# Delirium

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Rady Faculty of Health Sciences | UM

# Faculty/Presenter Disclosure

- **Faculty: Phil St John**
- **Relationships with commercial interests:**
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# Mitigating Potential Bias

- N/A

# ACKNOWLEDGEMENTS


- American Geriatrics Society Teaching Slides
- Pat Montgomery
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# OBJECTIVES

- Define delirium
- Recognize and diagnose delirium
- Name predisposing and precipitating risk factors for delirium in elderly patients
- Know how to evaluate and treat elderly patients with delirium
- State interventions to prevent delirium

- Federal election 2016: ABC wins election night coverage despite Leigh Sales' 'delirium'

# Mrs C

- 91 year old, retired teacher, single
- Previously independent and active
- Past hx: Heart block with CHF (Pacemaker), gout, OA, bilateral hip replacements (one complicated by “confusion”)
- Meds: Lasix 80 mg po daily, enalapril 10 mg po BID, colchicine prn

- Family brought her to GP with confusion for 10 days

# I would (Check all that apply)

1. Do a history and physical
2. Do some bloodwork
3. Do a urine analysis and culture
4. Send her to ER
5. Send her home

# In ER I would

1. Do a history and physical
2. Do some bloodwork
3. Do a urine analysis and culture
4. Admit her
5. Send her home

- Diagnosed with Raging UTI – got ciprofloxacin and went home
- Family brought her to different ER 2 days later – sent home
- Family brought her to 3rd ER – “Dyscopia” and GPAT consulted re: admission

# I would

1. Admit her to rehab
2. Suggest admission to acute care
3. Suggest sending her home
4. Panel her for PCH

- Looked unkempt
- Alert, not fully oriented
- MMSE 17/30 (poor attention noted by OT)
- Initial vitals (two days previous): afebrile, Sats good, BP 100/55, HR 60
- Chest clear, abd obese
- Na 133 lytes otherwise OK
- Cr 124
- CXR pacemaker

- Came for rehab
- BP 80/40
- MMSE 16/30

- Day 2
  - Received 3L of fluid
  - BP normalized
  - All medications held

- Day 3
  - Collateral from family – no one helping with medications – taken sporadically

# Week 1

- Still disoriented
- Ambulating well
- Eating and drinking well

# Friends want a prognosis. Which is true of delirium

1. Delirium is an acute reversible condition

2. Delirium is a strong predictor of mortality in hospital

3. 3- to 5-fold ↑ risk of nosocomial complications, prolonged stay, postacute nursing-home placement

4. Poor functional recovery and ↑ risk of death up to 2 years following discharge

5. Persistence of delirium → poor long-term outcomes

- Set in a world where love is deemed illegal and can be eradicated with a special procedure. With 95 days to go until her scheduled treatment, Lena Holoway does the unthinkable, she falls in love.

# AKA

- Acute confusional state
- Acute mental status change
- Altered mental status
- Organic brain syndrome
- Reversible dementia
- Toxic or metabolic encephalopathy
- Dysergastic reaction
- Subacute befuddlement

# Delirium

- From delirare (Latin)
  - To rave, to be crazy
  - To make the furrow awry in plowing
  - To deviate from a straight line

# Delirium

- Described by Hippocrates
  - Case series in Epidemics
  - Aphorisms
    - In every disease it is a good sign when the patient's intellect is sound, and he is disposed to take whatever food is offered to him; but the contrary is bad

“he tossed about, murmuring exclamations of pain or impatience, restlessly throwing his arms here and there, and turning constantly from side to side. At length he fell into that state of partial unconsciousness, in which the mind wanders uneasily from scene to scene, and from place to place, without the control of reason, but still without being able to divest itself of an indescribable sense of present suffering. Finding from his incoherent wanderings that this was the case, and knowing that in all probability the fever would not grow immediately worse, I left him, promising his miserable wife that I would repeat my visit next evening, and, if necessary, sit up with the patient during the night.”

# WHAT IS DELIRIUM?

- The *DSM-5* characterizes delirium as a disorder of attention and awareness that develops acutely and tends to fluctuate

# INCIDENCE OF DELIRIUM AMONG OLDER PATIENTS IS HIGH

- 1/3 of inpatients aged 70+ on general medical units, half of whom are delirious on admission
- In ICU: more than 75%
- At end of life: up to 85%

# MORBIDITY ASSOCIATED WITH DELIRIUM

- Meta-analysis: up to 3000 pts followed for almost 2 years showed increased risk:

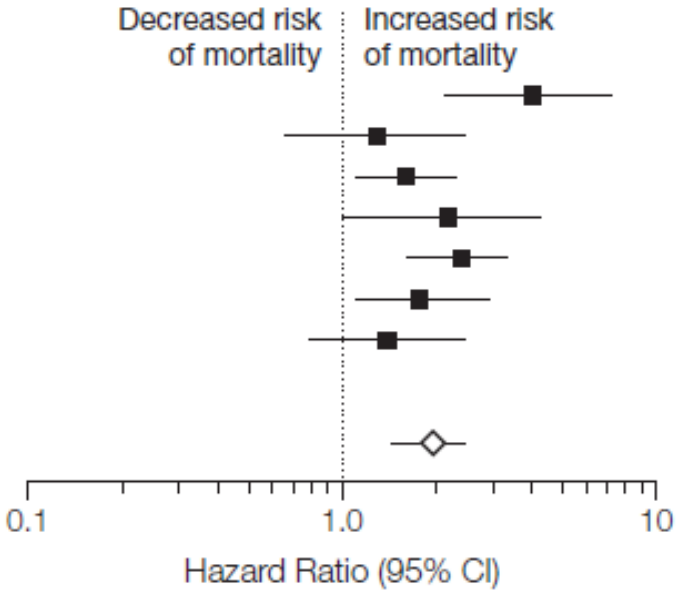
  2-fold for death

  2.4-fold for institutionalization

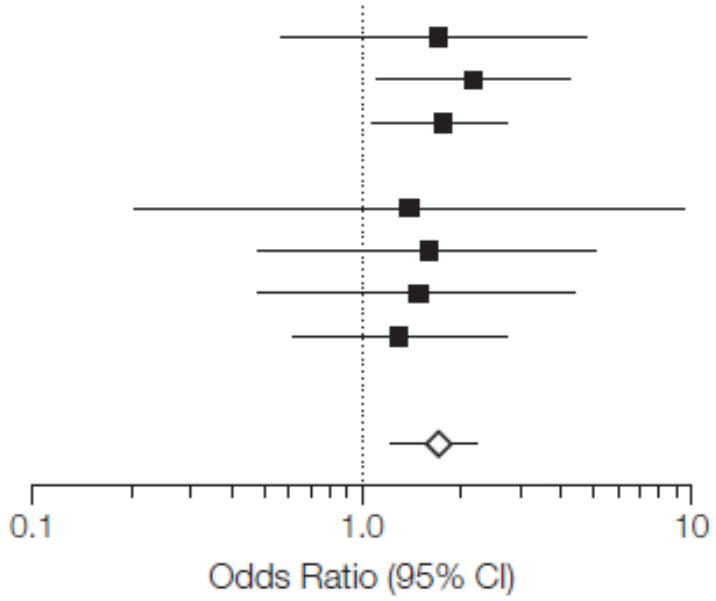
  12.5-fold for new dementia

- Persistent delirium → poor long-term outcomes

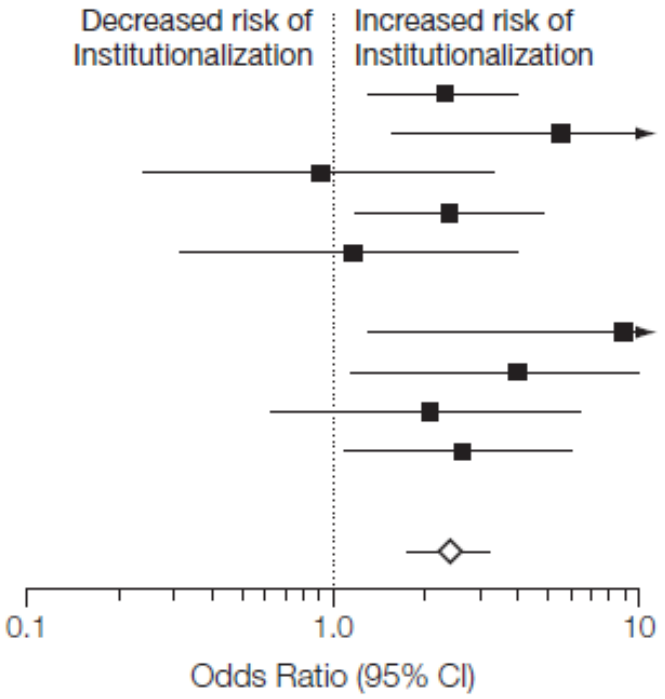
| Mortality | Hazard Ratio (95% CI) | Weight, % |
|---|---|---|
| González et al,[45] 2009 | 4.04 (2.19-7.46) | 11.63 |
| Furlaneto and Garcez-Leme,[41] 2007 | 1.28 (0.66-2.48) | 10.53 |
| Leslie et al,[52] 2005 | 1.62 (1.13-2.33) | 20.29 |
| McCusker et al,[6] 2002 | 2.16 (1.06-4.41) | 9.42 |
| Nightingale et al,[60] 2001 | 2.40 (1.66-3.48) | 19.93 |
| Rockwood et al,[65] 1999 | 1.80 (1.11-2.92) | 15.45 |
| Francis and Kapoor,[40] 1992 | 1.40 (0.79-2.48) | 12.76 |
| Heterogeneity: $I^2 = 44.0\%$; $P = .10$ | | |
| Random-effects model: $P < .001$ | 1.95 (1.51-2.52) | 100 |



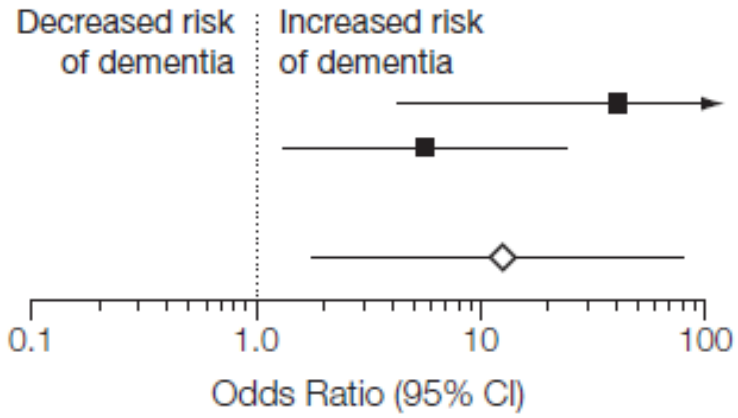
| | Odds Ratio (95% CI) | |
|---|---|---|
| Bickel et al,[32] 2008 | 1.70 (0.59-4.91) | 7.89 |
| de Rooij et al,[35] 2007 | 2.20 (1.12-4.32) | 19.52 |
| Pitkala et al,[63] 2005 | 1.76 (1.10-2.81) | 40.61 |
| Inouye et al,[7] 1998 | | |
| Chicago | 1.40 (0.20-9.60) | 2.39 |
| Cleveland | 1.60 (0.50-5.16) | 6.46 |
| Yale | 1.50 (0.50-4.55) | 7.20 |
| Levkoff et al,[51] 1992 | 1.30 (0.62-2.74) | 15.93 |
| Heterogeneity: $I^2 = 0\%$; $P = .98$ | | |
| Random-effects model: $P < .001$ | 1.71 (1.27-2.23) | 100 |



