

A new frontier in sedation and critical care: saving the injured brain



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I disclose having received grants and/or honoraria:
GSK, Hospira, Lilly, Cumberland, Masimo and Aspect

Front End vs. Back End of critical care

“Peeling back” critical care
Studying “iatrogenesis imperfecta”

Delirium: Snapshot Update (1)

- 40-60% nonvent & 60-80% of ventilated patients
- MODS = ALI + AKI + ...ABI
- ABI = Acute Brain Injury = Organ Dysfunction
- Hypoactive Delirium invisible and missed in 75%
- Most common organ dysfunction, > half ICU days

Spronk P, ICM 2009

Schweickert W, Lancet 2009

Vasilevskis E, Chest 2010

Devlin J, CCM 2010

Delirium: Snapshot Update (2)

- Predicts 3-fold increase death; 10% per day rise
- Predicts longer ICU and hospital LOS, higher cost of care, disposition other than home
- Acquired dementia-like long-term disability
- CIBI (Critical Illness-associated Brain Injury)
- Not TBI but CIBI

Pisani M, CCM 2010

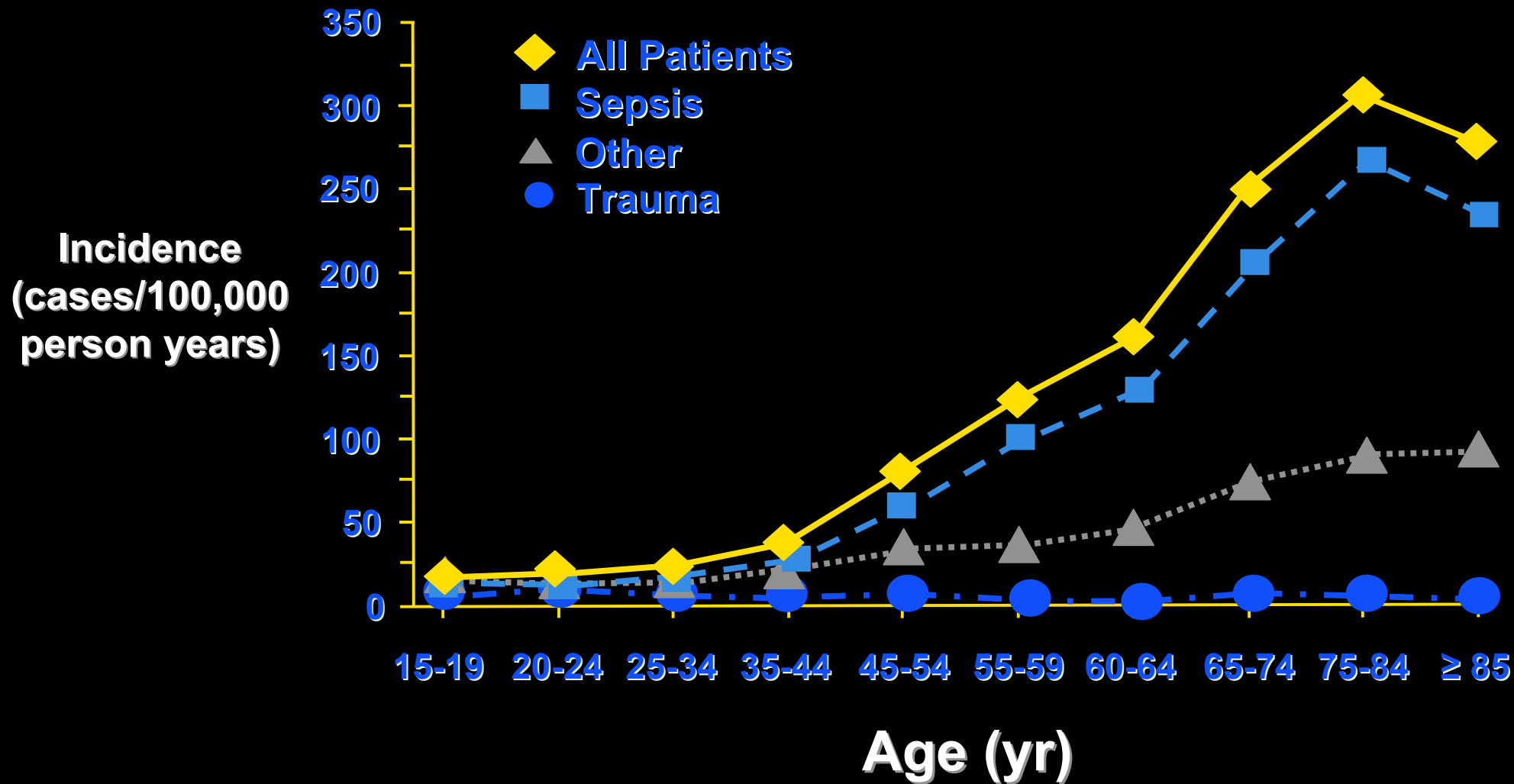
Shehabi Y, CCM 2010

Salluh J, Crit Care 2010

Girard T, CCM 2010

Vasilevskis E, CCM 2010

Aging and Critical Illness: ARDS & Sepsis



Association Between Acute Care and Critical Illness Hospitalization and Cognitive Function in Older Adults

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Context Studies suggest that many survivors of critical illness experience long-term cognitive impairment but have not included premorbid measures of cognitive functioning and have not evaluated risk for dementia associated with critical illness.

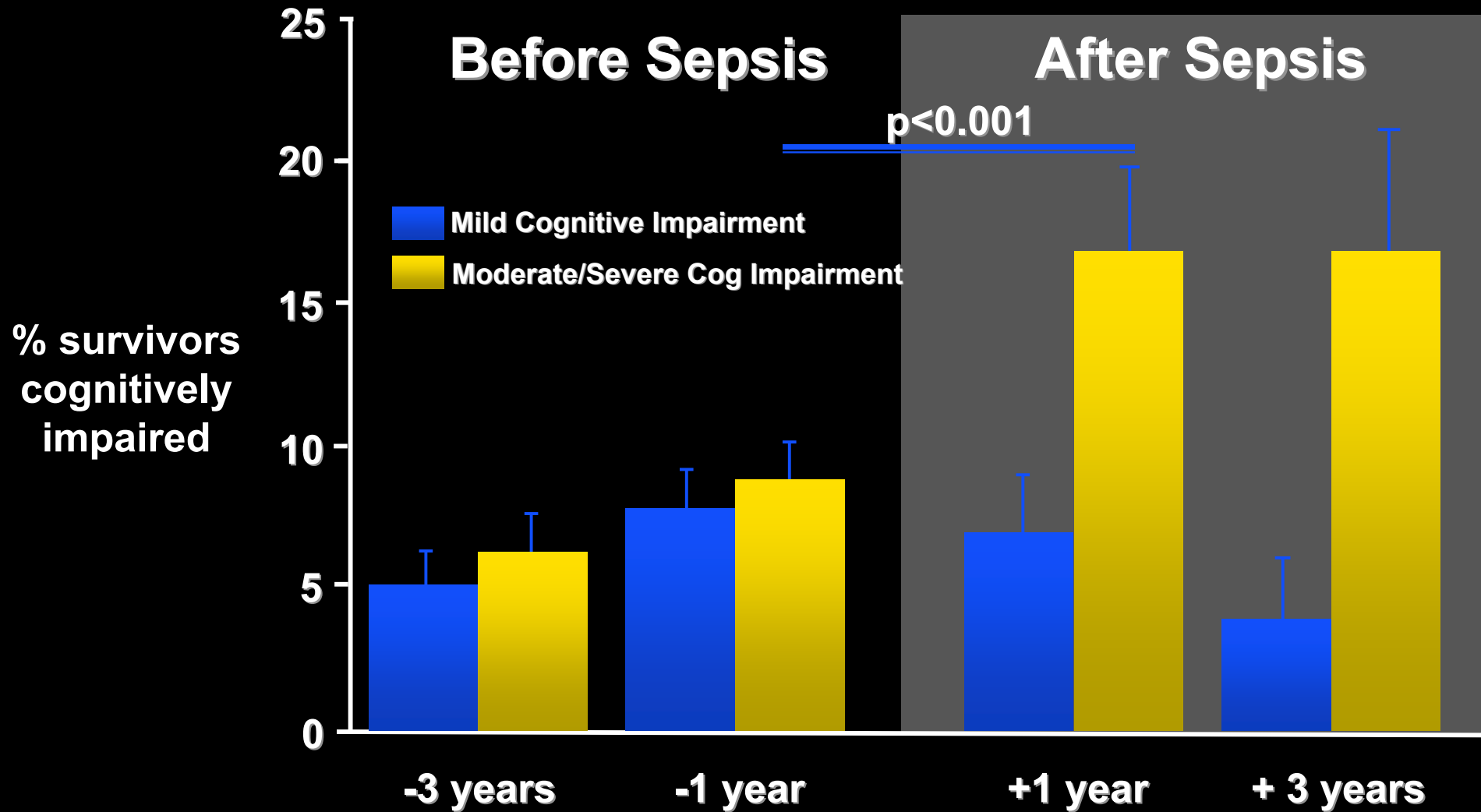
Objectives To determine whether decline in cognitive function was greater among older individuals who experienced acute care or critical illness hospitalizations relative to those not hospitalized and to determine whether the risk for incident dementia differed by these exposures.

Design, Setting, and Participants Analysis of data from a prospective cohort study from 1994 through 2007 comprising 2929 individuals 65 years old and older without

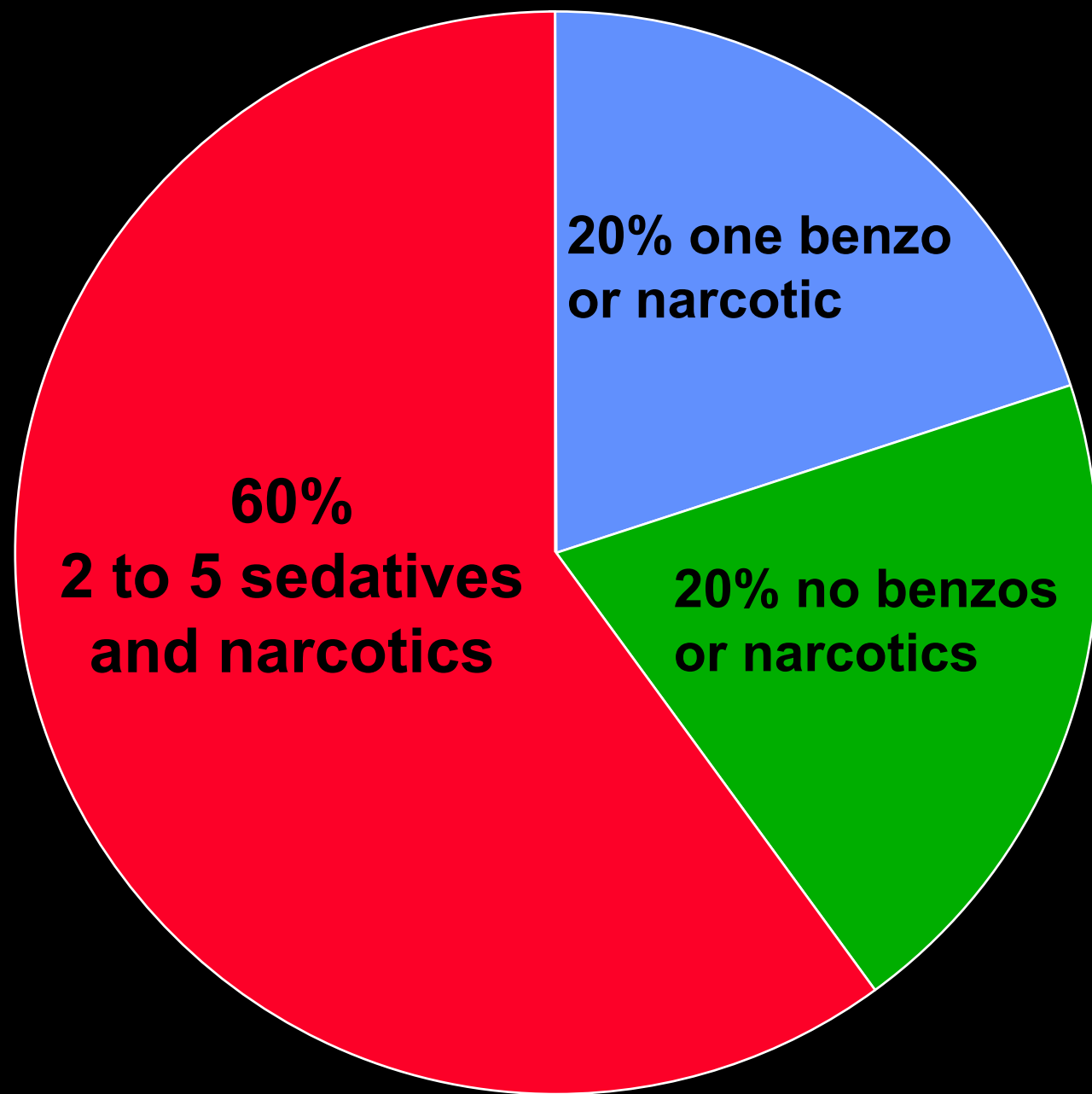
1. ~1300 patients >65 followed 6 years
2. Hospitalization independently associated with HR 1.4 and ICU with HR of 2.3 for Dementia
3. Of Dementias acquired during cohort, non-hospitalized patients had Alz Dz 76% vs. 60% in Hosp Patients and only 40% (meaning mostly non Alz Dz) in ICU patients



