

Defining and Measuring Light versus Moderate/Deep Sedation

Pratik Pandharipande, MD, MSCI
Professor of Anesthesiology and Surgery
Department of Anesthesiology
Vanderbilt University School of Medicine
VA TN Valley Health Care System



CRITICAL ILLNESS, BRAIN DYSFUNCTION,
and SURVIVORSHIP (CIBS) CENTER

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Indications for Sedation in Literature

1. Prevention of anxiety, removal of devices
2. Decrease oxygen consumption
3. Decrease the physiological stress response
4. Patient-ventilator synchrony
5. ? Prevention of neuropsychological dysfunction– depression, PTSD

Pitfalls of Continuous Sedatives

Deep sedation (with continuous infusions) may contribute to

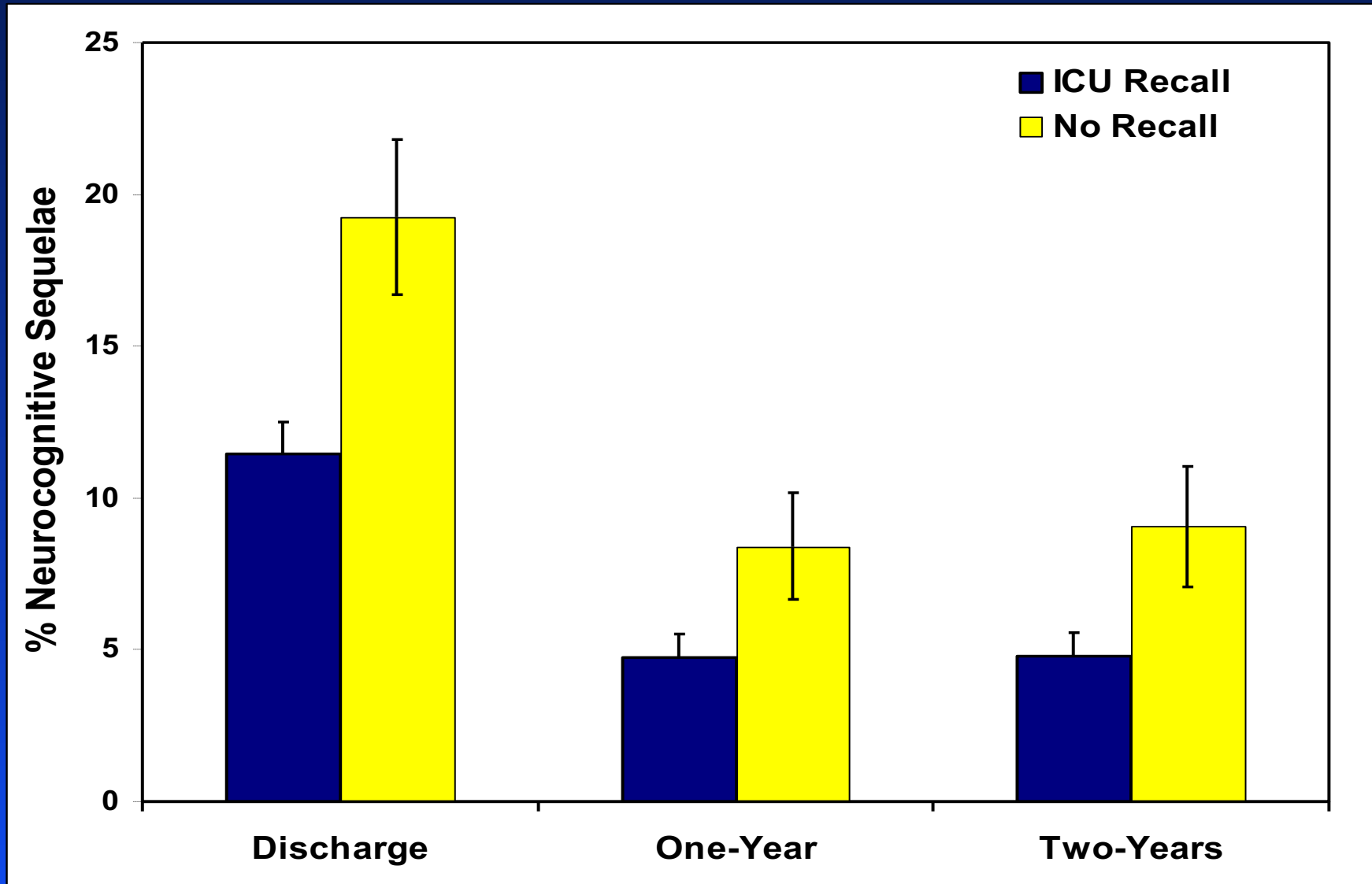
- Increased duration of mechanical ventilation
- Length of intensive care requirement
- Impede neurological examination
- Decreases mobility
- ? Increase mortality
- May predispose to delirium, ? Neuropsychological sequelae

