

# Long-Term Cognitive Impairment, Delirium, and the ABCDEs





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### Disclosures: ICU Physician Vanderbilt

- Abbott, Hospira, Orion
- NIH and VA U.S. Federal Funding
- Author of PAD Guidelines of SCCM 2013
- Chair of SCCM Delirium section for PAD
- Co-Chair of SCCM ICU Liberation project to aid worldwide implementation



# **Quote of the Day #1**

Dr. Swenson explained, "I'll tell you the truth. What I have discovered...is not what I expected. It is something greater, much more ambitious than anything we had hoped for...in science: Never be so focused on what you are looking for that you overlook the thing you actually find."

Ann Patchett - 2011, State of Wonder

# Quote of the Day #2

"I came awake on the fifth day. My first memory is that of **floating up from the ocean bottom**, my eyes still waterlogged and **with what felt like scuba gear stuffed in my mouth and throat**. I couldn't speak. As I broke to the surface, I understood that I was still in the ICU at Our Lady, but I **heard nothing of what anybody said**.

Abraham Verghese - 2009, Cutting for Stone





Barr J, et al. Crit Care Med. 2013;41:263-306.

# Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit

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April 2010 Suggested Sites ▼ Wanderbilt University Nas... 🞒 Web Slice Gallery ▼









# www.icudelirium.org

"ICU stays lead to Alzheimer's-like problems in one-third of patients"

**CBS News** 

WATCH THE REPORT

for Medical Professionals

for Patients and Families

Search

GC

#### ABCDEs of Prevention and Safety

ABCDE is a standard bundle of ICU measures that includes spontaneous

Awakening and Breathing coordination, attention to the Choice of sedation,

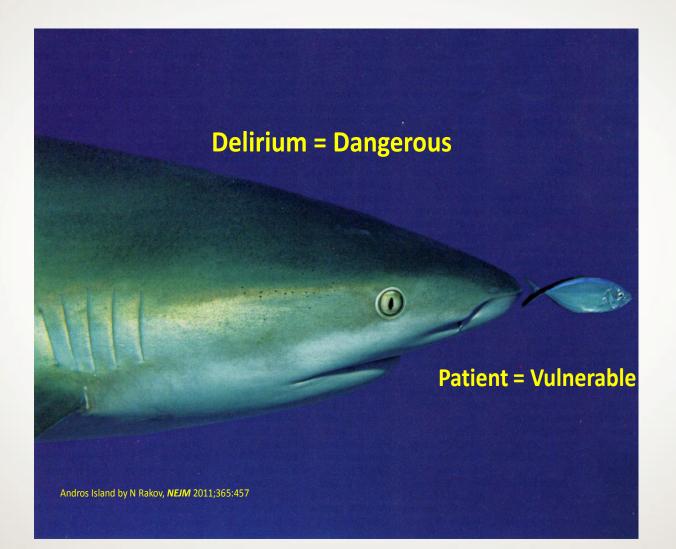
Delirium monitoring, and Early mobility and exercise. All individual components of this bundle are evidence based and can help standardize communication, improve interdisciplinary patient care, reduce mortality, and improve long-term cognitive and functional outcomes.

#### what is Delirium?

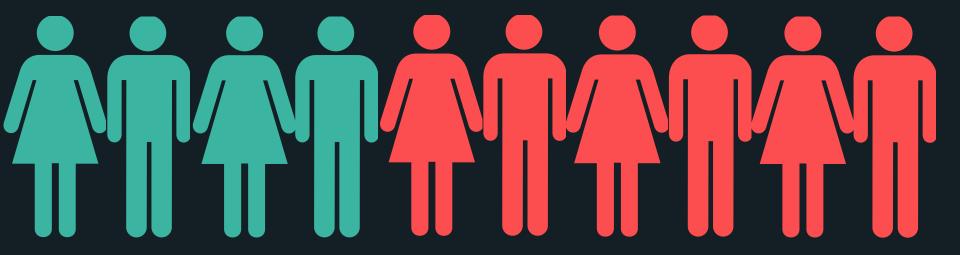
Delirium is basically inattention and confusion that represents the brain temporarily failing. A person who is delirious is unable to think clearly and can't make sense of what is going on around



### **Take Home Message**



# 6 out of 10 ICU patients are ≥ 65



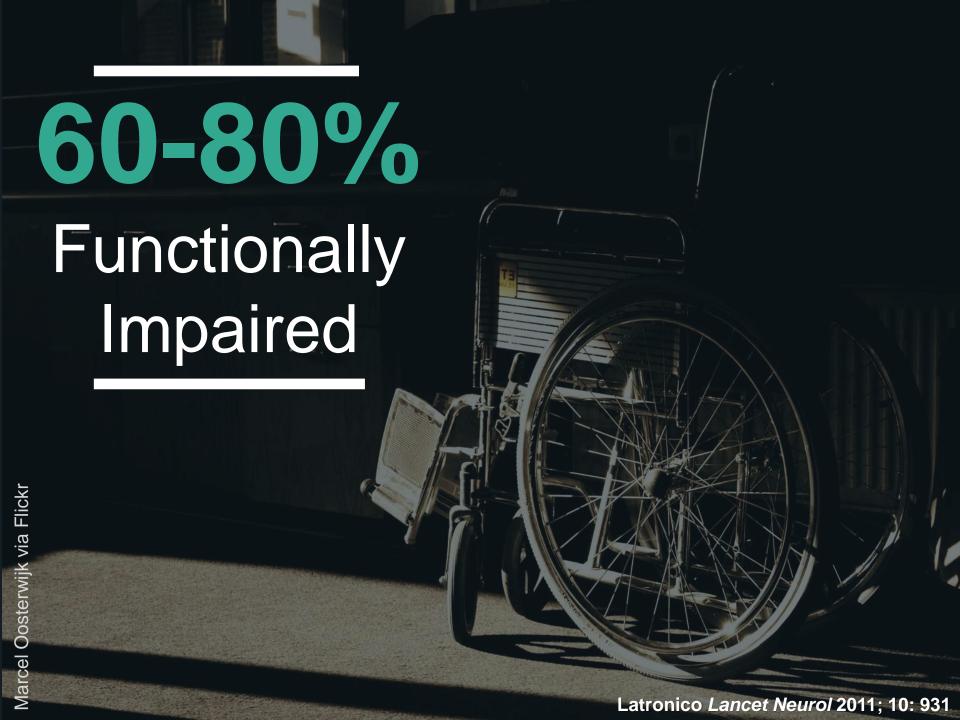
Angus Crit Care Med 2006; 34: 1016-1024

Angus *JAMA* 2000; 284: 2762-2770



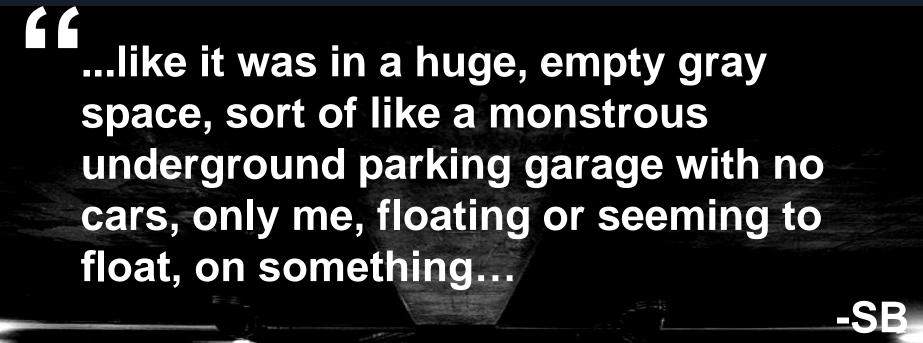
© rustyrhodes via Flickr

Wolters *Intensive Care Med* 2013; 39: 376 Jackson *AJRCCM* 2010; 182: 183 Girard *Crit Care Med* 2010; 38: 1513



# ICU Survivorship Family Hobbies Work

Iwashyna Annals of Int Med 2010; 153:204-5



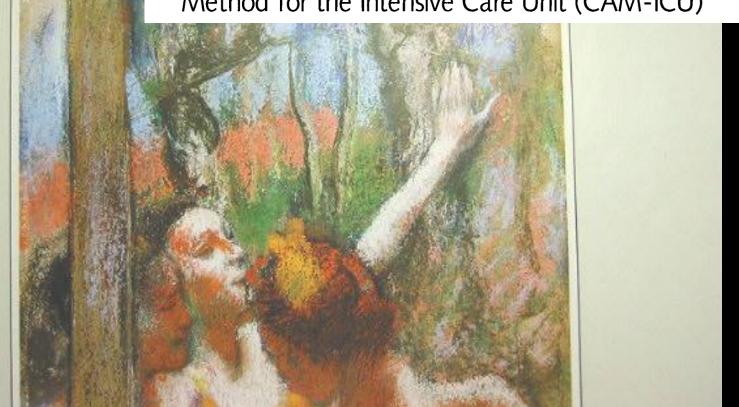


CRITICALLY ILL PATIENT

Ely EW, JAMA 2001;286:2703-10

# **Delirium in Mechanically Ventilated Patients**Validity and Reliability of the Confusion Assessment

Method for the Intensive Care Unit (CAM-ICU)

