

# Liberation and Animation: the ABCDEs of good sedation and delirium management practices in the ICU



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Pratik Pandharipande, MD, MSCI, has received honoraria from Hospira and Orion Pharma.

## Need for Sedation and Analgesia

1. Prevention of pain and anxiety
2. Decrease oxygen consumption
3. Decrease the stress response
4. Patient-ventilator synchrony
5. ? Prevention of psychiatric illnesses—depression, PTSD

Rotondi AJ, et al. *Crit Care Med*. 2002;30:746-52A.  
Weinert C, et al. *Curr Opin in Crit Care*. 2005;11(4):376-380.  
Kress JP, et al. *J Respir Crit Care Med*. 1996;153:1012-1018.

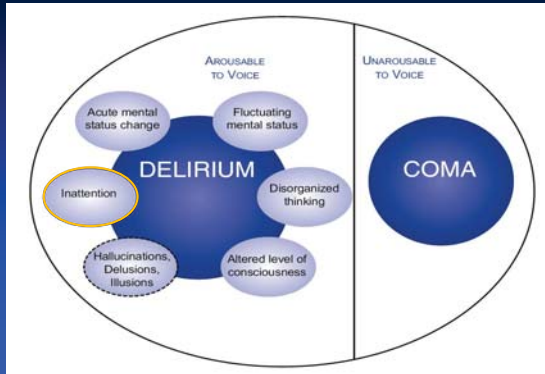
## Pitfalls of Sedatives and Analgesics

Sedatives and analgesics may contribute to

- Increased duration of mechanical ventilation
- Length of intensive care requirement
- Impede neurological examination
- May predispose to delirium

Kollef M, et al. *Chest*. 114:541-548.  
Pandharipande et al. *Anesthesiology*. 2006;124:21-26.

## Cardinal Symptoms of Delirium and Coma



Morandi A, et al. *Intensive Care Med.* 2008;34:1907-1915.

## Prevalence of ICU Delirium

- 60-80% MICU/SICU/TICU ventilated patients develop delirium
- 20-50% of lower severity ICU patients develop delirium
- Hypoactive or mixed forms most common
- Majority goes undiagnosed if routine monitoring is not implemented

Ely EW. *ICM.* 2001;27:1892-1900.  
 Ely EW. *JAMA.* 2001;286:2703-2710.  
 Pandharipande. *J Trauma.* 2008;65:34-41.  
 Ely EW. *CCM.* 2001;29:1370-1379.  
 Pandharipande. *ICM.* 2007;33:1726-1731.

Roberts B. *Aust Crit Care.* 2005;18:6:8-9.  
 Thomason J. *Crit Care.* 2005;9:375-381.  
 Ely EW. *CCM.* 2004;32:106-112.  
 Peterson. *JAGS.* 2006;54:479-484.  
 Ouimet S. *ICM.* 2007;33:66-73.

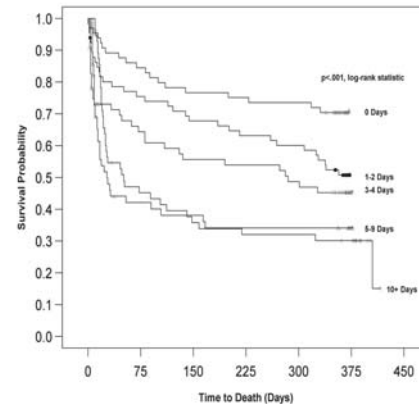
## Key Points: ICU Delirium

- \$15k to \$25k higher hospital costs
- Longer hospital stays
- 3 times higher risk of death by 6 months
- Prolonged neuropsychological dysfunction

Milbrandt E, et al. *Crit Care Med.* 2004;32:955-962.  
 Ely EW, et al. *JAMA.* 2004;291:1753-1762.  
 Ouimet S. *ICM.* 2007;33:66-73.  
 Lin, et al. *Crit Care Med.* 2004;32:2254-2259.

## Delirium duration and Mortality

Figure 2. Kaplan-Meier Survival Curves for an ICU Delirium Days Predictor



Pisani M. *Am J Respir Crit Care Med.* 2009 Dec 1;180(11):1092-7.

## Subsyndromal Delirium

Patients who present some symptoms of delirium, but do not fulfill all criteria for delirium.

## Subsyndromal Delirium and Clinical Outcomes

	No Delirium	Subsyndromal	Clinical Delirium	P-Value
ICU Mortality	2.4%	10.6%	15.9%	<.001
ICU LOS	2.5 (2.1)	5.2 (4.9)	10.8 (11.3)	<.001

Mean (SD) when applicable

Ouimet S. *Int Care Med.* 2007;33:1007-1013.

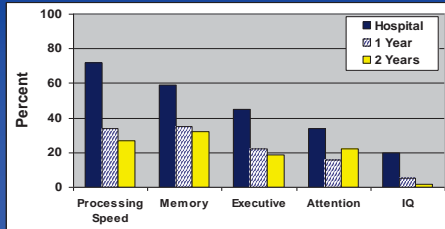
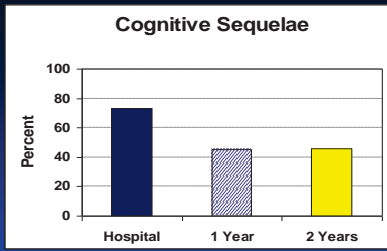
Is long-term cognitive impairment a significant problem among our ICU survivors (old and young)?