Cognitive Impairment: Sepsis



Iwashyna T, JAMA 2010



Liberation & Animation

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. Lancet 2008;371:126-34

Strom T, et al. Lancet 2010;375:475-480

Pandharipande PP, et al. JAMA 2007;298:2644-53

Riker R. et al, JAMA. 2009;301:489-499

Schweickert et al, Lancet 2009;373:1874-82

SBT

SAT

Remove (A+B)

Remove Sedation

Sedation choice

Sedation choice

Early Mobility

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

The ABCDE Bundle

Back End of Critical Care

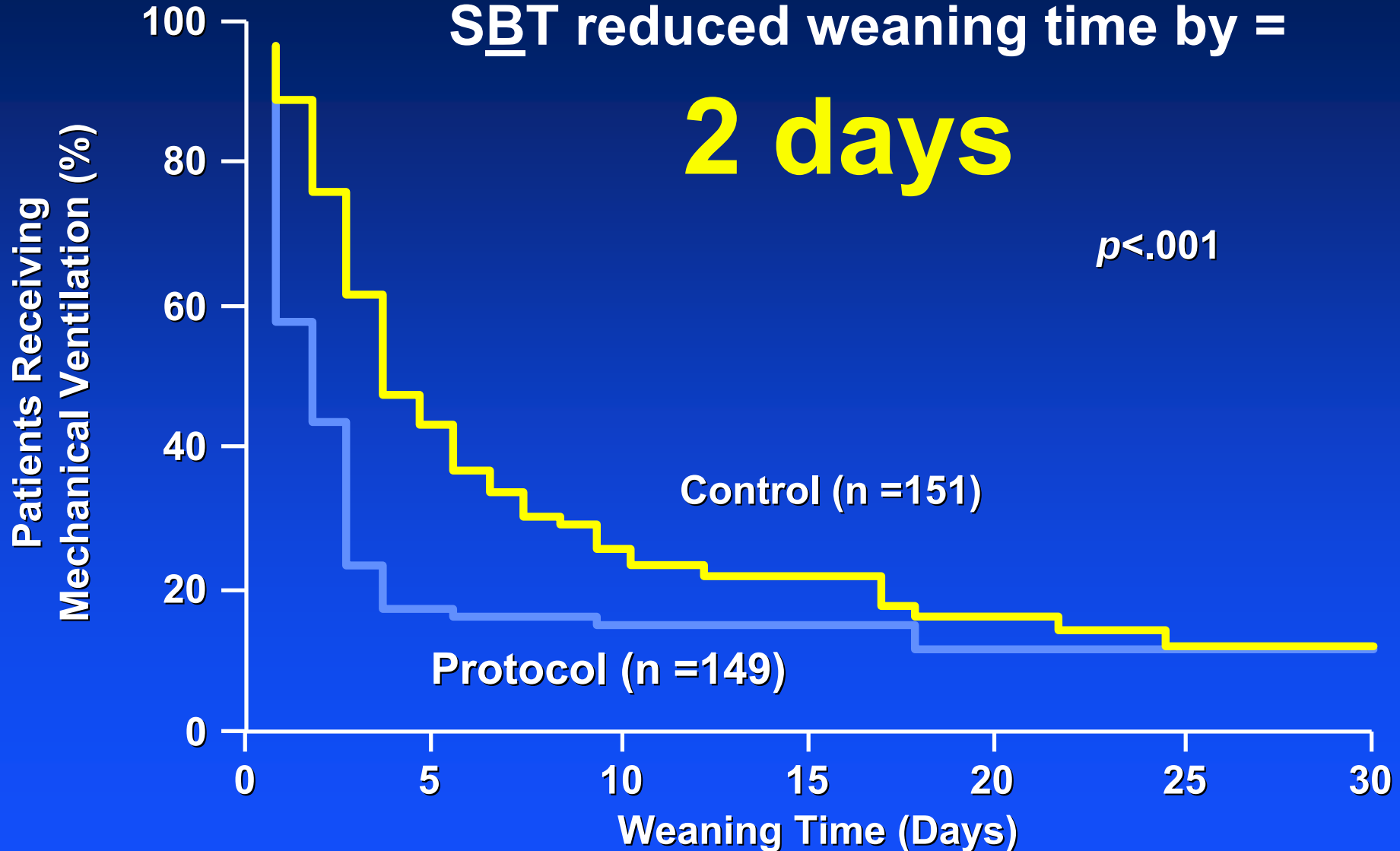
- Awakening
- Breathing
- Coordination, Choice
- Delirium monitoring/management
- Early mobility and Exercise

Weaning protocol

SBT reduced weaning time by =

2 days

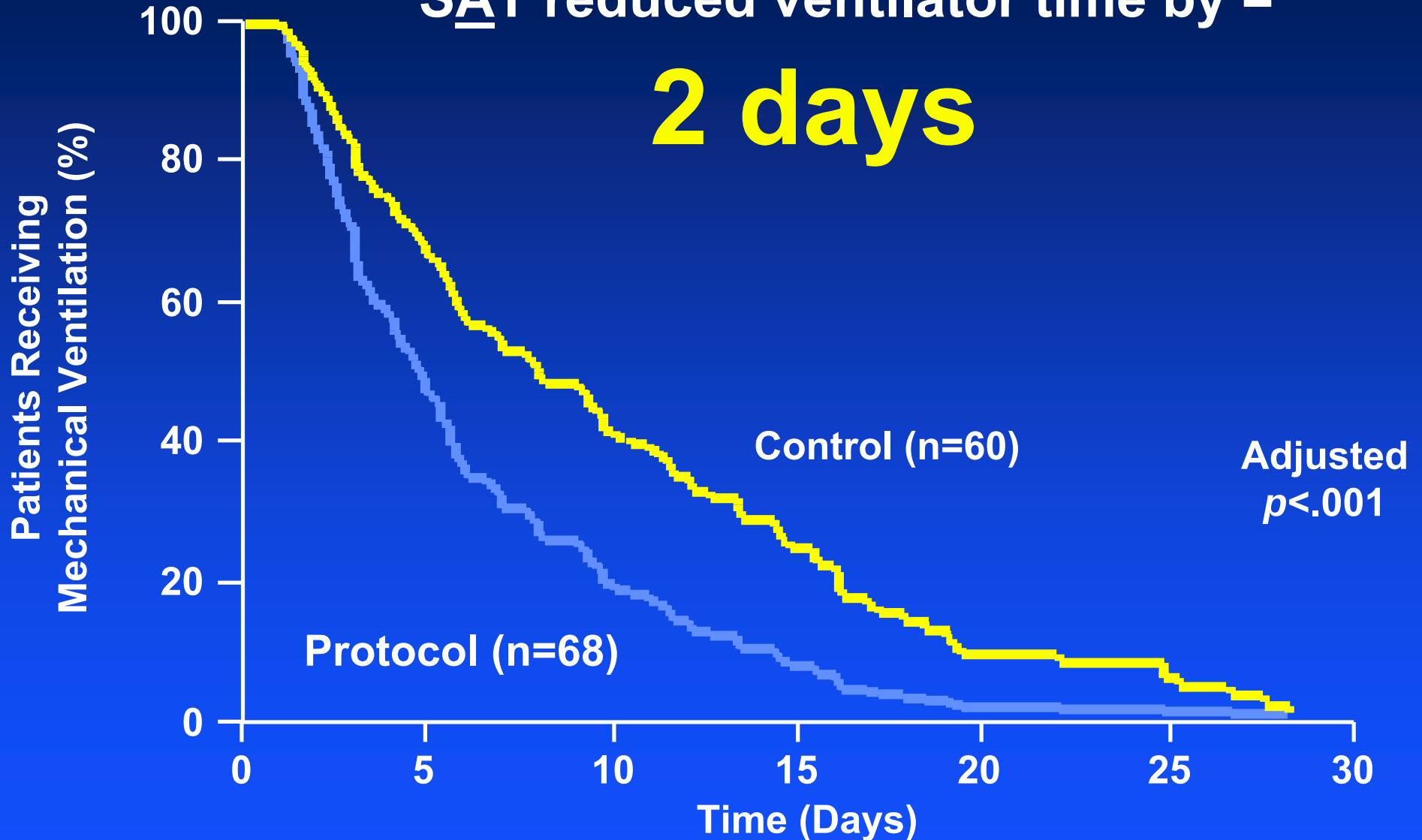
$p < .001$



Daily Interruption of Sedatives

SAT reduced ventilator time by =

2 days



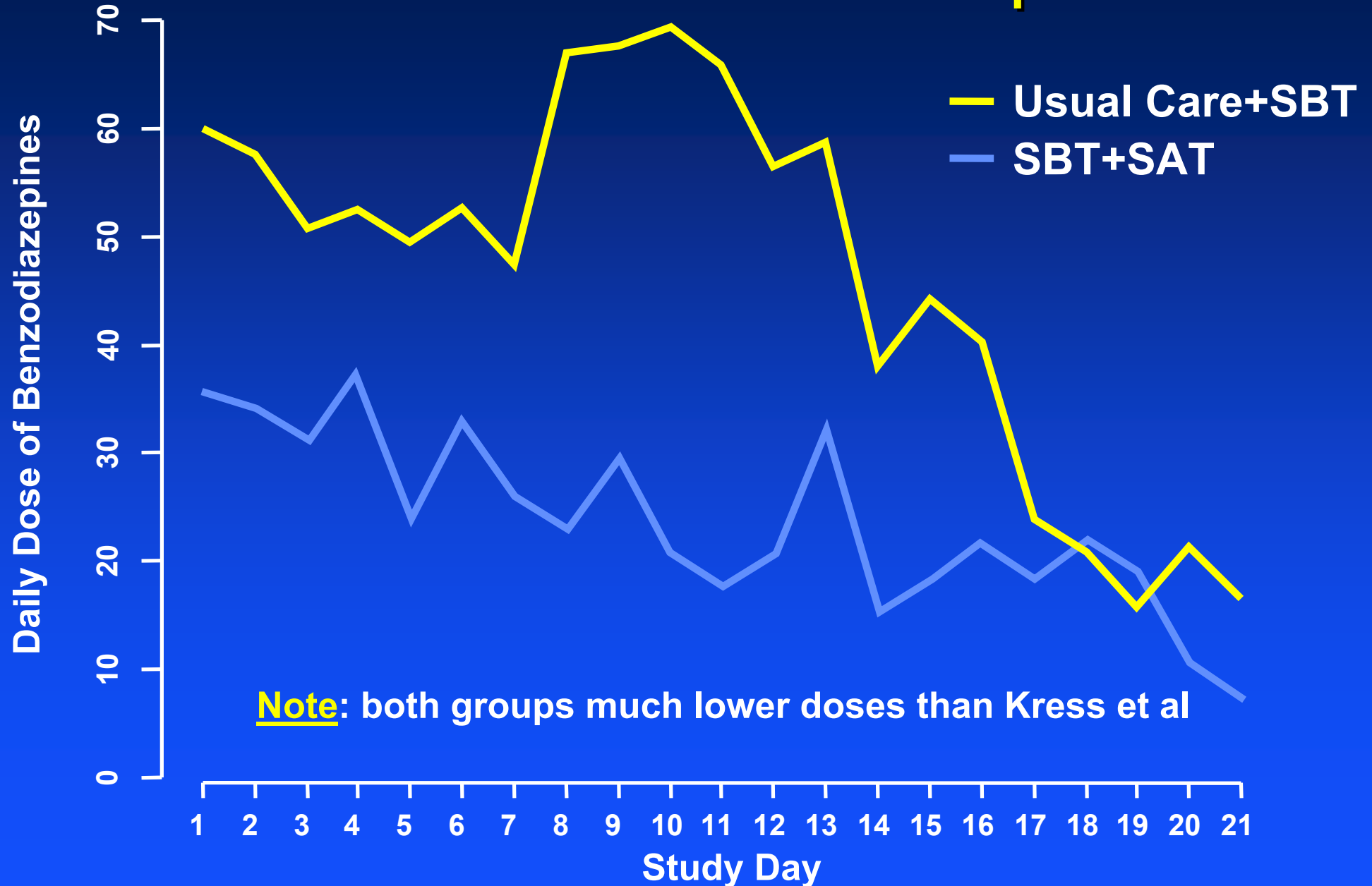
SATs (Daily Interruption) Used in Minority Around World