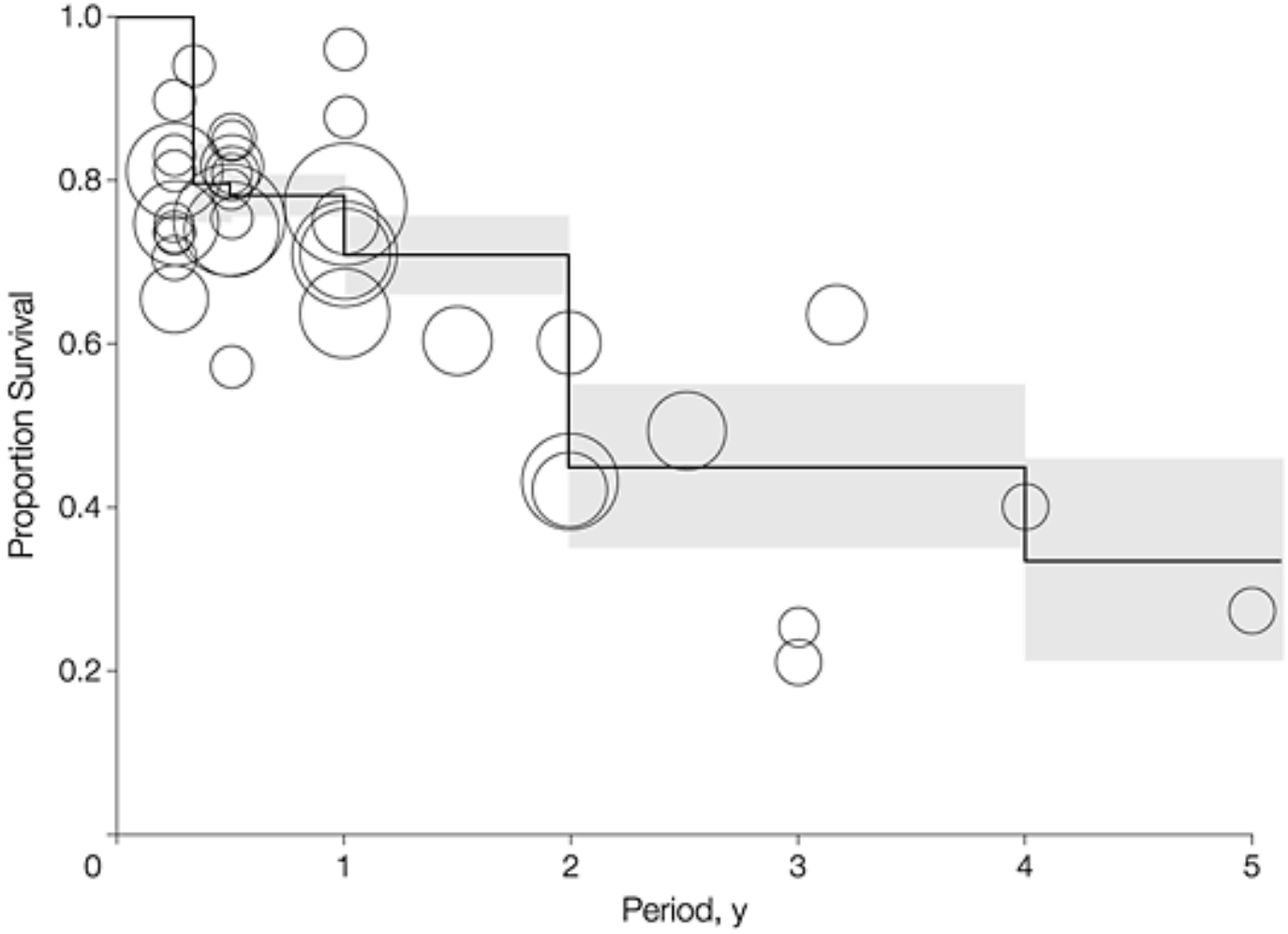
| | | |
|---|---|---|
| Institutionalization | | |
| Bellelli et al,[30] 2008 | 2.30 (1.33-3.98) | 32.35 |
| Bickel et al,[32] 2008 | 5.60 (1.60-19.65) | 6.17 |
| Giusti et al,[43] 2006 | 0.93 (0.25-3.47) | 5.61 |
| Pitkala et al,[63] 2005 | 2.45 (1.21-4.95) | 19.66 |
| McCusker et al,[6] 2002 | 1.15 (0.33-4.05) | 6.19 |
| Inouye et al,[7] 1998 | | |
| Chicago | 8.60 (1.31-56.45) | 2.74 |
| Cleveland | 3.90 (1.12-13.56) | 6.26 |
| Yale | 2.00 (0.63-6.33) | 7.34 |
| Francis and Kapoor,[40] 1992 | 2.56 (1.10-5.93) | 13.77 |
| Heterogeneity: $I^2 = 0\%$; $P = .48$ | | |
| Random-effects model: $P < .001$ | 2.41 (1.77-3.29) | 100 |



| Dementia | | |
|---|---|---|
| Bickel et al,[32] 2008 | 41.20 (4.29-395.48) | 40.0 |
| Lundström et al,[54] 2003 | 5.66 (1.34-24.00) | 60.0 |
| Heterogeneity: $I^2 = 52.4\%$; $P = .15$ | | |
| Random-effects model: $P = .009$ | 12.52 (1.86-84.21) | 100 |



# Meta-analytic Survival Curve




Witlox, J. et al. JAMA 2010;304:443-451.

Rady Faculty of Health Sciences | JAMA

# DIAGNOSING DELIRIUM

- 3 brief assessment tools have been developed recently to assess delirium
  - B-CAM
  - 4AT
  - 3D-CAM
- Also consider CAM-ICU as a screener in non-ICU patients

# CONFUSION ASSESSMENT METHOD

1. Acute change in mental status or fluctuating course
2. Inattention
3. Disorganized thinking
4. Altered level of consciousness

*Requires features 1 and 2 and either 3 or 4*

# CAM-ICU

- Version of CAM for non-verbal patients
- Uses same 4 features as CAM
  - Attention: Vigilance A, Attention Screening Exam
  - Disorganized thinking: Yes/no questions
- Excellent in ICU/non-verbal patients
  - Lower sensitivity in verbal patients

## B-CAM

- CAM-ICU adapted for non-ICU (ED)
- Starts with attention screener
- If “positive”, then do B-CAM
  - Some items adapted for verbal response
- Overall, works better than CAM-ICU in verbal populations (ED)

# 4AT

- Non-CAM based assessment
- Designed for general medicine patients
- Brief series of questions and observations
- Tally points—over threshold makes “diagnosis” of delirium
- Good sensitivity/specificity—near 90%

## 3D-CAM

- 3-minute diagnostic assessment for CAM-defined delirium
- Optimal items selected by IRT
- Items mapped to CAM Features
- One “positive” item triggers the feature
- CAM algorithm: presence of delirium
- Excellent sensitivity/specificity—95%

# Does This Patient Have Delirium?

## Value of Bedside Instruments

**Conclusion** The choice of instrument may be dictated by the amount of time available and the discipline of the examiner; however, the best evidence supports use of the CAM, which takes 5 minutes to administer.

# THE SPECTRUM OF DELIRIUM (1 of 2)

- Hyperactive, agitated, or mixed delirium — 25% of all cases
- Hypoactive delirium — ≥50% of all cases, but less often recognized and appropriately treated, and poorer prognosis

# THE SPECTRUM OF DELIRIUM (2 of 2)

- CAM-S – Delirium severity scale
  - Short and long forms available
  - Excellent predictive validity for important outcomes
- Patients who have some delirium features but do not meet all diagnostic criteria have attenuated delirium.

# NEUROPATHOPHYSIOLOGY (1 of 2)

Cholinergic deficiency

- Delirium is caused by anticholinergic drug overdose, reversed by physostigmine
- Acetylcholine is an important neurotransmitter for cognitive processes
- Scales available to measure anticholinergic burden of drug regimens
- Cholinesterase inhibitors have not been effective in preventing/treating delirium

# NEUROPATHOPHYSIOLOGY (2 of 2)

## Inflammation

- Especially important in postoperative, cancer, and infected patients
- ↑ C-reactive protein, ↑ interleukin-6, and ↑ TNFα
- Inflammation can break down blood-brain barrier, allowing medications and cytokines access to CNS
- Neuroinflammation may damage neurons, lead to long-term cognitive effects

# RISK FACTOR MODEL

- Delirium “caused” by “sum” of predisposing and precipitating factors
- The greater the burden of predisposing factors, the fewer precipitating factors required to cause delirium

# PREDISPOSING FACTORS

- Advanced age
- Dementia
- Functional impairment in ADLs
- Multi-morbidity
- History of alcohol abuse
- Male sex (maybe)
- Sensory impairment (↓ vision, ↓ hearing)

# PRECIPITATING FACTORS

- Acute cardiac events
- Acute pulmonary events
- Bed rest
- Drug withdrawal (sedatives, alcohol)
- Fecal impaction
- Fluid or electrolyte disturbances
- Indwelling devices
- Infections (esp. respiratory, urinary)
- Medications
- Restraints
- Severe anemia
- Uncontrolled pain
- Urinary retention

# DELIRIUM AND DEMENTIA

- Dementia: risk factor for delirium
- Delirium in a patient without dementia:
  - Associated with incident dementia
- Delirium in a patient with established dementia:
  - Associated with accelerated cognitive decline

# The interface between delirium and dementia in elderly adults

*Tamara G Fong*, Daniel Davis*, Matthew E Growdon, Asha Albuquerque, Sharon K Inouye*

| | Delirium | Dementia |
|---|---|---|
| Onset | Abrupt, although initial loss of mental clarity can be subtle | Insidious and progressive |
| Duration | Hours to days (although it can be prolonged in some cases) | Months to years |
| Attention | Reduced ability to focus, sustain, or shift attention is a hallmark feature that occurs early in presentation | Normal except in severe dementia |
| Consciousness (ie, awareness of the environment) | Fluctuating (thus assessment at multiple timepoints is necessary); reduced level of consciousness and impaired orientation | Generally intact |
| Speech | Incoherent and disorganised; distractible in conversation | Ordered, but development of anomia or aphasia is possible |
| Cause | Underlying medical condition, substance intoxication, or side-effect of drugs | Underlying neurological process (eg, amyloid β plaque accumulation in Alzheimer's disease) |
| Other features | Hyperactive, hypoactive, and mixed forms, as determined by the type of psychomotor disturbance, are possible; disruption in sleep duration and architecture; perceptual disturbances | Symptoms vary depending on underlying pathology (eg, fluctuations in cognition are a feature of Lewy body dementia) |

These two syndromes have substantial overlapping features and can coexist in an individual patient.