## Long-term cognitive impairment (LTCI) after ICU survival

- 10 cohorts (~500 pts) and the largest with neuropsychological testing was 74 patients
- Summary: ~2 out of 3 ICU survivors leave the ICU with long-term cognitive impairment that equates to mild/moderate dementia (sometimes severe)
- Deficits tend to be diffuse and occur in domains including memory, attention/concentration, language, executive functioning

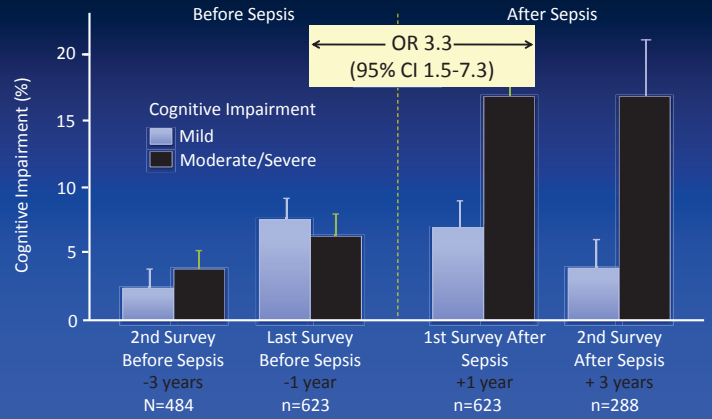
Rothenhausler, *Gen Hosp Psych* 2001;23:90-96  
Hopkins, *AJRCCM* 1999;160:50-56  
Jackson, *Crit Care Med* 2003;31:1226-34  
Hopkins, *JINS* 2004; 10:1005-1017  
Hopkins, *AJRCCM* 2005; 171:340-347

Marquis, *AJRCCM* 2000;161:A383 (Curtis)  
Al Sadi, *AJRCCM* 2003;167:A737 (Herridge)  
Sukantarat, *Anaesthesia* 2005;60:847-853  
Suchyta, *AJRCCM* 2004; 169:A18  
Christie, *AJRCCM* 2004; 169:A781



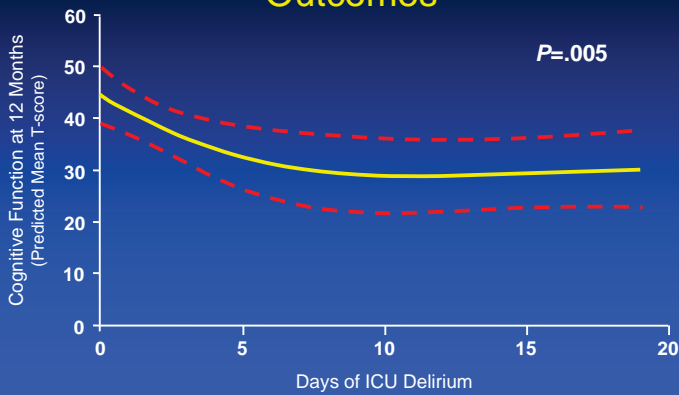
Hopkins AJRCCM 2005;171:340-7

## Cognitive Impairment after Sepsis



Iwashyna TJ, et al. JAMA 2010;304:1787-94

## Delirium and Long-Term Cognitive Outcomes



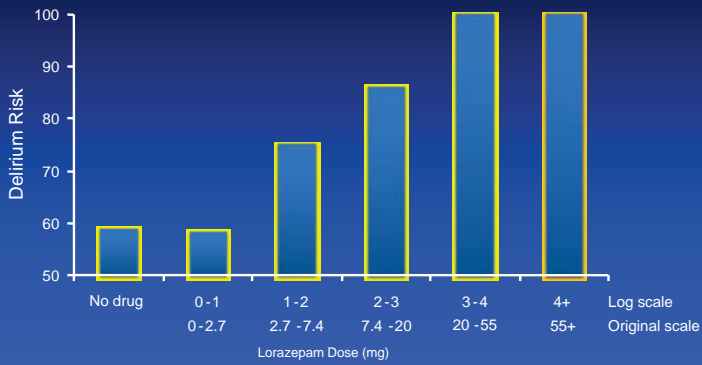
Girard TD, Jackson JC, Pandharipande P et al. CCM 2010 38(7):1513-20.

## Risk Factors for Delirium

- Aging
- Baseline dementia
- Psychiatric disorders
- Underlying illness
  - Inflammation
  - Coagulation
- Metabolic disturbances
- Hypoxemia
- Genetic predisposition (?)
- Psychoactive medications
- Sleep deprivation

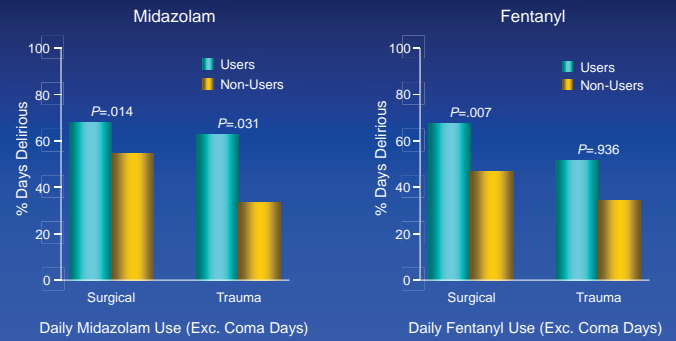
Inouye. JAMA. 1996;275:852-857.  
 Dubois. Intensive Care Med. 2001;27:1297-1304.  
 Inouye. NEJM. 1999;340:669-676.  
 Jacobi. Crit Care Med. 2002;30:119-141.  
 Milbrandt. Crit Care Med. 2005;33:226-229.  
 Ouimet S. Int Care Med. 2007;33:66-73  
 Pisani M. Crit Care Med. 2009 Jan;37(1):354-5