- Canada – 40% get SATs (273 physicians in 2005)
- U.S. – 40% get SATs (2004-05)
- Germany – 34% get SATs (214 ICUs in 2006)
- Brazil – 32% get SATs (1,015 MDs in 2008)
- UK – 28% get SATs, 82% use midazolam
- France – 90% continuous infusion (44 ICUs in 2005)

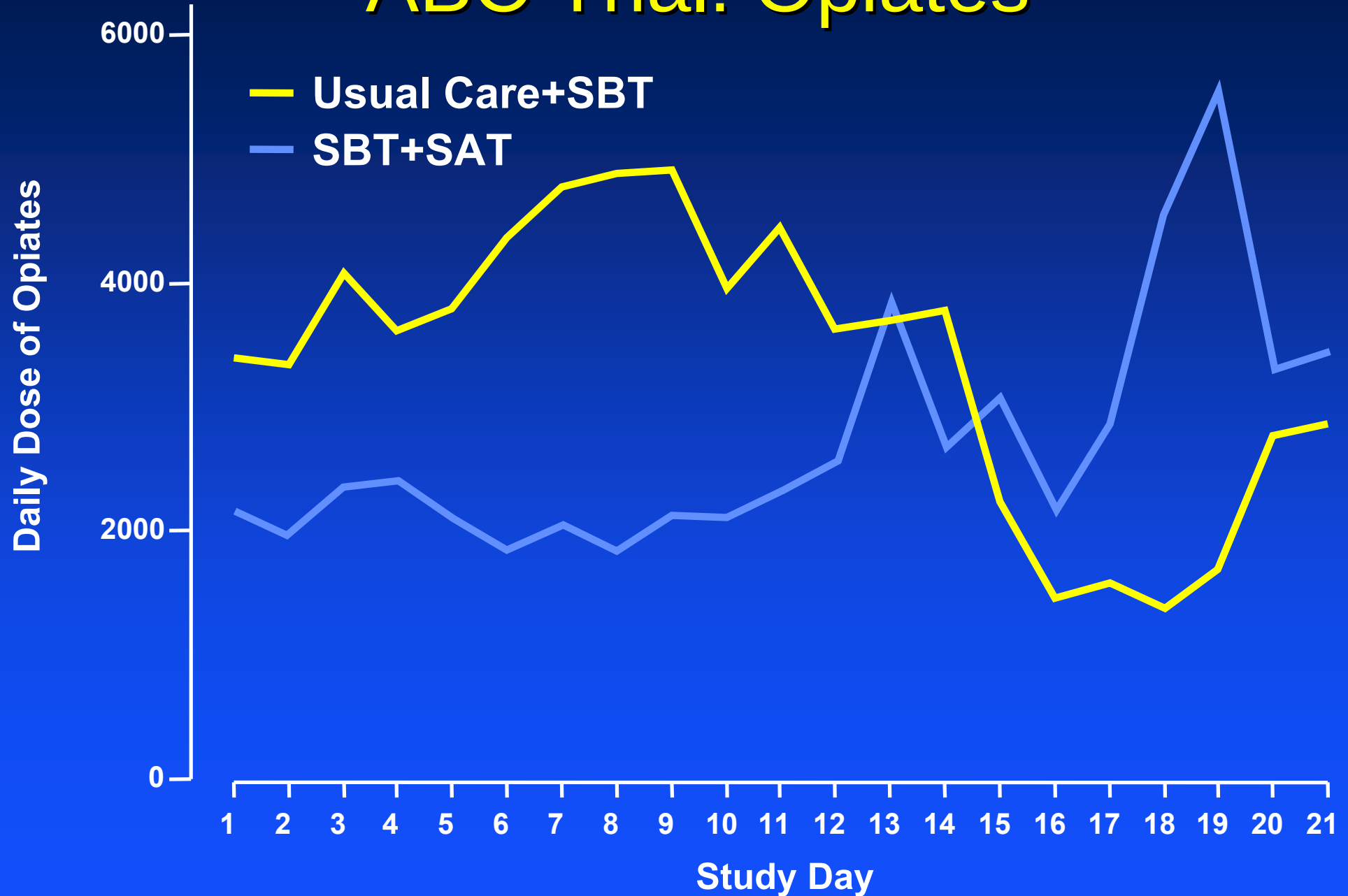
Mehta S, CCM 2006;34:374-80.
Devlin J, CCM 2006;34:556-57.
Payen JF, Anesthes 2007;106:687-95.

Tanios M, Proc Am Thorac Soc 2005;2:A793.
Martin J and Spies C, Crit Care 2007;11:R124
Ramaswamy S, Intens Care Med (ESICM 2009)
Salluh J, Brazil, J Crit Care 2009