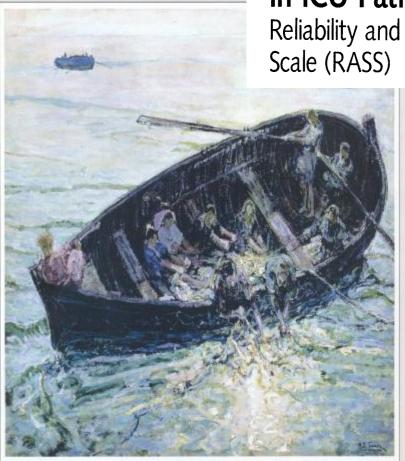


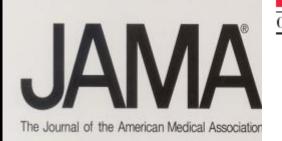


Ely EW, JAMA 2003;289:2983-91

# **Monitoring Sedation Status Over Time** in ICU Patients

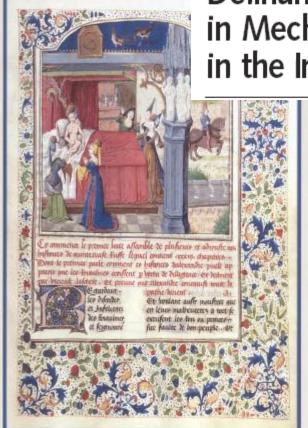
Reliability and Validity of the Richmond Agitation-Sedation Scale (RASS)



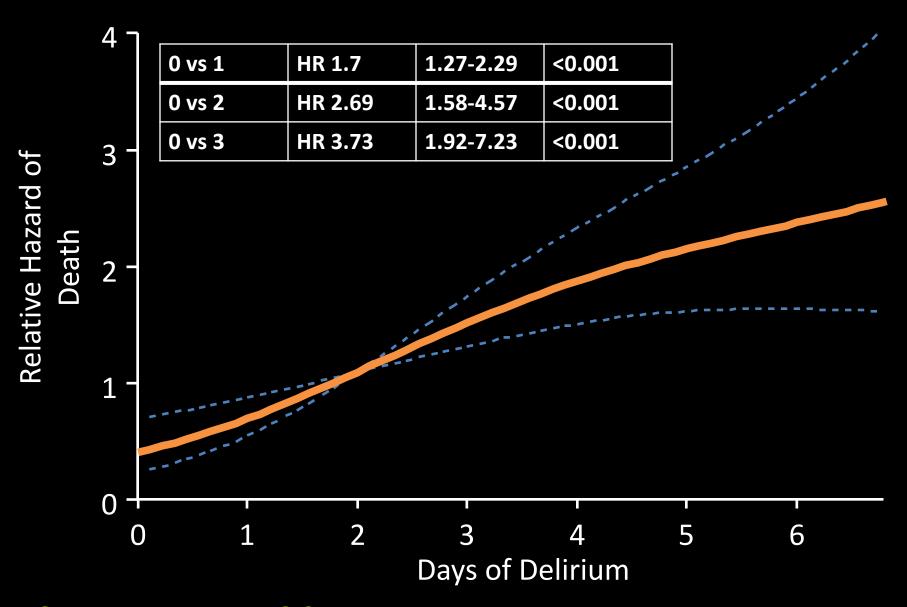


Ely EW, JAMA 2004;291:1753-62

Delirium as a Predictor of Mortality in Mechanically Ventilated Patients in the Intensive Care Unit

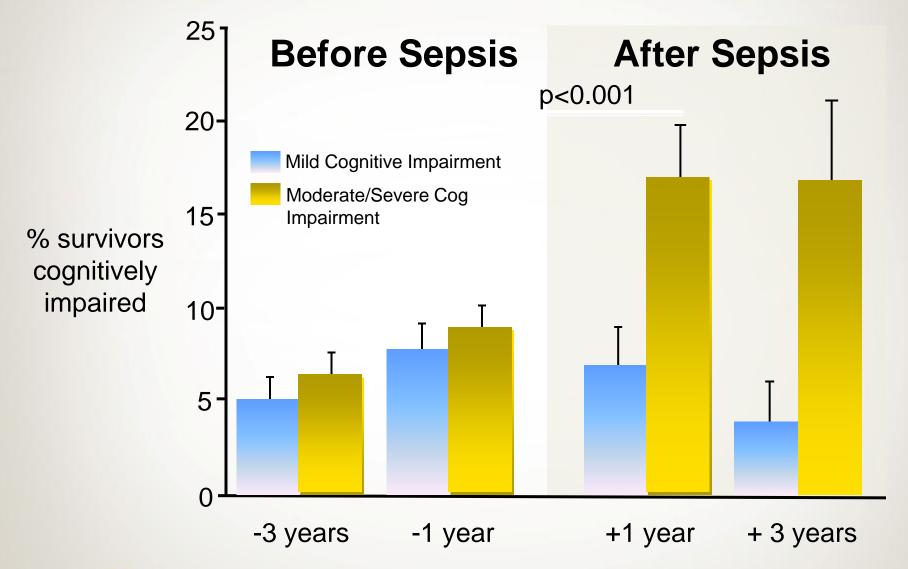


# **Delirium Duration & Mortality**



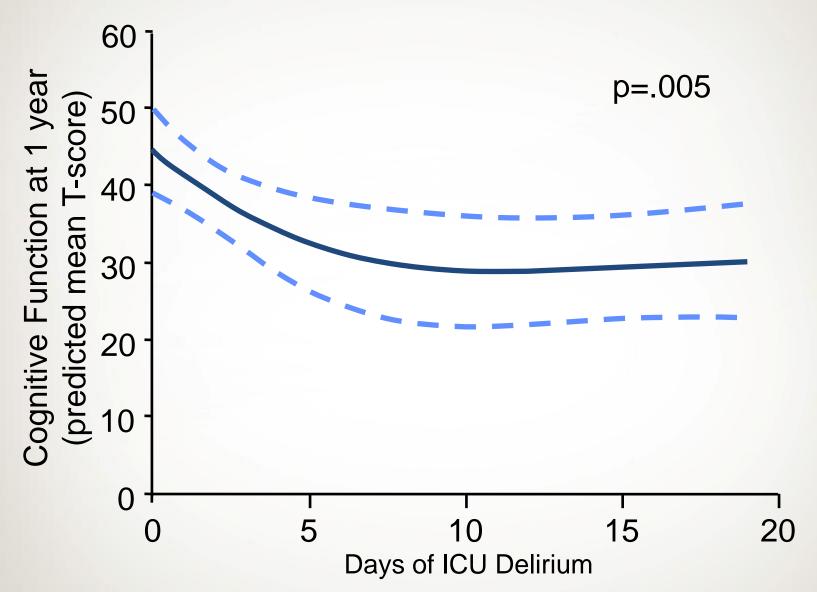
Shehabi Y, et al. CCM 2010; 38:2311-2318