## Lorazepam and Delirium



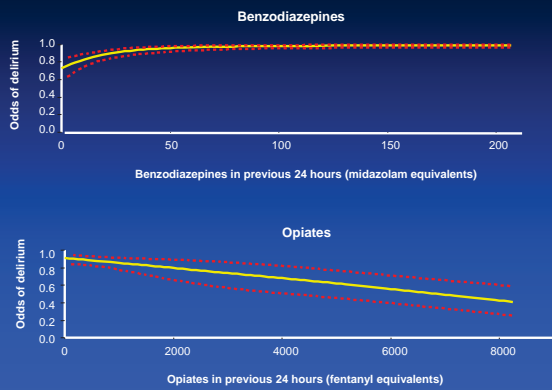
Pandharipande PP, et al. *Anesthesiology*. 2006;104:21-26.

## Midazolam and Fentanyl (?) as Risk Factors for Delirium (Trauma and SICU)



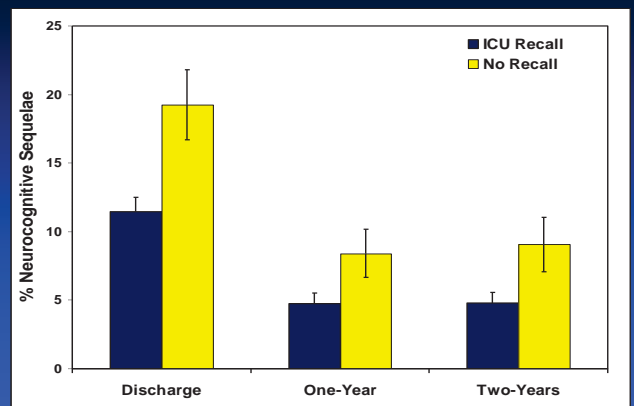
Pandharipande, et al. *J Trauma*. 2008;65:34-41.

## Risk factors of Delirium in Burn ICU patients



Agarwal et al. *J Burn Research and Rehab*. 2010 (epub)

## ARDS Patients



Larson MJ. *JINS* 2007;13:595-605

What should we do to “change” sedative exposure and improve outcomes?

Liberation and Animation

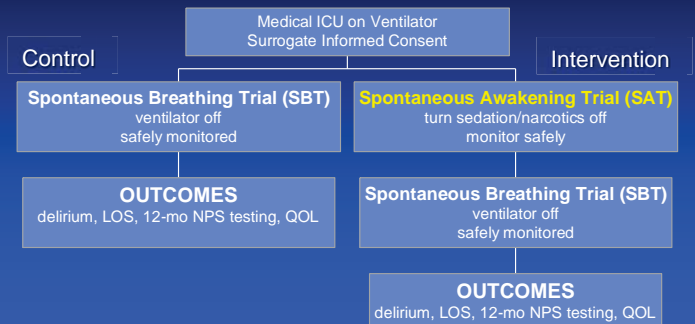
## The ABCDE approach of good sedation and delirium management

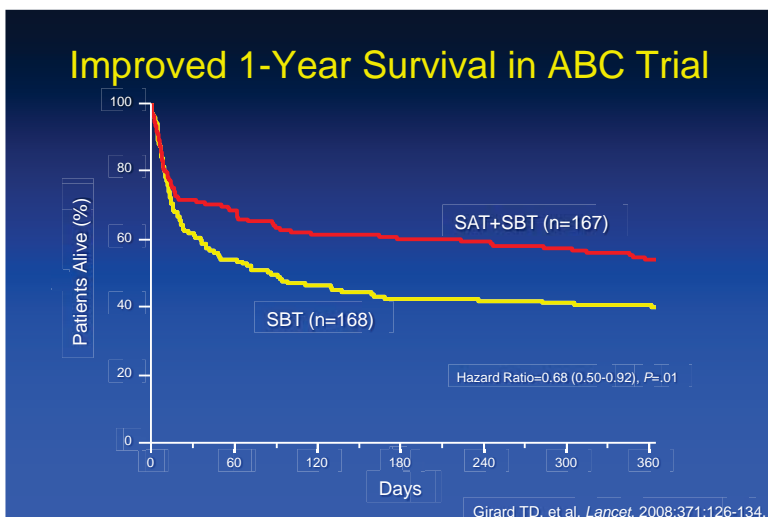
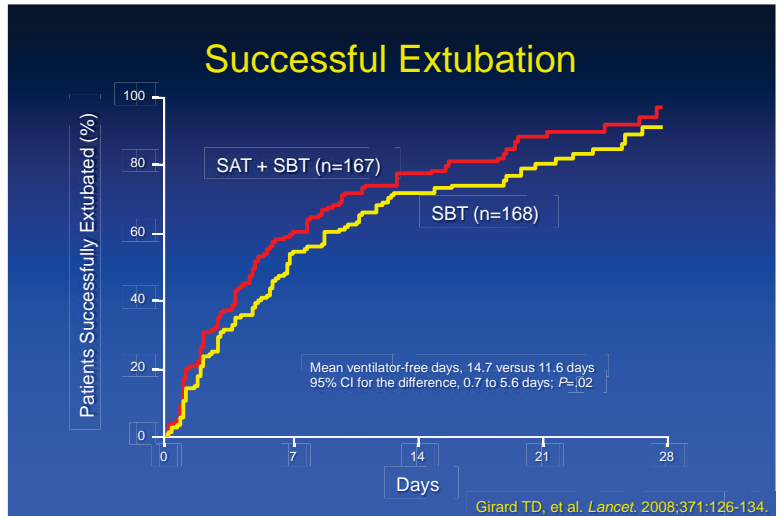
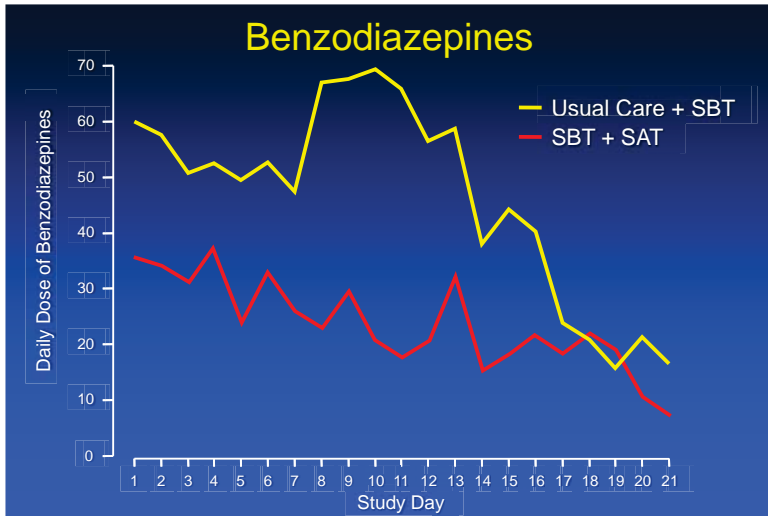
- **AB**- Awakening and Breathing Coordination
- **C**- Choice of Sedative
- **D**- Delirium monitoring and management
- **E**- Early mobility



