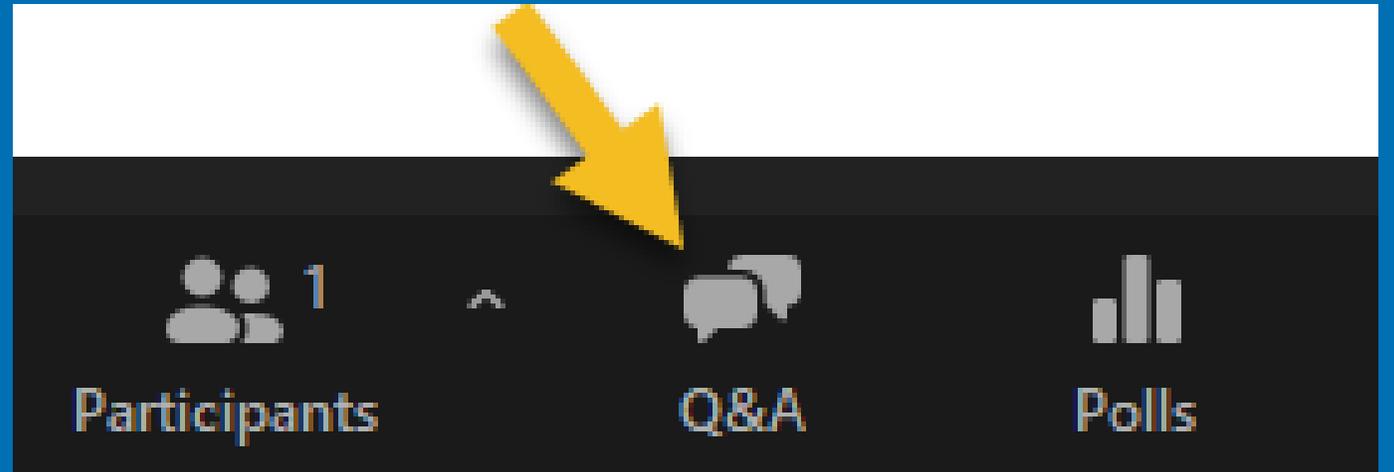
# Dr. Babar Ali Khan, MD

- **Professor of Medicine**
  - Floyd and Reba Smith Chair of Respiratory Diseases
- **Research Scientist**
  - Regenstrief Institute, Inc



# Please submit questions using Q&A feature

We will have Q&A time after



A blurred hospital hallway with medical professionals in the background. The scene is brightly lit, and the focus is on the foreground text.

# QUESTIONS

# Question 1

1. A 72-year-old female was brought to the emergency department (ED) for fever and altered mental status. The patient came from a skilled nursing facility (SNF) with one-week history of lethargy, drowsiness and urinary urgency. In the last two days, she had been increasingly confused and complained of pain on urination. The patient's past medical history was notable for mild cognitive impairment (MMSE=23), hypertension, and intermittent anxiety. Medications were paroxetine (20 mg daily), hydrochlorothiazide (25 mg daily), diphenhydramine (25 mg four times daily as needed), and oxybutynin (5 mg three times daily). On admission to the ED, her temperature was 101.6°F, pulse was 120/min, respirations were 33/min, and blood pressure was 90/60 mm Hg. She was lethargic and unable to answer questions. Neurologic examination showed no focal findings. Blood and urine cultures were collected, patient was given 2 liters of lactated ringer intravenous fluids and started on a norepinephrine drip. She was admitted to the ICU for two days and transferred to a medicine floor afterwards. During her ICU and hospital stay, she was positive for delirium on multiple days. She slowly improved and was discharged back to her SNF 15 days later. MMSE examination 3-months after her ICU stay showed a score of 16 with a negative delirium screen. **Which of the following is NOT a common outcome associated with delirium?**
- A. A) Increased length of hospital stay
  - B. B) Higher mortality rates
  - C. C) Improved long-term cognitive function
  - D. D) Increased risk for institutionalization

# Question 2

2. An 84-year-old male with past medical history significant for hypertension and diabetes mellitus type 2 was admitted to the ICU for shortness of breath and was found to have bilateral multi-lobar pneumonia secondary to Influenza A. He was initially maintained on heated high flow nasal cannula, but his FiO<sub>2</sub> requirements continued to increase, and he was promptly intubated and started on mechanical ventilation. During his ICU stay, patient developed new-onset confusion, inattention, and disorganized thinking. He was agitated and restless. Delirium was assessed through the CAM-ICU and was found to be positive. **Which of the following interventions has been shown to reduce the incidence of ICU delirium?**
- A. Routine use of antipsychotic medications such as haloperidol
  - B. Deep sedation
  - C. Assessment and treatment of pain, daily ventilator liberation trials, daily sedation breaks, assessment for delirium, early mobilization, family involvement in bedside care
  - D. Increased use of physical restraints

# Question 3

3. What is the benefit of utilizing antipsychotics in delirium?
- A. Preventing delirium
  - B. Decreasing duration of delirium
  - C. Maintaining patient and staff safety
  - D. Improving sleep-wake cycle

# Question 4

4. **What antipsychotic is preferred for non-redirectable agitation in patients with Parkinson's disease?**
- A. Haloperidol
  - B. Pimavanserin
  - C. Quetiapine
  - D. Aripiprazole





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# Delirium and Inpatient Psychotropics

Jennifer A. Woodard, MD

Clinical Assistant Professor

University of Wisconsin-Madison

# Agenda

1. Defining Delirium
2. Potentially Inappropriate Prescribing
3. Non-Pharmacologic Management
4. Antipsychotics & Alternatives



# Defining Delirium

# Defining Delirium

- **30-40% of delirium cases are preventable**
- **Delirium** is a clinical syndrome characterized by an alteration of attention, consciousness, and cognition, with a reduced ability to focus, sustain, or shift attention.
  - It develops over a short period and fluctuates during the day.
  - The clinical presentation can vary, usually with psychomotor behavioral disturbances such as hyperactivity or hypoactivity and with sleep duration and architecture impairment.