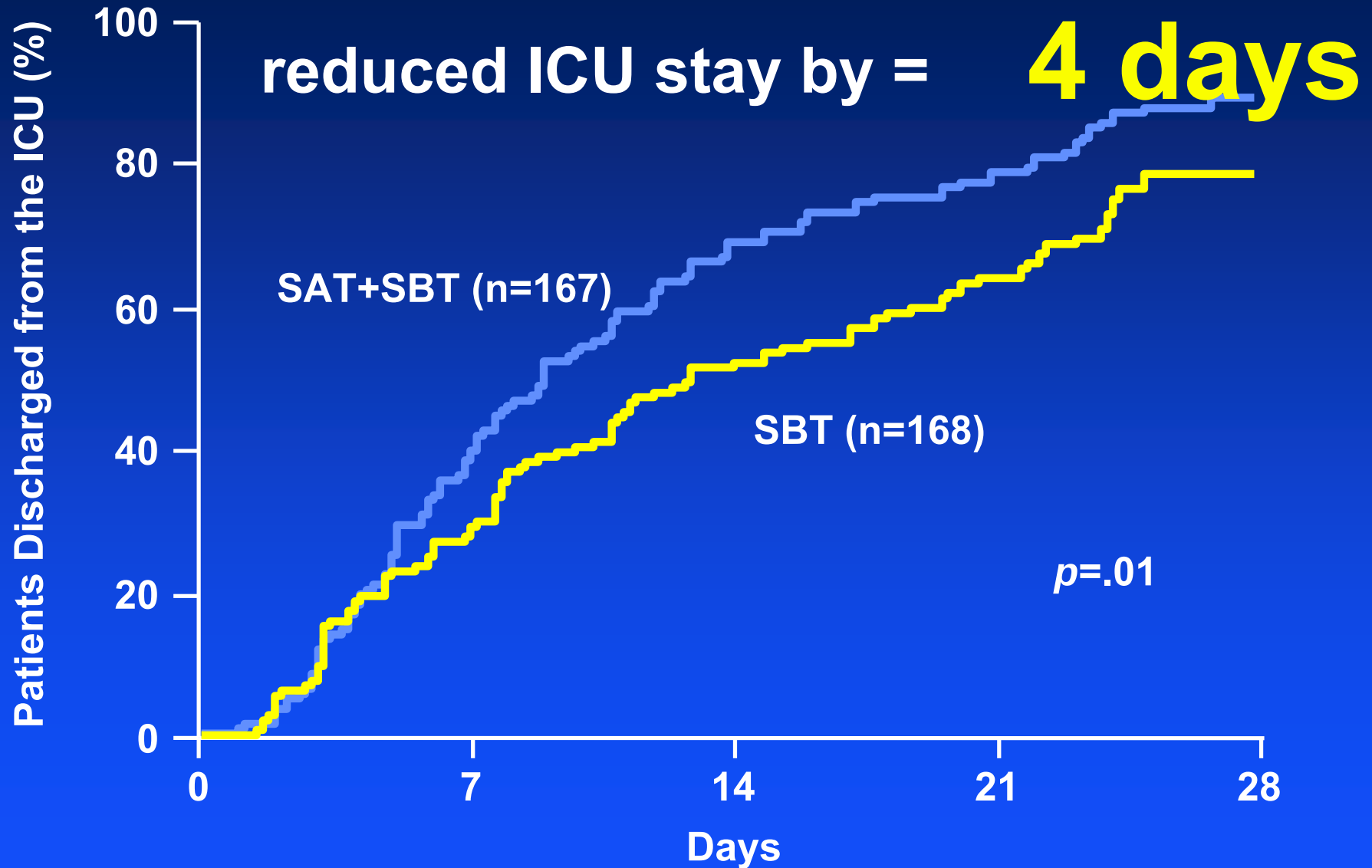
ABC Trial: Benzodiazepines



ABC Trial: Opiates

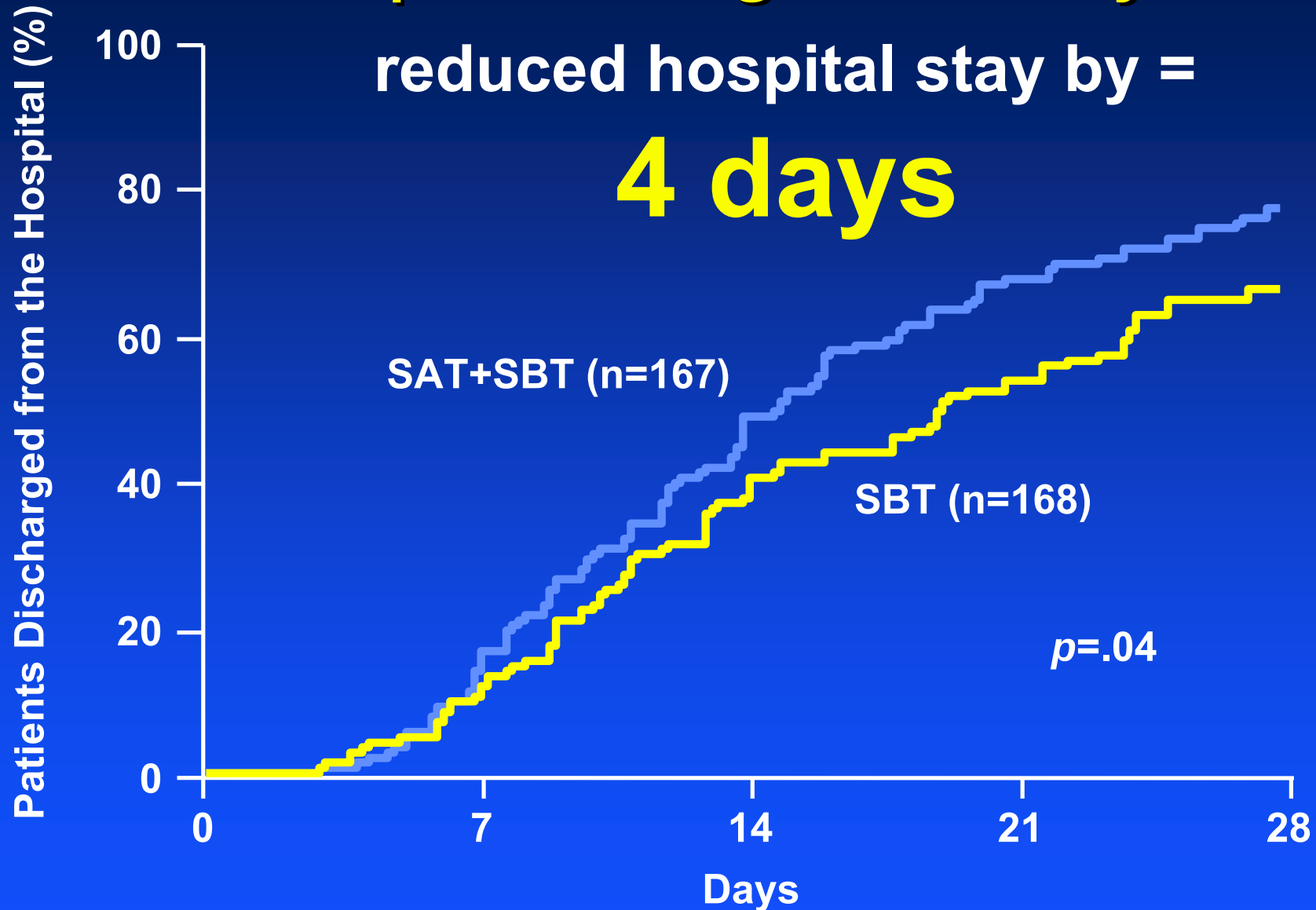


ICU Length of Stay

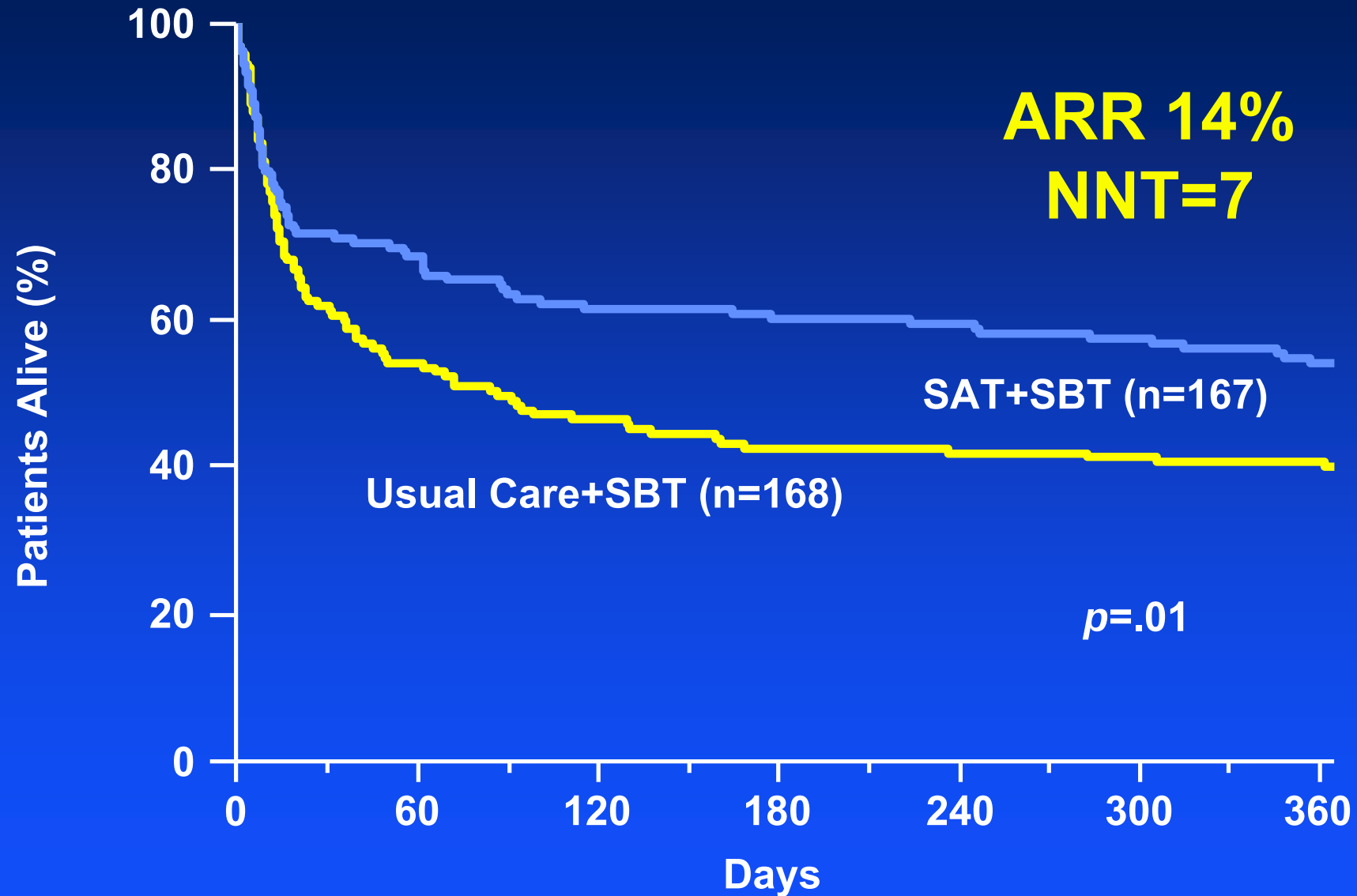


Hospital Length of Stay

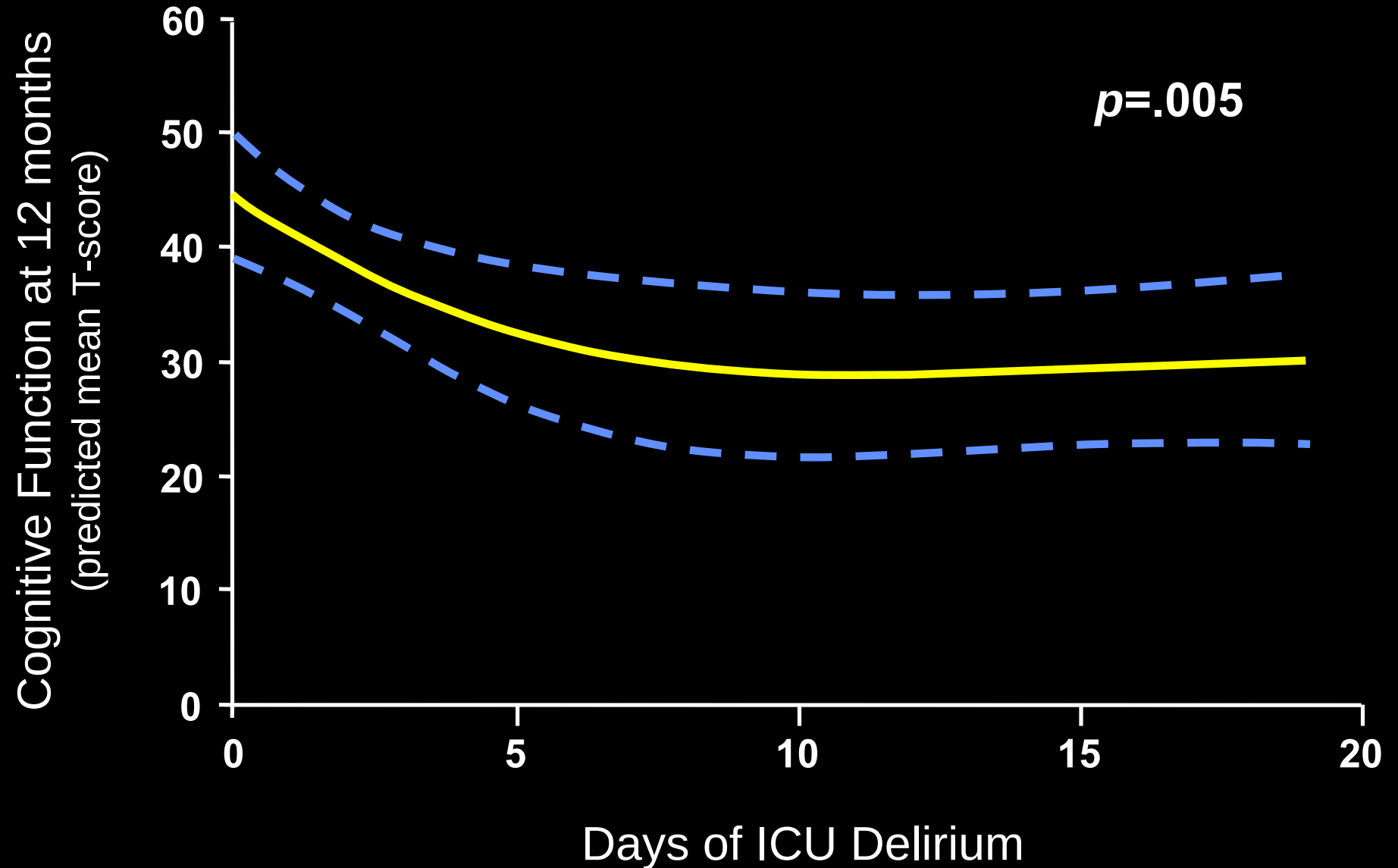
reduced hospital stay by =
4 days



One-Year Survival



Delirium and Long-Term Cognitive Outcomes



The ABCDEs of Peeling Back and Recovering from Critical Care

- Awakening
- Breathing
- Coordination, Choice
- Delirium monitoring/management
- Early mobility and Exercise