# Cognitive Impairment: Sepsis



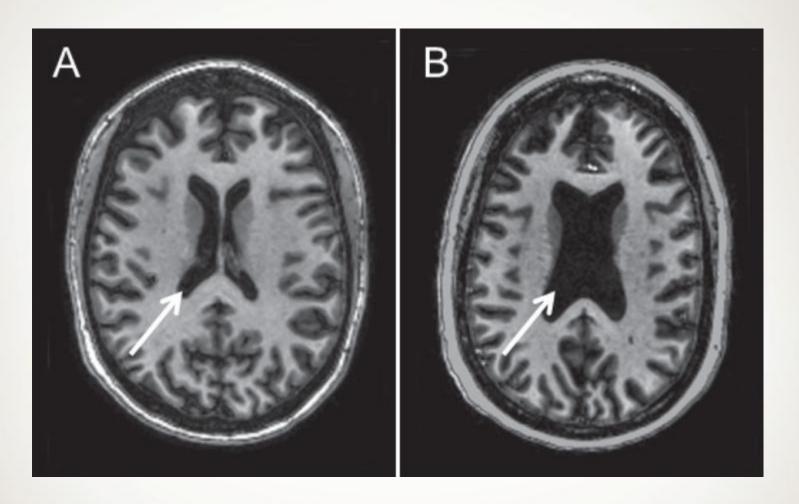


### Delirium and Long-Term Cognitive Outcomes





### Delirium and Brain Atrophy

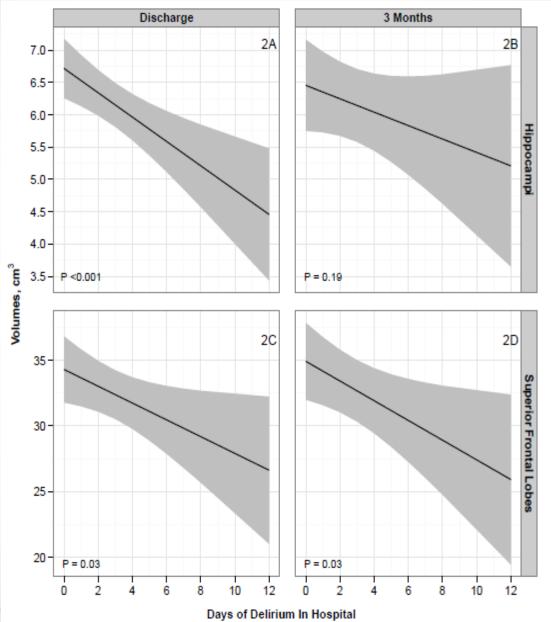


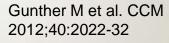
(A) 46 year old, no delirium

(B) 42 year old, 12 days of delirium



### The VISIONS MRI Studies







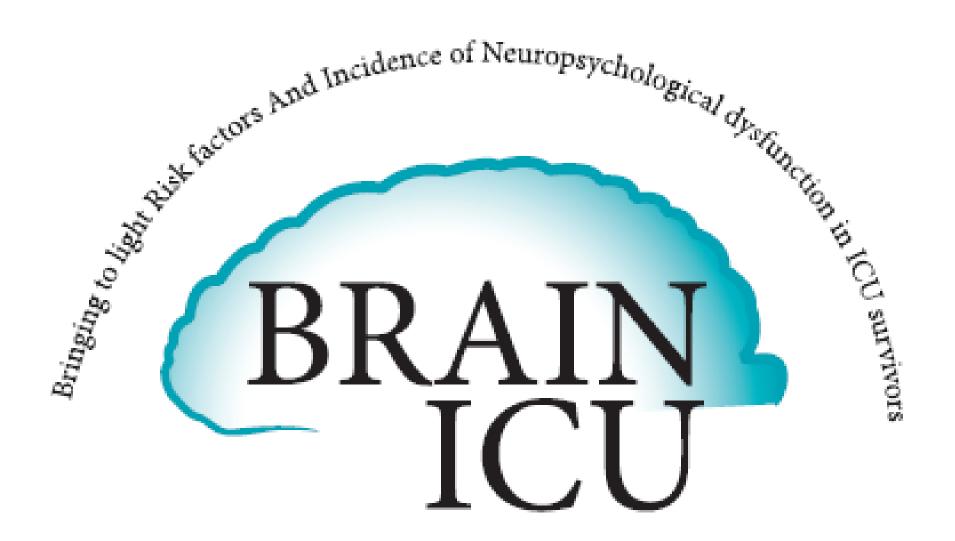
#### RESEARCH PAPER

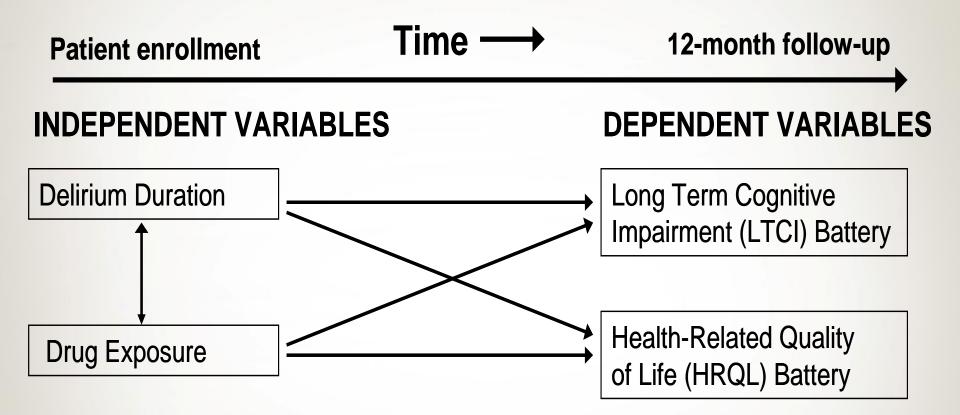
# Persistent cognitive impairment, hippocampal atrophy and EEG changes in sepsis survivors

Alexander Semmler,<sup>1,6</sup> Catherine Nichols Widmann,<sup>1</sup> Thorsten Okulla,<sup>1</sup> Horst Urbach,<sup>2</sup> Markus Kaiser,<sup>3,7</sup> Guido Widman,<sup>4</sup> Florian Mormann,<sup>4,8</sup> Julia Weide,<sup>1</sup> Klaus Fliessbach,<sup>4</sup> Andreas Hoeft,<sup>3</sup> Frank Jessen,<sup>5</sup> Christian Putensen,<sup>3</sup> Michael T Heneka<sup>1</sup>

- Bonn Germany, 2 center 6-24 month follow-up of 25 septic and 19 non-septic ICU survivors
- Sepsis survivors showed cognitive deficits in verbal learning and memory
- Significant reductions of hippocampal volume vs. controls
- More low frequency EEG activity indicating brain dysfunction









#### ORIGINAL ARTICLE

# Long-Term Cognitive Impairment after Critical Illness

P.P. Pandharipande, T.D. Girard, J.C. Jackson, A. Morandi, J.L. Thompson, B.T. Pun, N.E. Brummel, C.G. Hughes, E.E. Vasilevskis, A.K. Shintani, K.G. Moons, S.K. Geevarghese, A. Canonico, R.O. Hopkins, G.R. Bernard, R.S. Dittus, and E.W. Ely, for the BRAIN-ICU Study Investigators\*

#### ABSTRACT

#### BACKGROUND

Survivors of critical illness often have a prolonged and disabling form of cognitive impairment that remains inadequately characterized.



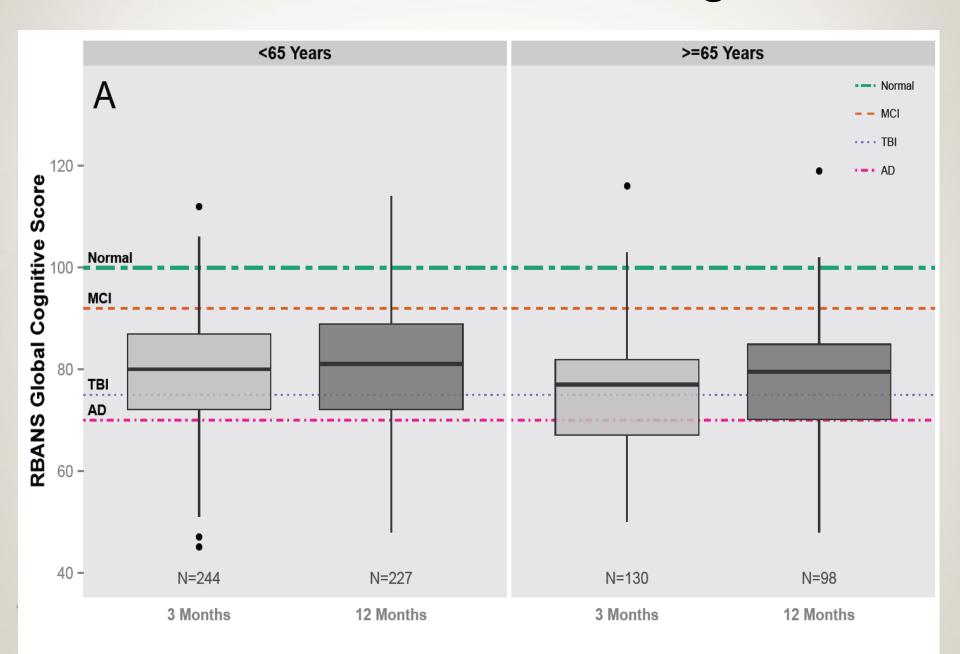
# Global Cognitive Scores

RBANS SCORES	3 months	12 months
	N (%)	N (%)
Extremely low (≤ 69)	90 (24%)	68 (21%)
Borderline (70-79)	106 (28%)	85 (26%)
Low average (80-89)	105 (28%)	103 (32%)
Average (90-109)	70 (19%)	67 (21%)
High Average (110-119)	2 (1%)	2 (1%)
Superior (120-129)	0 (0%)	0 (0%)
Very superior (≥130)	0 (0%)	0 (0%)