Tools for assessment:

- CAM
- Nu-DESC

# Defining Delirium

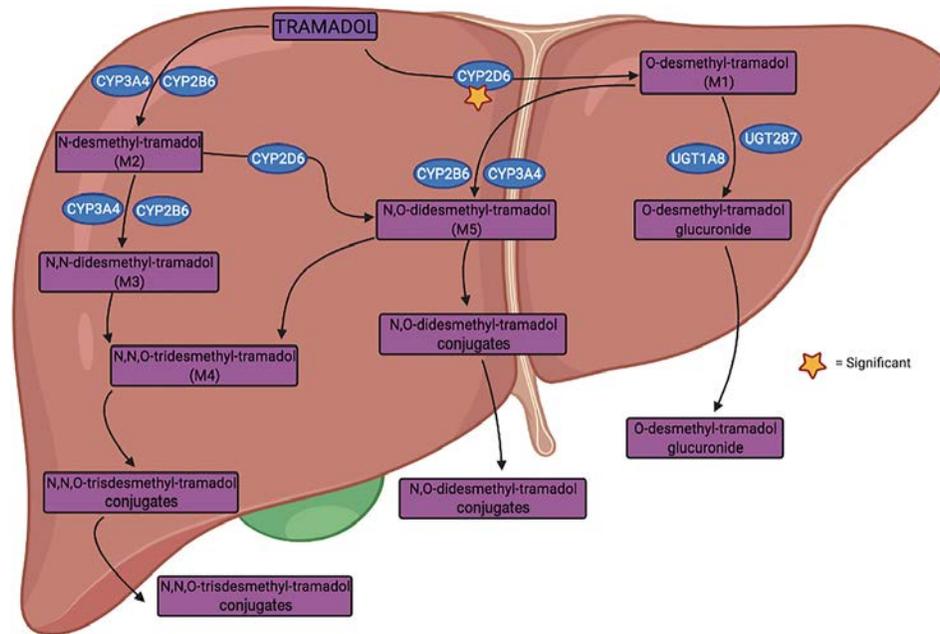
- **Behavioral and psychological symptoms of dementia (BPSD) includes emotional, perceptual, and behavioral disturbances that are similar to those seen in psychiatric disorders.**
  - Cognitive or perceptual (delusions, hallucinations)
  - Motor (pacing, wandering, repetitive movements, physical aggression)
  - Verbal (yelling, calling out, repetitive speech, verbal aggression)
  - Emotional (euphoria, depression, apathy, anxiety, irritability)
  - Vegetative (disturbances in sleep and appetite).
- Sundowning is common (seen in 2/3rds of patients with dementia)
- Often ***gradually worsening*** with progression of dementia – if acute or subacute onset, work up delirium.
- Up to **97%** of community-dwelling individuals with dementia will develop BPSD at some point

A blurred hospital hallway with medical staff in the background and a doctor and pharmacist in the foreground. The doctor is a woman in a white lab coat, and the pharmacist is a man in blue scrubs. They are both looking at a tablet. The background shows other staff members walking in a brightly lit hallway with large windows.

# Potentially Inappropriate Prescribing

# Potentially Inappropriate Prescribing

## PAIN



## Tramadol ☹️

- RCT – no more effective than Tylenol for pain control
- Unpredictable metabolism, drug interactions
  - Active metabolites
- Hepatically metabolized, renally cleared
- Worsens or causes hyponatremia in older adults
- Lowers seizure threshold

# Potentially Inappropriate Prescribing

## PAIN – Manage it better!

- **Maximize multimodal therapy – heat, ice, topical agents**

**Topical diclofenac** for knees, ankles, elbows, wrists

- My personal favorite for osteoarthritis
- Doesn't work well for deep joints (hips/shoulders)
- Minimal absorption, so safe in CKD, CHF!

**Lidocaine patches**

- Placebo effect is still an effect

- **Scheduled acetaminophen 1g three times daily – especially if cognitive impairment**
- **Consider renal function, comorbidities if oral NSAIDs are appropriate**
- **Oxycodone 2.5 mg q4-6 hours prn if all else fails**
- **Limit use of muscle relaxers, gabapentinoids**  
If necessary for spasticity, tizanidine or baclofen are preferred

# Potentially Inappropriate Prescribing

## ANXIETY & SLEEP

Nobody sleeps better in the hospital!



CS432426



"Try to get some rest. I'll be in every few minutes to make sure you don't."

# Potentially Inappropriate Prescribing

## ANXIETY & SLEEP – Manage it better!

- **Melatonin:** not well-regulated, effects variable  
Maybe some neuroprotective effects in Alzheimer's and Parkinson's?
- **Melatonin receptor agonists:** effects modest, expensive
- **Hydroxyzine:** still anticholinergic (though less than diphenhydramine)
- **Benzodiazepines:** can precipitate rebound delirium
- **Nonbenzodiazepine benzodiazepine receptor agonist hypnotics (Z drugs):** Not much better than benzos
- **Trazodone:** orthostatic hypotension common, used off-label for sleep
- **Doxepin (low dose):** better for sleep maintenance, also some orthostatic hypotension
- **Mirtazapine:** off-label use, mainly use if concerned for depression contributing (more sedation at lower doses)

Orzechowski RF, Currie DS, Valancius CA. Comparative anticholinergic activities of 10 histamine H1 receptor antagonists in two functional models. Eur J Pharmacol. 2005;506(3):257-264.

By the 2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. J American Geriatrics Society. 2023;71(7):2052-2081.

Laudon M, Frydman-Marom A. Therapeutic effects of melatonin receptor agonists on sleep and comorbid disorders. Int J Mol Sci. 2014;15(9):15924-15950.

Abad VC, Guilleminault C. Insomnia in elderly patients: recommendations for pharmacological management. Drugs Aging. 2018;35(9):791-817.

# Potentially Inappropriate Prescribing

## BOWEL & BLADDER – Manage it better!

- **Unfamiliar environments = evolutionary advantage for constipation**
- **Start with scheduled bowel regimen**  
Miralax daily + Senna 17.6 mg QHS
- **Examine for constipation if diarrhea**
- **If on opioids, always schedule stimulant laxative (senna)**
- **Scheduled toileting, minimize Purewick use**
- **Check PVR if any concern for new agitation or delirium – retaining is common!**  
Older adults may have 100-200 cc PVR  
Straight cath for >400-500 cc
  - If straight cath for > 1 L or more than twice, go for a Foley

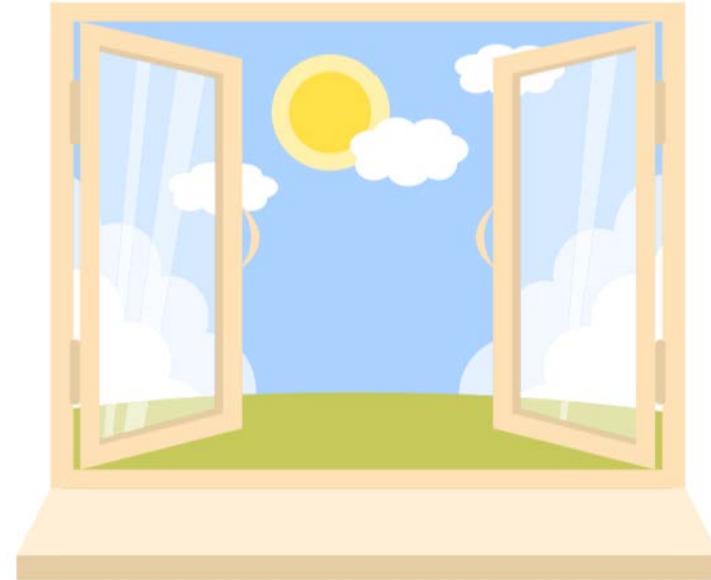


# Non-Pharmacologic Strategies

# Non-Pharmacologic Strategies

## *Not just for nursing staff!*

- Open the windows, turn on the lights when you go in (or turn off at night)
- Favorite TV show or channel? Music?
- **Pocket talkers – use them!**
  - Hearing impairment is linked to cognitive impairment
  - Most hearing loss is at higher frequencies – use low tones
- **Chaplains**
- **Family engagement**



# Non-Pharmacologic Strategies



- **Fingersticks – do you need them?**
- **Vital signs – how often?**
- **How you order meds matters**  
Three times daily  $\neq$  q 8 hours



A blurred photograph of a hospital hallway. In the center, a woman in a white lab coat and a man in blue scrubs are looking at a tablet together. Other people in white coats and scrubs are walking in the background, creating a sense of a busy medical environment.