•Awakening and Breathing

## The ABC Trial (Both groups get patient targeted sedation)





•Choice of sedation (after analgesia)

## Identifying and Treating Pain

### Behavioral Pain Scale (BPS)

Item	Description	Score
Facial expression	Relaxed	1
	Partially tightened (eg, brow lowering)	2
	Fully tightened (eg, eyelid closing)	3
	Grimacing	4
Upper limbs	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance with ventilation	Tolerating movement	1
	Coughing but tolerating ventilation for most of the time	2
	Fighting ventilator	3
	Unable to control ventilation	4

Payen JF, et al. *Crit Care Med*. 2001;29(12):2258-2263.

### Assessing Pain Improves Some Outcomes

Outcome	Day 2 Pain Assessment?		Unadj. OR	P-value	Adjusted OR	P-value
	No	Yes				
ICU Mortality	22%	19%	0.91	0.69	1.06	0.71
ICU LOS	18 d	13 d	1.70	< 0.01	1.43	0.04
MV duration	11 d	8 d	1.87	< 0.01	1.40	0.05
Vent-acquired pneumonia	24%	16%	0.61	< 0.01	0.75	0.21

Payen JF, et al. *Anesthesiology*. 2009;111:1308-1316.

### A Protocol of no sedation/analgo-sedation for mechanically ventilated patients

Prn morphine at 2.5- 5 mg for comfort



Physician consult if patient seemed uncomfortable  
Prn haloperidol for delirium



If still uncomfortable propofol infusion for 6 hours  
Transitioned to back to prn morphine  
3 such cycles allowed; if failed propofol infusion with DIS

Strom et al. *Lancet* 2010; 375:475-80



## Control group on "Sedation"

Sedation with propofol to achieve Ramsay score of 3-4



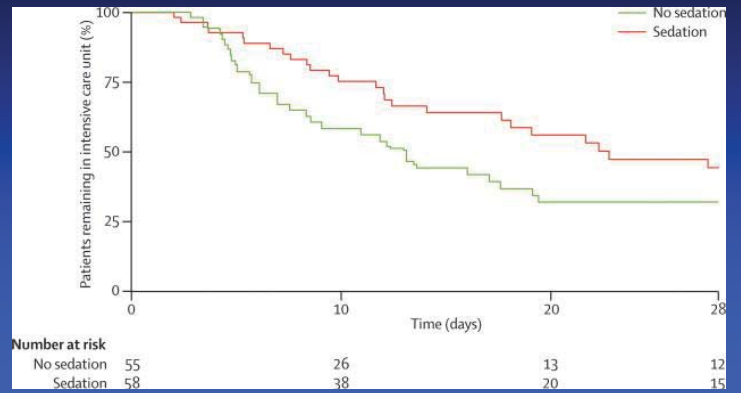
Morphine prn for pain  
Daily interruption of sedation; restart at half dose



After 48 hours of propofol, transitioned to midazolam titrated to Ramsay 3-4 with daily interruption of sedation