***Table 1:*** **Comparative features of delirium and dementia**

| | Sample | Sample size | Cognitive baseline | Delirium measure | Mean age at baseline (years) | Patients with delirium | Adjusted effect size (95% CI) |
|---|---|---|---|---|---|---|---|
| Kennedy et al[22] (2014) | Patients aged ≥65 years admitted to emergency department | 700 | Documented dementia by chart | Prevalent delirium by CAM | 77 | 9% | OR 4·3 (2·2–8·5) |
| Koster et al[23] (2013) | Patients aged ≥70 years undergoing elective cardiac surgery | 300 | MMSE <23 | DOSS | 74 | 17% | OR 4·5 (1·9–13·0) |
| Moerman et al[24] (2012) | Patients aged ≥65 years with acute hip fracture | 378 | Clinical diagnosis of dementia | Prevalent delirium by DSM-IV | 84 | 27% | OR 2·8 (1·7–4·6) |
| Bo et al[25] (2009) | Patients aged ≥70 years admitted to medical or geriatric wards | 252 | SPMSQ to establish presence and severity of cognitive impairment | Incident delirium by CAM | 82 | 11% | RR 2·1 (1·6–2·6) |
| Rudolph et al[26] (2009) | Patients aged ≥60 years undergoing elective cardiac surgery | 122 in development sample; 109 in validation sample | Preoperative MMSE ≤23 | Incident delirium by CAM | 75 | 44% | RR 1·3 (1·0–1·7) |
| Kalisvaart et al[27] (2006) | Patients aged ≥70 years undergoing elective hip surgery | 603 | Preoperative MMSE <24 | Postoperative delirium by DSM-IV and CAM | 78 | 12% | RR 5·5 (3·6–8·6) |
| Wilson et al[28] (2005) | Patients aged ≥75 years admitted to acute medical wards | 100 | IQCODE to establish presence of cognitive change over time | Incident delirium by DSM-III | 85 | 12% | OR 3·2 (1·2–9·0) |
| O'Keeffe et al[29] (1996) | Patients with acute medical admissions to geriatric units | 225 | Clinical diagnosis of dementia or BDRS ≥4 | Incident delirium by DSM-III | 82 | 28% | OR 4·8 (2·0–11·6) |
| Marcantonio et al[30] (1994) | Patients aged ≥50 years admitted to elective surgical units | 1341 | TICS <30 | Postoperative delirium by CAM | 68 | 9% | OR 4·2 (2·4–7·3) |
| Pompei et al[31] (1994) | Patients aged ≥65 years with no delirium admitted to acute hospital medical and surgical wards | 432 in development sample; 323 in validation sample | MMSE <24 (adjusted for education level) | Incident delirium by DSM-IIIR | 74 | 15% | OR 3·6 (2·1–6·2) |
| Inouye et al[32] (1993) | Patients aged ≥70 years with no dementia or delirium admitted to acute hospital medical wards | 107 in development sample; 174 in validation sample | MMSE <24 on admission | Incident delirium by CAM | 79 | 25% | RR 2·8 (1·2–6·7) |

CAM=Confusion Assessment Method. OR=odds ratio. MMSE=Mini-Mental State Examination. DOSS=Delirium Observation Screening Scale. DSM=Diagnostic and Statistical Manual of Mental Disorders. SPMSQ=Short Portable Mental Status Questionnaire. RR=relative risk. IQCODE=Informant Questionnaire on Cognitive Decline in the Elderly. BDRS=Blessed Dementia Rating Scale. TICS=Telephone Interview for Cognitive Status.

***Table 2:*** **Baseline cognitive impairment and dementia as an independent risk factor for delirium from predictive models**

| | Sample | Sample size | Delirium measure | Cognitive outcome | Mean age at baseline (years) | Patients with delirium | Adjusted effect size (95% CI) |
|---|---|---|---|---|---|---|---|
| Cognitive function and ageing study[42] (2014) | Population-based sample; multicentre sampling from health authority lists | 2197 | Algorithmic operationalisation of DSM-IV based on Geriatric Mental State examination | AGECAT-defined dementia at 2 years | 77 | 6% | OR 8·8 (2·8–28·0) |
| BRAIN-ICU[43] (2013) | Multicentre ICU admissions | 821 | CAM-ICU | RBANS score at 1 year | 61 | 74% | −5·6 (−9·5 to −1·8) points per day of delirium |
| Gross et al[44] (2012)* | Memory clinic patients with clinically diagnosed Alzheimer's dementia | 263 | Retrospective diagnosis of delirium from case notes (validated algorithm) | Worsening of Blessed IMC test score over 5 or more years | 78 | 56% | Additional 1·2 (0·5–1·8) points per year |
| Saczynski et al[45] (2012) | Patients aged ≥60 years undergoing elective CABG or valve surgery | 225 | CAM | Trajectory of MMSE change over 1 year | 73 | 46% | Prolonged impairment in recovery |
| Vantaa 85+[46] (2012) | Population-based sample of all residents aged ≥85 years | 553 | Participant and informant interview, along with medical record review | Dementia (DSM-IIIR; individual clinician) at 2·5 years | 89 | 13% | OR 8·7 (2·1–35·0) |
| Fong et al[47] (2009)* | Memory clinic patients with clinically diagnosed Alzheimer's disease | 408 | Retrospective diagnosis of delirium from case notes (validated algorithm) | Worsening of Blessed IMC test score over 0·7 years | 74 | 18% | Additional 2·4 (1·0–3·8) points |
| Bickel et al[48] (2008) | Patients aged ≥60 years undergoing elective hip surgery | 200 | CAM | Cognitive impairment or dementia, or both | 74 | 21% | OR 41·0 (4·3–396·0) |
| Lundström et al[49] (2003) | Dementia-free patients aged ≥65 years with acute hip fracture | 78 | DSM-IV | Consensus diagnosis of dementia at 5 years | 79 | 38% | OR 5·7 (1·3–24·0) |

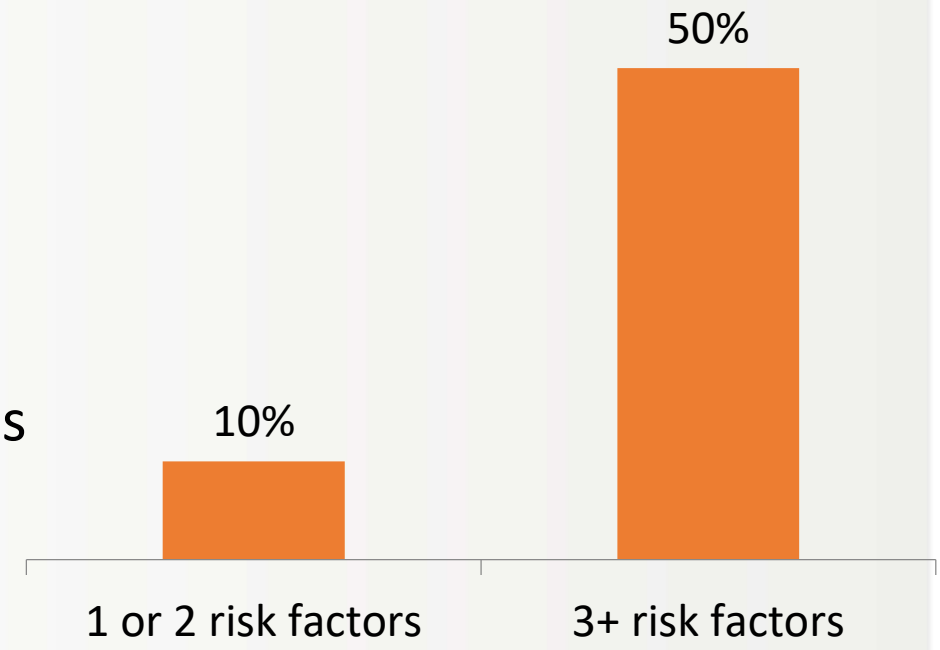
DSM=Diagnostic and Statistical Manual of Mental Disorders. AGECAT=Automated Geriatric Examination for Computer Assisted Taxonomy. OR=odds ratio. BRAIN-ICU=Bringing to Light the Risk Factors and Incidence of Neuropsychological Dysfunction in Intensive Care Unit Survivors. ICU=intensive care unit. CAM=Confusion Assessment Method. RBANS=Repeatable Battery for the Assessment of Neuropsychological Status. IMC=Information-Memory-Concentration. CABG=coronary artery bypass grafting. MMSE=Mini-Mental State Examination. *Related analyses with some overlap of data.

***Table 3*: Delirium as an independent risk factor for long-term cognitive decline and dementia**

# INCIDENCE & RISKS FOR POSTOPERATIVE DELIRIUM

Increased risk with preoperative risk factors:

- Advanced age
- Cognitive impairment
- Physical functional impairment
- History of alcohol abuse
- Abnormal serum chemistries
- Intrathoracic and aortic aneurysm surgery



# KEYS TO PREVENTING POSTOPERATIVE DELIRIUM

- Peak onset: 1st postoperative day
- Peak prevalence: 2nd postoperative day
- Associated with postoperative pain, anemia, use of sedatives and opioids
- Recent randomized trial used bispectral monitor to titrate intraoperative sedation (propofol):
  - Delirium rate: light sedation—19%, usual care—40%

# DELIRIUM AND POSTOPERATIVE COGNITIVE DYSFUNCTION

Postoperative cognitive dysfunction measured by declining performance on serial testing with a neurocognitive battery.

Emerging studies suggest that delirium and POCD are associated but do not fully explain each other.