Kollef M, et al. *Chest*. 114:541-548.

Pandharipande et al. *Anesthesiology*. 2006;124:21-26.

Shehabi et al. *Am J Respir Crit Care Med*. 2012 Oct 15;186(8):724-31

Sedation and Neuropsychological Sequelae



Guideline Recommendations of Light versus Moderate/Deep Sedation

The SCCM 2013 PAD guidelines

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

Juliana Barr, MD, FCCM¹; Gilles L. Fraser, PharmD, FCCM²; Kathleen Puntillo, RN, PhD, FAAN, FCCM³;

Depth of Sedation and Clinical Outcomes

Question: Should adult ICU patients be maintained at a light level of sedation? (actionable)

2. Agitation and Sedation

a. Depth of sedation vs. clinical outcomes

- i. Maintaining light levels of sedation in adult ICU patients is associated with improved clinical outcomes (e.g., shorter duration of mechanical ventilation and a shorter ICU length of stay [LOS]) (B).
- ii. Maintaining light levels of sedation increases the physiologic stress response, but is not associated with an increased incidence of myocardial ischemia (B).
- iii. The association between depth of sedation and psychological stress in these patients remains unclear (C).
- iv. We recommend that sedative medications be titrated to maintain a light rather than a deep level of sedation in adult ICU patients, unless clinically contraindicated (+1B).

The SCCM 2018 PADIS guidelines

Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU

John W. Devlin, PharmD, FCCM (Chair)^{1,2}; Yoanna Skrobik, MD, FRCP(c), MSc, FCCM (Vice-Chair)^{3,4}; Céline Gélinas, RN, PhD⁵; Dale M. Needham, MD, PhD⁶; Arjen J. C. Slooter, MD, PhD⁷; Pratik P. Pandharipande, MD, MSCI, FCCM⁸; Paula L. Watson, MD⁹; Gerald L. Weinhouse, MD¹⁰;

Question: Does light sedation (vs deep sedation), regardless of the sedative agent(s) used, significantly affect outcomes in critically ill, mechanically ventilated adults?

Light Versus Deep Sedation

Recommendation:

We suggest using light (vs. deep) sedation in critically ill, mechanically ventilated adults (conditional recommendation, low quality of evidence).

Evidence gaps:

- There is no consensus on definitions of light, moderate, and deep sedation.
- The relationship between changing sedation levels over time and clinical outcomes remains unclear.
- The effect of light sedation on post-ICU, patient-specific factors needs to be evaluated in RCTs.
- There is a dearth of information about interactions between sedative choice, depth, and patient-specific factors.

Defining Light versus Moderate/Deep Sedation in Guidelines

- 2018 PADIS
 - Evaluated studies where light vs. deep sedation was defined *a priori*, measured and explicitly reported with objective sedation scales
 - Described if those targets were met over time
 - No surrogate measures (plasma levels) or subjective clinical assessments of wakefulness were considered
 - Studies looking at spontaneous awakening trials were not considered since those reported lightening of sedation at single time point

Should we be using Objective
(relatively) Sedation Scales to
Define Light Sedation?