# Antipsychotics & Alternatives

# Antipsychotics & Alternatives

A 79 year old man is hospitalized after surgery for a hip fracture. History includes hypertension and mild cognitive impairment. On day 2 post-op, he refuses medications and pulls out his IV lines. He is oriented to self and has difficulty reciting days of the week backwards. His nurse requests administration of haloperidol.

**Which is most likely to result from administering haloperidol to this patient?**



- A. Longer hospital stay
- B. Increased short-term mortality
- C. Increased risk of drug interactions
- D. Reduction in severity of symptoms

# Antipsychotics & Alternatives

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**Which is most likely to result from administering haloperidol to this patient?**



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- D. Reduction in severity of symptoms

# Antipsychotics & Alternatives

- **Use of antipsychotics exceeds 70-80% for management of delirium in hospitalized patients**
- Short-term use – main concern is QTc interval and drug interactions
- Long-term use carries a black box warning for mortality in older adults with dementia – but needs to consider caregiver burden, quality of life
- Poor quality evidence but no mortality effect with short term use
- No change in length of stay or ICU length of stay with antipsychotic use
- No trial reported on hospital length of stay, hospital discharge disposition, or health-related quality of life.

# Antipsychotics & Alternatives

- **Olanzapine: 2.5 – 5 mg/day**

More sedating, less EPS  
Less QTc interval effect

- **Quetiapine: 12.5 – 25 mg/day**

\*Preferred in Parkinson's

- **Haloperidol: 0.5 – 2 mg/day**

Less sedating, best studied

- **Aripiprazole: 2 - 3 mg/day**

Minimal QTc effect, should be avoided in dementia with Lewy bodies

- **Valproic acid: 250-500 mg/day**

No QTc effect, questionable efficacy

Antipsychotics DO NOT prevent or shorten duration of delirium.

These chemical restraints should be reserved ONLY for behaviors with imminent risk of harm to self or staff and not responsive to redirection or non-pharm strategies.

# Antipsychotics & Alternatives

## Pimavanserin: Parkinson's disease hallucinations

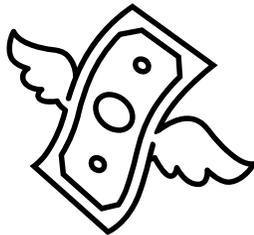
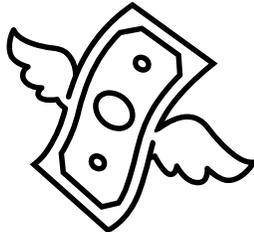
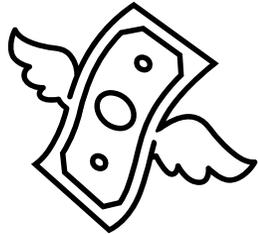
FDA approved in 2016

Still has a black box warning

Prolongs QTc interval

Takes several weeks for effect – NOT appropriate for acute management

Modest effects



## Brexpiprazole: Alzheimer's dementia agitation

FDA approved in 2023 (FastTrack)

Still has a black box warning

No/minimal effect on QTc interval

Modest effects

Can be activating, will usually need to trial aripiprazole first

# Thank you!

Jennifer A. Woodard, MD  
[jwoodard@medicine.wisc.edu](mailto:jwoodard@medicine.wisc.edu)  
[jwoodardmd.bsky.social](#)



<https://www.geriatricfastfacts.com/>  
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# Delirium in the ICU and Beyond

Babar A. Khan MD, MS



ESKENAZI  
HEALTH



INDIANA UNIVERSITY

IU Center for  
Aging Research



School of Medicine  
Department of Medicine  
Division of Pulmonary/ Critical care, Allergy and Occupational medicine

IU Geriatrics

# Disclosure

- No conflicts relevant to this presentation
- NIH-NIA R01 AG055391, R01 AG052493, R01 AG067631, R01 AG061161, R21 AG074179, R01 AG076489, NHLBI R01 HL131730, R01 HL16115, CDC NU581P000004
- Regenstrief Institute Inc.
- Mayo Clinic
- Showalter Trust

# Objectives

- Discuss the screening tools for Delirium recognition
- Describe the current state of literature on Delirium Prevention and Treatment
- Appreciate the long-term effects of Delirium

# Case

- 80-year-old female who presented with altered mental status. Per family, they noted a gradual decline in her mentation over the last few months. This was accompanied by decreased oral intake. Prior to that she was ambulating and feeding herself. Of note, she was aggressive with knives and had outbursts of yelling. She tended to throw away her clothes, waking up frequently at night and roam around, and was feeding cat food to herself. On the day of admission, she was found naked by her grandson, semi-responsive and EMS was called. Her chronic home medicines were atenolol and Vitamin D.
- In the ER she was hypothermic, altered, other vitals were HR 65, BP 110/72, RR 14, 94% RA
- Not oriented, not responsive to verbal stimuli but to pain
- Dry mucus membranes, PERL, CTA, No murmurs, cold extremities
- Dependent for all IADL, ADL: independent on feeding and ambulation
- **Her serum sodium level was 186**

- IV fluids were started, and serial sodium levels were monitored.
- She was assessed for delirium which was positive.
- Delirium protocol given.
- Nursing based interventions (sleep, orientation, family interaction, activity, pain, constipation, dehydration, d/c foley, restraints, IV lines)
- Manage agitated delirium (electrolytes, CBC, d/c anticholinergics, sleep protocols)

# Burden

- In the U.S., 5 older persons develop delirium every minute, affecting a total of more than 2.6 million adults aged 65 and older each year, and costing more than \$164 billion in annual healthcare expenditures.