PROBABILITY THAT YOU'LL BE KILLED BY THE THING YOU STUDY
BY FIELD
MORE LIKELY
ASTRONOMY
LAW
CRIMINOLOGY
MARINE BIOLOGY
ECONOMICS
MATHEMATICS
METEOROLOGY
CHEMISTRY
VOLCANOLOGY
GERONTOLOGY

# EVALUATION: HISTORY & PHYSICAL

History

- Focus on time course of cognitive changes, esp. their association with other symptoms or events
- Medication review, including OTC drugs, alcohol

Physical examination

- Vital signs
- Oxygen saturation
- General medical evaluation
- Neurologic examination to assess for new focal findings

# EVALUATION: LABORATORY TESTING

- Base on history and physical
- Include complete blood count, electrolytes, renal function tests
- Also helpful in selected situations: UA, urine toxicology, LFTs, serum drug levels, arterial blood gases, chest x-ray, electrocardiogram, cultures
- Consider imaging in some situations
- Consider EEG and CSF in some situations

# MANAGEMENT: GENERAL PRINCIPLES

- Requires interdisciplinary effort by clinicians, nurses, family, others
- Multifactorial approach is most successful because multiple factors contribute to delirium
- Failure to diagnose and manage delirium → costly, life-threatening complications; loss of function

# KEYS TO EFFECTIVE MANAGEMENT

- Identify and treat reversible contributors
  - Optimize medications (*see next slide*)
  - Treat infections, pain, fluid balance disorders, sensory deprivation
- Maintain behavioral control
  - Behavioral and pharmacologic interventions
- Anticipate and prevent complications
  - Urinary incontinence, immobility, falls, pressure ulcers, sleep disturbance, feeding disorders
- Restore function
  - Hospital environment, cognitive reconditioning, ADL status, family education, discharge planning

# MANAGEMENT:
# DRUGS TO REDUCE OR ELIMINATE

**Almost any medication if time course is appropriate**

- Alcohol
- Anticholinergics
- Anticonvulsants
- Antidepressants (anticholinergic only)
- Antihistamines (anticholinergic only)
- Antiparkinsonian agents
- Antipsychotics
- Barbiturates
- Benzodiazepines
- Chloral hydrate
- $H_2$-blocking agents
- Non-benzodiazepine hypnotics
- Opioid analgesics (esp. meperidine)

# MANAGEMENT: NONPHARMACOLOGIC

- Use orienting stimuli (clocks, calendar, radio)
- Provide adequate socialization
- Use eyeglasses and hearing aids appropriately
- Mobilize patient as soon as possible
- Ensure adequate intake of nutrition and fluids, by hand feeding if necessary
- Educate and support the patient and family

# MANAGEMENT: BEHAVIORAL PROBLEMS (1 of 2)

- Provide “social” restraints: consider a sitter or allow family to stay in room
- Avoid physical or pharmacologic restraints if possible
- If absolutely necessary for agitation in delirium, medications can be considered
  - Antipsychotics are treatment of choice in low doses
  - Contraindicated in Parkinson disease, Lewy-body dementia or history of neuroleptic malignant syndrome

# MANAGEMENT: BEHAVIORAL PROBLEMS (2 of 2)

More about managing delirium with medications:

- Assess for akathisia and extrapyramidal (EPS) effects
- Avoid in older people with parkinsonism
- In Parkinson disease or Lewy body dementia, a second-generation antipsychotic with fewer EPS effects can be substituted (quetiapine)
- Monitor for QT interval prolongation, torsade de pointes, neuroleptic malignant syndrome, withdrawal dyskinesias
- Use benzodiazepines for sedative and alcohol withdrawal and history of neuroleptic malignant syndrome

REVIEW

Annals of Internal Medicine

# Antipsychotics for Preventing Delirium in Hospitalized Adults

## A Systematic Review

Esther S. Oh, MD, PhD; Dale M. Needham, MD, PhD; Roozbeh Nikooie, MD; Lisa M. Wilson, ScM; Allen Zhang, BS; Karen A. Robinson, PhD*; and Karin J. Neufeld, MD, MPH*

## DISCUSSION

Our systematic review of 14 RCTs (4281 participants) found insufficient or no evidence supporting the routine use of antipsychotics for the prevention of delirium in adult inpatients.

Annals of Internal Medicine

REVIEW

# Antipsychotics for Treating Delirium in Hospitalized Adults

## A Systematic Review

Roozbeh Nikooie, MD; Karin J. Neufeld, MD, MPH; Esther S. Oh, MD, PhD; Lisa M. Wilson, ScM; Allen Zhang, BS; Karen A. Robinson, PhD*; and Dale M. Needham, MD, PhD*

**Conclusion:** Current evidence does not support routine use of haloperidol or second-generation antipsychotics to treat delirium in adult inpatients.

# ANTIPSYCHOTICS

- Occasionally needed for quality of life/death reasons
- Occasionally needed for aggression
- Use at lowest possible dose for shortest possible period

# THE BEST MANAGEMENT IS PREVENTION

- HELP Interventions: cognitive impairment, sleep deprivation, immobility, sensory impairment, dehydration
- Focus on nonpharmacologic approaches (eg, sleep protocol involving warm milk, back rubs, soothing music)
- Limit or avoid psychoactive and other high-risk medications
- Proactive geriatrics consultation

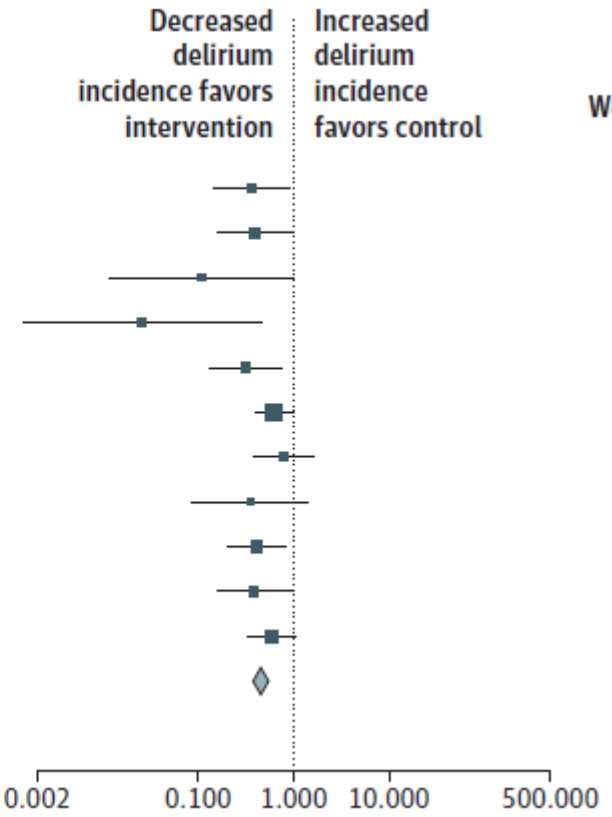
Original Investigation | HEALTH CARE REFORM

# Effectiveness of Multicomponent Nonpharmacological Delirium Interventions

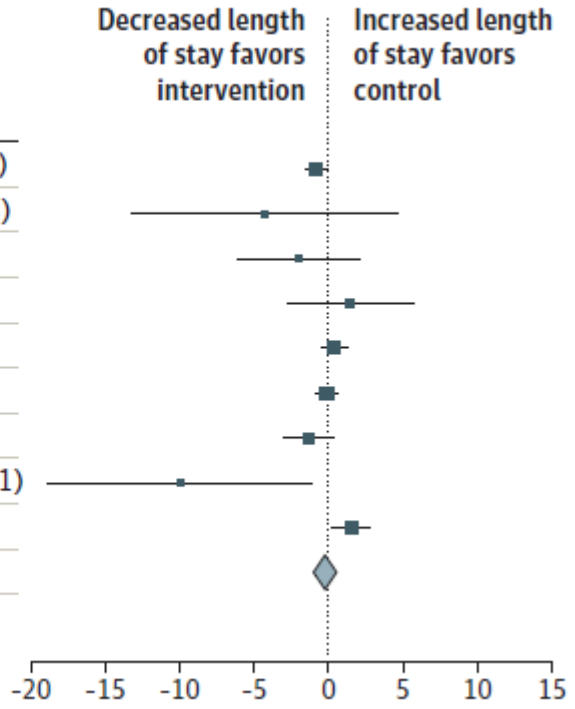
## A Meta-analysis

Tammy T. Hshieh, MD; Jirong Yue, MD; Esther Oh, MD; Margaret Puelle; Sarah Dowal, MSW, MPH; Thomas Travison, PhD; Sharon K. Inouye, MD, MPH

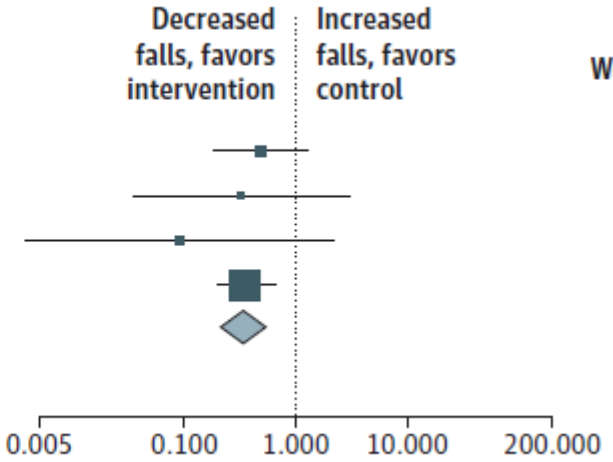
| Delirium Incidence | Odds Ratio (95% CI) |
|---|---|
| Andro et al,[27] 2012 | 0.36 (0.15-0.89) |
| Bo et al,[28] 2009 | 0.39 (0.17-0.93) |
| Caplan and Harper,[20] 2007 | 0.11 (0.01-0.99) |
| Chen et al,[16] 2011 | 0.03 (0.00-0.44) |
| Holt et al,[29] 2013 | 0.31 (0.13-0.74) |
| Inouye et al,[5] 1999 | 0.62 (0.41-0.94) |
| Jeffs et al,[30] 2013 | 0.79 (0.40-1.57) |
| Kratz,[31] 2008 | 0.35 (0.09-1.39) |
| Lundström et al,[17] 2007 | 0.42 (0.21-0.80) |
| Martinez et al,[32] 2012 | 0.38 (0.16-0.91) |
| Vidán et al,[26] 2009 | 0.59 (0.34-1.00) |
| Fixed-effect model: $P < .001$ | 0.47 (0.38-0.58) |
| Heterogeneity: $I^2 = 18\%$, $P = .27$ | NNT = 14.3 (95% CI, 11.1-20.0) |



| Length of Stay | Mean Difference (95% CI) | Weight, % |
|---|---|---|
| Bo et al,[28] 2009 | -0.79 (-1.49 to -0.09) | 21.3 |
| Caplan and Harper,[20] 2007 | -4.30 (-13.25 to 4.65) | 0.8 |
| Chen et al,[16] 2011 | -2.00 (-6.10 to 2.10) | 3.4 |
| Holt et al,[29] 2013 | 1.46 (-2.73 to 5.65) | 3.2 |
| Inouye et al,[5] 1999 | 0.40 (-0.44 to 1.24) | 19.9 |
| Jeffs et al,[30] 2013 | -0.10 (-0.74 to 0.54) | 22.0 |
| Martinez et al,[32] 2012 | -1.35 (-2.98 to 0.28) | 12.4 |
| Lundström et al,[17] and Stenvall et al,[18] 2007 | -10.00 (-18.79 to -1.21) | 0.8 |
| Vidán et al,[26] 2009 | 1.55 (0.34 to 2.76) | 16.2 |
| Random-effect model: $P = .69$ | -0.16 (-0.97 to 0.64) | 100 |
| Heterogeneity: $I^2 = 63\%$, $P = .006$ | | |



| Falls | Odds Ratio (95% CI) | Weight, % |
|---|---|---|
| Babine et al,[14] 2013 | 0.49 (0.19-1.27) | 10.9 |
| Caplan and Harper,[20] 2007 | 0.33 (0.04-2.93) | 2.5 |
| Martinez et al,[32] 2012 | 0.11 (0.01-2.05) | 3.3 |
| Stenvall et al,[18] 2007 | 0.38 (0.23-0.65) | 38.2 |
| Fixed-effect model: $P < .001$ | 0.38 (0.25-0.60) | 100 |
| Heterogeneity: $I^2 = 0\%$, $P = .78$ | | |