GABA

GABA

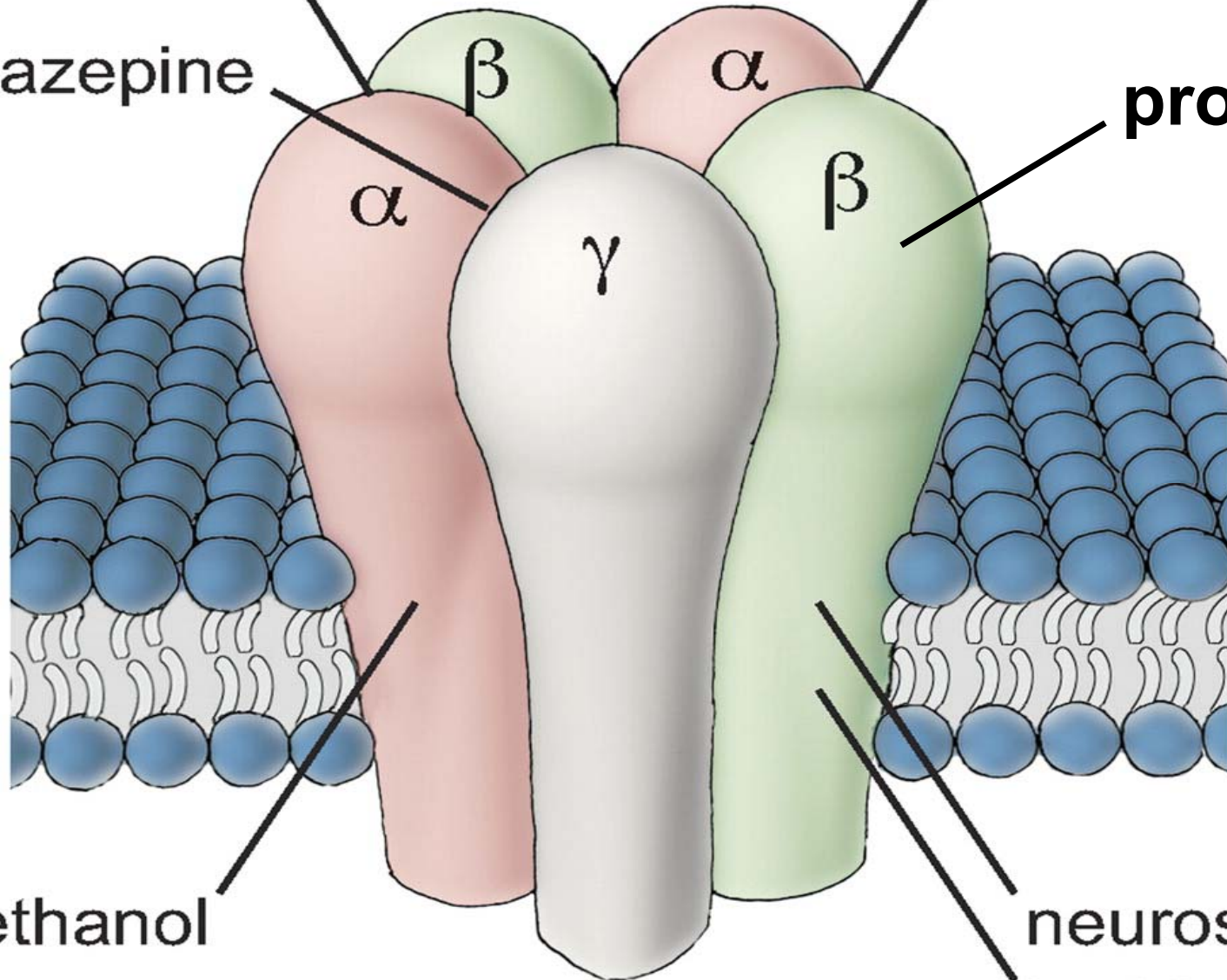
benzodiazepine

propofol

ethanol

neurosteroids
barbiturates

$\text{Cl}^- \downarrow$





Worldwide Sedation Practices

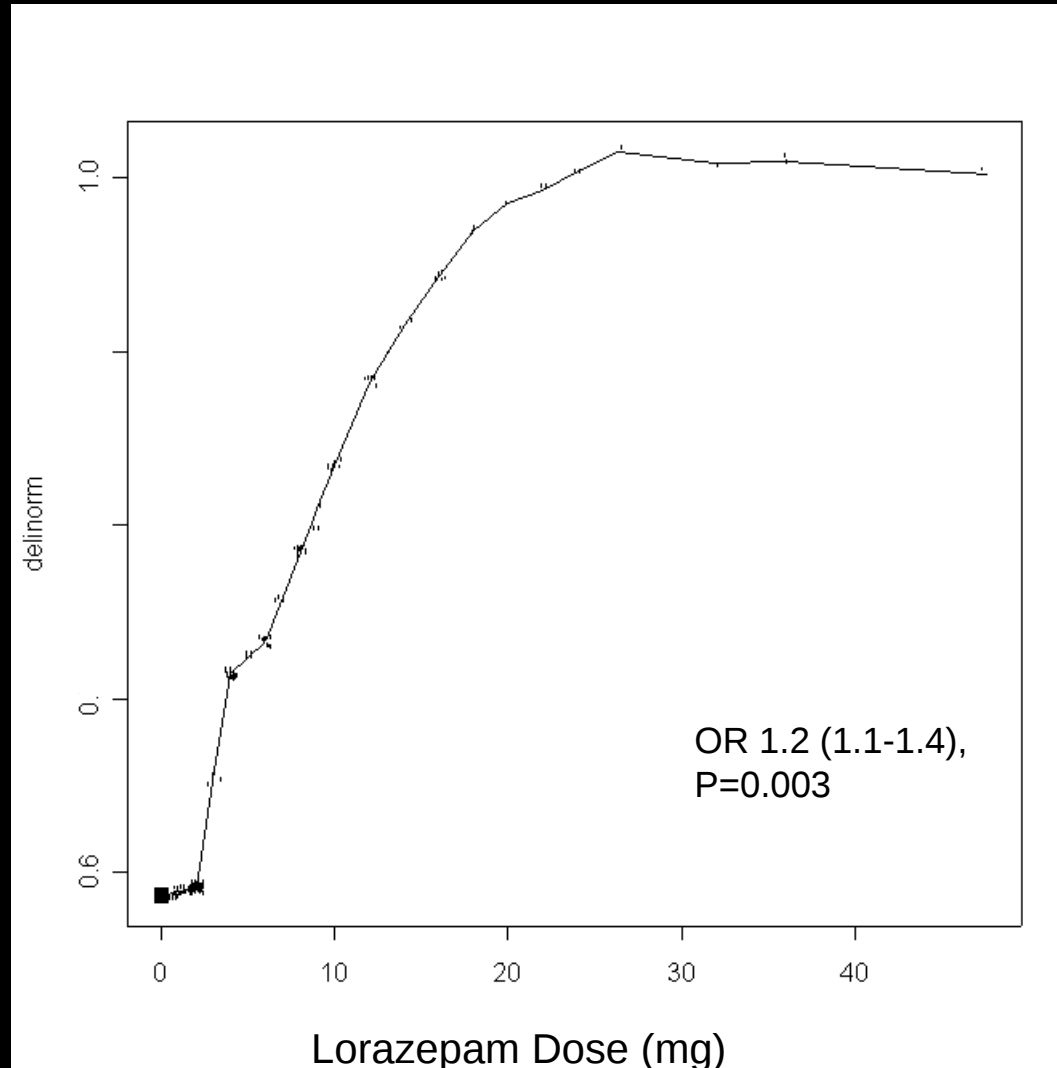
- GABA-ergics have been most widely used sedative agents for 20 years
 - Propofol #1 sedative infusion in U.S.
 - Benzodiazepines most common sedatives worldwide
- “Less is more” data support trends in use of analgo-sedation or dexmedetomidine

Wunsch H, CCM 2010;37:3031-37
Patel R, CCM 2009;37:825-32
Salluh J, Crit Care 2010;14:R210

Kress JP, NEJM 2000
Girard T, Lancet 2007
Strom T, Lancet 2010
Treggiari M, CCM 2009

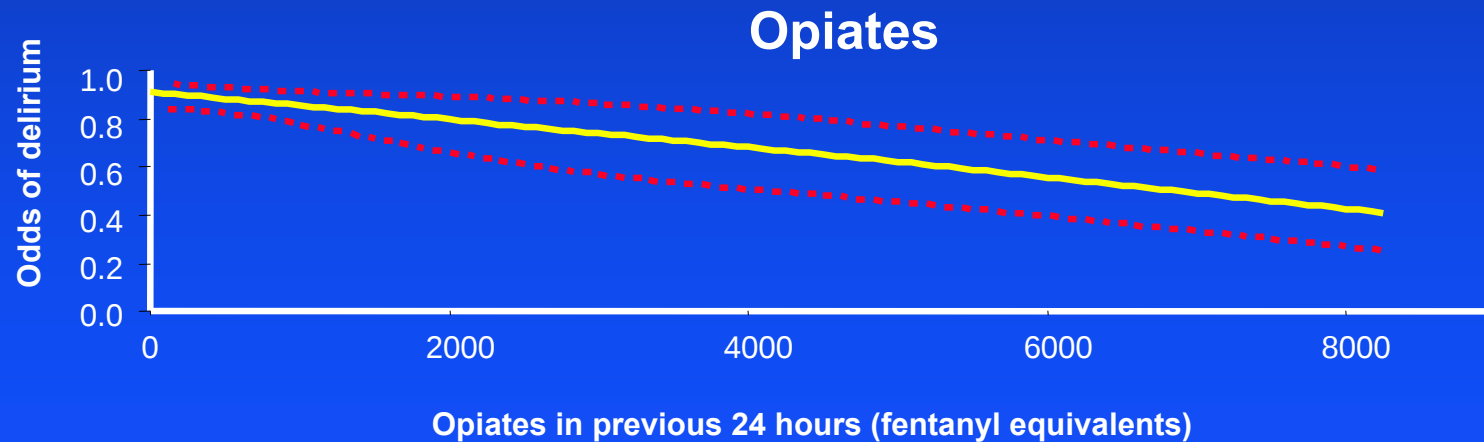
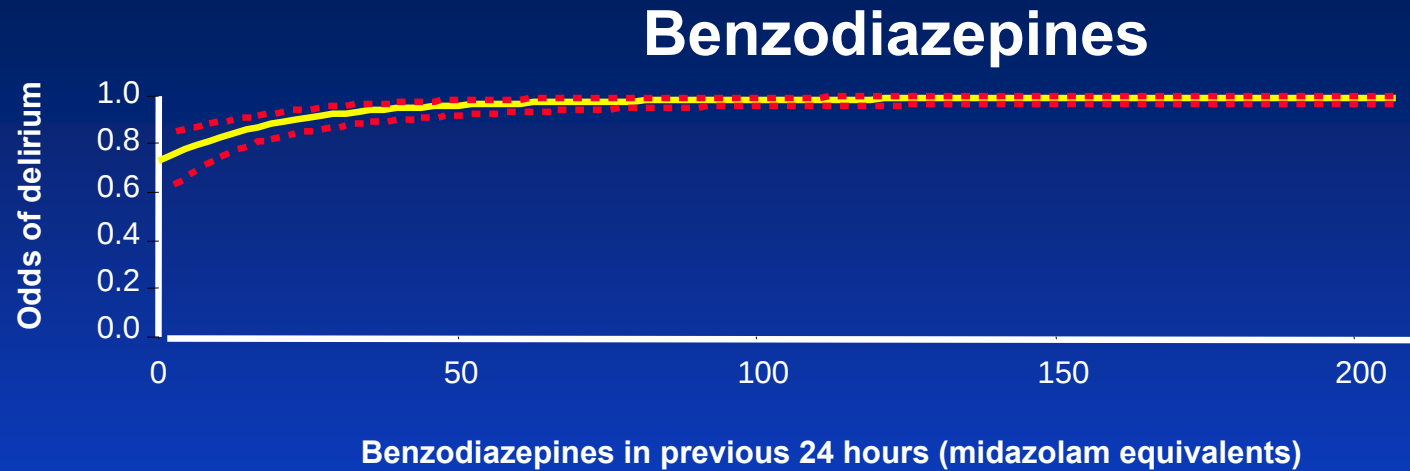
Benzodiazepines and Delirium: Medical ICU

