


Center of Excellence for Delirium in Aging Research



**UPDATE ON DELIRIUM**  
**2016**

**CEDARTREE**

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**DSM5 CRITERIA FOR DELIRIUM**

- Disturbance in attention and awareness (reduced orientation to the environment)
- Disturbance develops acutely and tends to fluctuate
- An additional disturbance in cognition, (e.g., memory deficit, language, visuoperceptual)
- Not better explained by a preexisting dementia
- Not in face of severely reduced level of arousal or coma
- Evidence of an underlying organic etiology or multiple etiologies

*Used with permission. American Psychiatric Association, 2013*

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## Why is delirium important?

- Common problem
- Serious complications
- Often unrecognized
- Typically multifactorial etiology
- Up to 40% cases preventable

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## In U.S. hospitals today

***5 older patients become delirious every minute***

2.6 million older adults develop delirium each year

U.S. Dept HHS, AoA Report, Profile of Older Americans 2011

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## **Delirium is common**

### **Delirium Rates**

Hospital:	
• Prevalence (on admission)	14-24%
• Incidence (in hospital)	6-56%
Postoperative:	15-53%
Intensive care unit:	70-87%
Nursing home/post-acute care:	20-60%
Palliative care:	up to 80%

### **Mortality**

Hospital mortality:	22-76%
One-year mortality:	35-40%

Ref: Inouye SK, NEJM 2006;354:1157-65;  
Lancet 2014; 383:911-922

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## **Delirium has serious complications**

- Delirium associated with:
  - Increased morbidity and mortality
  - Functional and cognitive decline
  - Increased rates of dementia
  - Institutionalization
  - Increased LOS and healthcare costs
  - Post-traumatic stress disorder
  - Caregiver burden

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## **Delirium is expensive**

Hospital costs (> \$8 billion/year)

Post-hospital costs (>\$150 billion/year)

- Rehospitalization
- Institutionalization
- Rehabilitation
- Home care
- Caregiver burden

Ref: Leslie DL, et al. Arch Intern Med 2008;168:27-32

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## **Delirium is often unrecognized**

Previous studies: 32-66% cases  
unrecognized by physicians and nurses

***Pearl: We cannot manage delirium or  
decrease its complications unless we  
recognize it***

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## **How do we recognize delirium?**

[many approaches]

- Confusion Assessment Method (CAM)
- CAM for the Intensive Care Unit (CAM-ICU)
- 3-Minute Diagnostic Interview for CAM delirium (3D-CAM)
- Intensive Care Delirium Screening Checklist (ICDSC)
- Delirium Index (DI)
- Delirium Observation Screening Scale(DOSS)
- Delirium Rating Scale (DRS)-Revised-98
- Delirium Symptom Interview (DSI)
- Memorial Delirium Assessment Scale (MDAS)
- Neelon/Champagne Confusion Scale (NEECHAM)
- Nursing Delirium Screening Scale (NuDESC)

....and more

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## **Confusion Assessment Method (CAM)**

- Most widely used method worldwide
- Used in >5000 original studies to date, translated into over 20 languages
- Short CAM (4-item)—diagnostic algorithm
  - Commonly used for screening
- Long CAM (10-item):
  - Provides information on severity/subtypes
  - Diagnostic/Reference standard purposes

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## **CONFUSION ASSESSMENT METHOD (CAM)**

- (1) acute onset and fluctuating course  
-and-  
(2) inattention  
-and either-  
(3) disorganized thinking  
-or-  
(4) altered level of consciousness

[score based on cognitive testing]