Cochrane Library

Cochrane Database of Systematic Reviews

# Interventions for preventing delirium in hospitalised non-ICU patients (Review)

Siddiqi N, Harrison JK, Clegg A, Teale EA, Young J, Taylor J, Simpkins SA

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**Figure 3. Forest plot of comparison: 1 Multi-component delirium prevention intervention (MCI) versus usual care, outcome: 1.1 Incident delirium.**

| Study or Subgroup | MCI Events | MCI Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| **1.1.1 Medical patients** | | | | | | |
| Abizanda 2011 | 27 | 186 | 39 | 184 | 12.8% | 0.68 [0.44, 1.07] |
| Bonaventura 2007 | 0 | 30 | 5 | 30 | 0.3% | 0.09 [0.01, 1.57] |
| Jeffs 2013 | 15 | 305 | 21 | 343 | 6.1% | 0.80 [0.42, 1.53] |
| Martinez 2012 | 8 | 144 | 19 | 143 | 4.0% | 0.42 [0.19, 0.92] |
| **Subtotal (95% CI)** | | **665** | | **700** | **23.3%** | **0.63 [0.43, 0.92]** |
| Total events | 50 | | 84 | | | |
| Heterogeneity: Tau² = 0.03; Chi² = 3.53, df = 3 (P = 0.32); I² = 15% | | | | | | |
| Test for overall effect: Z = 2.40 (P = 0.02) | | | | | | |
| **1.1.2 Surgical patients** | | | | | | |
| Hempenius 2013 | 12 | 127 | 19 | 133 | 5.5% | 0.66 [0.33, 1.31] |
| Lundstrom 2007 | 56 | 102 | 73 | 97 | 57.9% | 0.73 [0.59, 0.90] |
| Marcantonio 2001 | 20 | 62 | 32 | 64 | 13.4% | 0.65 [0.42, 1.00] |
| **Subtotal (95% CI)** | | **291** | | **294** | **76.7%** | **0.71 [0.59, 0.85]** |
| Total events | 88 | | 124 | | | |
| Heterogeneity: Tau² = 0.00; Chi² = 0.32, df = 2 (P = 0.85); I² = 0% | | | | | | |
| Test for overall effect: Z = 3.70 (P = 0.0002) | | | | | | |
| **Total (95% CI)** | | **956** | | **994** | **100.0%** | **0.69 [0.59, 0.81]** |
| Total events | 138 | | 208 | | | |
| Heterogeneity: Tau² = 0.00; Chi² = 4.32, df = 6 (P = 0.63); I² = 0% | | | | | | |
| Test for overall effect: Z = 4.53 (P < 0.00001) | | | | | | |
| Test for subgroup differences: Chi² = 0.33, df = 1 (P = 0.56), I² = 0% | | | | | | |

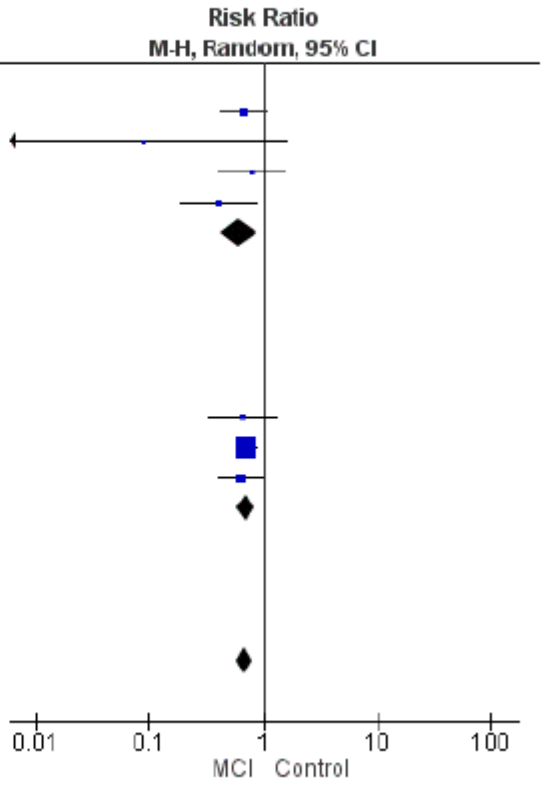


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**Figure 4. Forest plot of comparison: 2 Prophylactic cholinesterase inhibitor versus placebo, outcome: 2.1 Incident delirium.**

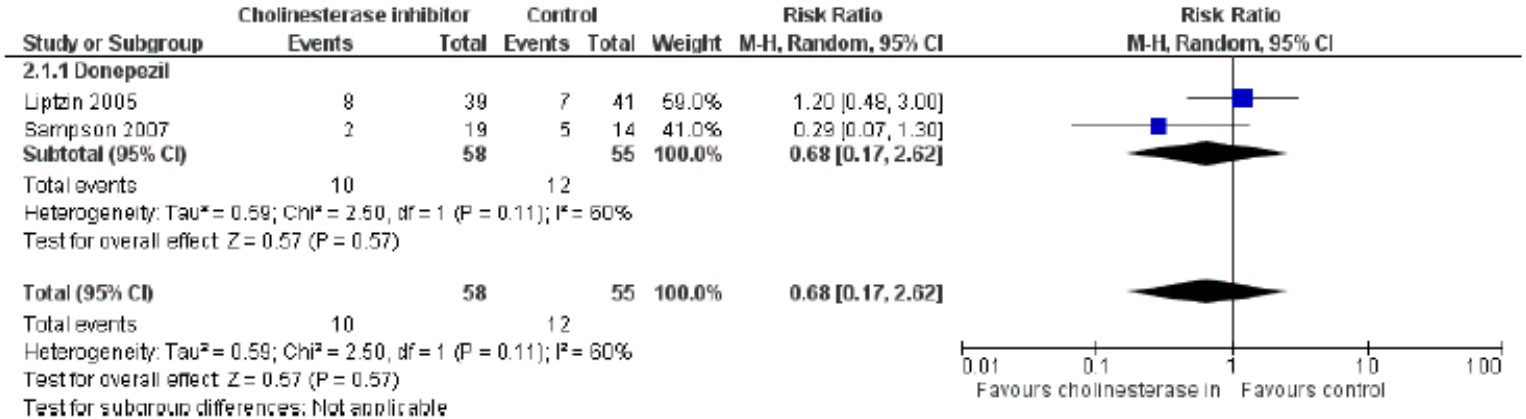


**Figure 5. Forest plot of comparison: 3 Prophylactic antipsychotic versus control, outcome: 3.1 Incidence of delirium.**

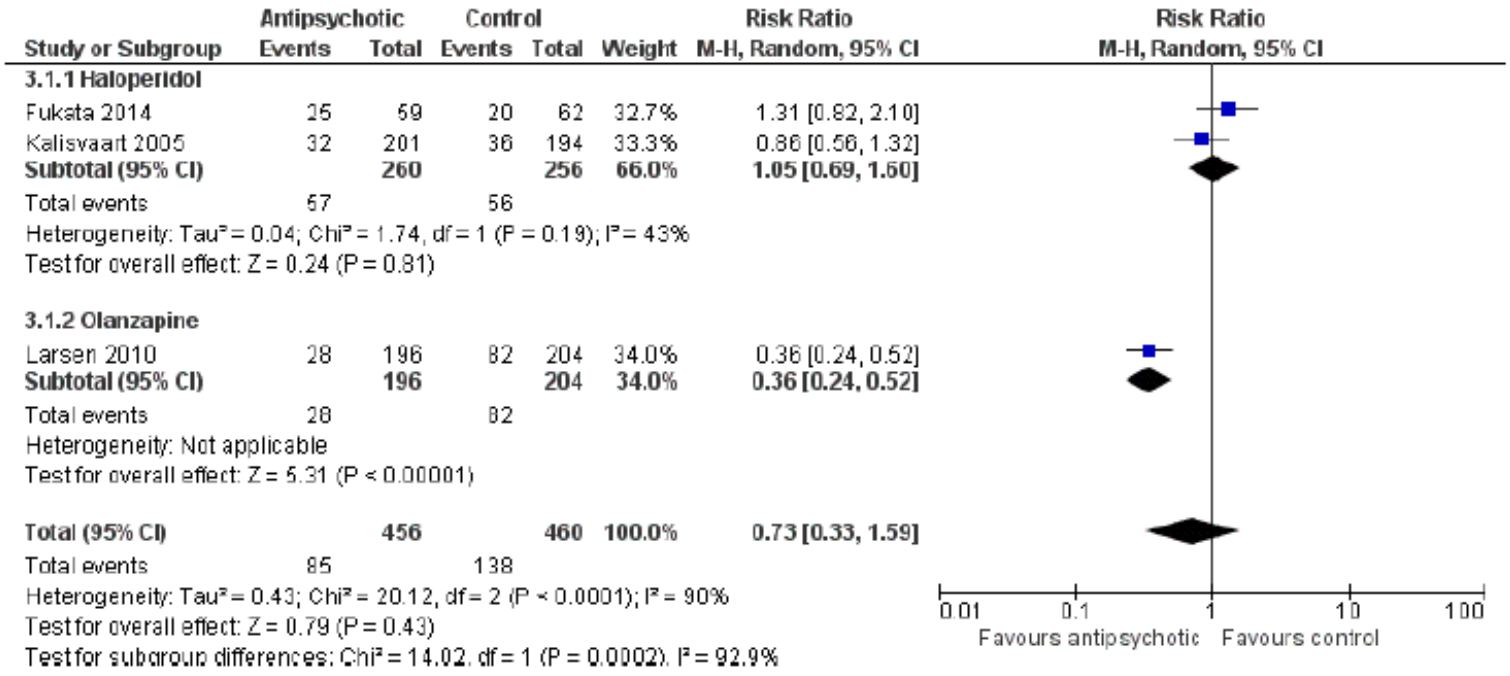
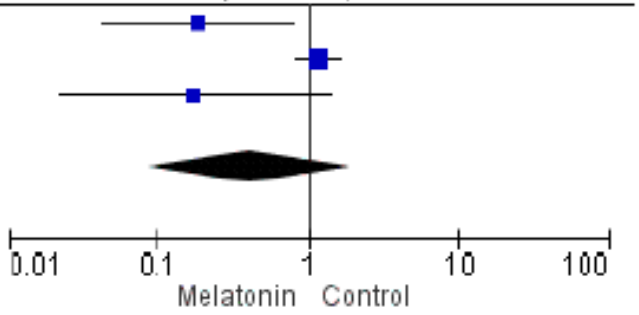