# Risk factors

- **Systematic Review**
- **33 Studies**

Age  
Dementia  
Hypertension  
Emergency Surgery/Trauma  
APACHE II  
Mechanical Ventilation  
Metabolic Acidosis  
Delirium on prior day  
Coma

# Prevalence

- Older adults hospitalized for Medical illness: 11% to 41%
- Post-operative: Older adults undergoing surgical repair of hip fracture: 40% to 52%
- Post-operative: Older adults undergoing elective major non-cardiac surgery: 10% to 39%
- Post-operative: Older adults undergoing cardiac surgery: 13% to 44%
- Post-operative: Thoracic Surgery at IU: 25%

# Delirium Screening

- **Confusion Assessment Method (CAM)**
- **3 Minute Confusion Assessment Method (3DCAM)**
- **Ultra-Brief CAM**
  - *Months of the Year Backwards, and What is the Day of the Week?*
  - All tools are freely available at <https://help.agscocare.org/table-of-contents/delirium-instruments/H00101>
- **4AT**
  - Freely available at <https://www.the4at.com>

# CAM

Table 2 **Confusion Assessment Method**

Feature*	Assessment	
#1 Acute onset and fluctuating course	Usually obtained from a family member or nurse and shown by positive responses to the following questions: <ul style="list-style-type: none"> <li>• “Is there evidence of an acute change in mental status from the patient’s baseline?”</li> <li>• “Did the abnormal behavior fluctuate during the day, that is, tend to come and go, or increase and decrease in severity?”</li> </ul>	
#2 Inattention	Shown by a positive response to the following: <ul style="list-style-type: none"> <li>• “Did the patient have difficulty focusing attention, for example, being easily distractible or having difficulty keeping track of what was being said?”</li> </ul>	
#3 Disorganized thinking	Shown by a positive response to the following: <ul style="list-style-type: none"> <li>• “Was the patient’s thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?”</li> </ul>	
#4 Altered level of consciousness	Shown by any answer other than “alert” to the following: <ul style="list-style-type: none"> <li>• “Overall, how would you rate this patient’s level of consciousness?”</li> </ul>	
	- Normal = alert	- Hyperalert = vigilant
	- Drowsy, easily aroused = lethargic	- Difficult to arouse = stupor
	- Unarousable = coma	

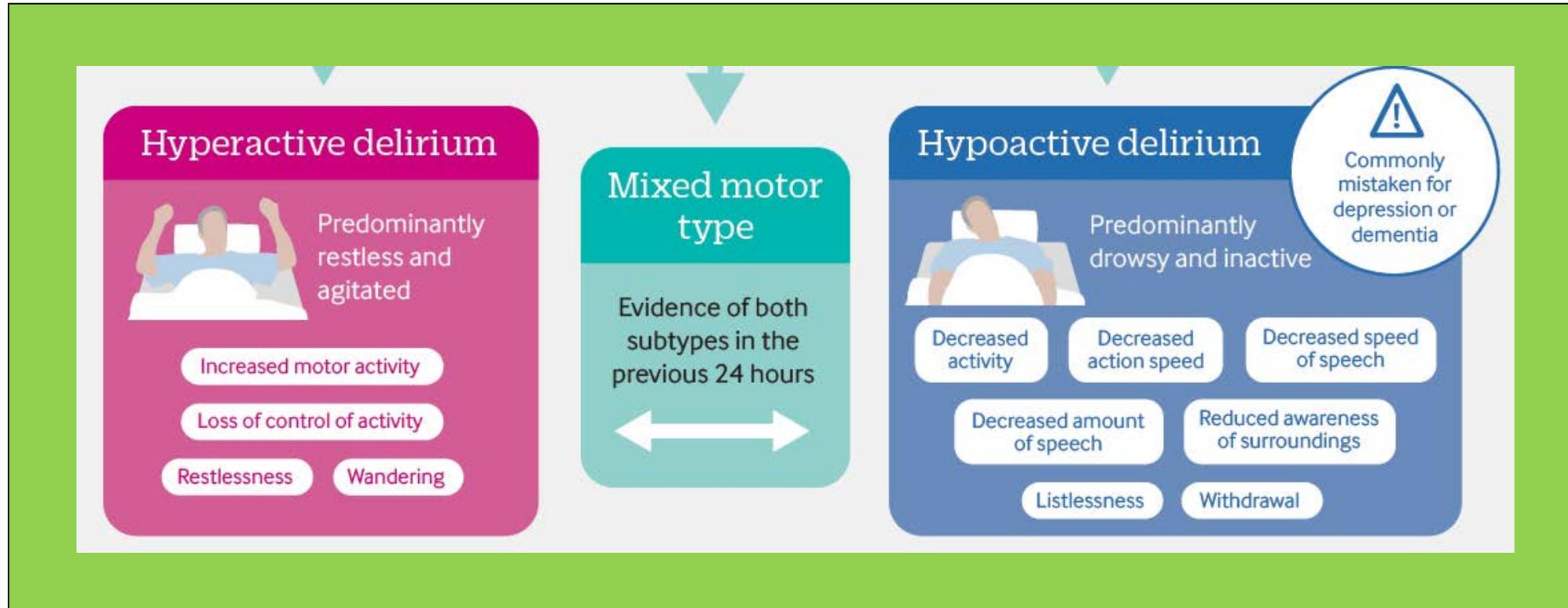
\* The diagnosis of delirium requires the presence of features #1 AND #2 plus either #3 OR #4.

Source: Adapted from: Gower LE, et al. *Western J Emerg Med.* 2012;13:194-201.

**TABLE 1. The Confusion Assessment Method for the ICU-7 Delirium Severity Scale**

Items	Grading	Score
1. Acute onset or fluctuation of mental status  Is the patient different than his/her baseline mental status? or Has the patient had any fluctuation in mental status in the past 24hr as evidenced by fluctuation on a sedation/level of consciousness scale (i.e., RASS/Sedation-Agitation Scale), Glasgow Coma Scale, or previous delirium assessment?	0 for absent  1 for present	
2. Inattention  Say to the patient, "I am going to read you a series of 10 letters. Whenever you hear the letter 'A,' indicate by squeezing my hand." Read letters from the following letter list in a normal tone 3 s apart. "SAVEAHAART" (Errors are counted when patient fails to squeeze on the letter "A" and when the patient squeezes on any letter other than "A.")	0 for absent (correct: $\geq 8$ ) 1 for inattention (correct: 4–7) 2 for severe inattention (correct: 0–3)	
3. Altered level of consciousness  Present if the actual RASS score is anything other than alert and calm (zero)	0 for absent (RASS: 0) 1 for altered level (RASS: 1, –1) 2 for severe altered level (RASS: $> 1$ , $< -1$ )	
4. Disorganized thinking  Yes/no questions 1. Will a stone float on water? 2. Are there fish in the sea? 3. Does one pound weigh more than two pounds? 4. Can you use a hammer to pound a nail?  Errors are counted when the patient incorrectly answers a question. Command: Say to patient "Hold up this many fingers" (Hold two fingers in front of patient). "Now do the same with the other hand" (Do not repeat number of fingers)  An error is counted if patient is unable to complete the entire command.	0 for absent (correct: $\geq 4$ ) 1 for disorganized thinking (correct: 2, 3) 2 for severe disorganized thinking (correct: 0, 1)	
Total score		<div style="border: 1px solid black; padding: 10px; text-align: center;"> <p>No delirium: 0 - 2 Mild-moderate: 3 - 5 Severe: 6 - 7 <b>Maximum score: 7</b></p> </div>