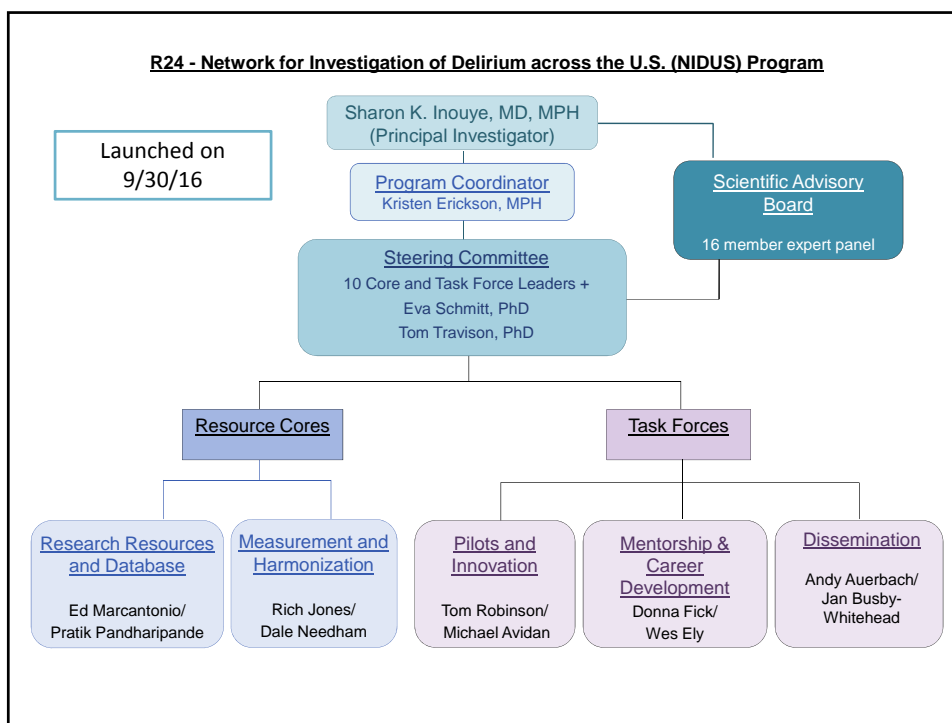
Ref: Inouye SK, et. al. Ann Intern Med. 1990, 113: 941-8

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## **Pearls for delirium screening**

- For screening purposes, important to maximize sensitivity (don't miss cases)
- Consider as a vital sign in older adults
- Assessment *must be* based on cognitive testing
- Cognitive screen can be brief
  - Orientation (5 items)—place, time, context
  - Sustained attention (months of year backwards, days backwards, digit spans)
  - Mini-Cog or SPMSQ used by many

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## What causes delirium?

### Major mechanistic hypotheses

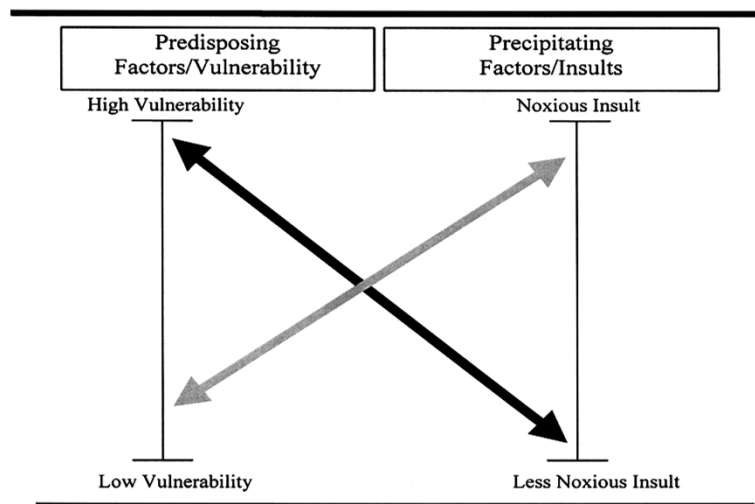
- Neurotransmitter dysregulation
- Neuro-inflammation
- Aberrant stress response
- Oxidative stress
- Metabolic disorders
- Sleep-wake dysregulation
- Network disconnectivity
- Genetic factors

## Biomarkers in Delirium

Types of Biomarkers	Use of Biomarkers
Fluid Biomarkers (blood, CSF) <ul style="list-style-type: none"> <li>· Inflammatory (eg, CRP, IL-6)</li> <li>· Neuronal injury</li> <li>· Genetic</li> <li>· Alzheimer-associated</li> </ul> Neurophysiology <ul style="list-style-type: none"> <li>· Quantitative EEG</li> </ul> Neuroimaging <ul style="list-style-type: none"> <li>· Diffusion tensor imaging (DTI)</li> <li>· Functional MRI (fMRI)</li> </ul> Animal models	<ul style="list-style-type: none"> <li>• Advance pathophysiologic understanding</li> <li>• Allow for earlier or more accurate diagnosis</li> <li>• Utilize for risk stratification</li> <li>• Develop predictive models</li> <li>• Follow clinical course</li> <li>• Use for prognostication</li> <li>• Monitor effectiveness of interventions</li> </ul>

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## Delirium is typically multifactorial



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Ref: Inouye SK et al. JAMA 1996; 275:852-857



## Predictive Models for Delirium

**Annals of Internal Medicine**  
**A Predictive Model for Delirium in Hospitalized Elderly Medical Patients Based on Admission Characteristics**  
 Sharon K. Inouye, MD, MPH; Catherine M. Viscoli, PhD; Ralph I. Horvitz, MD; Leslie D. Hurst, MS, and Mary E. Tinetti, MD  
*Ann Intern Med.* 1999;131:424-431.