Strom et al. Lancet 2010; 375:475-80

## Study Outcomes



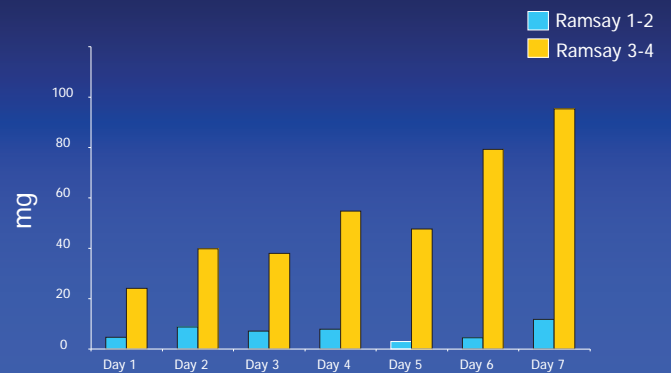
Strom et al. Lancet 2010; 375:475-80

## Randomized Trial of Light versus Deep Sedation on Mental Health after Critical Illness

- Randomized trial, open label
- Concealed allocation to one of two groups
  - **Light sedation group** (Ramsay 1-2)
    - Intermittent sedation
  - **Deep sedation group** (Ramsay 3-4)
    - Continuous sedation
- Balanced demographics and severity of illness

Treggiari MM, Crit Care Med. 2009;37:2527-34.

## Midazolam use reduced



Treggiari MM, Crit Care Med. 2009;37:2527-34.

## Mortality and Length of Stay

Outcome	Ramsay 1-2 n = 65	Ramsay 3-4 n = 64	P
ICU mortality, n (%)	9 (14)	9 (14)	>.99
Hospital mortality, n (%)	12 (18)	11 (17)	.65
Days of MV	2.9 ± 5.0	5.5 ± 10.8	.02
Ventilator free days (1 to 7)	6.6	5.7	.02
ICU length of stay	4.0	5.5	.03
ICU free days (1 to 7)	4	1	.03
Hospital length of stay	16	20	.47

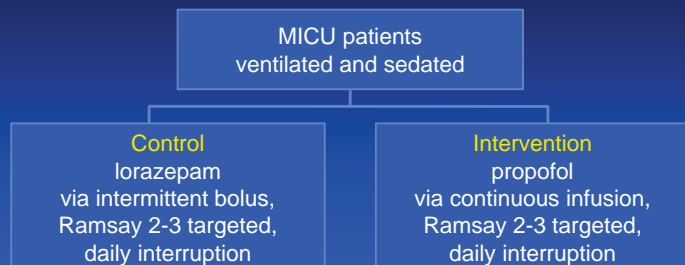
Treggiari MM, Crit Care Med. 2009;37:2527-34.

## Neuropsychological outcomes

4 weeks after ICU discharge

Outcome	Ramsay 1-2 n = 52	Ramsay 3-4 n = 50	P
PTSD score (ranks)	46 ± 29	56 ± 29	.07
Anxiety, mean score	5.3 ± 5.0	5.0 ± 4.2	.64
Depression, mean score	3.4 ± 3.7	3.1 ± 3.7	.72
Composite – sum of ranks	116 ± 68	123 ± 66	.69

## Propofol-Based Sedation Randomized Controlled Trial



University of North Carolina and University of Chicago Hospitals

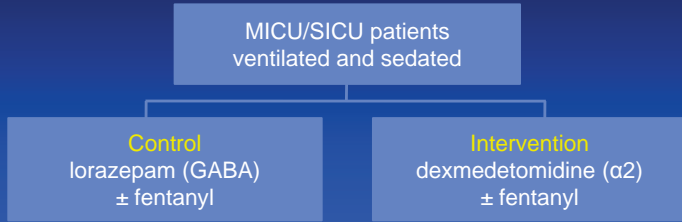
Carson SS, et al. Crit Care Med. 2006;34:1326-1332.

## Outcomes with Propofol-based sedation

Outcome	Lorazepam (n=64)	Propofol (n=68)	P-Value
Ventilator days			
All patients	8.4 [4.6-14.7]	5.8 [3.5-10.3]	.04
Survivors	9.0 [5.3-16.8]	4.4 [3.0-8.7]	.006
ICU length of stay, days			
Survivors	12.7 [7.8-19.1]	8.6 [5.0-14.7]	.05
Hospital mortality	38	37	.82

Carson SS, et al. Crit Care Med. 2006;34:1326-1332.

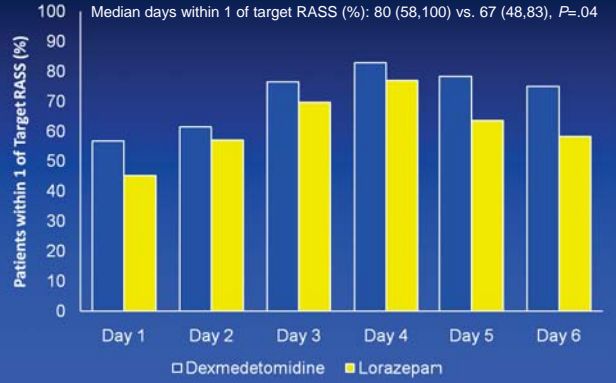
## Dexmedetomidine-based sedation MENDS double blind RCT



\*Doses of Dexmedetomidine up to 1.5 mcg/kg.hr  
\*\* Duration of Dexmedetomidine infusion up to 5 days or 120 hours

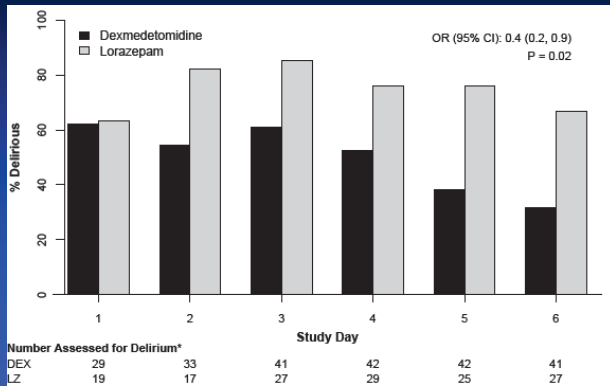
Pandharipande PP, et al. JAMA. 2007;298:2644-2653.