**Figure 6. Forest plot of comparison: 4 Prophylactic melatonin versus placebo, outcome: 4.1 Incident delirium.**

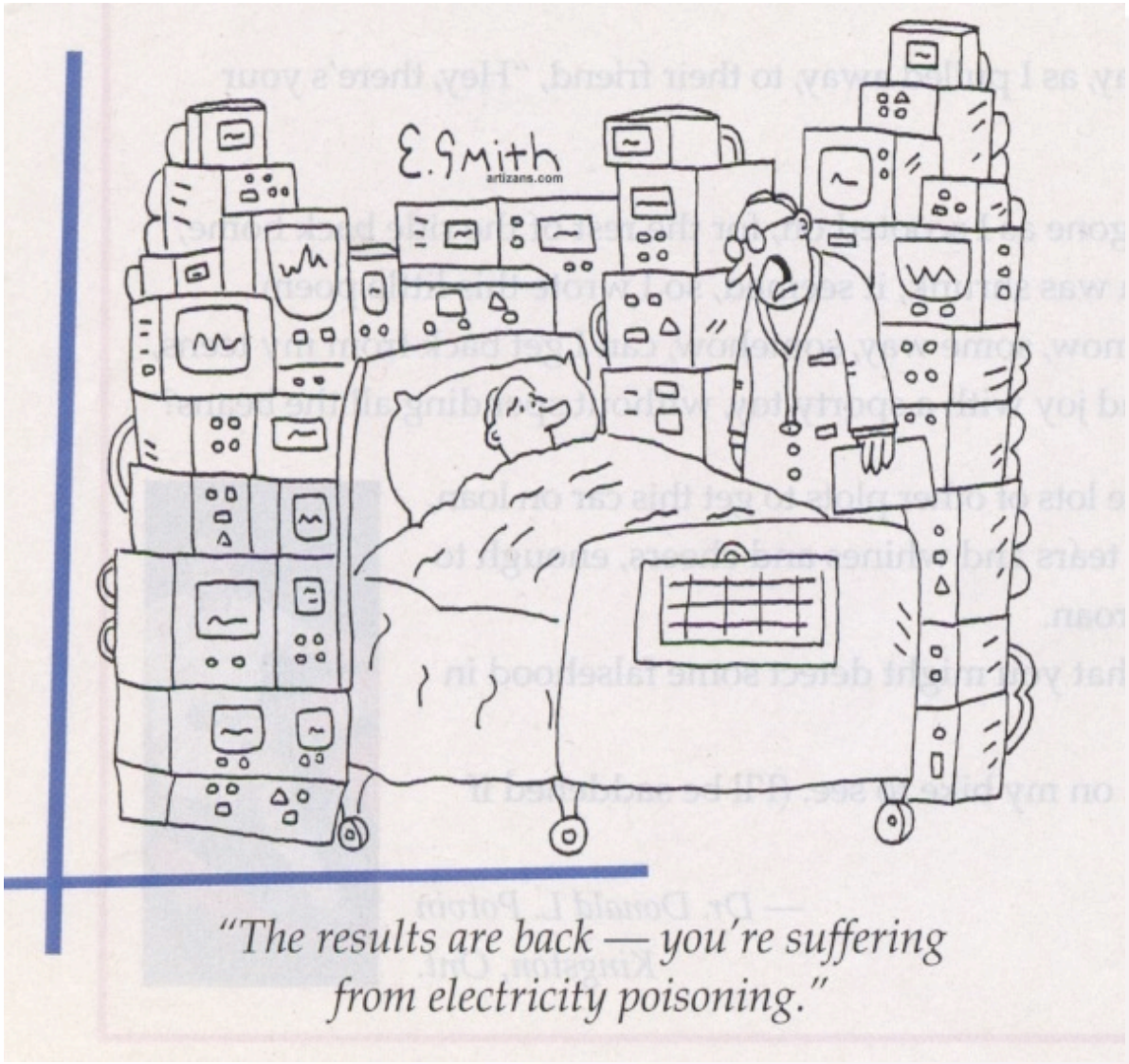
| Study or Subgroup | Melatonin Events | Melatonin Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Al-Aama 2011 | 2 | 56 | 10 | 52 | 31.6% | 0.19 [0.04, 0.81] |
| de Jonghe 2014 | 55 | 186 | 49 | 192 | 43.7% | 1.16 [0.83, 1.61] |
| Hatta 2014 | 1 | 23 | 5 | 20 | 24.7% | 0.17 [0.02, 1.37] |
| **Total (95% CI)** | | **265** | | **264** | **100.0%** | **0.41 [0.09, 1.89]** |
| Total events | 58 | | 64 | | | |

Heterogeneity: $Tau^2 = 1.37$; $Chi^2 = 8.97$, $df = 2$ ($P = 0.01$); $I^2 = 78\%$

Test for overall effect: $Z = 1.15$ ($P = 0.25$)



- The bar's name comes from the beer Delirium Tremens, whose pink elephant symbol also decorates the café's entrance




*"The results are back — you're suffering from electricity poisoning."*

# DELIRIUM AND CARE TRANSITIONS

- Improved documentation of patient's baseline cognitive status by "sending" facility.
- Presence of delirium at hospital discharge to a skilled nursing facility is a risk factor for readmission and can lead to misdiagnosis of dementia.
- Prolonged cognitive functional disability from delirium can make care planning difficult.
- Intensive therapy can facilitate cognitive recovery but not shorten the duration of delirium.
- Continue therapy as log as patient shows signs of improvement and not make permanent decisions about care needs until patient's status plateaus.

# DELIRIUM GUIDELINES

AGS Guideline for Postoperative Delirium provides recommendations with various levels of evidence

*Choosing Wisely Recommendations:*

- Avoid physical restrains to manage behavioral symptoms of hospitalized older adults
- Do not use benzodiazepines or other sedative-hypnotics in older adults as first choice for insomnia, agitation, or delirium

# SUMMARY (1 of 2)

- Delirium is common and associated with substantial morbidity for older people
- Delirium can be diagnosed with high sensitivity and specificity using the CAM
- A thorough history, physical, and focused labs should be performed to identify the underlying cause(s) of delirium

# SUMMARY (2 of 2)

- A careful medication review is mandatory; discontinue any agent likely to contribute to delirium, if possible
- Managing delirium involves treating the underlying cause(s), avoiding complications, managing behavioral problems, providing rehabilitation
- The best treatment for delirium is prevention

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# TRANSITORY MENTAL CONFUSION AND DELIRIUM IN OLD AGE

CHARLES W. BURR, M.D.

Professor of Mental Diseases, University of Pennsylvania

PHILADELPHIA

consciously—or subconsciously, to use the more fash-
ionable word—form the belief that all mental distur-
bances in the aged are but forerunners of incurable
illness, if not of speedy death. In a sense this belief is
true. Even acute attacks that are recovered from are
at best warnings of possible future permanent mental
trouble, if the patient does not in the meantime die of
some physical affection; but it should never be forgotten
that they may be mere preliminary signals that the
human machine is getting seriously out of order but not
necessarily, for the time being, irremediably so. Not

...actively engaged in a large business.

Not infrequently in senile dementia, even in the late stages, episodal attacks of acute excitement occur which may leave the patient just as he was before the attack, or, and this is more usual, may pass off but leave him each time at a somewhat lower level than before.

too far on in the disease to have mind enough to dream. In the very beginning of mentally diseased old age there is often a daily variation in mental clearness, the nights being cloudy, even stormy, while in the day the patient may be quite clear. This periodic variability

Bleeding can do no harm in the latter case and in the former often does much good.

# How often delirium misspelled in the academic literature?

- 0.1%
- 0.5%
- 1%
- 2.5%
- 5%
- 10%

# Which decades were worst?

- 30-40
- 40-50
- 50-60
- 60-70
- 70-80
- 80-90
- 90-0000
- 2000+

# What is the most common misspelling?

- Dilirium
- Delireum
- Delireum
- Delerium
- Delereum

# Delerium had to be manually verified because

- It is the name of a Canadian electronic band
- It is the name of a bar in Belgium
- It is the name of a “coffee shop” in Amsterdam
- It is the B movie (Sequel of the movie Frailty)

- **Delerium** is a Canadian new age electronic musical duo that formed in 1987, originally as a side project of the influential industrial act Front Line Assembly
- The single Silence, featuring Sarah McLachlan hit number three in electronic music in the UK
- The song has been described as one of the greatest trance songs of all time.

- A Penn colleague described Burr as "conservative." That may be putting it mildly. Burr had harsh words for psychoanalysis, for standardized education, and for young people who strove to cross class, ethnic, racial, or other lines and to climb social and economic ladders. Writing in *The New York Times in 1913, he called for "segregation of the defective classes," including government-imposed lifetime confinement in institutions.*

- In his piece in *The New York Times, Burr spent nearly half his space on undesirable immigrants, then cautioned against "the intermarriage of races as far apart as the negro and the Caucasian. . . . It leads to degeneracy." In that same piece, Burr had cited the need for "segregation," an approach often advocated by eugenicists.*

# CASE 1 (1 of 3)

- An 84-year-old man is brought to the ED by his family. His daughter thinks that he has mouth pain.
- She says that he does not want to open his mouth, and he grimaces when others try to open it.
  - He usually eats well, but he has accepted only some liquids for the last 7 days.
- He has been more lethargic and less interactive with family over the past 5 days.
- History: CAD, CABG, prostate cancer, moderate cognitive impairment, osteoarthritis, bilateral knee replacement

# CASE 1 (2 of 3)

Which one of the following is the most likely diagnosis?

A. Worsening of dementia
B. Delirium
C. Depression
D. Acute stroke

# CASE 1 (3 of 3)

Which one of the following is the most likely diagnosis?

A. Worsening of dementia
***B. Delirium***
C. Depression
D. Acute stroke

# CASE 2 (1 of 3)

- An 82-year-old woman is brought to the ED because she is coughing and short of breath.
- She is lethargic, confused, and easily distracted, and she is trying to pull out IV lines.
- History: systolic heart failure, CAD, hypertension, renal insufficiency
- Heart failure is diagnosed.
- Confusion Assessment Method (CAM) is positive for delirium.

# CASE 2 (2 of 3)

Which one of the following is the best initial treatment for managing this patient's delirium?

A. Administer haloperidol.
B. Administer lorazepam.
C. Encourage family to spend time at bedside.
D. Apply soft wrist restraints.

# CASE 2 (3 of 3)

Which one of the following is the best initial treatment for managing this patient's delirium?

A. Administer haloperidol.
B. Administer lorazepam.
***C. Encourage family to spend time at bedside.***
D. Apply soft wrist restraints.

# CASE 3 (1 of 3)

An 80-year-old woman is admitted to the hospital because of worsening agitation that began a few days ago.

- History: moderate Parkinson disease
- She refuses physical examination.
- Lab tests indicate UTI.
- CT of the head shows a new subdural hematoma.
- She is trying to leave and cannot be redirected. Her family is at her bedside.
- At 1:00 AM the agitation worsens, and the patient tries to hit the nursing staff.
- She has been receiving her routine medications.

# CASE 3 (2 of 3)

Which one of the following should be started to lessen the patient's agitation?