The Motor Activity Assessment Scale

Score	Description	Definition
0	Unresponsive	Does not move with noxious stimulus ^a
1	Responsive only to noxious stimuli	Opens eyes OR raises eyebrows OR turns head toward stimulus OR moves limbs with noxious stimulus ^a
2	Responsive to touch or name	Opens eyes OR raises eyebrows OR turns head toward stimulus OR moves limbs when touched or name is loudly spoken
3	Calm and cooperative	No external stimulus is required to elicit movement AND patient is adjusting sheets or clothes purposefully and follows commands
4	Restless and cooperative	No external stimulus is required to elicit movement AND patient is picking at sheets or tubes OR uncovering self and follows commands
5	Agitated	No external stimulus is required to elicit movement AND attempting to sit up OR moves limbs out of bed AND does not consistently follow commands (e.g., will lie down when asked but soon reverts back to attempts to sit up or move limbs out of bed)
6	Dangerously agitated, uncooperative	No external stimulus is required to elicit movement AND patient is pulling at tubes or catheters OR thrashing side to side OR striking at staff OR trying to climb out of bed AND does not calm down when asked

^aNoxious stimulus, suctioning OR 5 secs of vigorous orbital, sternal, or nail bed pressure.

Sedation-Agitation Scale (SAS)

Score	State	Behaviors
7	Dangerous Agitation	Pulling at ET tube, climbing over bedrail, striking at staff, thrashing side-to-side
6	Very Agitated	Does not calm despite frequent verbal reminding, requires physical restraints
5	Agitated	Anxious or mildly agitated, attempting to sit up, calms down to verbal instructions
4	Calm and Cooperative	Calm, awakens easily, follows commands
3	Sedated	Difficult to arouse, awakens to verbal stimuli or gentle shaking but drifts off
2	Very Sedated	Arouses to physical stimuli but does not communicate or follow commands
1	Unarousable	Minimal or no response to noxious stimuli, does not communicate or follow commands

Richmond Agitation-Sedation Scale

Score	Term	Description
+4	Combative	Overtly combative or violent; immediate danger to staff
+3	Very agitation	Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff
+2	Agitated	Frequent nonpurposeful movement or patient-ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	
-1	Drowsy	Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice
-2	Light sedation	Briefly (less than 10 seconds) awakens with eye contact to voice
-3	Moderate sedation	Any movement (but no eye contact) to voice
-4	Deep sedation	No response to voice, but any movement to physical stimulation
-5	Unarousable	No response to voice or physical stimulation

Early Intensive Care Sedation Predicts Long-Term Mortality in Ventilated Critically Ill Patients

Yahya Shehabi^{1,2}, Rinaldo Bellomo^{3,4,5,6}, Michael C. Reade^{7,8}, Michael Bailey⁵, Frances Bass², Belinda Howe⁵, Colin McArthur⁹, Ian M. Seppelt¹⁰, Steve Webb^{11,12}, and Leonie Weisbrodt¹³;
Sedation Practice in Intensive Care Evaluation (SPICE) Study Investigators and the ANZICS Clinical Trials Group*

- Multicenter (25 Australia and New Zealand)
- 251 medical/surgical patients
- Deep sedation occurred in 191 (76.1%) patients within 4 hours and in 171 (68%) patients at 48 hours
- Delirium occurred in 51% of patients
- Only about 25% of ICUs had sedation protocols and had targeted sedation