## Patients Accurately Sedated



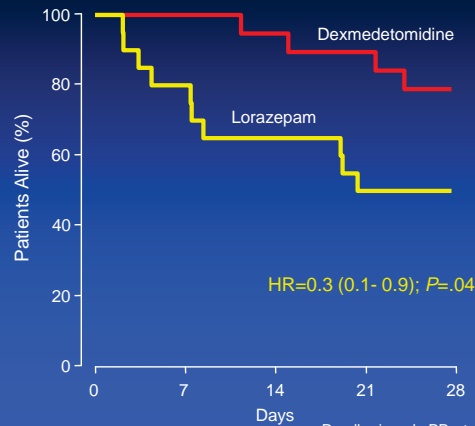
Pandharipande PP, et al. JAMA. 2007;298:2644-2653.

## Risk of Developing Delirium



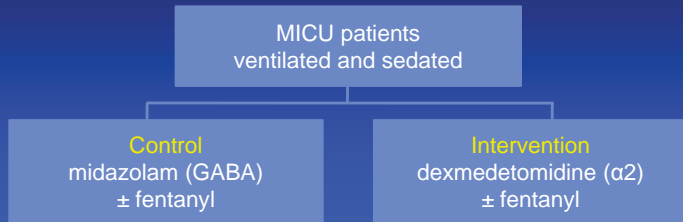
Pandharipande PP, et al. Crit Care. 2010;14(2):R38

## 28-Day Survival, Sepsis Patients



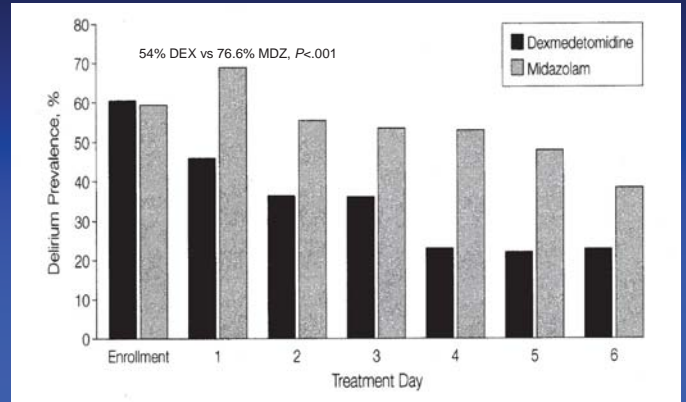
Pandharipande PP, et al. Crit Care. 2010;14(2):R38

## Dexmedetomidine Long-Term Study (SEDCOM)



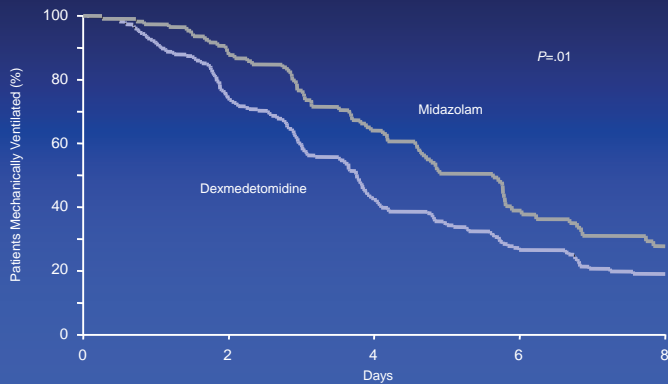
Riker RR, et al. JAMA. 2009;301:489-499.

## Prevalence of Delirium



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

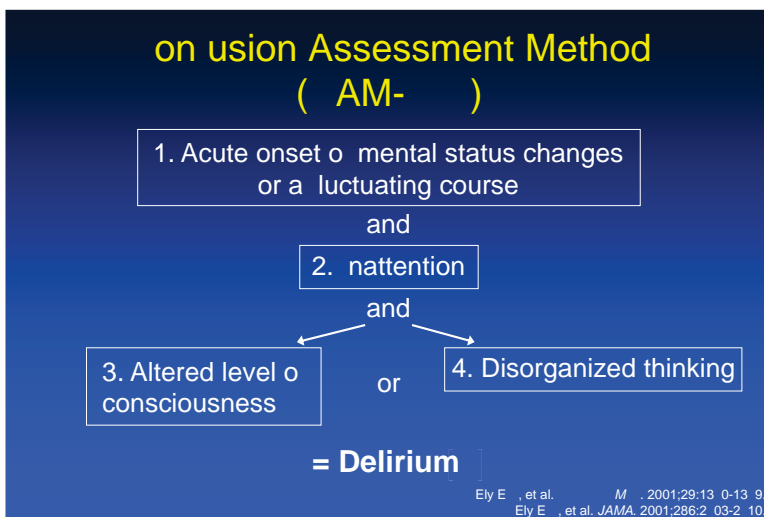
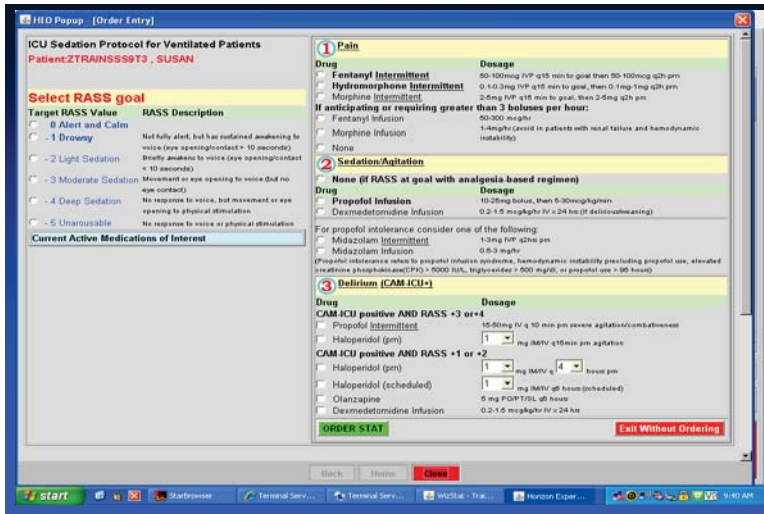
## Dexmedetomidine – Extubation