**JAMA**  
 The Journal of the American Medical Association  
**A Clinical Prediction Rule for Delirium After Elective Noncardiac Surgery**  
 Edward H. Marmorstein, MD, SM; Lee Goldman, MD, MPH; Carol M. Mangione, MD, SM; Lynn R. Lurie, PhD, MD; Brenda Murray, PhD; Christine M. Hultman; Christopher C. Donnan, MD; Anthony E. Whitmore, MD; David A. Sugarbaker, MD; Robert Press, MD; Susan Hass, MD, SM; E. Harold Cook, MD; E. John Chan, PhD; Thomas H. Lee, MD, SM  
*JAMA.* 1999;281:1334-1339

**Circulation**  
**Derivation and Validation of a Preoperative Prediction Rule for Delirium After Cardiac Surgery**  
 James L. Rudolph, MD, SM; Richard N. Jones, ScD; Sue E. Levkoff, ScD; Christopher Rockoff, PhD; Sharon K. Inouye, MD, MPH; Daniel Ramirez, MD, MPH; Frank B. Sletten, MD; Shakti F. Khan, MD; Lewis A. Lipsitz, MD; Chandra, MD; Sidney Levinsky, MD; Edward R. McCosham, MD, SM  
*Circulation.* 2009;119:226-234

**...and many, many more**

## Predisposing Factors from Predictive Models

Predisposing Factors	General Medicine	Surgery		ICU
		Non-cardiac	Cardiac	
	Relative Risks			
Dementia	2.3-4.7	2.8		
Cognitive impairment	2.1-2.8	3.5-4.2	1.3	
History of delirium		3.0		
Functional impairment	4.0	2.5-3.5		
Vision impairment	2.1-3.5	1.1-3.0		
Hearing impairment		1.3		
Comorbidity/severity of illness	1.3-5.6	4.3		1.1
Depression	3.2		1.2	
History of transient ischemia/ stroke			1.6	
Alcohol abuse	5.7	1.4-3.3		
Older age	4.0	3.3-6.6		1.1

Inouye SK et al. Lancet 2014; 383:911-922

### **Precipitating Factors from Predictive Models**

Precipitating Factors	Medicine	Surgery		ICU
		Non-cardiac	Cardiac	
Medications				
Multiple medications added	2.9			
Psychoactive medication use	4.5			
Sedative-hypnotics				4.5
Use of physical restraints	3.2-4.4			
Use of bladder catheter	2.4			
Physiologic				
Elevated BUN/creatinine ratio	2.0-5.1	2.9		
Abnormal sodium, glucose, potassium		3.4		
Metabolic acidosis				1.4
Infection				3.1
Any iatrogenic event	1.9			
Surgery		3.5-8.3		

Inouye SK et al. Lancet 2014; 383:911-922

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### **Who is at risk for delirium?**

- Identifies who we need to be extra cautious about during hospitalization
- Allows us to proactively put into place prevention strategies
- Some targeted vulnerability factors are amenable to intervention

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## Medications Associated with Delirium

[2012 AGS Beers Criteria: Potentially Inappropriate Medications for Elderly]

- All tricyclic antidepressants
- Anticholinergics (eg, diphenhydramine)
- Benzodiazepines
- Corticosteroids
- H2-receptor antagonists
- Meperidine
- Sedative hypnotics
- Thioridazine/chlorpromazine

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## NONPHARMACOLOGIC DELIRIUM PREVENTION: HOSPITAL ELDER LIFE PROGRAM (HELP)

Multicomponent intervention strategy targeted at 6 delirium risk factors

<u>Risk Factor</u>	<u>Intervention</u>
Cognitive Impairment.....	Reality orientation Therapeutic activities protocol
Sleep Deprivation.....	Nonpharmacological sleep protocol Sleep enhancement protocol
Immobilization.....	Early mobilization protocol Minimizing immobilizing equipment
Vision Impairment.....	Vision aids Adaptive equipment
Hearing Impairment.....	Amplifying devices Adaptive equipment and techniques
Dehydration.....	Early recognition and volume repletion

Inouye SK. N Engl J Med 1999;340:669-76.