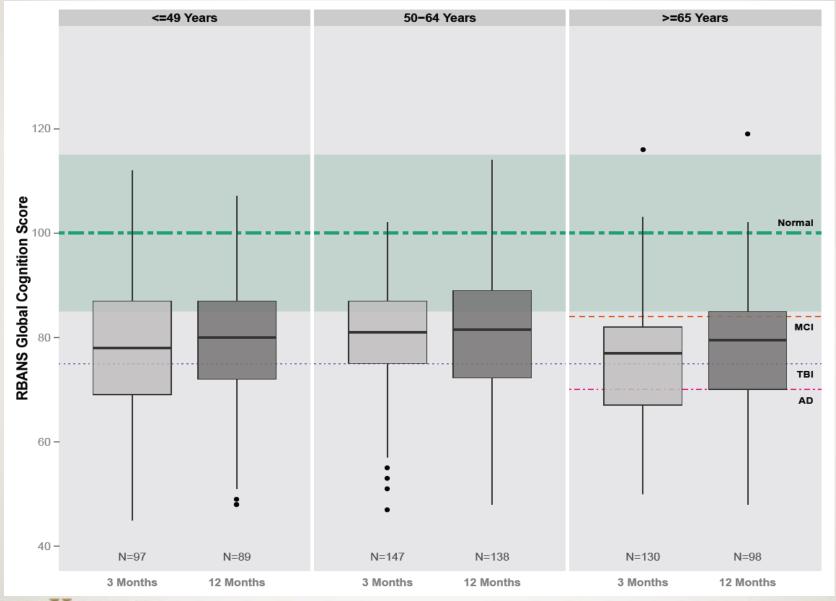
Scores of <70 seen in patients with Alzheimer's disease; mild MCI have scores around 84. Dementias in 80s



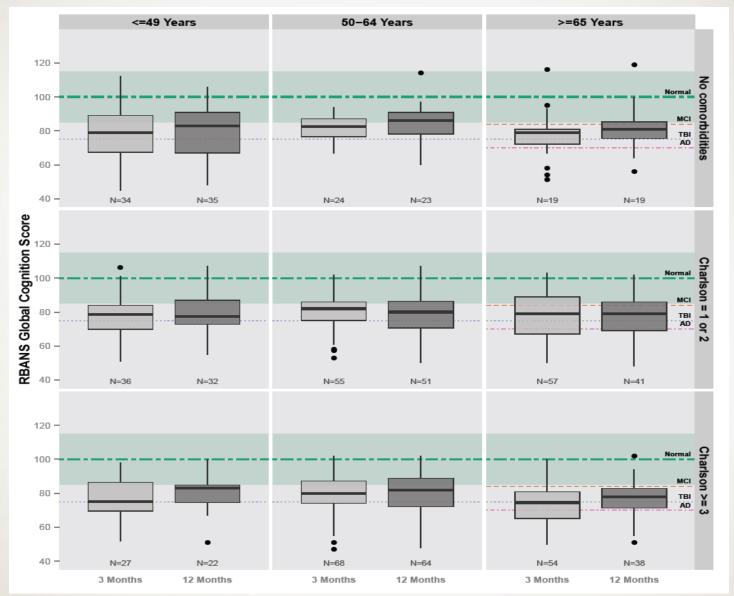
# The Picture of Dementia Following ICU Care



# Global Cognitive Scores by Age

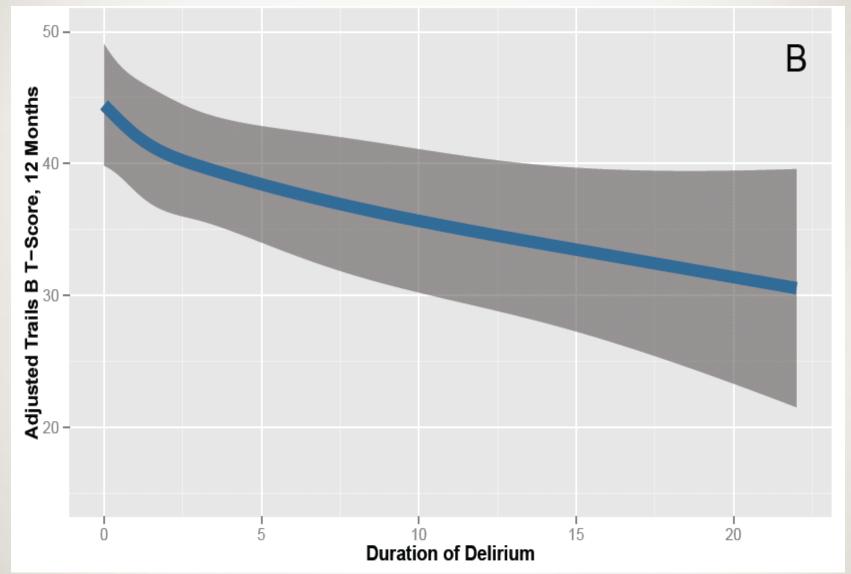


### Global Cognitive Scores by Age and Comorbidity





# Delirium and Executive Function





# THE LANCET

Wokume 372 · Number 9634 · Pages 177-262 · July 19-25, 2008

www.thelancet.com

"Dementia is perhaps the cruellest manifestation of ageing, inexorably melting away all that which makes us individual and human."

See Editorial page 177

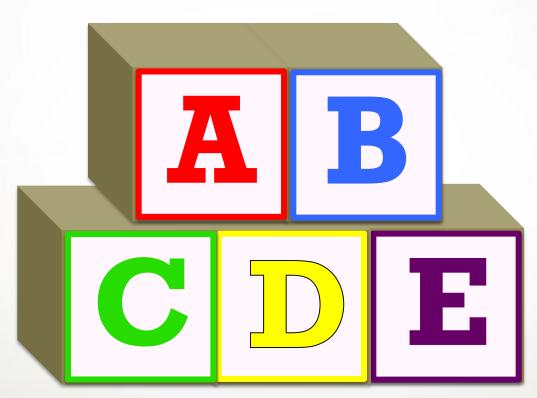




Barr J, et al. Crit Care Med. 2013;41:263-306.

## **ABCDEs:**

# Building blocks of managing Pain, Agitation & Delirium





# Birth of the ABCDEs

Ely EW, et al. N Engl J Med 1996;335:1864-9

Kress JP, et al. N Engl J Med 2000;342:1471-7

Girard TD, et al. <u>Lancet</u> 2008;371:126-34

Strom T, et al. <u>Lancet</u> 2010;375:475-480

Pandharipande PP, et al. <u>JAMA</u> 2007;298:2644-53

Riker R. et al, <u>JAMA</u>. 2009;301:489-499

Schweickert et al, <u>Lancet</u> 2009;373:1874-82

**SBT** 

SAT

Remove (A+B)

Remove Sedation

Sedation choice

Sedation choice

Early Mobility

...quick tour of the RCT literature...







ABCDE's of Prevention and Safety

Awakening and Breathing Coordination

CHOICE OF SEDATION

**D**ELIRIUM MONITORING

EXERCISE

Additional Resources

LONG-TERM OUTCOMES

PEDIATRIC CARE

TERMINOLOGY AND MNEMONICS

HISTORICAL REFERENCE

LINKS AND TIMELIN

#### Delirium Prevention and Safety: Starting with the ABCDE's

It is essential to consider delirium management in the broader picture of ICU patient care as a major piece of the current guidelines for Pain, Agitation, and Delirium (PAD) of the Society of Critical Care Medicine (SCCM). Advancements in research and technology are resulting in higher acuity and increased complexity of care, which is resulting in drastic increases in workload and demands on staff. More than ever, there is a great need to develop simpler ways of implementing safer and better care into practice for our sickest patients.

The ABCDE bundle is one way to align and coordinate care, which includes specific focus on delirium as a component of the overall care patients receive including sedation and pain medications, breathing machines, and mobilization. This bundle has multiple, evidenced based components, interdependent, and designed to:

- · Improve collaboration and coordination among clinical team members
- Standardize care processes
- Decrease delirium
- · Break the cycle of oversedation and prolonged ventilation

What are the components of the ABCDE bundle?