# Hyper and Hypoactive Delirium

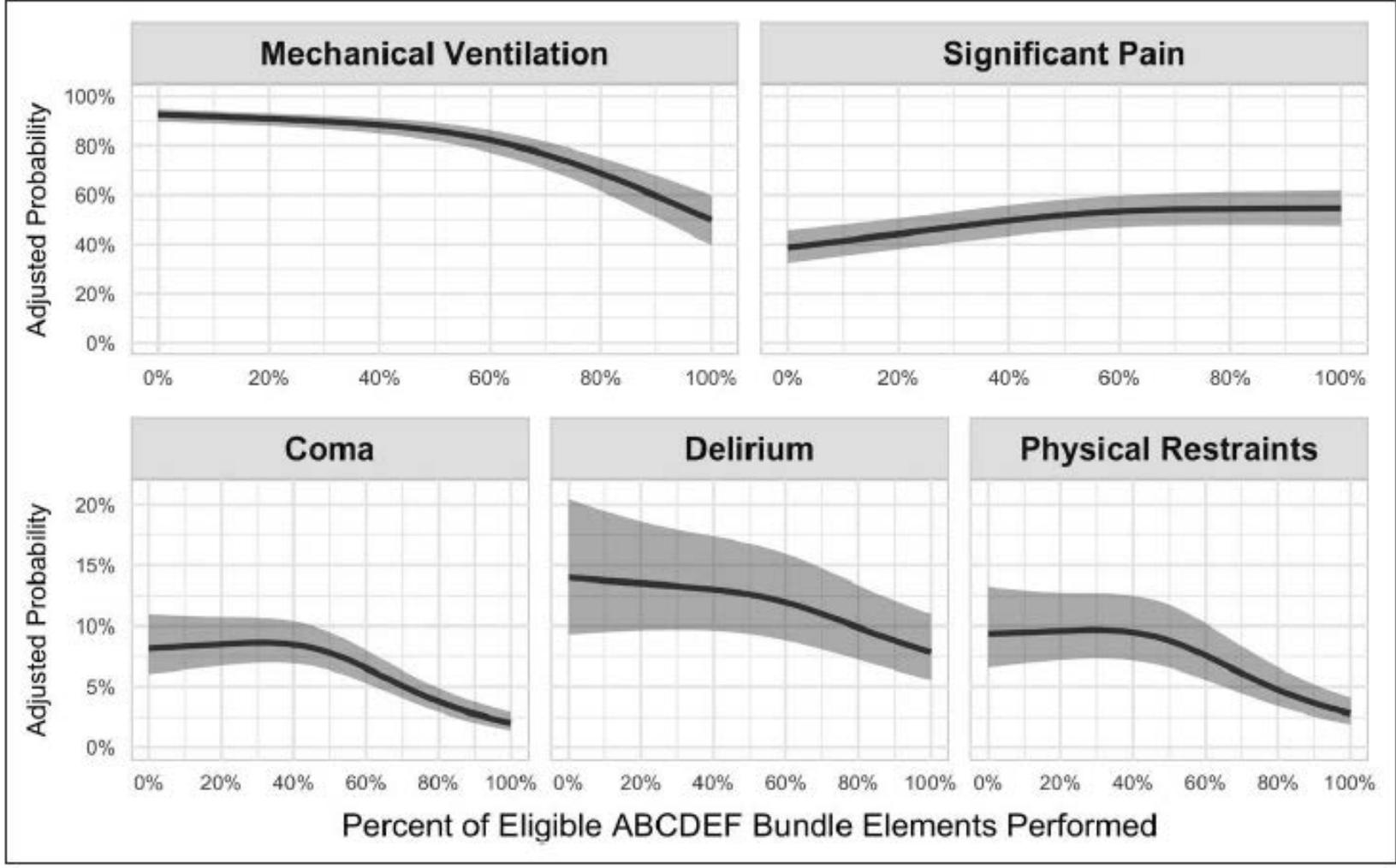


# Prevention

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

**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
<b>Patient-Related Outcomes</b>	<b>AHR (95% CI)</b>	
ICU discharge <sup>a</sup>	1.17 (1.05–1.30)	< 0.004
Hospital discharge <sup>b</sup>	1.19 (1.01–1.40)	< 0.033
Death <sup>c</sup>	0.32 (0.17–0.62)	< 0.001
<b>Symptom-Related Outcomes<sup>d</sup></b>	<b>AOR (95%CI)</b>	
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
<b>System-Related Outcomes</b>	<b>Adjusted OR (95%CI)</b>	
ICU readmission <sup>e</sup>	0.54 (0.37–0.79)	< 0.001
Discharge destination <sup>f</sup>	0.64 (0.51–0.80)	< 0.001



# Delirium Prevention- HELP

- Intervention was targeted towards minimizing six risk factors in elderly patients admitted to a general medicine service
- Orientation activities for cognitively impaired, early mobilization, preventing sleep deprivation, minimizing the use of psychoactive drugs, use of eyeglasses and hearing aids, and treating volume depletion

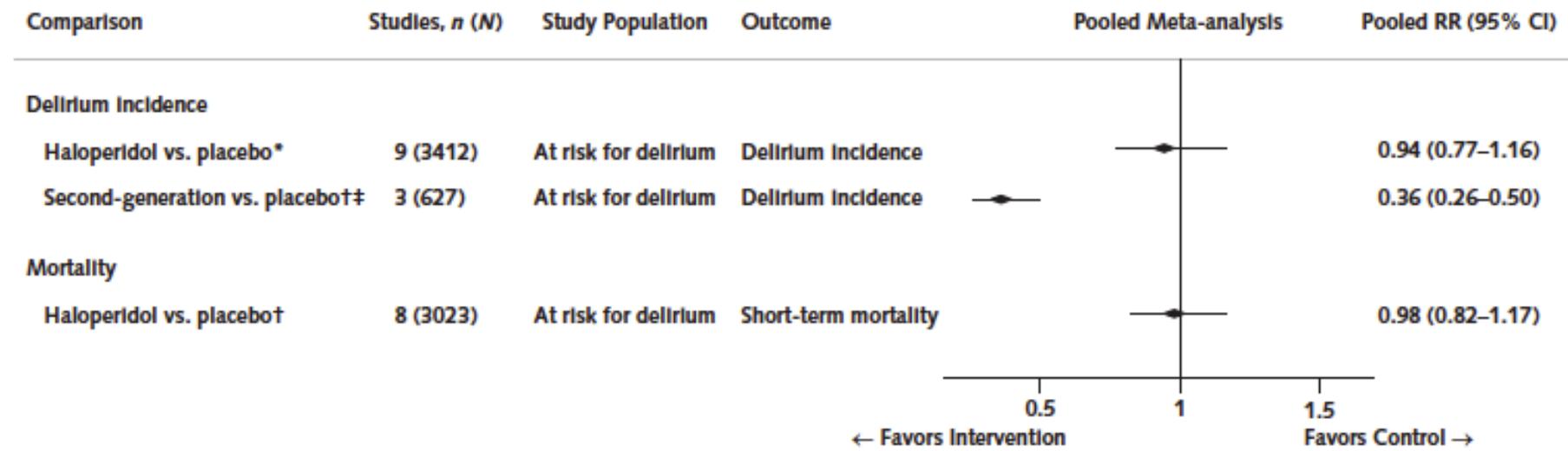
# Prevention

- The incidence of delirium was 9.9% with this intervention compared with 15% in the usual care group (OR, 0.60; 95% CI, 0.39- 0.92)
- Cost saving \$9000 per patient per year

# Antipsychotics for Prevention of Delirium

- **No difference between haloperidol vs. placebo**
  - Delirium incidence, duration, hospital length of stay, mortality

Figure 3. Pooled outcome meta-analysis for delirium incidence and mortality.