A. Lorazepam
B. Haloperidol
C. Quetiapine
D. Citalopram

# CASE 3 (3 of 3)

Which one of the following should be started to lessen the patient's agitation?

A. Lorazepam
B. Haloperidol
***C. Quetiapine***
D. Citalopram

| | |
|---|---|
| GRS10 Slides Editor: | Danielle Snyderman, MD, CMD |
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| GRS10 Question Writers: | Manisha Parulekar, MD, FACP, AGSF, CMD |
| | Arunima Sarkar MD, FACP, CMD |
| Managing Editor: | Andrea N. Sherman, MS |

# Which discipline has the most?

- Geriatrics
- Psychiatry
- Neurology
- General medicine
- Anesthesia
- Surgery

# Primary Analyses of the Association Between Delirium and Mortality, Institutionalization, and Dementia in Studies Adjusted for Age, Sex, Comorbid Illness or Illness Severity, and Baseline Dementia

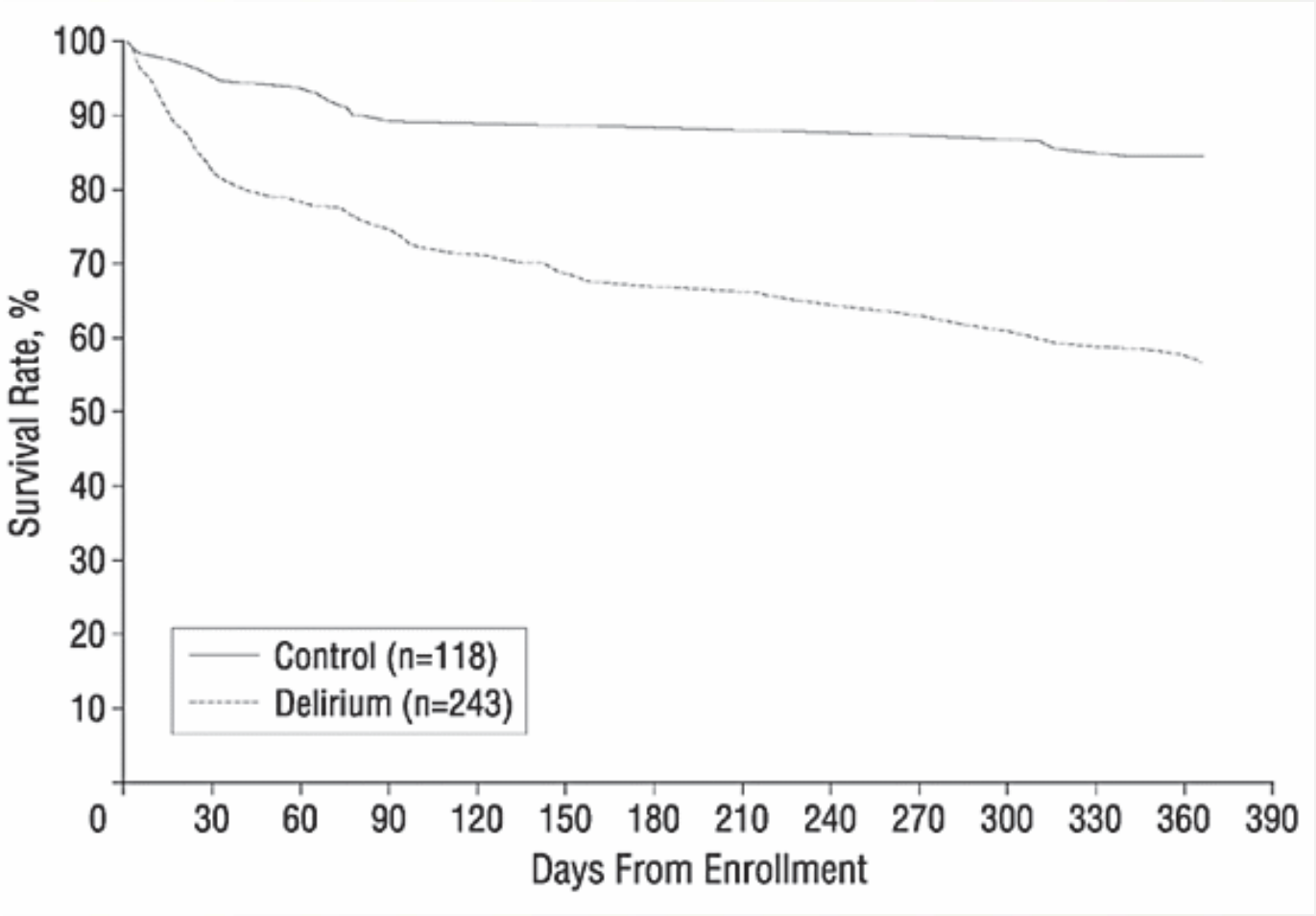
**Table 1.** Primary Analyses of the Association Between Delirium and Mortality, Institutionalization, and Dementia in Studies Adjusted for Age, Sex, Comorbid Illness or Illness Severity, and Baseline Dementia

| | Delirium, No. | | No Delirium, No. | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Events | Total Patients[a] | Events | Total Patients[a] | $k$[b] | References | HR (95% CI)[c] | $I^2$, % |
| Mortality | | | | | | | | |
| Fixed effects | 271 | 714 | 616 | 2243 | 7 | 6, 40, 41, 45, 52, 60, 65 | 1.95 (1.62-2.34) | 44.0 |
| Random effects | 271 | 714 | 616 | 2243 | 7 | 6, 40, 41, 45, 52, 60, 65 | 1.95 (1.51-2.52) | 44.0 |
| Postdischarge mortality only | 160 | 414 | 318 | 1298 | 5 | 6, 40, 41, 52, 65 | 1.62 (1.29-2.04) | 0 |
| | | | | | | | OR (95% CI) | |
| Fixed effects | 183 | 483 | 316 | 1583 | 7 | 7, 32, 35, 51, 63 | 1.71 (1.27-2.30) | 0 |
| Random effects | 183 | 483 | 316 | 1583 | 7 | 7, 32, 35, 51, 63 | 1.71 (1.27-2.30) | 0 |
| Postdischarge mortality only | 15 | 41 | 17 | 158 | 1 | 32 | 1.70 (0.59-4.91) | NA |
| Institutionalization | | | | | | | | |
| Fixed effects | 176 | 527 | 219 | 2052 | 9 | 6, 7, 30, 32, 40, 43, 63 | 2.41 (1.77-3.29) | 0 |
| Random effects | 176 | 527 | 219 | 2052 | 9 | 6, 7, 30, 32, 40, 43, 63 | 2.41 (1.77-3.29) | 0 |
| Incident cases only | 89 | 302 | 161 | 1829 | 7 | 6, 7, 30, 32, 40, 43, 63 | 2.37 (1.63-3.45) | 12.7 |
| Dementia | | | | | | | | |
| Fixed effects | 35 | 56 | 15 | 185 | 2 | 32, 54 | 10.06 (2.98-34.0) | 52.4 |
| Random effects | 35 | 56 | 15 | 185 | 2 | 32, 54 | 12.52 (1.86-84.21) | 52.4 |
| Incident cases only | 21 | 30 | 9 | 48 | 1 | 54 | 5.66 (1.34-24.0) | NA |

Abbreviations: CI, confidence interval; HR, hazard ratio; NA, data not applicable; OR, odds ratio.
[a] The sum total of participants in each subgroup is an estimate because the event rates entered in statistically adjusted analyses were not consistently reported for all studies.
[b] Indicates the number of individual effect estimates in aggregated analyses.
[c] The HRs and ORs that are greater than 1 indicate increased risk of mortality, institutionalization, and dementia among participants who experienced delirium.

**Witlox, J. et al. JAMA 2010;304:443-451.**

## Unadjusted Kaplan-Meier survival curves of the 12-month mortality rate by study group




McCusker, J. et al. Arch Intern Med 2002;162:457-463.