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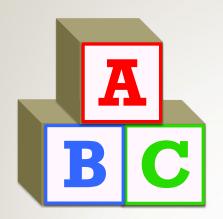












#### **Awake and Breathing Coordination**

- **▶** Duration of mechanical ventilation
- **▶** Duration of coma
- **♦** Mortality



#### **Choose light sedation & avoid benzos**

- **▶** Duration of mechanical ventilation
- **Ψ** Mortality
- **♦** Delirium



#### **Delirium monitoring & management**

- **↑** Delirium detection
- **↑** Delirium predictor of mortality and morbidity

#### **Early Mobility & Environment**

- **▶** Duration of delirium
- **♦** Disability
- **Ψ** ICU Length of Stay
- **▶** Rehospitalization/Mortality

Morandi et al Curr Opin Crit Care 2011;17:43-9 Vasilevskis et al Crit Care Med 2010;38:S683-91 Vasilevskis et al Chest 2010;138:1224-1233

Zaal et al, ICM 2013;39:481-88

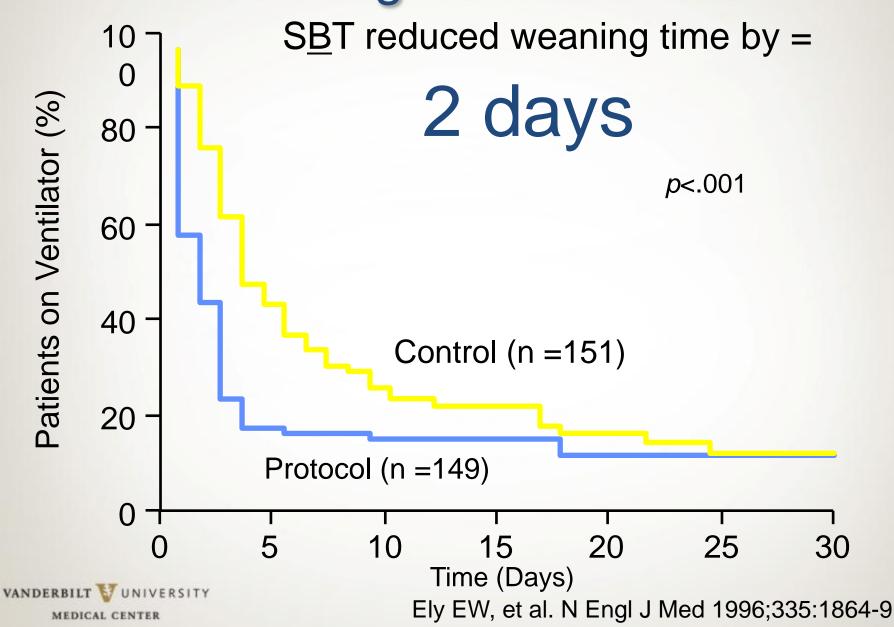
Colombo et al, Minerva Anest 1012;78:1026-33



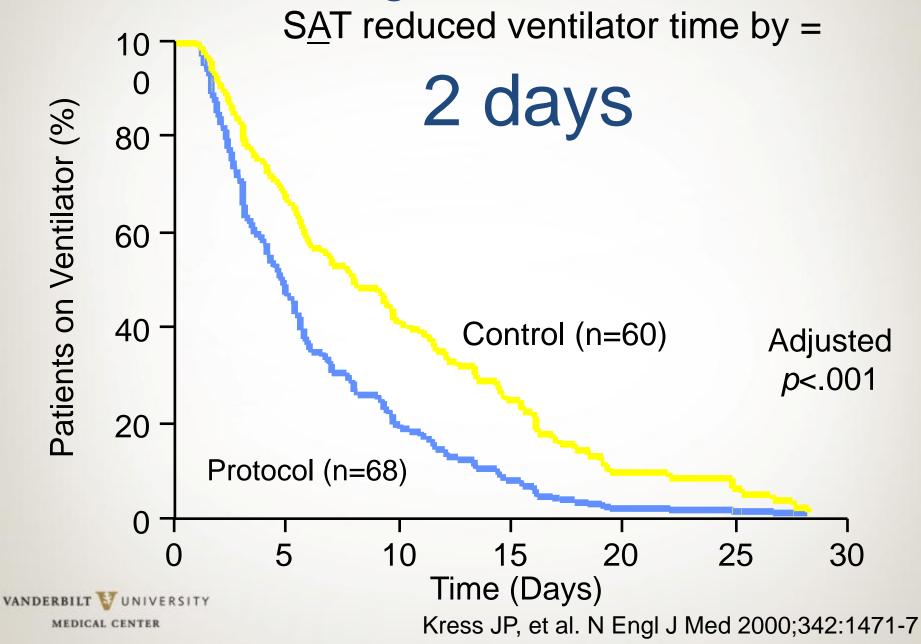




# Liberating from Ventilator







# SATs (Daily Interruption) Used in Minority Around World

- Canada 40% get SATs (273 physicians in 2005)
- U.S. 40% get SATs (2004-05)
- France 10% get SATs (44 ICUs in 2005)
- Germany 34% get SATs (214 ICUs in 2006)
- Brazil 32% get SATs (1,015 MDs in 2008)
- UK 28% get SATs, 82% use midazolam (2009)
- Belgium 18% get SATs (587 nurses / 99 hospitals in 2012)

Mehta S, CCM 2006;34:374-80. Tanios M, Proc Am Thorac Soc 2:A793, 2005 Devlin J, CCM 2006;34:556-57. Payen JF, Anesthes 2007;106:687-95 Martin J and Spies C, Crit Care 2007;11:R124
Ramaswamy S, Intens Care Med (ESICM 2009)
Salluh J, Brazil, J Crit Care 2009
Sneyers B, Brussels, Abst #324 2012



# THE LANCET

Volume 371 - Number 9607 - Pages 89-176 - January 12-18, 2008

www.thelancet.com

#### **Articles**

#### SAT + SBT = 4 day shorter ICU/hosp LOS

Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial

Lancet 2008; 371: 126-34 See Comment page 95

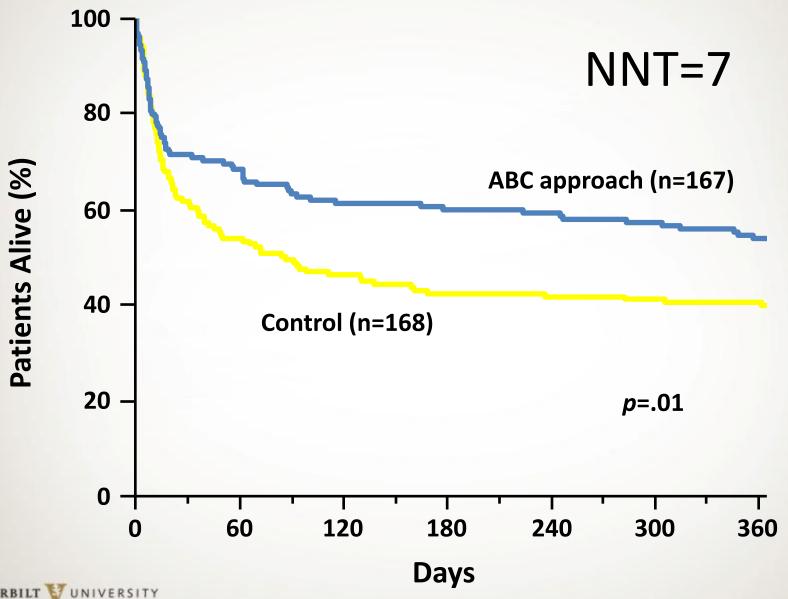
Founded 1823 - Published weekly

Timothy D Girard, John P Kress, Barry D Fuchs, Jason W W Thomason, William D Schweickert, Brenda T Pun, Darren B Taichman, Jan G Dunn, Anne S Pohlman, Paul A Kinniry, James C Jackson, Angelo E Canonico, Richard W Light, Ayumi K Shintani, Jennifer L Thompson, Sharon M Gordon, Jesse B Hall, Robert S Dittus, Gordon R Bernard, E Wesley Ely

Statins for diabetic patients meta-analysis	Protocols for mechanically	Clinical sigms predictive of	Acute pancreatitis	Preterm Birth 2:
	ventilated patients in	severe illness in babies aged	Serpape (4)	Interventions to reduce
Seic page LLT	Intensive care See page SJ6	Sess than 2 months Serpage 135		morbidity and mortalit see page 364.