# Treatment

Efficacy and safety of quetiapine in critically ill patients with delirium: A prospective, multicenter, randomized, double-blind, placebo-controlled pilot study\*

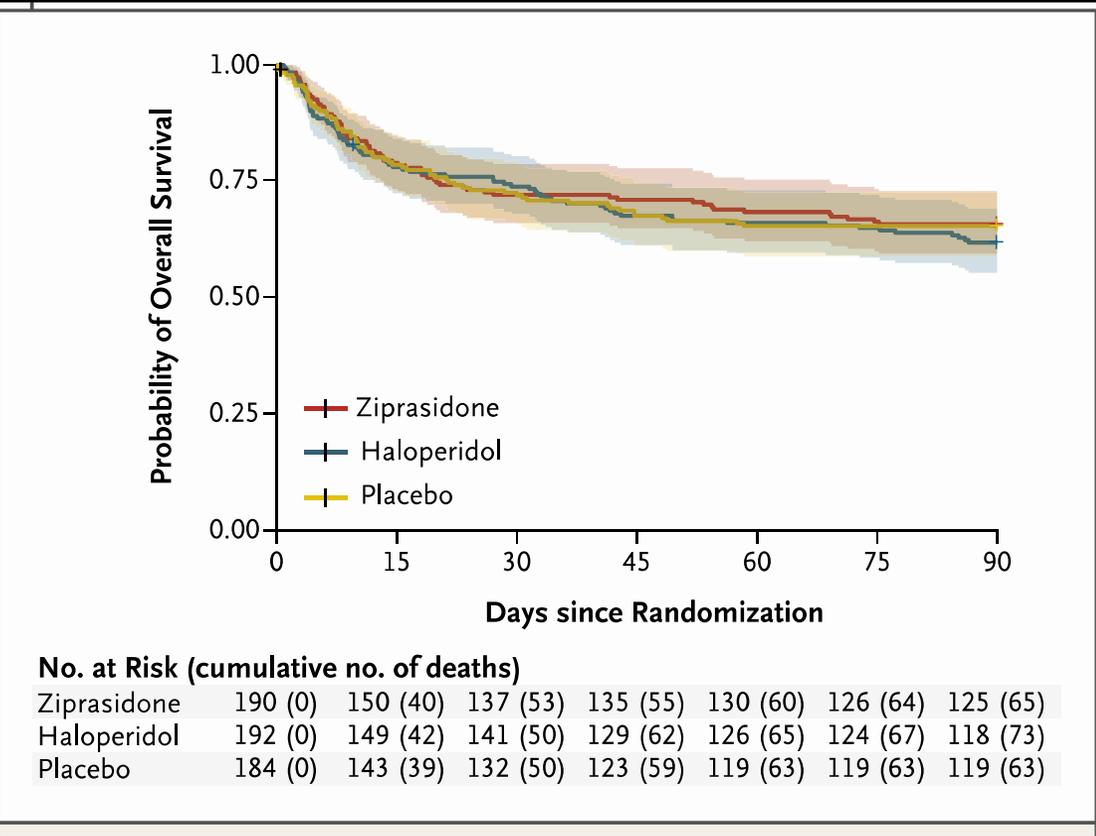
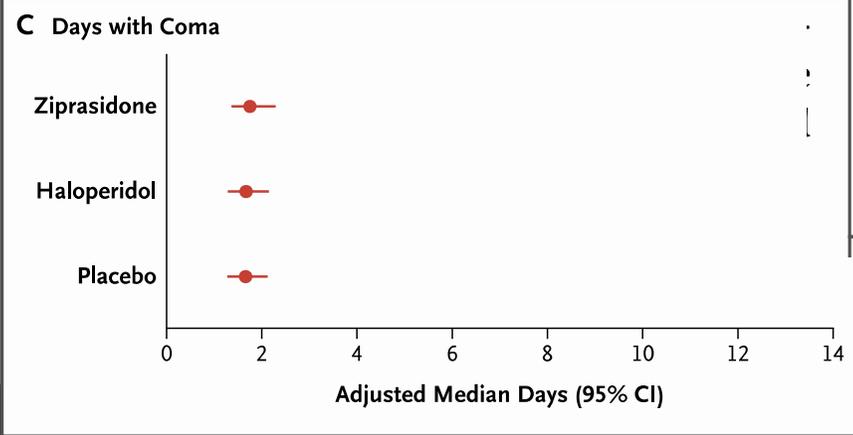
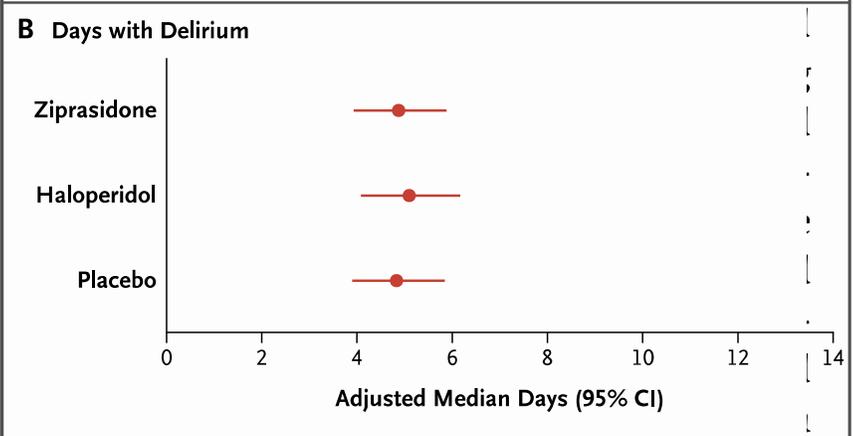
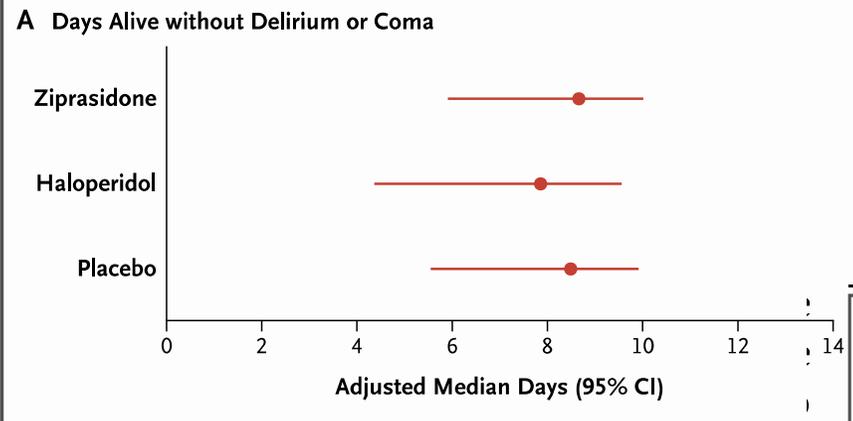
- Prospective, randomized, double-blind, placebo-controlled study
- Thirty-six adult intensive care unit patients with delirium
- Patients were randomized to receive quetiapine 50 mg every 12 hours or placebo
- Primary end point was time to first resolution of delirium