Delirium Risk

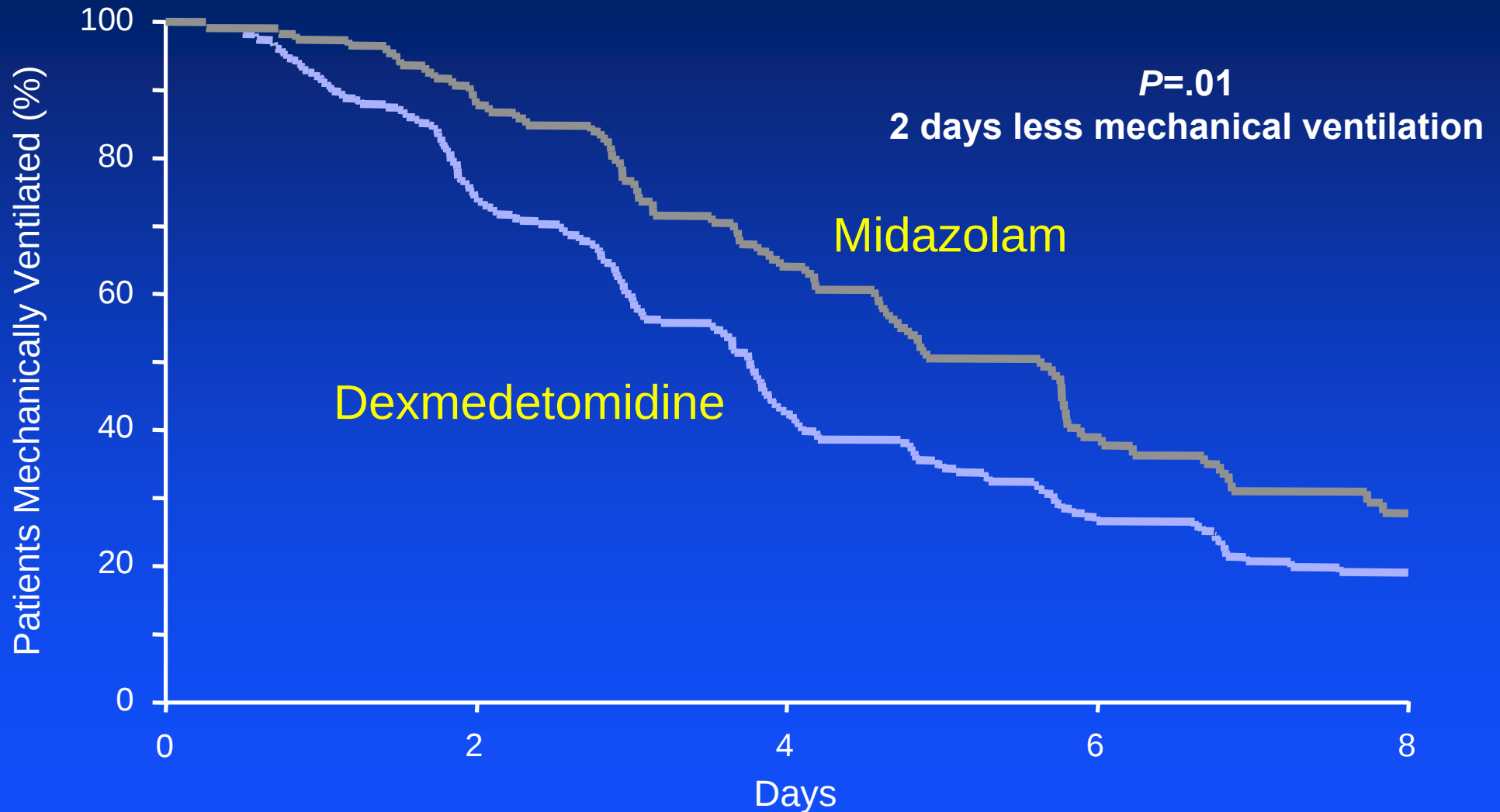


Pandharipande et al.
Anesthesiology 2006:
124:21-6

Benzodiazepine and Delirium: Burn ICU

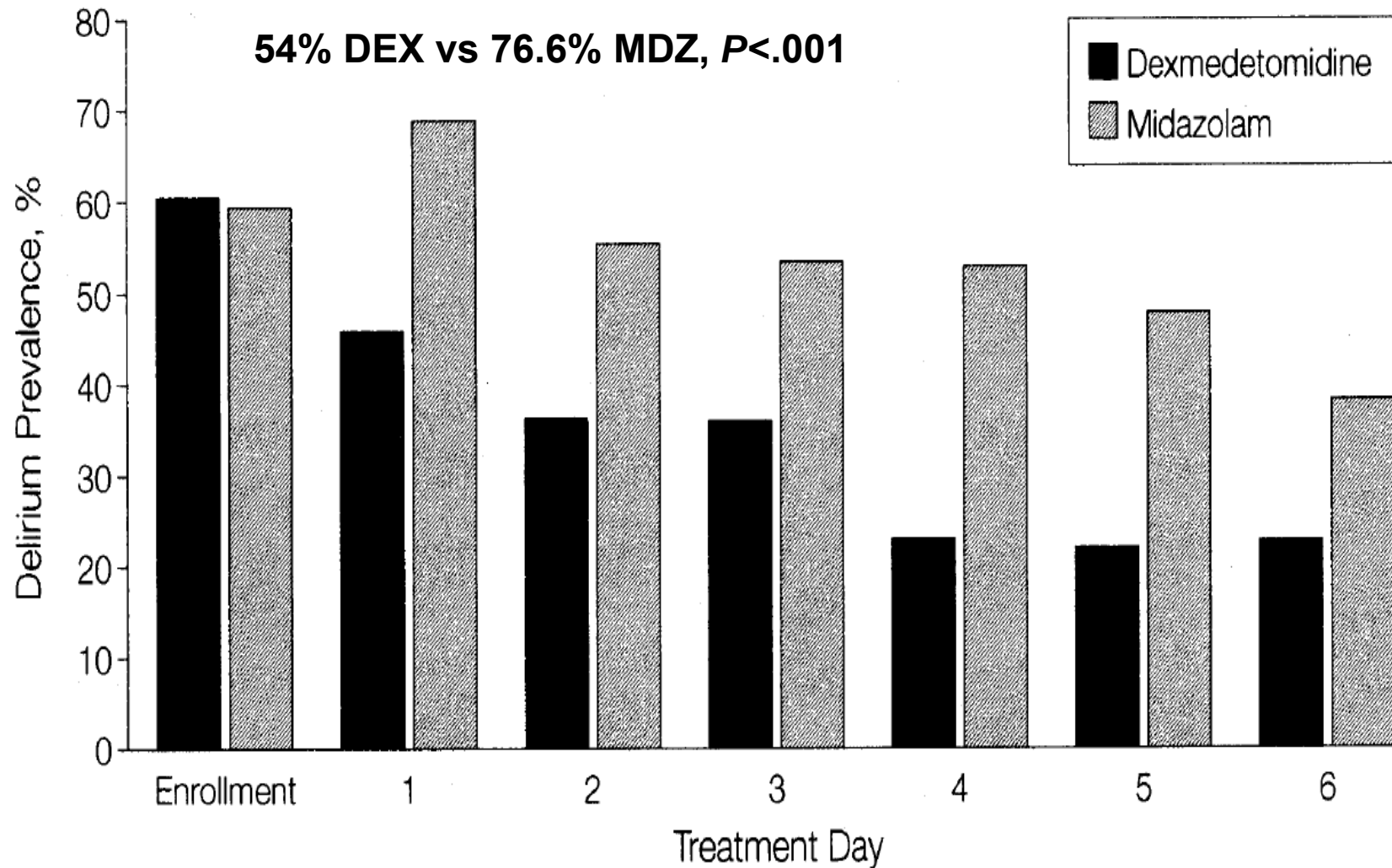


SEDCOM Trial – Extubation

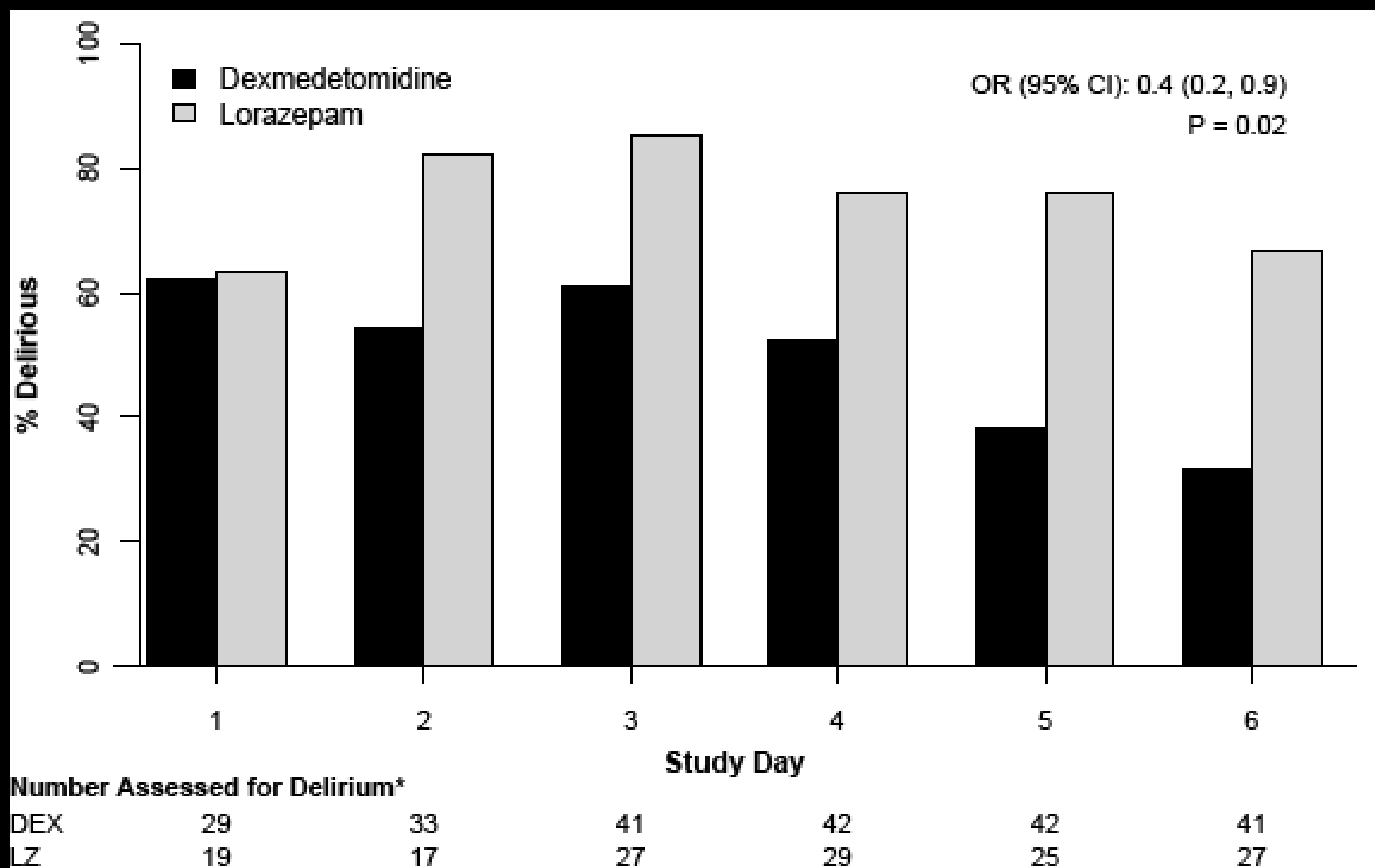


Riker RR, et al. JAMA. 2009;301:489-499

SEDCOM Prevalence of Delirium

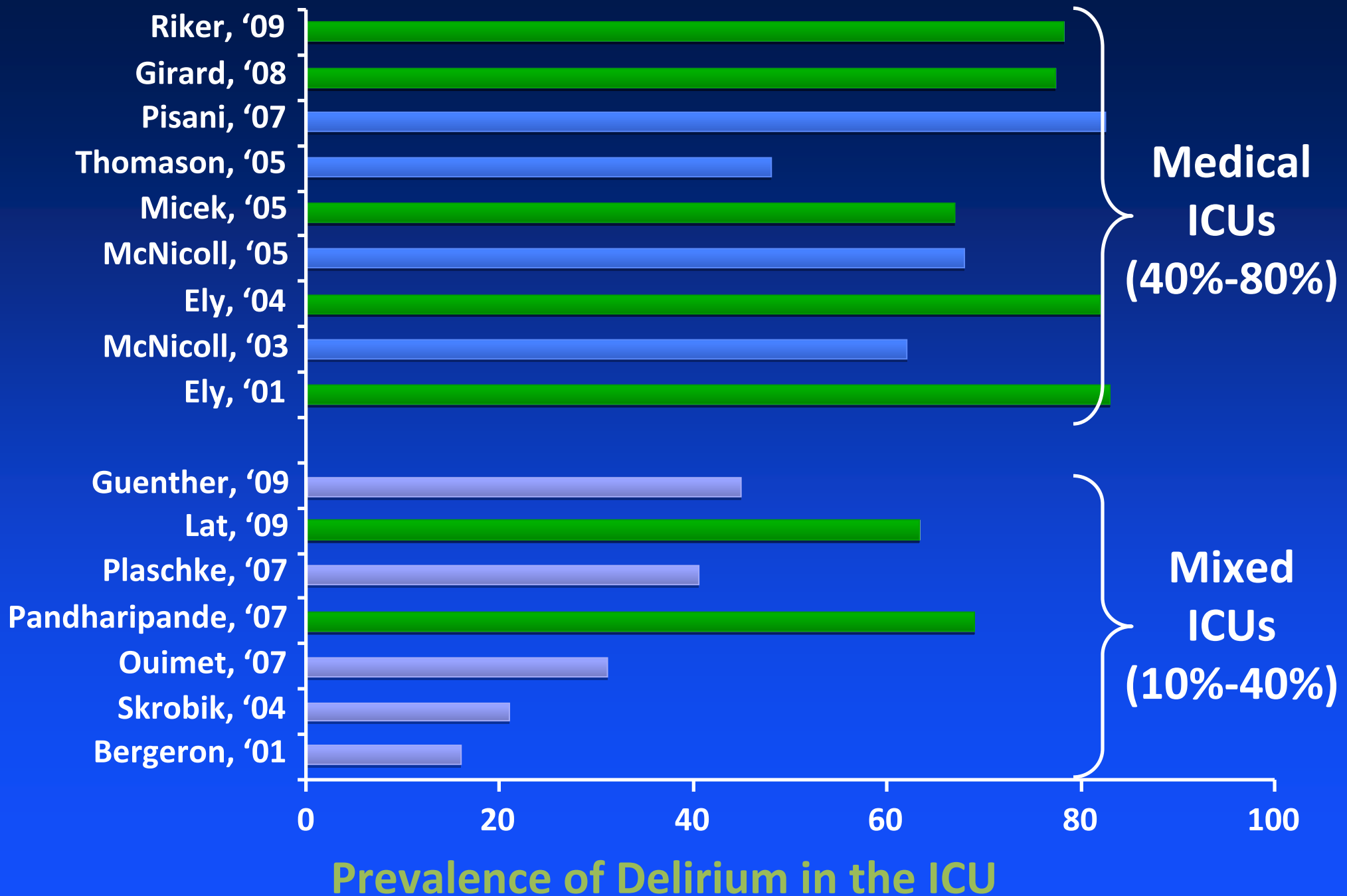


MENDS Prevalence of Delirium



The ABCDEs of Peeling Back and Recovering from Critical Care

- Awakening
- Breathing
- Coordination, Choice
- Delirium monitoring/management
- Early mobility and Exercise



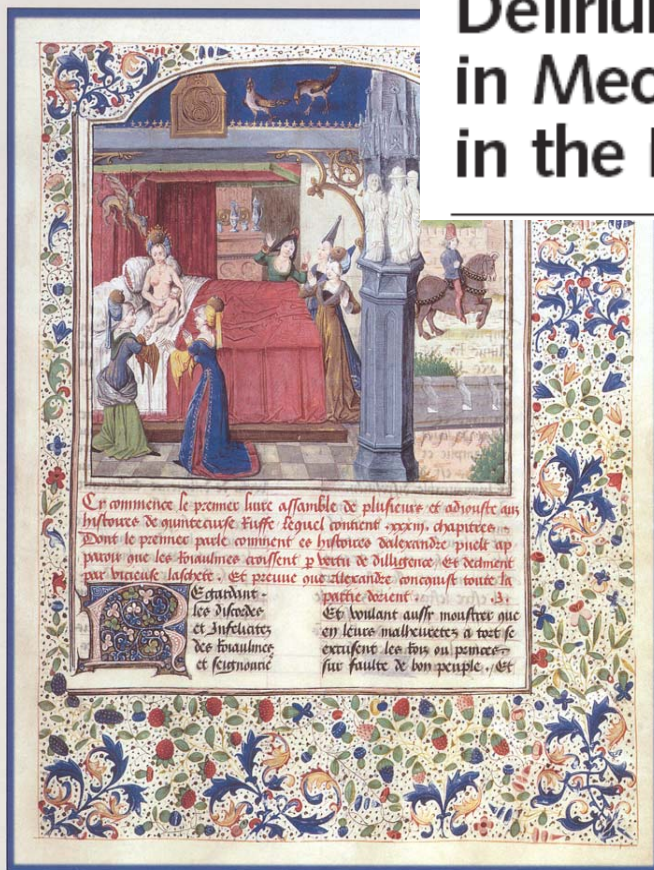
JAMA[®]