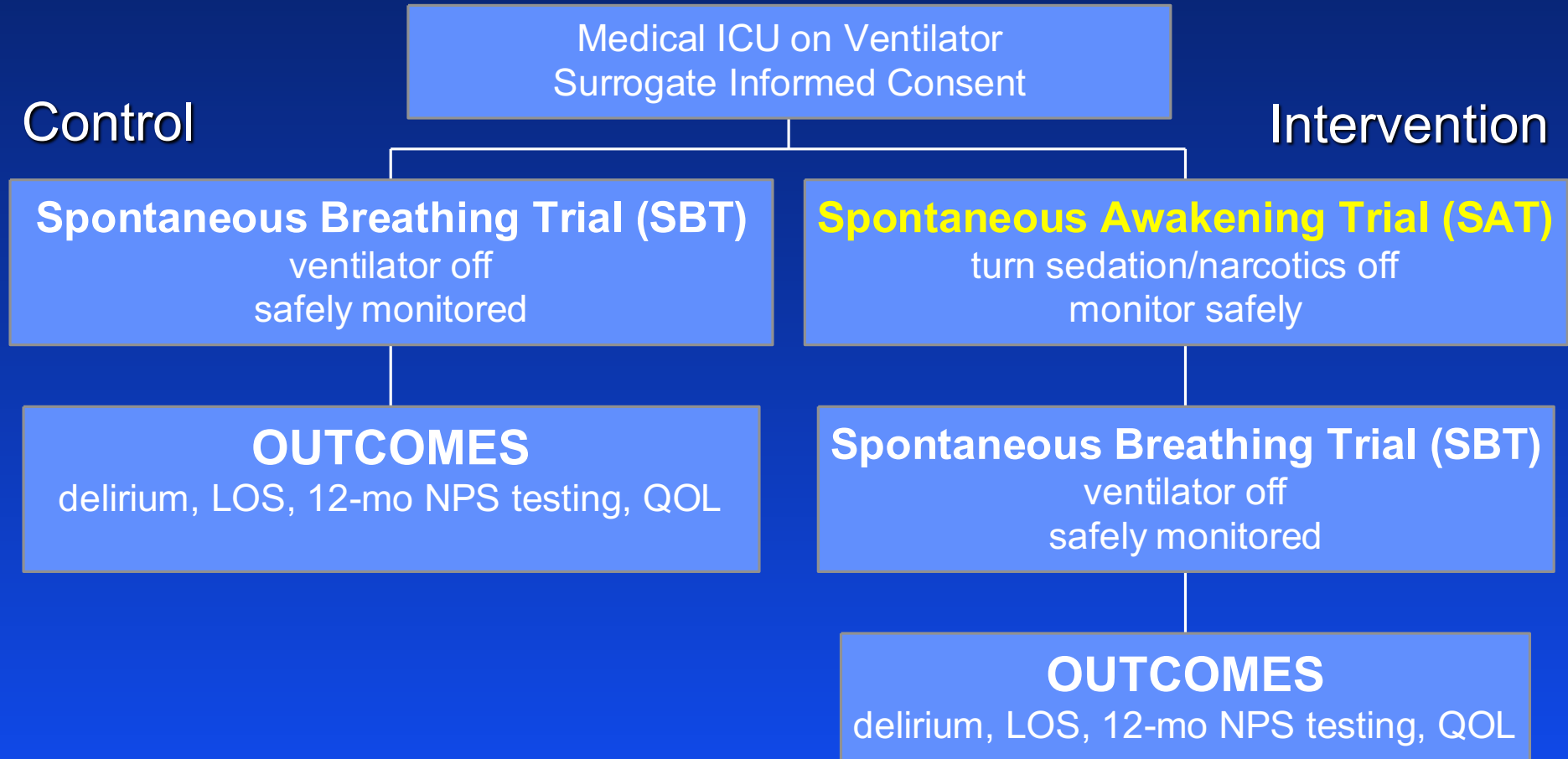
Deep sedation and Outcomes

	Time to extubation			delirium after 48 hrs			180 day mortality		
	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
RASS -3 to -5 ^A	0.90	0.87- 0.94	<0.001	1.05	0.99-1.11	0.10	1.08	1.01-1.16	0.027
APACHE II ^B	0.99	0.97-1.02	0.79	1.01	0.99-1.04	0.47	1.02	0.99-1.06	0.21
Age	0.99	0.98-1.00	0.71	1.00	0.99-1.01	0.62	1.03	1.01-1.05	0.009
Male	0.63	0.46-0.87	0.02	1.10	0.72-1.70	0.64	1.05	0.78-2.34	0.25
Operative	0.77	0.48-1.24	0.33	0.98	0.48-2.01	0.96	1.20	0.52-2.79	0.67
Elective	1.25	0.74-2.11	0.36	0.41	0.16-1.09	0.07	1.18	0.50-2.85	0.71