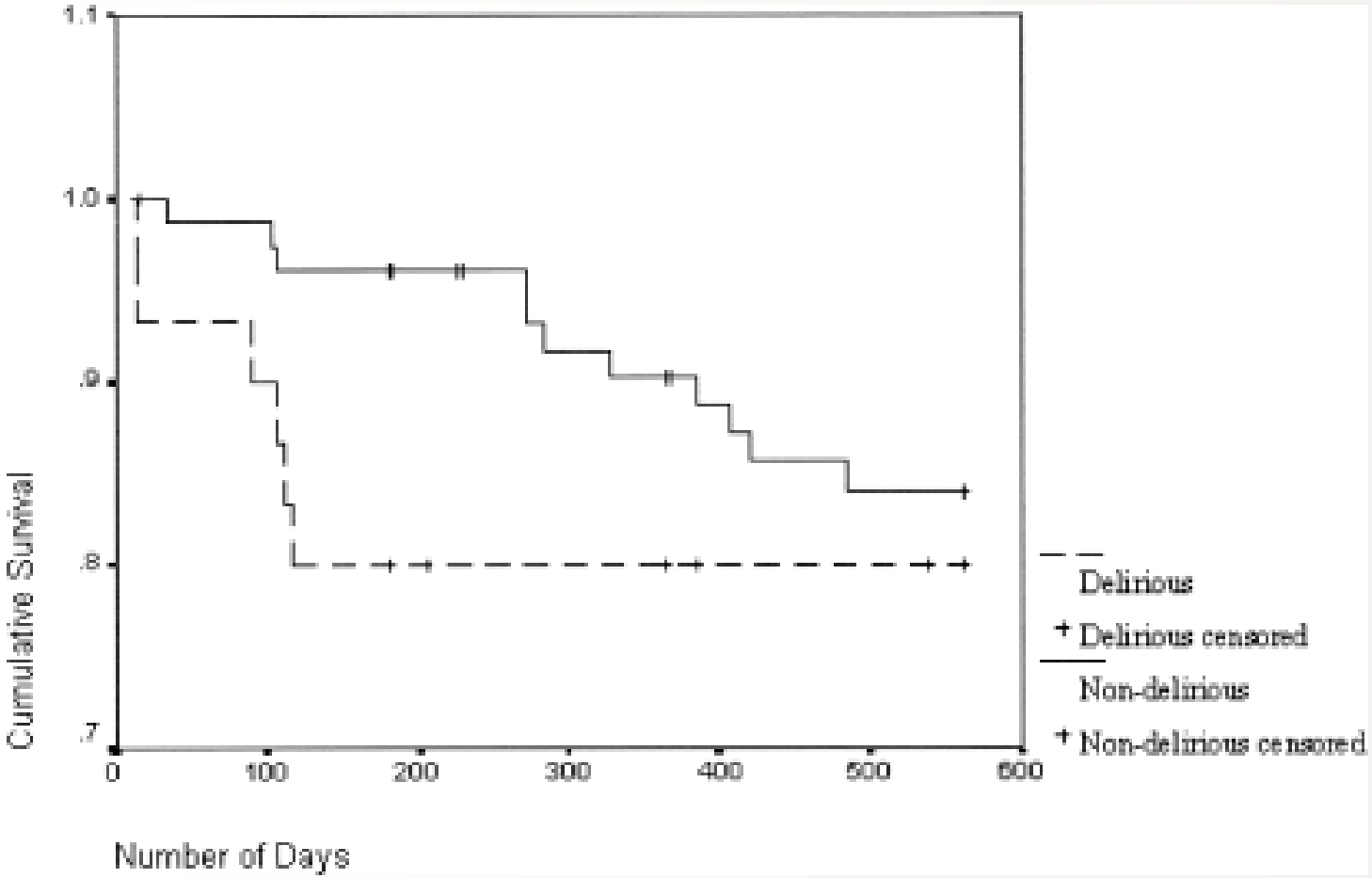
ARCHIVES OF INTERNAL MEDICINE

**Table 2. Results of Proportional Hazards Analyses of 1-Year Mortality***

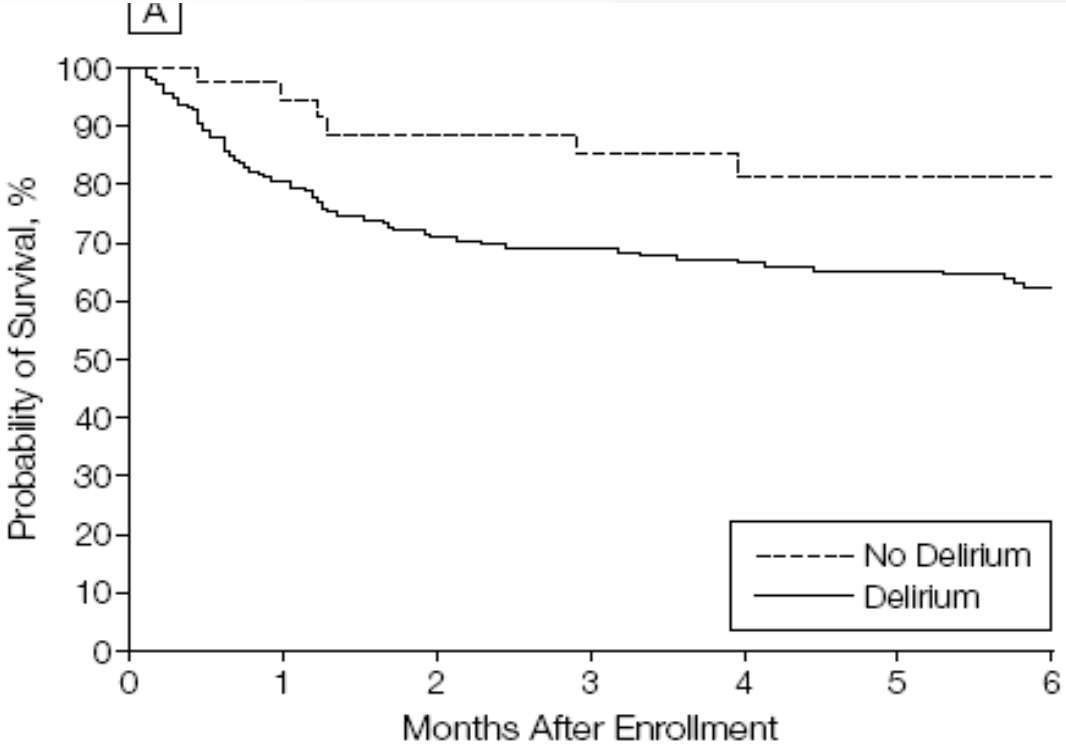
| Variable | Statistical Model | |
|---|---|---|
| | Univariate | Multivariable |
| Delirium/control | 3.44† (2.05-5.75) | 2.11‡ (1.18-3.77) |
| Age, y | 1.01 (0.99-1.04) | 1.04§ (1.01-1.07) |
| Male/female | 1.80§ (1.25-2.58) | 1.48 (0.98-2.24) |
| Married/single‖ | 1.10 (0.75-1.62) | 0.61‡ (0.38-0.99) |
| Institution/home | 1.33 (0.91-1.96) | 1.14 (0.74-1.75) |
| Charlson Comorbidity Index | 1.31† (1.23-1.40) | 1.27† (1.18-1.38) |
| Acute Physiology Score | 1.18† (1.13-1.24) | 1.14† (1.08-1.20) |
| Clinical severity of illness | 1.57† (1.38-1.79) | 1.28§ (1.09-1.50) |
| Dementia (present)/absent | 1.03 (0.69-1.55) | 0.62‡ (0.40-0.97) |
| Dementia (missing)/absent | 1.09 (0.52-2.28) | 1.86 (0.85-4.09) |
| Medical/geriatric | 2.33† (1.50-3.63) | 1.13 (0.68-1.89) |
| Likelihood ratio statistic¶ | . . . | 123.38† |

*Data are hazard ratio (95% confidence interval). Ellipses indicate not applicable. Of 361 patients, 118 died.
†$P<.001$.
‡$.01 \leq P < .05$.
§$.001 \leq P < .01$.
‖Single includes widowed, divorced, and separated.
¶Likelihood ratio statistics for testing the significance of the model.

# Delirium in Older Emergency Department Patients Discharged Home: Effect on Survival



# Delirium – Prognosis in ICU




| No. at Risk | | | | | | | |
|---|---|---|---|---|---|---|---|
| No Delirium | 41 | 34 | 28 | 25 | 22 | 21 | 19 |
| Delirium | 183 | 138 | 116 | 111 | 104 | 98 | 88 |

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# POST - OP

Table 4. Association of Adverse Hospital Outcomes by Complication and Delirium Status[a]

| | Adjusted Relative Risk (95% CI)[b] | | |
|---|---|---|---|
| Status | Length of Stay >5 d | Institutional Discharge | 30-d Readmission |
| No complications or delirium (n = 404) | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| Complications only (n = 27) | 2.8 (1.9-4.0) | 1.0 (0.7-1.5) | 1.6 (0.6-4.2) |
| Delirium only (n = 115) | 1.9 (1.4-2.7) | 1.5 (1.3-1.7) | 2.3 (1.4-3.7) |
| Complications and delirium (n = 20) | 3.4 (2.3-4.8) | 1.8 (1.4-2.5) | 3.0 (1.3-6.8) |

Table 5. Association of any Adverse Hospital Outcomes by Complication and Delirium Status[a]

| Status | Any Adverse Outcome | | |
|---|---|---|---|
| | Patients, No. (%) | Adjusted RR (95% CI)[b] | PAR, % (95% CI)[c] |
| No complications or delirium (n = 404) | 252 (62.4) | 1 [Reference] | 1 [Reference] |
| Complications only (n = 27) | 22 (81.5) | 1.2 (1.0-1.6) | 0.8 (0.0-1.5) |
| Delirium only (n = 115) | 105 (91.3) | 1.4 (1.3-1.5) | 5.8 (4.7-6.8) |
| Complications and delirium (n = 20) | 20 (100) | 1.6 (1.4-1.8) | 1.3 (1.0-1.6) |

**CONCLUSIONS AND RELEVANCE** Major postoperative complications and delirium are separately associated with adverse events and demonstrate a combined effect. Delirium occurs more frequently and has a greater effect at the population level than other major complications.

# Risk factors for incident delirium among older people in acute hospital medical units: a systematic review and meta-analysis

Suman Ahmed[1], Baptiste Leurent[2,3], Elizabeth L. Sampson[2,3]

Rady Faculty of Health Sciences | UM

Table 3. Meta-analysis of risk factors for incident delirium in older medical inpatients

| Risk factor | Studies/total sample (*n*/*n*) | Statistical method | Pooled OR or MD* (95% CI) | Heterogeneity $I^2$ (%) |
|---|---|---|---|---|
| Demographic factors | | | | |
| Old age | 5/1,300 | IV, Random | 2.74 [0.11, 5.38]* | 86 |
| Male sex | 5/1,148 | M–H, Fixed | 0.86 [0.65, 1.14] | 0 |
| Mental status | | | | |
| Dementia | 2/501 | M–H, Fixed | 6.62 [4.30, 10.19] | 0 |
| Physical illness | | | | |
| Illness severity (APACHE II) | 2/653 | IV, Random | 3.91 [2.22, 5.59]* | 69 |
| Physical status | | | | |
| Visual impairment | 4/1,077 | M–H, Random | 1.89 [1.03, 3.47] | 64 |
| Urinary catheterisation | 2/692 | M–H, Random | 3.93 [2.51, 6.14] | 62% |
| Medication | | | | |
| Polypharmacy | 3/944 | IV, Fixed | 0.64 [0.17, 1.11]* | 0 |
| Laboratory findings | | | | |
| Low albumin | 2/518 | IV, Random | −3.14 [−5.99, −0.29]* | 68 |
| Hospitalisation related | | | | |
| Length of hospital stay | 2/537 | IV, Random | 4.85 [2.20, 7.50] | 69 |

OR, odds ratio; MD, mean difference; CI, confidence interval; M–H, Mantel–Haenszel method; IV, inverse variance method.
*indicates that mean difference is reported.

We would like to thank Bridget Candy for her assistance with literature searching. E.L.S. is employed in a post funded by Marie Curie Cancer Care UK.

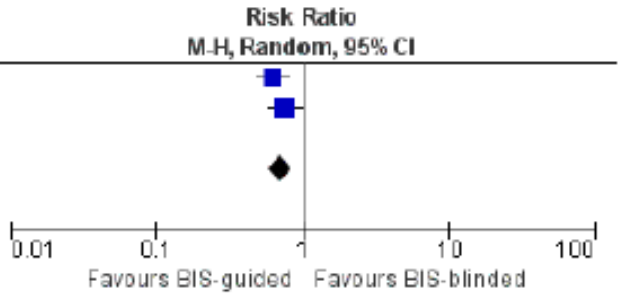
# Whatever that is….

**Figure 7. Forest plot of comparison: 11 Bispectral index (BIS)-guided anaesthesia versus BIS-blinded anaesthesia, outcome: 11.1 Incident delirium.**

| Study or Subgroup | BIS-guided Events | BIS-guided Total | BIS-blinded/clin judge Events | BIS-blinded/clin judge Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Chan 2013 | 70 | 450 | 109 | 452 | 44.3% | 0.65 [0.49, 0.85] |
| Radtke 2013 | 95 | 575 | 124 | 580 | 55.7% | 0.77 [0.61, 0.98] |
| **Total (95% CI)** | | **1025** | | **1032** | **100.0%** | **0.71 [0.60, 0.85]** |
| Total events | 165 | | 233 | | | |

Heterogeneity: Tau² = 0.00; Chi² = 0.96, df = 1 (P = 0.33); I² = 0%

Test for overall effect: Z = 3.68 (P = 0.0002)



# Evidence for Cholinesterase Inhibitors is Overshot

Cochrane Library

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**Cholinesterase inhibitors for delirium (Review)**

Overshott R, Karim S, Burns A

Health Sciences | UMI

**Authors' conclusions**

There is currently no evidence from controlled trials that donepezil is effective in the treatment of delirium. Further trials using cholinesterase inhibitors for the treatment of delirium are needed.