The Journal of the American Medical Association

CARING FOR THE
CRITICALLY ILL PATIENT

Ely EW, JAMA 2004;291:1753-62

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



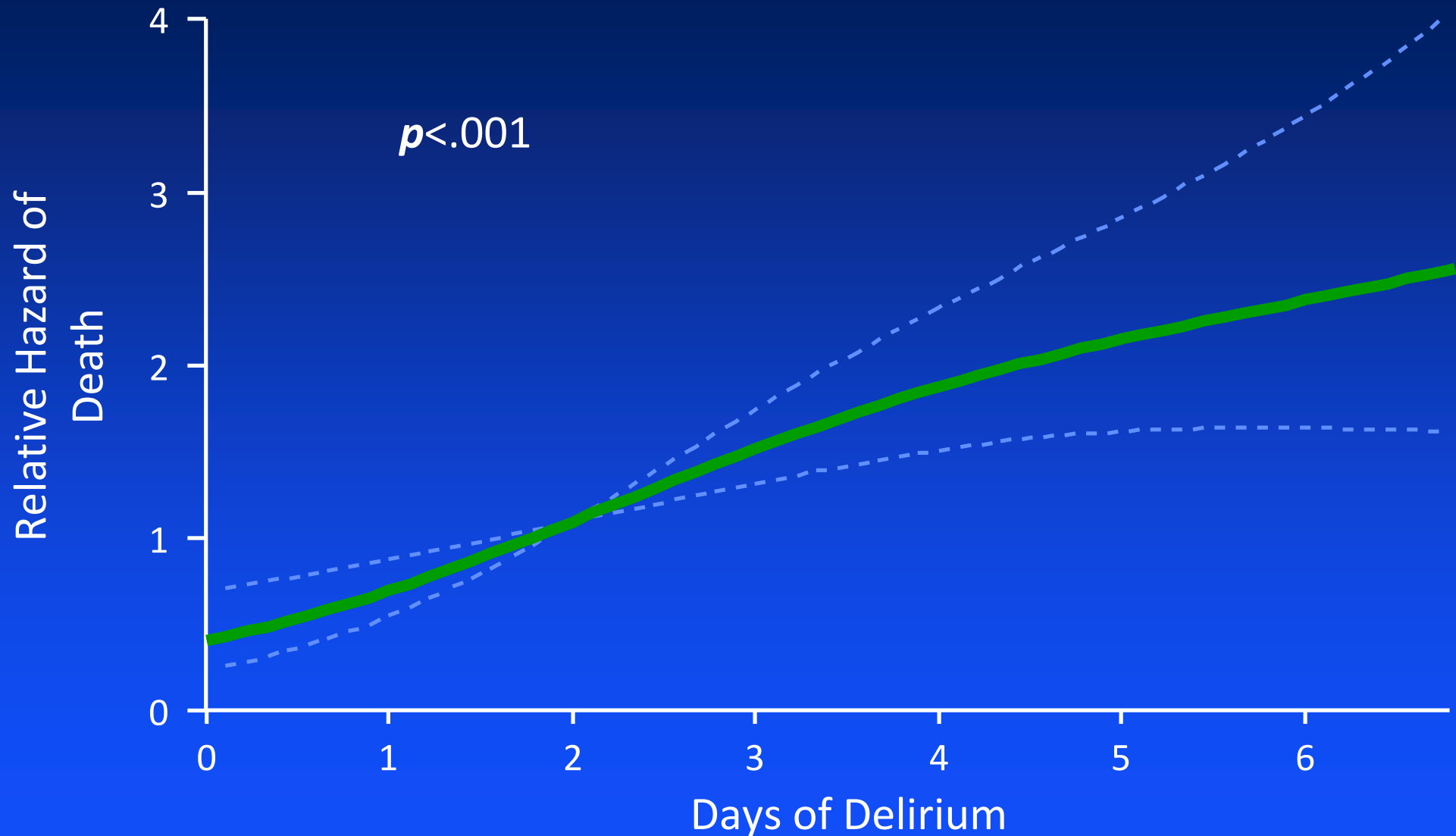
Risk of death rises 10% per day

1. After adjusting for covariates, each day spent in delirium was associated with **10% increased risk of death** at 6 mo (HR, 1.10; 95% CI, 1.0-1.3).
2. After adjusting for covariates, each day spent in delirium was associated with **10% increased risk of death** at 1 yr (HR, 1.10; 95% CI, 1.0-1.2).

1. Ely EW, JAMA 2004;291:1753-62

2. Pisani M, AJRCCM 2009;180:1092-7

Delirium Duration & Mortality



Shehabi Y, et al. Crit Care Med 2010 Sep 9. [Epub]

Brain autopsy findings in intensive care unit patients previously suffering from delirium: A pilot study[☆]

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Keywords:

Delirium;
Brain autopsy;
Neuropathology

Abstract

Purpose: Delirium affects 50% to 80% of intensive care unit (ICU) patients and is associated with increased risk of mortality. Given the paucity of data reporting the neuropathologic findings in ICU patients experiencing delirium, the purpose of this pilot, hypothesis-generating study was to evaluate brain autopsies in ICU patients who suffered from delirium to explore possible neuroanatomical correlates.

Materials and Methods: Using delirium databases at Vanderbilt University, we identified patients who had delirium in the ICU and subsequently died and received a brain autopsy during the same hospitalization. Brain autopsy reports were collected retrospectively on all 7 patients who met these criteria.

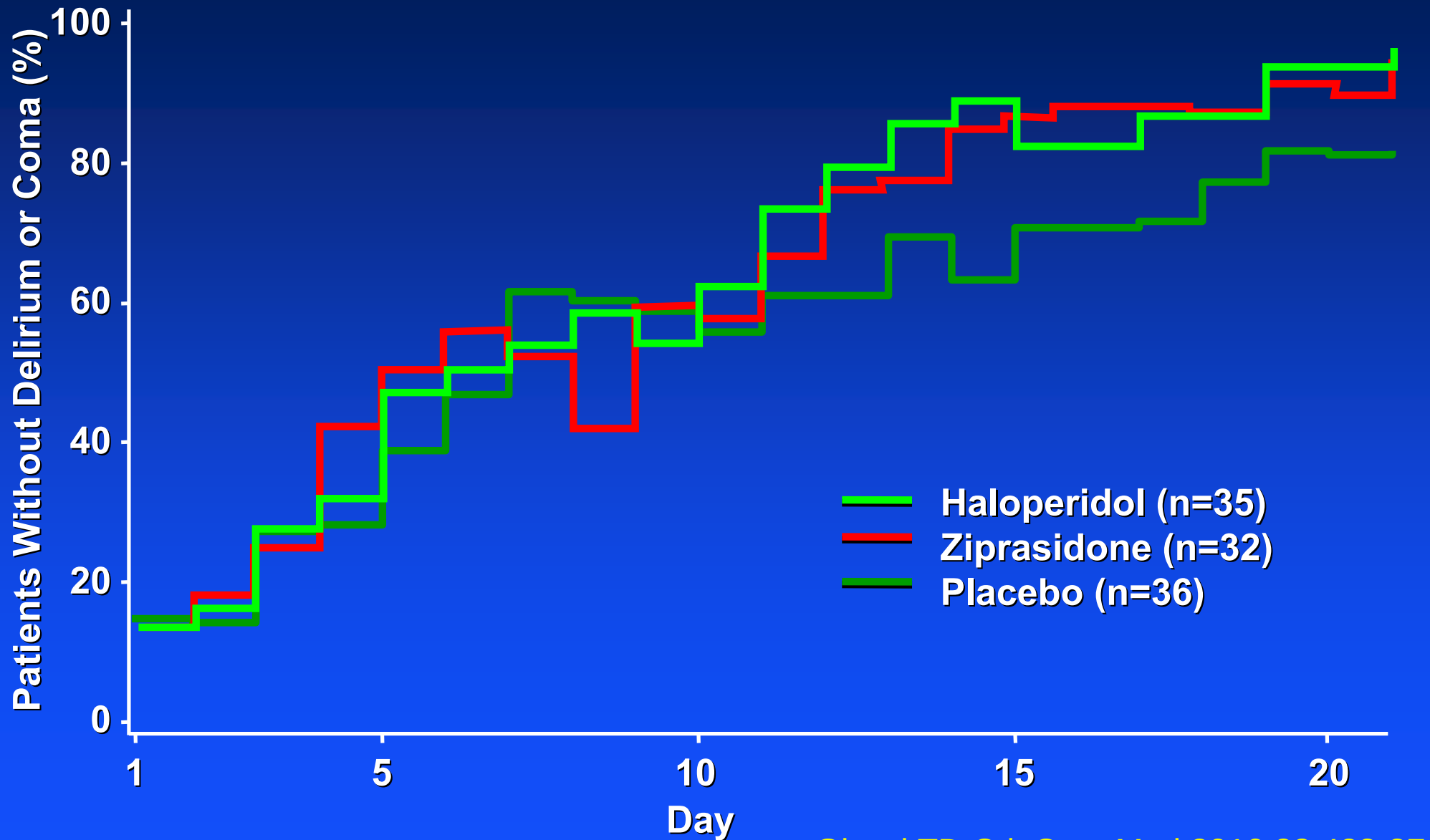
Results: Patients' mean age was 55 (SD $\pm$ 8.4) years, and median number of days spent with delirium was 7 ($\pm$ 5 interquartile range). In 6 (86%) of 7 patients, pathologic lesions normally attributed to hypoxia or ischemia were noted in the hippocampus, pons, and striatum. Hippocampal lesions represented the most common neuropathologic site of injury, present in 5 (71%) of 7 patients.

Conclusions: Hypoxic ischemic injury in multiple locations of the brain was a common finding. The biological plausibility of hippocampal lesions as a contributor to long-term cognitive impairment warrants postmortem investigation on a larger scale with comparison to patients not experiencing ICU delirium.

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Nonpharm and Pharm in Delirium Management

Resolution of Delirium and Coma



The ABCDEs of Peeling Back and Recovering from Critical Care

- Awakening
- Breathing
- Coordination, Choice
- Delirium monitoring/management
- Early mobility and Exercise

Mobilization = Less Delirium

Variable	Intervention (n=49)	Control (n=55)	P-value
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

Schweickert et al, Lancet 2009;373:1874-82

Milestones Achieved Safely ~3 days earlier ($p < 0.001$)

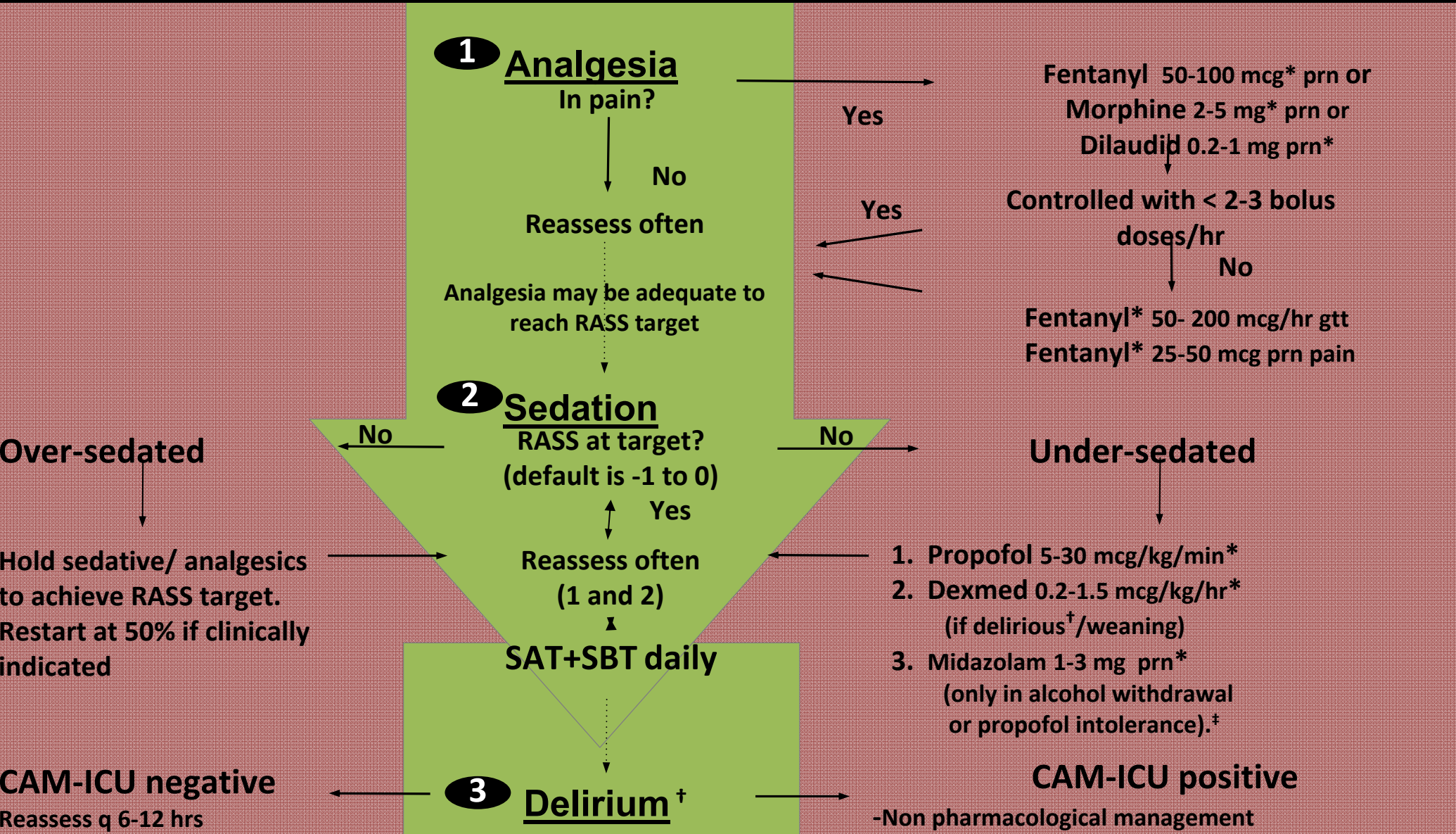
1. Standing
2. Marching
3. Walking
4. Transferring

Screening/Presenting on Rounds 4 items in 10 seconds

1. Target RASS (where going?)
2. Actual RASS (where now?)
3. CAM-ICU (where now?)
4. Drugs (how got here?)



Analgesia/Sedation Protocol for Mechanically Ventilated Patients



*Detailed dosing information available in WizOrder.