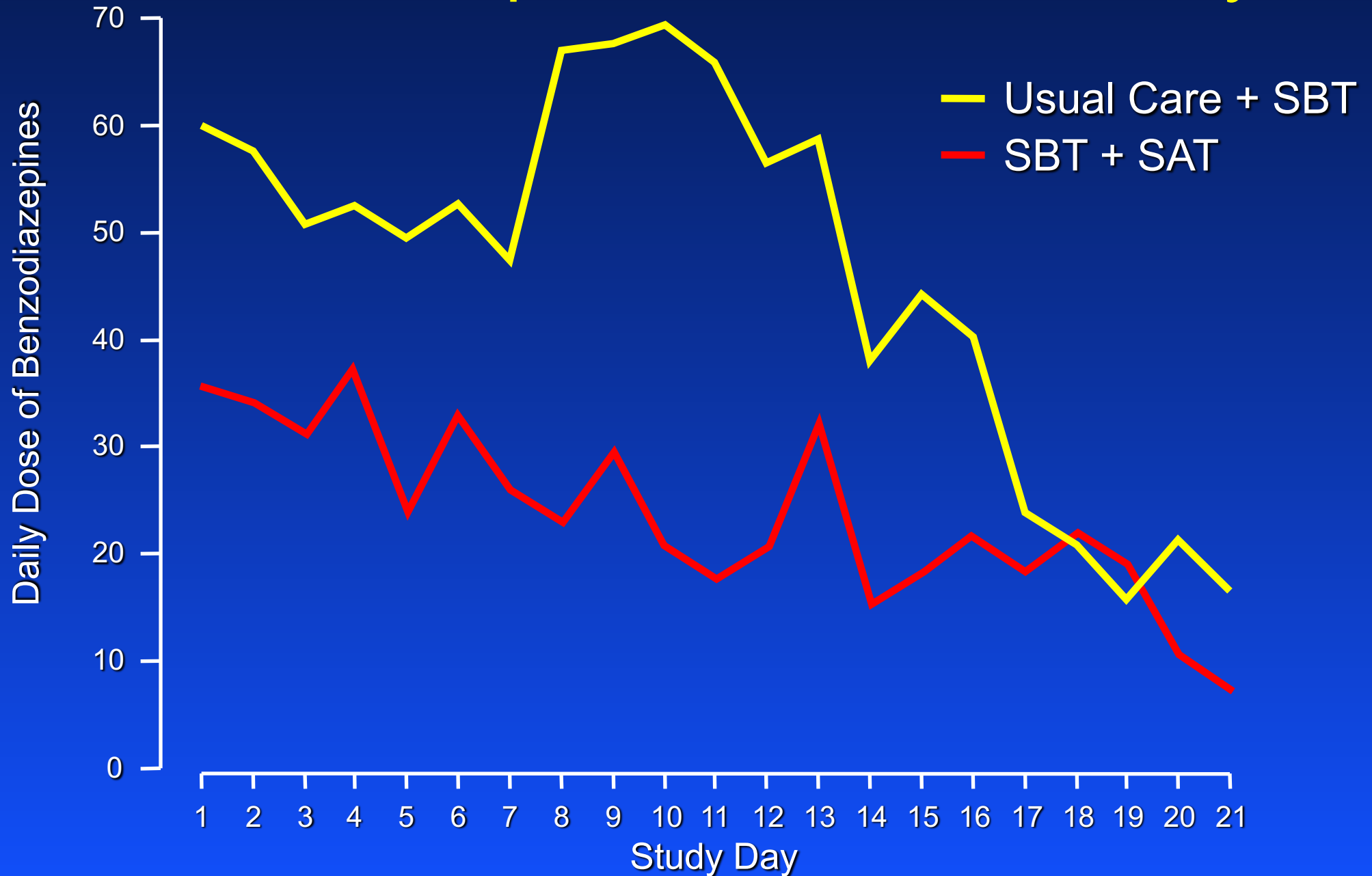
- Independent variable: number of RASS between -3 and -5 in first 48 hours
- Dependent variable: time to extubation, delirium or time to death