- Quetiapine was associated with a shorter time to first resolution of delirium (1.0 vs. 4.5 days; p: 0.01), and a reduced duration of delirium (36 vs. 120 hours; p:0.006)
- Subjects treated with quetiapine required fewer days of as-needed haloperidol (3 vs. 4 days)

ORIGINAL ARTICLE

# 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\*



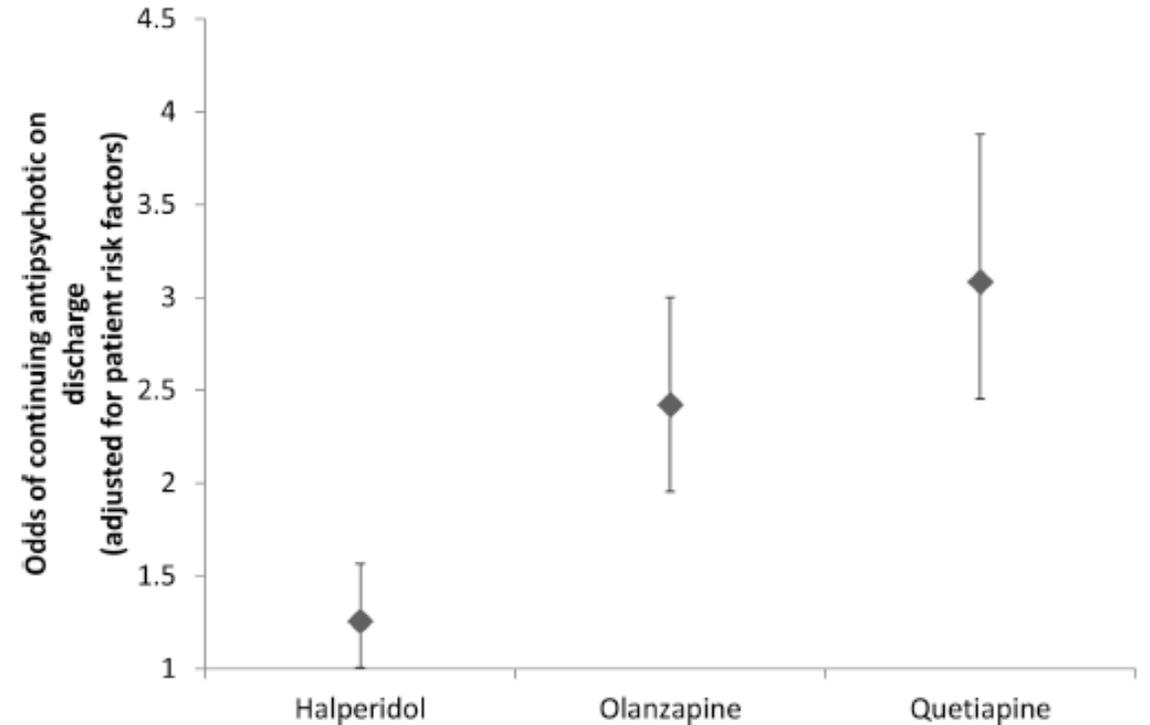
**Figure 2.** Effects of Haloperidol, Ziprasidone, and Placebo on Days Alive without Delirium or Coma, Days with Delirium, and Days with Coma.

# Antipsychotics for Treatment of Delirium

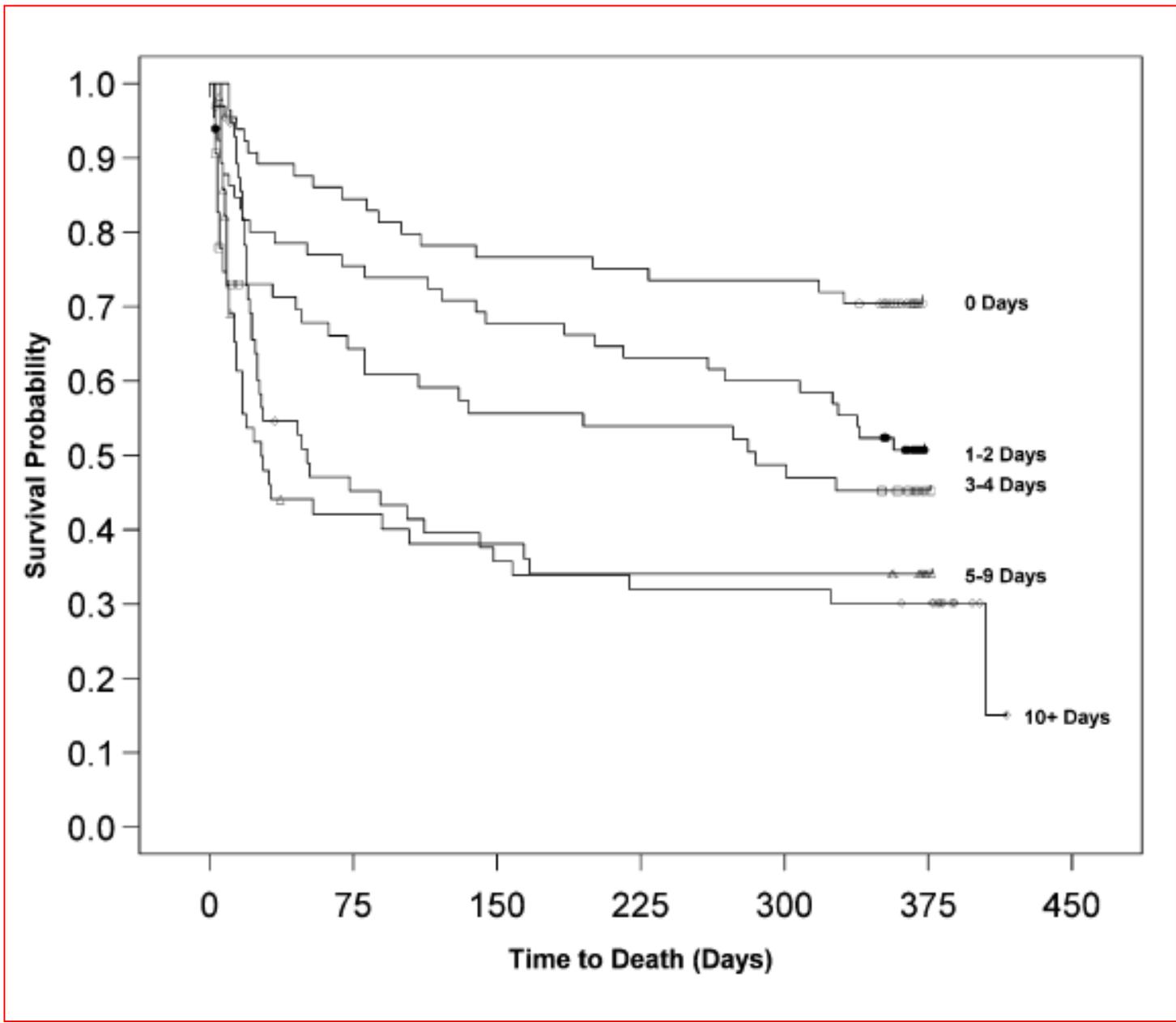
- No difference between haloperidol vs. placebo or second-generation antipsychotics vs. placebo
- Delirium duration, sedation status, hospital length of stay, mortality