VANDE

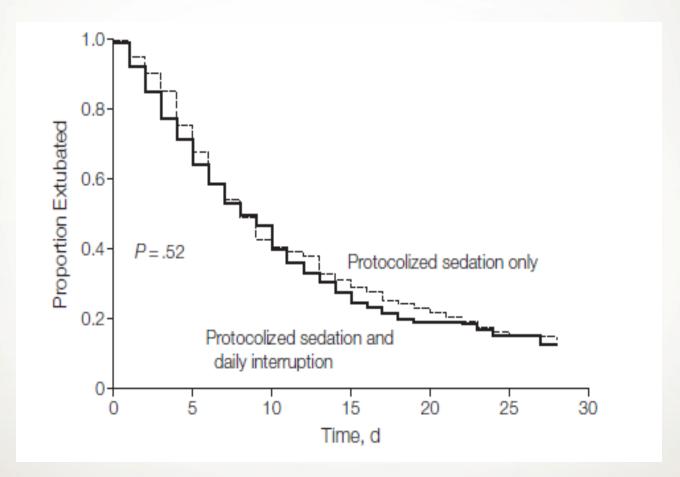
## **ABC Trial: One-Year Survival**





Girard TD, et al. Lancet 2008;371:126-34

# Sedation Interruption in SLEAP





## Benzodiazepine Use in Trials \*

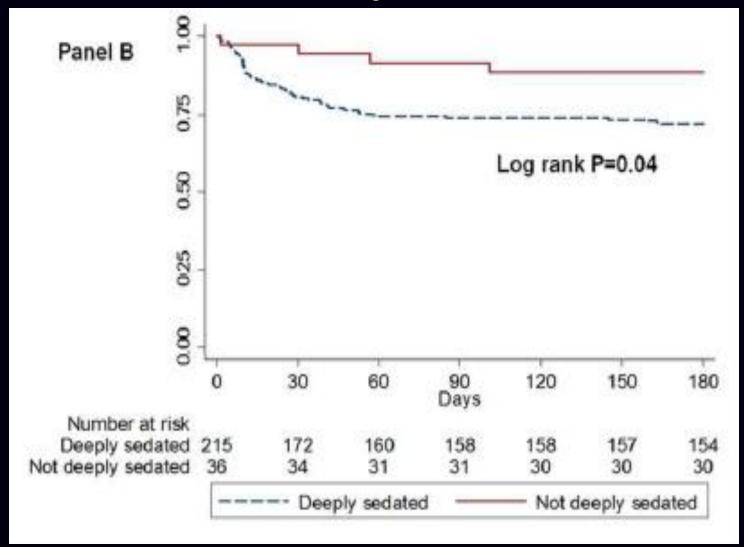
Study	Control	Treatment
Kress NEJM 2000	90 mg/day	53 mg/day
Girard ABC Lancet 2007	84 mg/day	54 mg/day
Mehta SLEAP JAMA 2012	82 mg/day	102 mg/day
OSCILLATE NEJM 2013	141 mg/day	199 mg/day

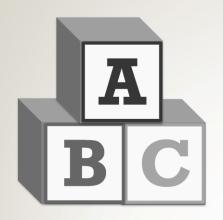


<sup>\*</sup> All values converted and expressed as mean midazolam dose per patient, median for ABC study were 8 mg and 5 mg, respectively

#### SPICE Study – first 48 hours

mean 50 mg/d benzos





#### **Awake and Breathing Coordination**

- **▶** Duration of mechanical ventilation
- **▶** Duration of coma
- **♦** Mortality



#### **Choose light sedation & avoid benzos**

- Duration of mechanical ventilation
- **Ψ** Mortality
- **♦** Delirium



#### **Delirium monitoring & management**

- **↑** Delirium detection
- **↑** Delirium predictor of mortality and morbidity

#### **Early Mobility & Environment**

- **▶** Duration of delirium
- **♦** Disability
- **Ψ** ICU Length of Stay
- **▶** Rehospitalization/Mortality

Morandi et al Curr Opin Crit Care 2011;17:43-9 Vasilevskis et al Crit Care Med 2010;38:S683-91 Vasilevskis et al Chest 2010;138:1224-1233

Zaal et al, ICM 2013;39:481-88

Colombo et al, Minerva Anest 1012;78:1026-33













Articles

# A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial



Thomas Strøm, Torben Martinussen, Palle Toft

#### Summary

Background Standard treatment of critically ill patients undergoing mechanical ventilation is continuous sedation. Daily interruption of sedation has a beneficial effect, and in the general intesive care unit of Odense University Hospital, Denmark, standard practice is a protocol of no sedation. We aimed to establish whether duration of mechanical ventilation could be reduced with a protocol of no sedation versus daily interruption of sedation.

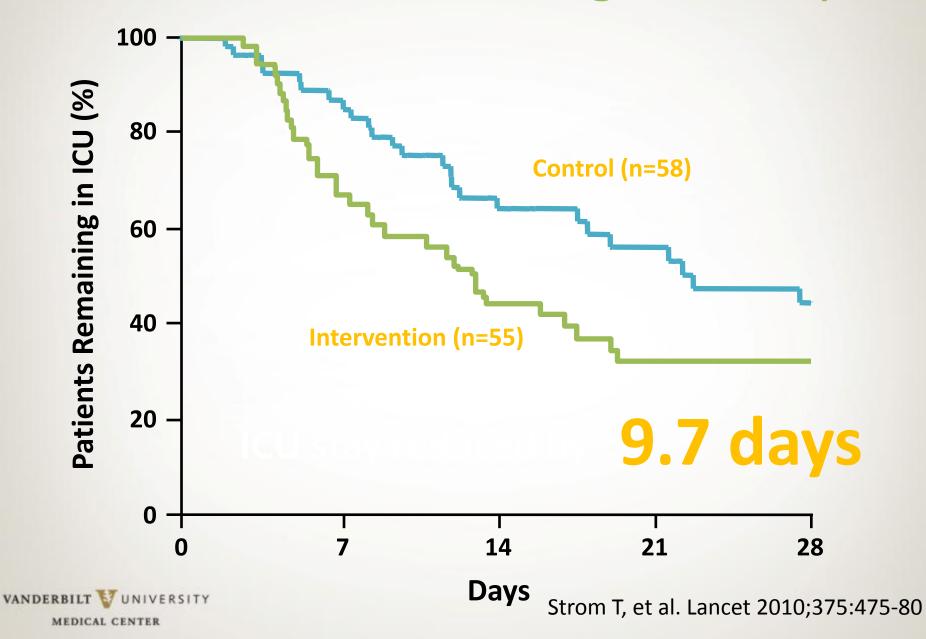
Lancet 2010; 375: 475-80

Published Online January 29, 2010 DOI:10.1016/S0140-6736(09)62072-9

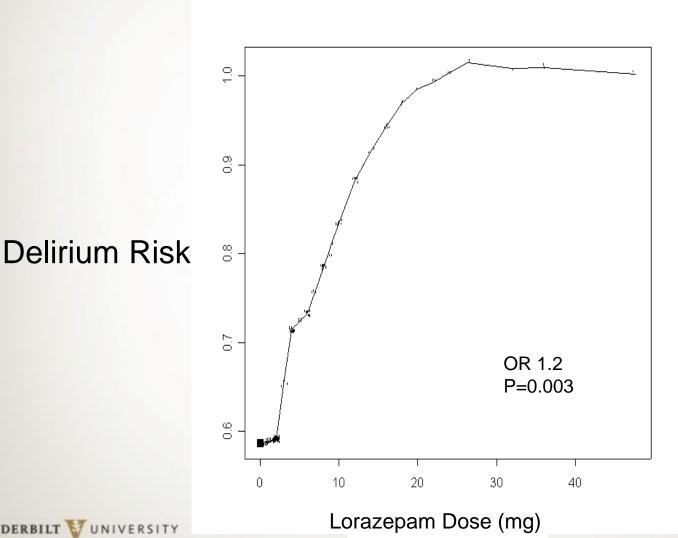
See Comment page 436



## No Sedation: ICU Length of Stay



#### Benzodiazepines and Delirium Risk





Pandharipande et al. Anesthesiology 2006: 124:21-6

#### **Buffalos to Beer to Brain Cells**

Cliff the mailman and philosopher

Cliff: "Well you see, Norm, it's like this . . A herd of buffalo can only move as fast as the slowest buffalo. And when the herd is hunted, it is the slowest and weakest ones at the back that are killed first. This natural selection is good for the herd as a whole, because the general speed and health of the whole group keeps improving by the regular killing of the weakest members."



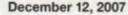


#### Buffalos to Beer to Brain Cells

"In much the same way, Norm, the human brain can only operate as fast as the slowest brain cells. Now, as we know, excessive intake of alcohol kills brain cells. But naturally, it attacks the slowest and weakest brain cells first. In this way, regular consumption of beer eliminates the weaker cells, making the brain a faster and more efficient machine. And that, Norm, is why you always feel smarter after a few beers."











CARING FOR THE CRITICALLY ILL PATIENT

# Effect of Sedation With Dexmedetomidine vs Lorazepam on Acute Brain Dysfunction in Mechanically Ventilated Patients

The MENDS Randomized Controlled Trial

Pratik P. Pandharipande, MD, MSCI
Brenda T. Pun, RN, MSN, ACNP
Daniel L. Herr, MD
Mervyn Maze, MB, ChB
Timothy D. Girard, MD, MSCI
Russell R. Miller, MD, MPH
Ayumi K. Shintani, MPH, PhD
Jennifer L. Thompson, MPH
James C. Jackson, PsyD
Stephen A. Deppen, MA, MS
Renee A. Stiles, PhD
Robert S. Dittus, MD, MPH
Gordon R. Bernard, MD
E. Wesley Ely, MD, MPH