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

## Dexmedetomidine – Adverse Events

Outcome <sup>a</sup>	No. (%)		P Value
	Dexmedetomidine (n = 244)	Midazolam (n = 122)	
Cardiovascular			
Bradycardia	103 (42.2)	23 (18.9)	<.001
Bradycardia with intervention	12 (4.9)	1 (0.8)	.07
Tachycardia	62 (25.4)	54 (44.3)	<.001
Tachycardia with intervention	24 (9.8)	12 (9.8)	>.99
Hypotension	137 (56.1)	68 (55.7)	>.99
Hypotension with intervention	69 (28.3)	33 (27)	.90
Hypertension	106 (43.4)	54 (44.3)	.91
Hypertension with intervention	46 (18.9)	36 (29.5)	.02
Metabolic (hyperglycemia)	138 (56.6)	52 (42.6)	.02
Infections	25 (10.2)	24 (19.7)	.02
30-d mortality <sup>b</sup>	55 (22.5)	31 (25.4)	.60



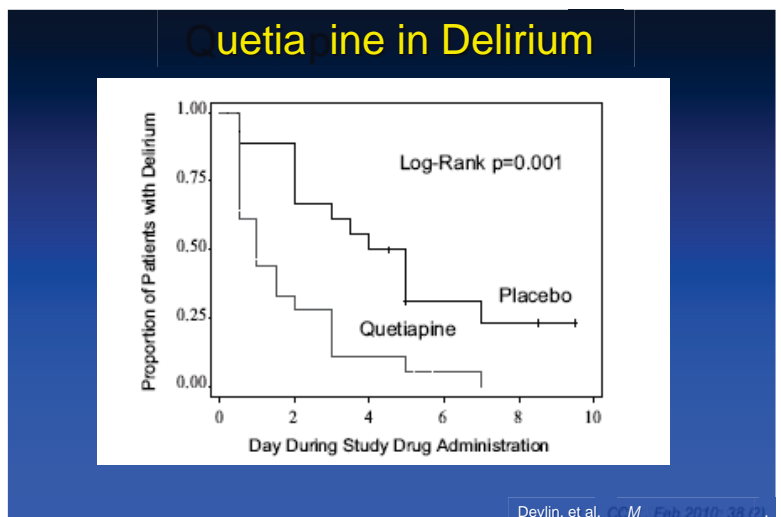
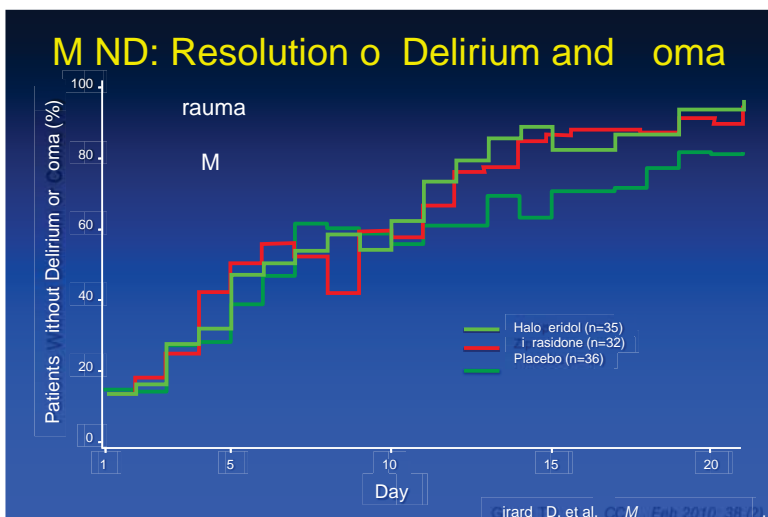
- ntensive are Delirium creening hecklist**
1. Altered level o consciousness
  2. nattention
  3. Disorientation
  4. Hallucinations
  5. Psychomotor agitation or retardation
  6. na ro riate s each
  7. lee ake cycle disturbances
  8. ym tom luctuation
- ergeron, et al. M. 2001;2 :859-864.



## Prevention Protocols for Delirium

- Reorientation, continuity of caregivers
- Promoting sleep architecture
- Decreased use of restraints
- Cognitive stimulation, providing eye glasses and hearing aids
- Removal of catheters
- Role of geriatrician visits or trained personnel in neuro-psychological disorders

houye, et al. *NEJM*. 1999;340:669-676.