# Persistent Use of Antipsychotics after Hospital Discharge

- A single-center retrospective observational study
- Adult patients who received antipsychotics for ICU delirium
- Approximately one in five patients were discharged from the hospital with continued antipsychotics

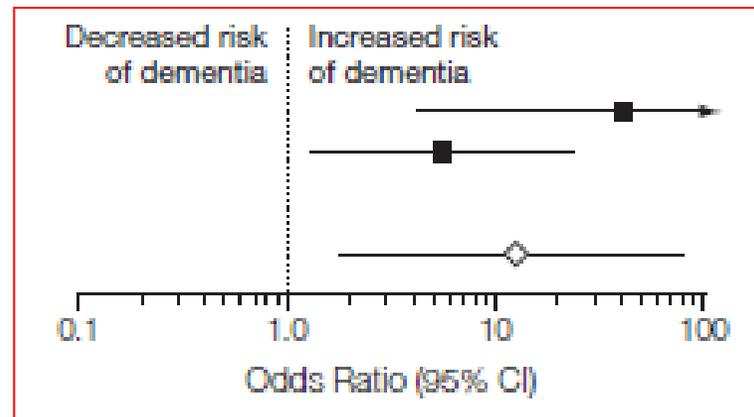
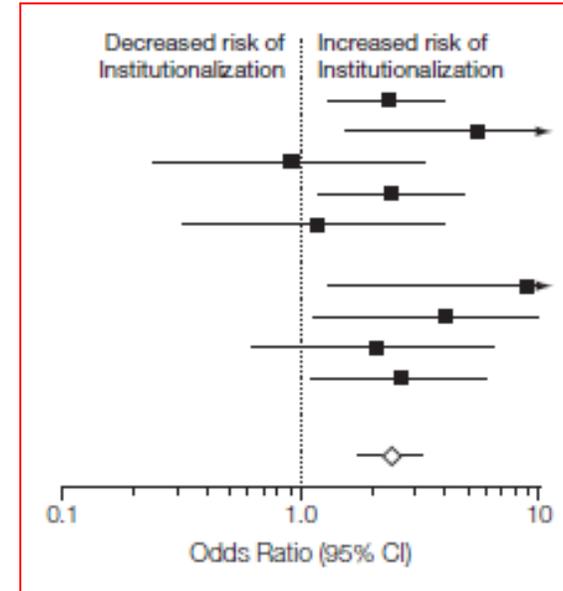
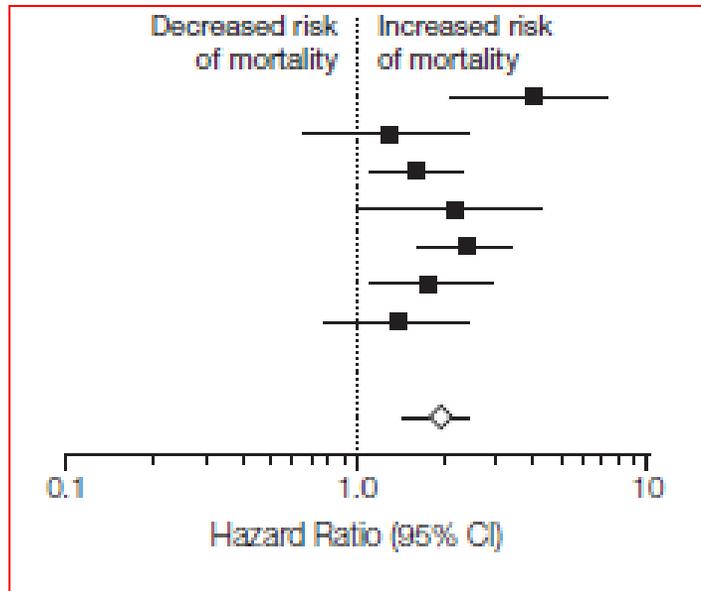


# Outcomes



# Delirium in Elderly Patients and the Risk of Postdischarge Mortality, Institutionalization, and Dementia

A Meta-analysis



# Summary

- Delirium is highly prevalent and persistent
- Delirium is associated with poor clinical outcomes
- There is very little evidence for using antipsychotics for prevention or treatment of delirium
- Multicomponent non-pharmacological interventions has the best evidence for delirium prevention



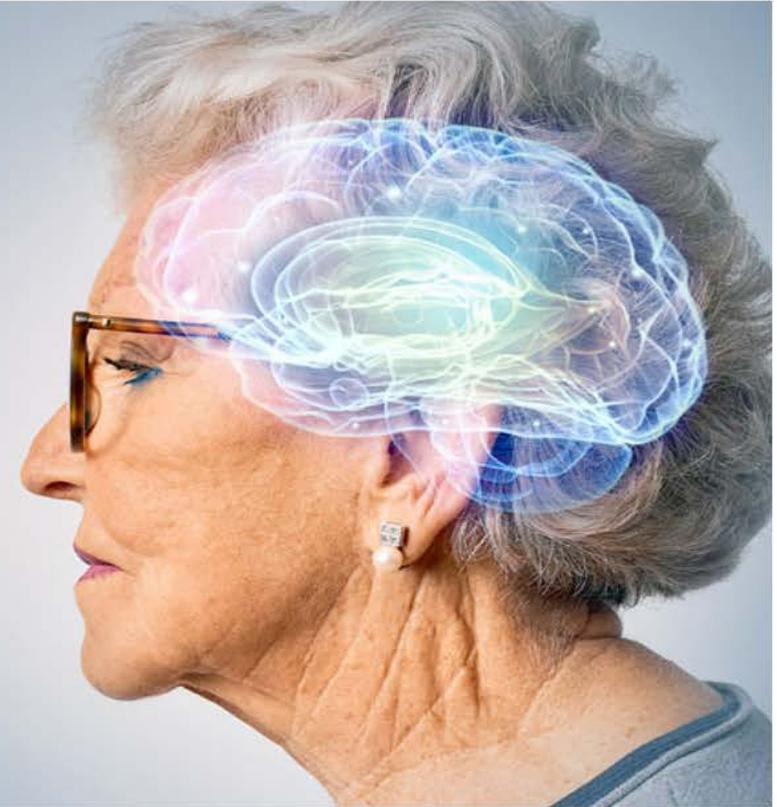
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# Improving Delirium Care

Fostering research, education, quality improvement, advocacy & implementation science to minimize the impact of delirium on patients.

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[www.americandeliriumsociety.org](http://www.americandeliriumsociety.org)

Questions ?????

[bakhan@iu.edu](mailto:bakhan@iu.edu)