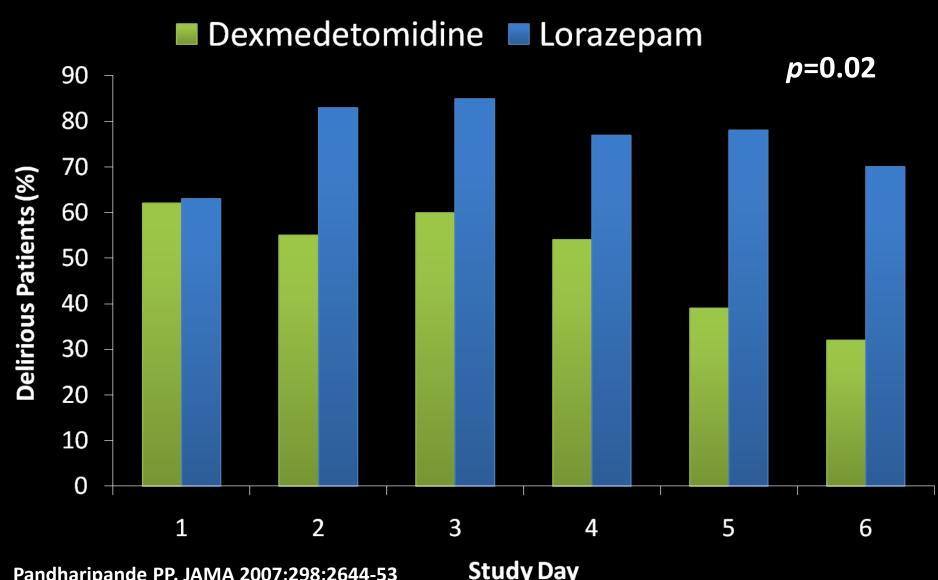
**Context** Lorazepam is currently recommended for sustained sedation of mechanically ventilated intensive care unit (ICU) patients, but this and other benzodiazepine drugs may contribute to acute brain dysfunction, ie, delirium and coma, associated with prolonged hospital stays, costs, and increased mortality. Dexmedetomidine induces sedation via different central nervous system receptors than the benzodiazepine drugs and may lower the risk of acute brain dysfunction.

**Objective** To determine whether dexmedetomidine reduces the duration of delirium and coma in mechanically ventilated ICU patients while providing adequate sedation as compared with lorazepam.

**Design, Setting, Patients, and Intervention** Double-blind, randomized controlled trial of 106 adult mechanically ventilated medical and surgical ICU patients at 2 tertiary care centers between August 2004 and April 2006. Patients were sedated with dexmedetomidine or lorazepam for as many as 120 hours. Study drugs were titrated to achieve the desired level of sedation, measured using the Richmond Agitation-Sedation Scale (RASS). Patients were monitored twice daily for delirium using the Confusion Assessment Method for the ICU (CAM-ICU).

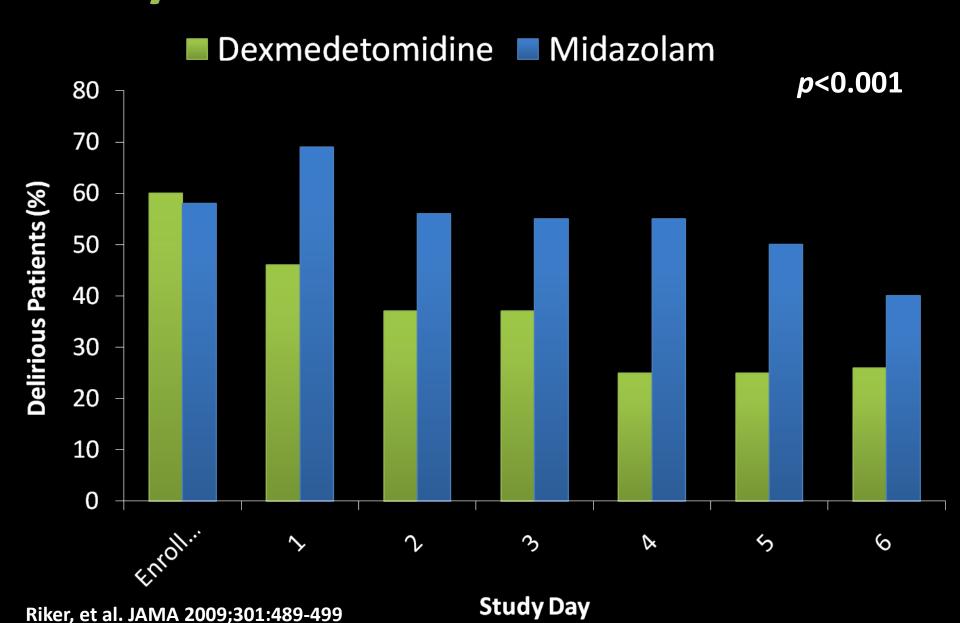
**Main Outcome Measures** Days alive without delirium or coma and percentage of days spent within 1 RASS point of the sedation goal.

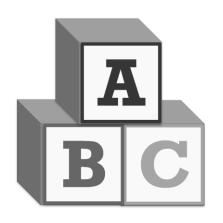
# Daily Risk of Delirium in MENDS



Pandharipande PP. JAMA 2007;298:2644-53 Pandharipande PP. Crit Care 2010;14:R38

# Daily Risk of Delirium in SEDCOM





#### **Awake and Breathing Coordination**

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#### **Choose light sedation & avoid benzos**

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#### **Early Mobility & Environment**

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Morandi et al Curr Opin Crit Care 2011;17:43-9 Vasilevskis et al Crit Care Med 2010;38:S683-91 Vasilevskis et al Chest 2010;138:1224-1233

Zaal et al, ICM 2013;39:481-88

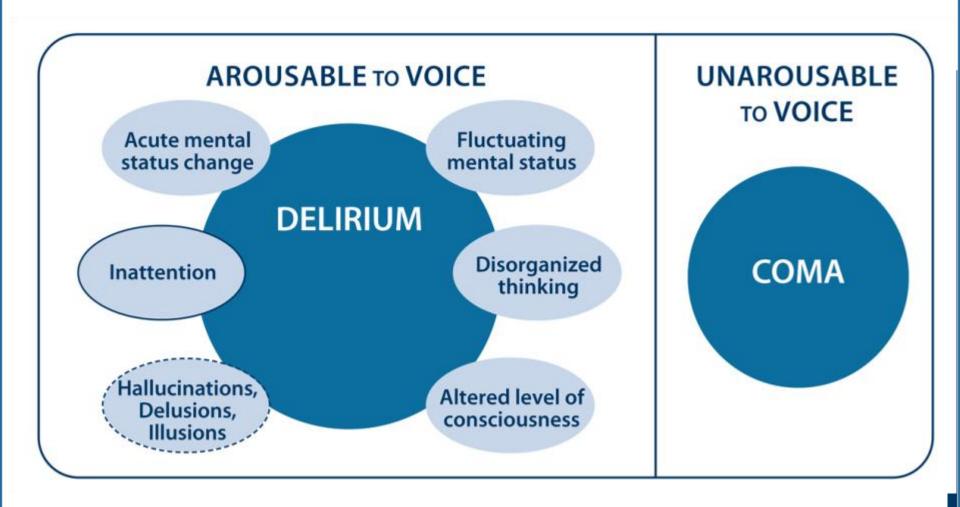
Colombo et al, Minerva Anest 1012;78:1026-33

www.SEDATION-cme.org





#### **Cardinal Symptoms of Delirium and Coma**



#### 2013 PAD Guidelines:

# "We recommend routine monitoring for delirium in adult ICU patients"

Grade 1B Recommendation



# If delirium is not screened for using a validated delirium screening tool it is missed ~75% of time.

Inouye SK *Arch Intern Med.* 2001;161:2467-2473. Devlin JW *Crit Care Med.* 2007;35:2721-2724. Spronk PE *Intensive Care Med.* 2009;35:1276-1280. van Eijk MM *Crit Care Med.* 2009;37:1881-1885.



# Don't forget about Dr. DRE



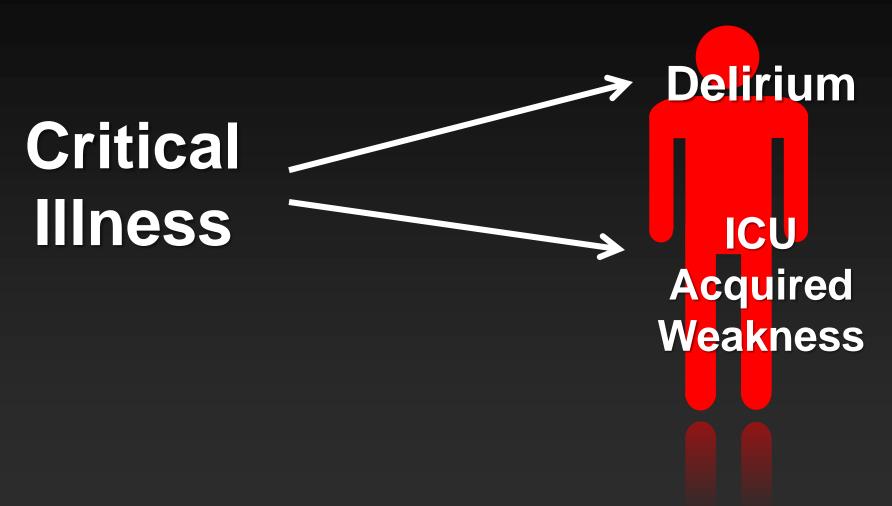
<u>D</u>iseases Sepsis, COPD, CHF

<u>Drug Removal</u>
SATs and stopping benzodiazepines/
narcotics

**E**nvironment

Immobilization, sleep and day/night, hearing aids, glasses, noise

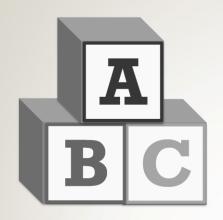
# Critical Illness



Ely, et al., *JAMA* 2004; 291: 1753-62 Devlin et al., *Intensive Care Med* 2007; 35:2721-4 Bergeron et al., *Intensive Care Med* 2001; 27:859-Needham DM *JAMA* 2008; 300: 1685-84 DeJonghe, et al., *JAMA* 2002; 288: 2859-67 Baseball (like life) is 90% mental...