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## HELP Impact on Outcomes

Reference	No. of Patients	Rate in HELP	Rate in Controls	Improvement with HELP
<b>PREVENTION OF DELIRIUM</b>				
Rubin 2011	>7,000	18%	41%	23%
Chen 2011	179	0%	17%	17%
Caplan 2007	37	6%	38%	32%
Rubin 2006	704	26%	41%	15%
Inouye 1999	852	10%	15%	5%
<b>REDUCED COGNITIVE DECLINE (MMSE decline by 2+ points)</b>				
Inouye 2000	1,507	8%	26%	18%
<b>REDUCED FUNCTIONAL DECLINE (ADL decline by 2+ points)</b>				
Inouye 2000	1,507	14%	33%	19%
<b>DECREASED HOSPITAL LENGTH OF STAY</b>				
Rubin 2011	>7,000	5.3 days	6.0 days	0.7 days
Caplan 2007	37	22.5 days	26.8 days	4.3 days
Rubin 2006	704	---	---	0.3 days
<b>REDUCED INSTITUTIONALIZATION</b>				
Caplan 2007	37	25%	48%	23%
<b>DECREASED FALLS</b>				
Inouye 2009	--	2%	4%	2%
Inouye 2009	--	3.8/1000 p-y	11.4/1000 p-y	7.6/1000 p-y
Inouye 2009	--	1.2/1000 p-y	4.7/1000 p-y	3.5/1000 p-y
Caplan 2007	37	6%	19%	13%
<b>DECREASED SITTER USE</b>				
Caplan 2007	37	330 hours	644 hours	314 hours

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## HELP Impact on Costs

Reference	No. of Patients	Impact on Cost
Rubin 2011	>7,000	>\$7.3 million per year savings in hospital costs (> \$1000 savings per patient)
Rizzo 2001	852	\$831 cost savings per person-yrs in hospital costs
Leslie 2005	801	\$9,446 savings per person-yrs in long-term nursing home costs
Caplan 2007	111	\$121,425 per year savings in sitter costs

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### Geriatric Consultation or Assessment\*

Study	Population	Intervention	Results
<i>Marcantonio 2001</i>	126 hip fracture pts	Proactive geriatric consultation	Lower incident delirium
<i>Cole 2002</i>	227 medical pts	Multidisciplinary consultation	Negative study
<i>Pitkala 2006</i>	174 medical pts	Multicomponent geriatric assessment	Faster improvement in delirium
<i>Yoo 2012</i>	518 medical pts	Multidisciplinary team	Decreased nursing home placement
<i>Deschodt 2012</i>	171 orthopedic pts	Geriatric consultation	Lower incident delirium

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### Other Nonpharmacologic Approaches

Study	Population	Intervention	Results
<i>Milisen 2001</i>	120 hip fracture pts	Enhanced nursing care and nursing consultation	Shorter duration and severity of delirium
<i>Caplan 2006</i>	104 medical pts	Rehab-at-home by team approach	Lower incident delirium; lower costs
<i>Schweikert 2009</i>	104 intubated ICU patients	Exercise, PT/OT	Decreased ICU and hospital delirium-days
<i>Martinez 2012</i>	287 medical pts	Multicomponent intervention by family members	Lower incident delirium and falls

*Note: specialized delirium rooms or units: No RCTs*

## **PHARMACOLOGIC APPROACHES**

[IOM-based Systematic review, AGS 2014]

- 16 high quality RCTs of:
  - Haloperidol, olanzapine, risperidone
  - Melatonin/Ramelteon
  - Rivastigmine, donepezil
  - Dexmedetomidine (OR, ICU)
- Studies hampered by methodologic limitations (nonblinded outcomes, dropouts, measurement)
  - 6 trials: no difference in delirium rates
  - 8 trials: delirium reduced; no impact on any clinical outcomes
  - 2 trials: clinical outcomes worsened (increased delirium duration or severity, increased LOS or mortality)

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## **PHARMACOLOGIC APPROACHES**