Early mobility

## Early Mobilization Protocol

### Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial

William D Schwabiker, Mark C Pohlman, Anne S Pohlman, Celeina Nigos, Amy J Poulak, Cheryl L Esbrook, Linda Spears, Megan Miller, Mistka Franczyk, Deanna Depizzo, Gregory A Schmidt, Amy Bowman, Rhonda Barr, Kathryn E McCallister, Jesse B Hall, John P Kress

#### Summary

**Background** Long-term complications of critical illness include intensive care unit (ICU)-acquired weakness and neuropsychiatric disease. Immobilisation secondary to sedation might potentiate these problems. We assessed the efficacy of combining daily interruption of sedation with physical and occupational therapy on functional outcomes in patients receiving mechanical ventilation in intensive care.

**Methods** Sedated adults (≥18 years of age) in the ICU who had been on mechanical ventilation for less than 72 h, were expected to continue for at least 24 h, and who met criteria for baseline functional independence were eligible for enrolment in this randomised controlled trial at two university hospitals. We randomly assigned 104 patients by computer-generated, permuted block randomisation to early exercise and mobilisation (physical and occupational therapy) during periods of daily interruption of sedation (intervention; n=49) or to daily interruption of sedation with therapy as ordered by the primary care team (control; n=55). The primary endpoint—the number of patients returning to independent functional status at hospital discharge—was defined as the ability to perform six activities of daily living and the ability to walk independently. Therapists who undertook patient assessments were blinded to treatment assignment. Secondary endpoints included duration of delirium and ventilator-free days during the first 28 days of hospital stay. Analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00322010.



Published Online  
May 14, 2009  
DOI:10.1016/S0140-6736(09)60628-9  
See Online/Comment  
DOI:10.1016/S0140-6736(09)60628-9  
Department of Medicine,  
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A S Pohlman MD, C Nigos RN,  
K E McCallister RN,  
Jesse B Hall MD, J P Kress MD

ch eickert et al., lancet 2009;3 3:18 4-82

Milestones Achieved a day 3 days earlier ( <0.001)

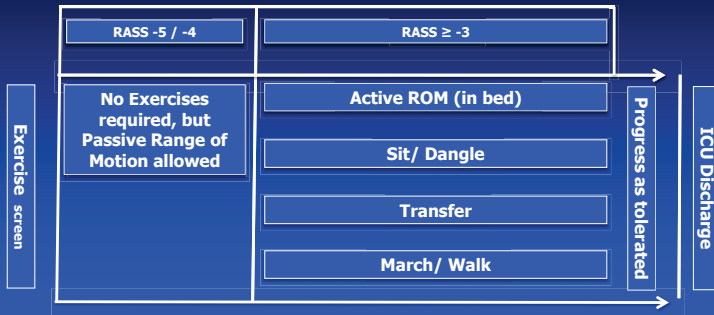
1. Standing
2. Marching
3. Walking
4. Transferring

## Daily Wake- Early Mobility

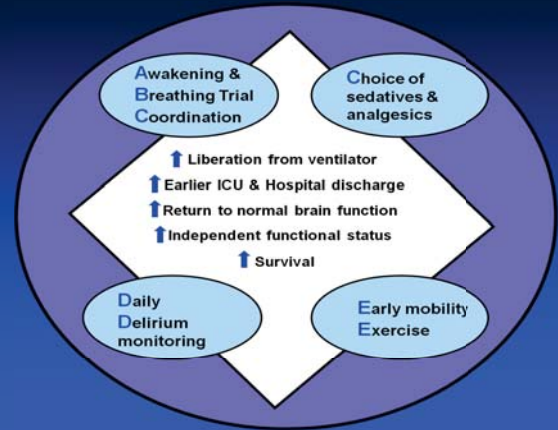
Outcome	Intervention (n=49)	Control (n=50)	P
functionally independent at discharge	29 (59%)	19 (35%)	.02
delirium (days)	2.0 (0.0-6.0)	4.0 (2.0-.0)	.03
time in delirium (%)	33% (0-58)	5% (33-69)	.02
Hospital delirium (days)	2.0 (0.0-6.0)	4.0 (2.0-8.0)	.02
Hospital days with delirium (%)	28% (26)	41% (2)	.01
Barthel index score at discharge	5 (.5-95)	55 (0-85)	.05
-acquired paresis at discharge	15 (31%)	2 (49%)	.09
Ventilator-free days	23.5 (.4-25.6)	21.1 (0.0-23.8)	.05
length of stay in (days)	5.9 (4.5-13.2)	.9 (6.1-12.9)	.08
length of stay in hospital (days)	13.5 (8.0-23.1)	12.9 (8.9-19.8)	.93
Hospital mortality	9 (18%)	14 (25%)	.53

ch eickert D, et al. . 2009;3 3:18 4-1882.

## Early Exercise and Mobility Protocol Progression



## Benefits of ABCDE Protocol



Morandi A et al. *urr in rit are*,2011;1 :43-9

## conclusion

- Important to balance the benefits and risks associated with sedative/analgesic medications
- Analgesia important, sedation/amnesia may not be necessary in all patients
- Delirium occurs in majority of mechanically ventilated patients and is associated with worse outcomes
- Sedatives and analgesics may be modifiable risks factors
- The “ABCDE” approach is one organizational framework of good practices that can improve patient outcomes