# Baseball (like life) is 90% mental... the other half is physical

Yogi Berra



#### **Awake and Breathing Coordination**

- **▶** Duration of mechanical ventilation
- **▶** Duration of coma
- **♦** Mortality



#### **Choose light sedation & avoid benzos**

- **▶** Duration of mechanical ventilation
- **Ψ** Mortality
- **♦** Delirium



#### **Delirium monitoring & management**

- **↑** Delirium detection
- **↑** Delirium predictor of mortality and morbidity

#### **Early Mobility & Environment**

- **▶** Duration of delirium
- **♦** Disability
- **Ψ** ICU Length of Stay
- **▶** Rehospitalization/Mortality

Morandi et al Curr Opin Crit Care 2011;17:43-9 Vasilevskis et al Crit Care Med 2010;38:S683-91 Vasilevskis et al Chest 2010;138:1224-1233

Zaal et al, ICM 2013;39:481-88

Colombo et al, Minerva Anest 1012;78:1026-33

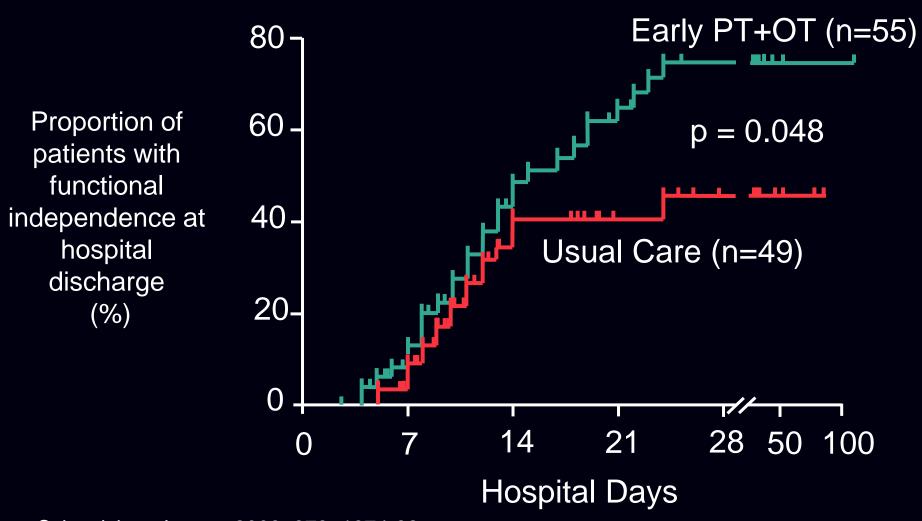








# Early physical rehabilitation



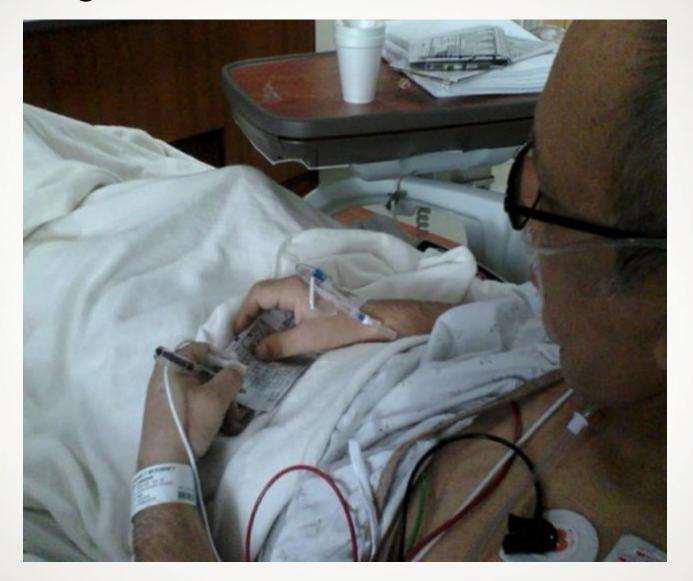
Schweickert, Lancet 2009; 373: 1874-82

# Mobilization = Less Delirium

Variable	Intervention	Control	P-value
	(n=49)	(n=55)	
ICU/Hosp Delirium Days	2 days	4 days	0.03
Time in ICU with Delirium	33%	57%	0.02
Time in Hosp. with Delirium	28%	41%	0.01



#### Mobilizing the Brain with Sudoku & Scrabble



I survived and that is the main thing. And I am so grateful to God that I survived and am now off all oxygen and consider myself all well except that I can't remember to take my medications...



-SB

#### **Quote of the Day #1**

Dr. Swenson explained, "I'll tell you the truth. What I have discovered...is not what I expected. It is something greater, much more ambitious than anything we had hoped for...in science: Never be so focused on what you are looking for that you overlook the thing you actually find."

Ann Patchett - 2011, State of Wonder

#### Quote of the Day #2

"I came awake on the fifth day. My first memory is that of **floating up from the ocean bottom**, my eyes still waterlogged and **with what felt like scuba gear stuffed in my mouth and throat**. I couldn't speak. As I broke to the surface, I understood that I was still in the ICU at Our Lady, but I **heard nothing of what anybody said**.

Abraham Verghese - 2009, Cutting for Stone

icudelirium.org

RESEARCH DESIGNED TO TURN
MIRRORS INTO WINDOWS



# ICU Delirium and Cognitive Impairment Study Group: selected local members

Pratik Pandharipande

Jim Jackson

Jin Han

**Ed Vasilevskis** 

Chris Hughes

Alessandro Morandi

Paula Watson

**Lorraine Ware** 

**Gordon Bernard** 

**Bob Dittus** 

**Ted Speroff** 

Wes Ely

Leanne Boehm

Joyce Okahashi

Cayce Strength

Brenda Pun

Lauren Hardy

**Amy Lipsey** 

Ryan Black

Jessica McCurley

Michael Santoro

**Carrie Jones** 

Morgan Crawford

Mayur Patel

Tim Girard

John Gore

**Baxter Rogers** 

Stephan Heckers

Cathy Fuchs

Heidi Smith

Ty Berutti

**Brad Strohler** 

Elizabeth Card

Jennifer Thompson

Ayumi Shintani

**Stephanie Hamilton** 



## Key Epidemiological Points:

- Patients suffer from long-lasting and disabling aspects of critical illness that demand our attention as a medical community
- 2) Acquired or accelerated cognitive impairment is a major public health problem following ICU care for both the old and young
- 3) This cognitive impairment appears most pronounced in domains of executive dysfunction and memory
- 4) Frontal lobe and hippocampal atrophy are being consistently found in recent studies
- 5) This injury is likely distinct from or complementary to Alzheimer's pathology, though we are in our infancy in learning about this entity (e.g., large pathology study under review)
- 6) Delirium and drug exposure appear to be the most modifiable aspects of care, with need for more trials to delineate next steps



## Key Management Points:

- Establish an overarching protocolized approach to daily ICU patient management using 2013 PAD Guidelines
- 2) Assess & treat pain first (may be sufficient)
- 3) If patient remains agitated after adequately treating pain, use prn/bolus sedation initially, if frequent boluses (>3/hr) use continuous sedation
- 4) Avoid traditional benzodiazepines in most patients
- 5) Turn off sedation daily and restart only if needed at lowest dose to maintain chosen target level of consciousness
- 6) Deep sedation (RASS -4/-5) appears harmful; target awake/alert
- 7) Screen for delirium (CAM-ICU or ICDSC); If delirious, first seek reversible causes and attempt non-pharmacologic management
- 8) Use the ABCDEs to improve outcomes for your patients



## 2013 PAD Guidelines: Benzodiazepines

- General Choice: non-benzodiazepine sedation strategies preferred (propofol or dex), with statistically shorter ICU LOS (~0.5 day, p=0.04)
- 2. Benzodiazepines risk factor for delirium
- 3. Ventilated patients at risk for delirium prefer dexmedetomidine to benzodiazepine
- Delirious ICU patients (excluding DTs and benzo w/drawal) - give dexmedetomidine (alpha-2) and not benzo (GABA)