(cont)

- Drug treatment may reduce agitation but prolong delirium and cognitive decline
- Conclusion reached by several systematic review and guideline panels:
 

**No recommendation for drug treatment for prevention or management of delirium at this time**

Ref: NICE 2010, VA HSRD 2011, AGS 2014, Neufeld JAGS 2016

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## AGS-ACS Clinical Practice Guidelines:

Area	Recommendation
Multicomponent Non-pharmacologic Interventions	<ul style="list-style-type: none"> <li>Delivered by interdisciplinary team for at-risk older adults</li> <li>Includes mobility and walking, avoiding physical restraints, orienting to surroundings, sleep hygiene, adequate oxygen, fluids and nutrition</li> </ul>
Educational Programs	<ul style="list-style-type: none"> <li>Ongoing, provided for healthcare professionals</li> </ul>
Medical Evaluation	<ul style="list-style-type: none"> <li>Identify and manage underlying organic contributors to delirium</li> </ul>
Pain Management	<ul style="list-style-type: none"> <li>Should be optimized, preferably with non-opioid medications</li> </ul>
Medications to Avoid	<ul style="list-style-type: none"> <li>Minimize medications associated with precipitating delirium</li> <li>Benzodiazepines should not be used as first-line treatment of delirium-associated agitation</li> <li>Benzodiazepines and antipsychotics should be avoided for treatment of hypoactive delirium</li> <li>Cholinesterase inhibitors should not be newly prescribed to prevent or treat postoperative delirium</li> </ul>
Antipsychotics (weak recommendation)	<ul style="list-style-type: none"> <li>The use of antipsychotics (haloperidol, risperidone, olanzapine, quetiapine, or ziprasidone) at the lowest effective dose for shortest possible duration may be considered to treat delirious patients who are severely agitated, distressed or threatening substantial harm to self and/or others</li> </ul>

<http://geriatricscareonline.org/toc/american-geriatrics-society-clinical-practice-guideline-for-postoperative-delirium-in-older-adults/CL018>

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## DELIRIUM MANAGEMENT PHARMACOLOGIC (cont)

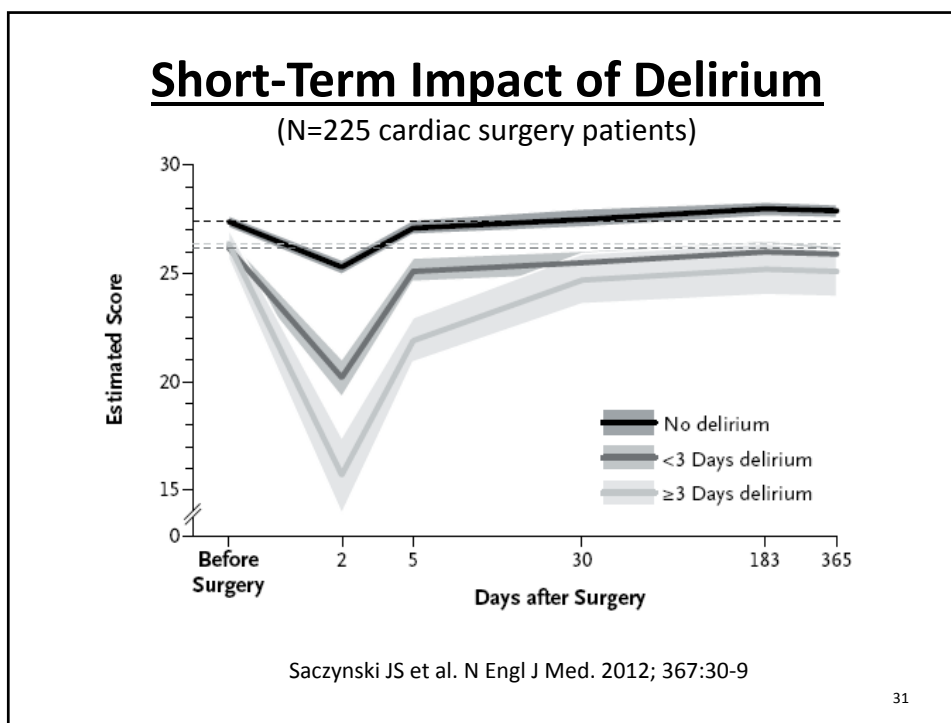
***Pearl: Reserve for patients with severe agitation which will:***