[†]Delirium diagnosed using the CAM-ICU (see Delirium Protocol for details)

[‡]Midazolam 1-3 mg/hr gtt rarely if > 3 midaz boluses/hr, propofol intolerance or >96 hrs propofol

Sedating - Below the Water Level

“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.” Marion Stone

Cutting for Stone by Abraham Verghese

Public Health Problem: Brain Dysfunction in ICU

- Acute brain dysfunction (delirium) occurs in 60-80% of high severity ICU patients and independently predicts poor outcomes
- Over 50% of ICU survivors suffer a functionally debilitating dementia-like illness
- Every additional day of delirium appears to be an independent predictor of death and a dementia-like illness
- Intensive care should be restructured to prioritize maximizing brain function including optimization of sedative exposure and rehabilitation



The JEDI Study: **Japanese Epidemiology of Delirium in the ICU**

Tsuruta R.

http://www.icudelirium.org



assessment resources for ICU Delirium

The current clinical practice guidelines of the Society of Critical Care Medicine (SCCM) for the sustained use of analgesics and sedatives are geared toward the maintenance of optimal comfort in critically ill patients by focusing on 3 central components - pain, anxiety and delirium. The third component of these guidelines, delirium, is an independent predictor of death, length of stay, cost, and cognitive outcomes at discharge. Although, it is experienced by 60-80% of mechanically ventilated patients, it remains unrecognized in 66% to 84% of patients. The SCCM guidelines recommend that the emergence and/or persistence of delirium be regularly monitored in critically ill patients. Two of the validated tools for assessing delirium in ICU patients are the CAM-ICU and ICDSC.

Ely EW, Inouye SK, Bernard GR, Gordon S, Francis J, May L, et al. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). *JAMA* 2001; 286:2703-2710.

Ely EW, Margolin R, Francis J, May L, Truman B, Dilks R, et al. Evaluation of delirium in critically ill patients: validation of the confusion assessment method for the intensive care unit (CAM-ICU). *Crit Care Med* 2001; 29:1370-1376.

The Confusion Assessment Method for the ICU (CAM-ICU) is a delirium monitoring instrument for ICU patients. The CAM-ICU was adapted for use in nonverbal ICU patients from the original Confusion Assessment Method (CAM) (Inouye, *Ann Intern Med* 1990). The CAM-ICU is a well validated delirium assessment scale that is widely used and easy to administer. It performs well even among difficult patient populations (i.e. patients with suspected dementia, patients over 65 years old, and those with very high severity of illness). The CAM-ICU was designed to be a serial assessment tool for use by bedside clinicians (e.g. nurses, physicians, etc). Thus it is easy to use, taking less than 2 minutes to complete and requiring minimal training.

The Intensive Care Delirium Screening Checklist is an eight item checklist based on DSM-IV Criteria and features of delirium. It is intended to be a bedside screening tool for delirium in the ICU. Rates complete the checklist based on data from the previous 24 hours. The eight items are scored 1 (present) or 0 (absent), for a total of 8 points. A score of 4 or greater is a positive screen for delirium. The ICDSC is also a well validated screening tool.

Reference: Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y. *Intensive Care Med*. 2001 May;27(5):539-54.

Education

Use the education tools below, as well as the videos "10 Key Points Tutorial" and "Using the CAM-ICU."



Download

CAM-ICU Training Manual
This is a training manual for physicians, nurses and other health care professionals who wish to use the Confusion Assessment Method for the ICU (CAM-ICU).



Download

CAM-ICU Worksheet
The Richmond Agitation and Sedation Scale (RASS) and the Confusion Assessment Method for the ICU (CAM-ICU) worksheet.



Download

CAM-ICU Flowchart
This flowchart is a modification of the original CAM-ICU worksheet made facilitate implementation at the bedside by healthcare professionals.



Download

CAM-ICU Pocket Cards
Helpful reference materials readily available at the bedside. They include detailed instructions for each of the four features of the CAM-ICU in addition to a complete guide to the RASS scale.



Download

FAQ
CAM-ICU Training Manual
Frequently asked questions.



Download

ICDSC
The Intensive Care Delirium Screening Checklist is an eight item checklist based on DSM-IV Criteria and features of delirium. It is intended to be a bedside screening tool for delirium in the ICU.



Vanderbilt University
DEPARTMENT OF VETERANS AFFAIRS

- Overview
- Risk Factors
- Assessment, Adult and Pediatric Tools, Implementation, FAQ
- Patient and Family Information



Video: 10 Key Points Tutorial



Video: Dr. Valerie Page - Delirium in ICU



Video: Using the CAM-ICU



Video (youtube.com): CAM-ICU Video without ppt



Video (youtube.com / Portuguese): CAM ICU treatments



Video (youtube.com / Portuguese): Diagnóstico com CAM

Teaching Resources

This slide set has been created by Dr. Ely and Ms. Fun of the Vanderbilt and VA ICU Delirium and Cognitive Impairment Study group to help you educate others regarding this very dangerous condition, which is experienced by so many millions of patients every year. Please contact us through the website if you have any suggestions or questions regarding this material.



Download

ICU Delirium: Epidemiology, Monitoring & Management

CAM-ICU Resources in Foreign Languages

Resources - select a language



Ordering Printed Materials

You can order the Adult Pocket Cards and ASE Picture Cards. We will be glad to assist you in ordering printed materials. Send Stephanie Hamilton an email with the subject line "CAM-ICU order" and we will assist you.

ICU のためのせん妄評価法

(CAM-ICU)

トレーニング・マニュアル

これは ICU のためのせん妄マニュアル (CAM-ICU) の使用を望む医師、看護師、医療従事者のためのトレーニング・マニュアルです。CAM-ICU は ICU 患者のためのせん妄モニタリング法です。このトレーニング・マニュアルはよくある質問に答えると同時に CAM-ICU の使用方法を詳細に説明します。

疑問な点は以下にご連絡ください。

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Grant Support: The CAM-ICU was developed through funds from Dr Ely's Paul Beeson Faculty Scholar Award from the Alliance for Aging Research, a K23 from the National Institute of Health (AG01023-01A1), and support from the VA Tennessee Valley Healthcare System Geriatric Research, Education, and Clinical Center (GRECC). Dr Ely is now the Associate Director of Research for the GRECC.

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Background

- ICU delirium
 - 1) High incidence (80%)
 - 2) Many unavoidable risk factors
 - 3) Predictor of six month mortality
- Evaluation of delirium using validated tool
Japanese CAM-ICU

http://www.icudelirium.org/docs/CAM_ICU_training_Japanese.pdf

Cohort study at the ICU of Yamaguchi University Hospital

April 1, 2008-June 30, 2008

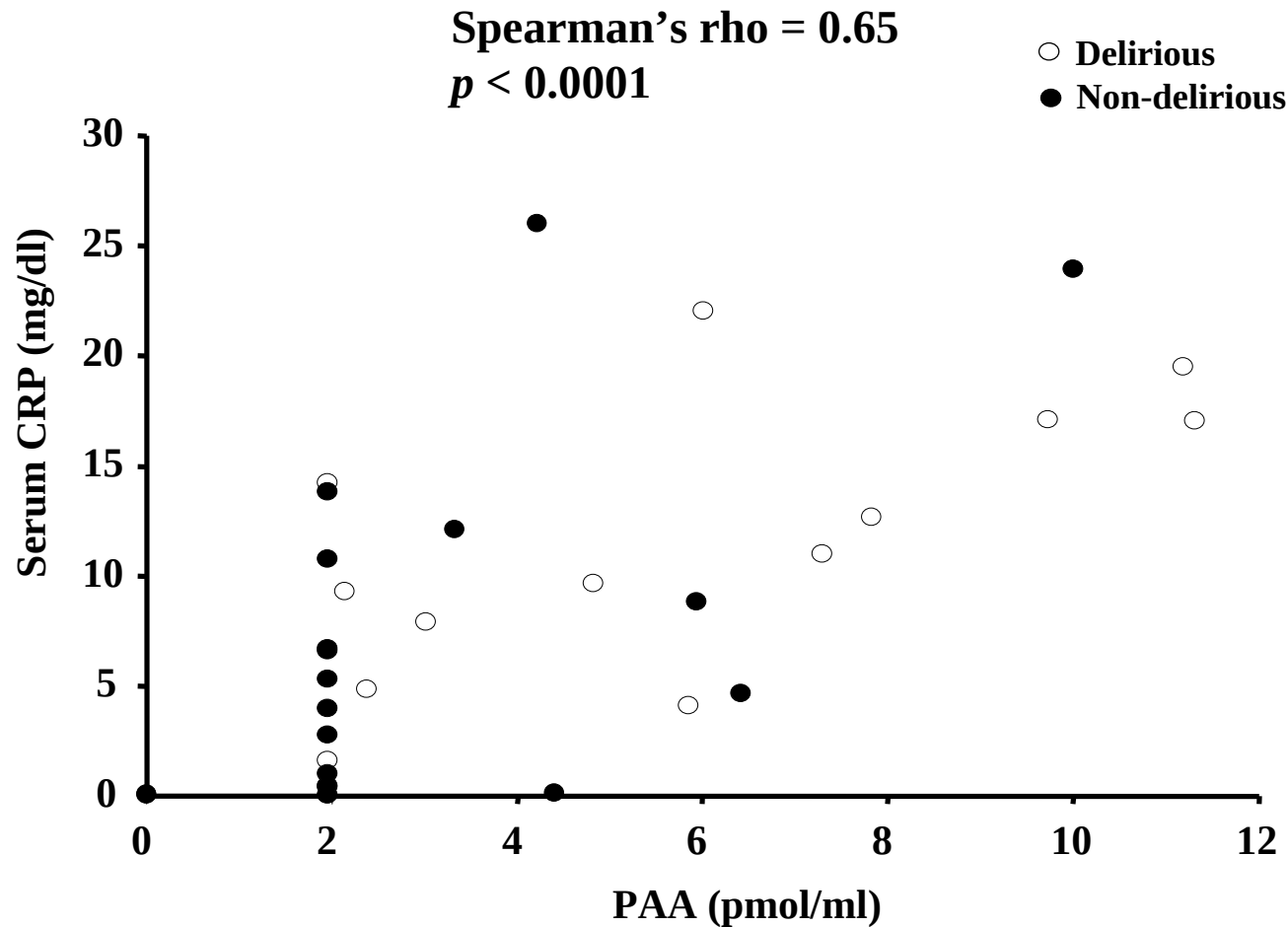
10-12 am, once-daily delirium evaluation

- 20% of enrolled patients (21/103)
- 76% of ventilated patients (13/17)
- All hypoactive delirium

Cohort study at the ICU of Yamaguchi University Hospital

Variable	OR (95%CI)	<i>P</i> Value
Use of mechanical ventilator	10.50 (2.36-46.72)	0.002
Serum max-CRP (mg/dL)	1.42 (1.03-1.95)	0.032
Length of ICU stay (days)	1.11 (1.00-1.23)	0.043

Correlation between serum CRP and plasma anticholinergic activity



(Tsuruta R, et al. Bull Yamaguchi Med School. 2008; 55: 35-42)

Purpose and necessity of the JEDI

- Prevalence of delirium in the Japanese ICU using the common evaluation tool
- Prevalence of ICU delirium among the different kinds of ICU (medical, surgical, and critical care & trauma center)
- Risk factors for ICU delirium (severity, infection, sedation, etc.)

What will we learn from JEDI?

- Prevalence of ICU delirium in Japan
- Relationship between delirium duration and 28-day mortality
- Risk factors for ICU delirium
- Other epidemiological aspects of delirium in Japan
- Relationship between sedation/analgesia practices and prevalence of ICU delirium
- Appropriate frequency of routine delirium monitoring

Patients

- Inclusion;
 - Mechanically ventilated adult ICU patients ($48 \geq$ hours)
- Exclusion;
 - i. DNAR patients
 - ii. Persistent disturbed consciousness (i.e., due to anoxic encephalopathy, brain stem hemorrhage or head trauma)
 - iii. Neurosurgical patients
 - iv. History of chronic dementia, psychosis, mental retardation and neuromuscular disease
 - v. Visual and hearing disturbance
 - vi. Unable to understand Japanese language

Methods of the JEDI

1) Design: observational cohort study

2) Outline

(1) Entry

June 1, 2011-July 31, 2011 (the 1st choice)

Oct 1, 2011-Nov 30, 2011 (the 2nd choice)

(2 months entry)

+ follow up for 28 days

Methods of the JEDI (2)

(2) Primary end points

- 1) 28 day outcome after intubation
- 2) ventilator free days
- 3) incidence of VAP
- 4) incidence of re-intubation

compared between delirious and nondelirious patients or 2-3 day delirious and 0-1 day delirious patients.