- 1. cause interruption of essential medical therapies (e.g., intubation)***
- 2. pose safety hazard to patient or staff***

**Recommended Approach:**

- Haloperidol 0.25-0.50 mg po or IM (IV short acting, risk of torsades). Atypicals equal efficacy.
- Repeat dose Q 30 minutes until patient manageable (maximum haloperidol dose 3-5 mg/24 hours)
- Maintenance: 50% loading dose in divided doses over next 24 hours
- Taper dose over next few days

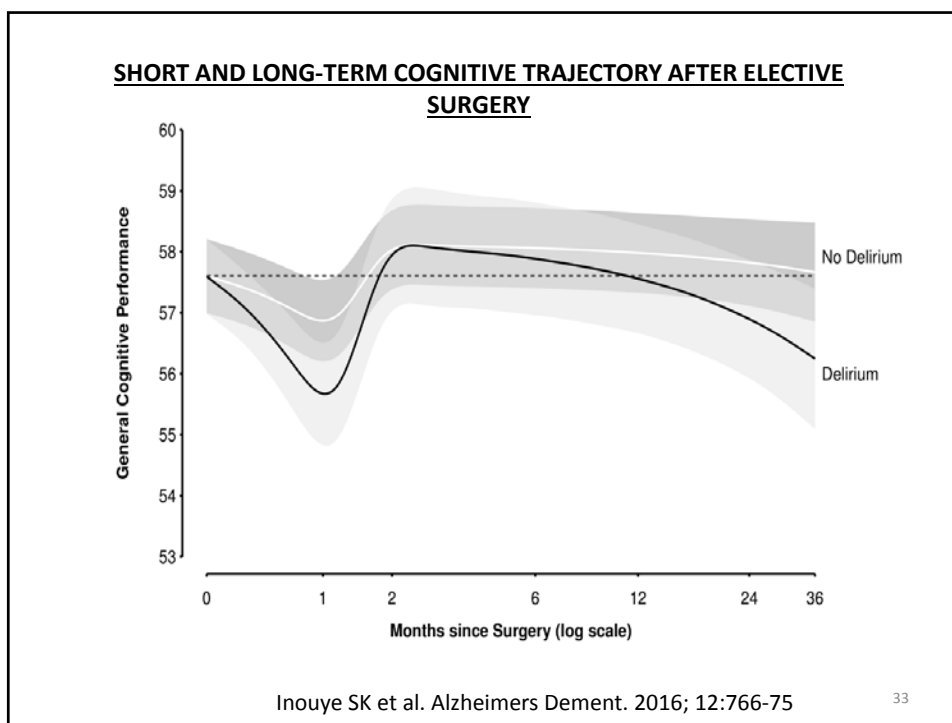
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### **Impact of Delirium (cont)**

- Delirium occurred in 46% patients following cardiac surgery in 225 patients
- Cognitive trajectory characterized by abrupt initial decline followed by gradual recovery over 6 months
- Patients did not get fully back to baseline even at 1 year





## Longer Term Impact: SAGES Study

- Delirium occurred in 24% patients following major elective surgery
- Delirium group, recovers above baseline at 2 months, then gradual decline out to 36 months substantially below baseline (equal to MCI).

### **Relationship of AD and Delirium**

- SAGES cohort (free of dementia at baseline) :
  - APOE-E4 not a risk factor for delirium in SAGES
  - MRI volumetric changes typical of AD not a risk factor for delirium in SAGES
- Thus, in SAGES important risk factors for AD do not confer increased risk for delirium— suggesting separate pathways.

Refs: Vasunilashorn, AJGP 2015; Cavallari, Neurobiol Aging. 2015

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### **BACK TO THE BEDSIDE:** **Pearls for Practice**

1. *Assess for delirium* in all older hospitalized patients: cognitive screening and CAM. Find out baseline.
2. *Evaluate medications* and reduce psychoactive drugs.
3. *Use nonpharmacologic approaches* to manage sleep, anxiety, and agitation.
4. *Reserve pharmacologic approaches* for patients with severe agitation or psychosis.
5. *Involve family members* for reorientation.
6. *Avoid bedrest orders*; encourage mobility.
7. Make sure patients have their *glasses, hearing aids, and dentures*.
8. *Communicate*: Keep patients/families involved.

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