The ABC Trial

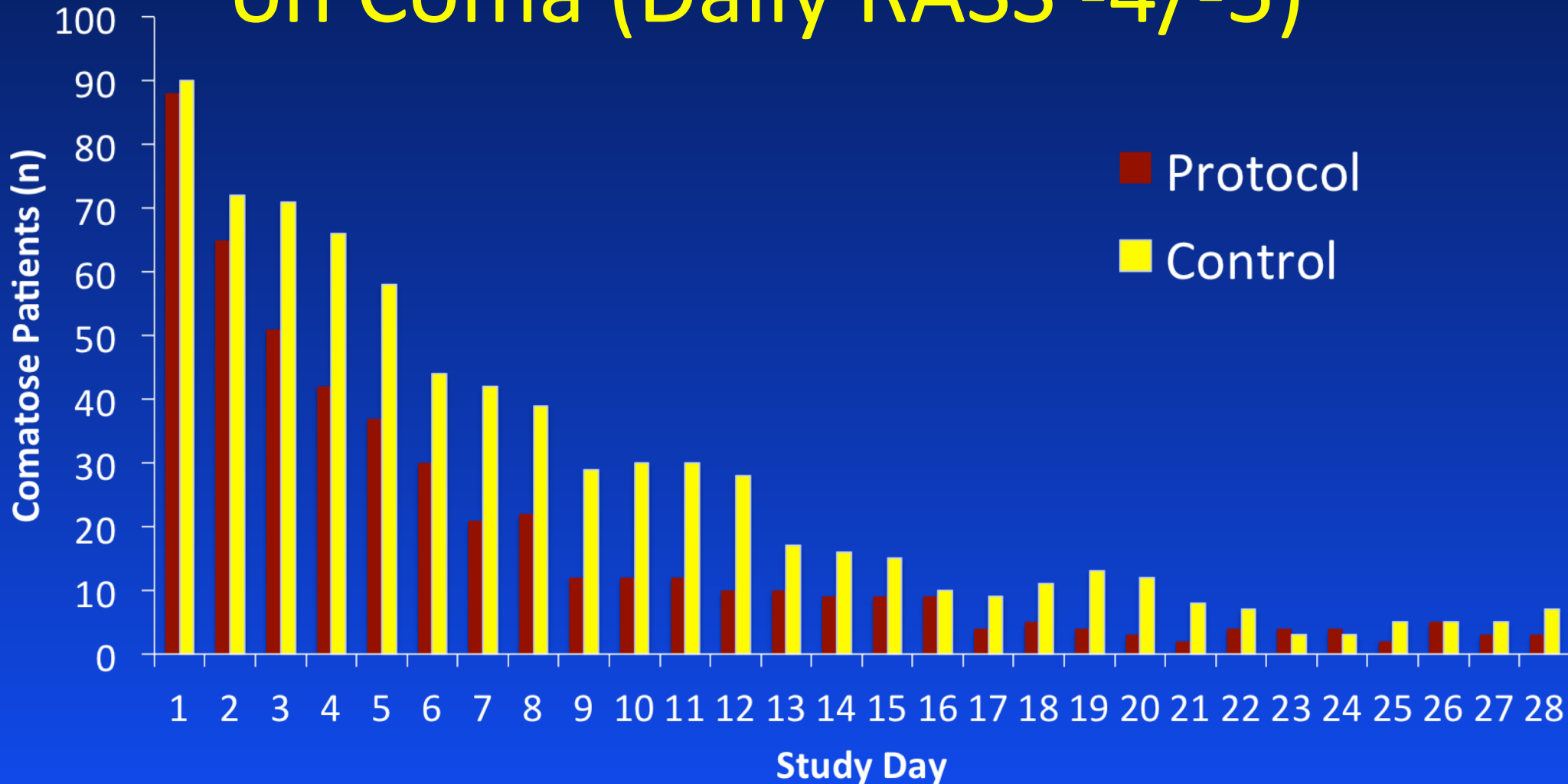
(Both groups get patient targeted sedation)



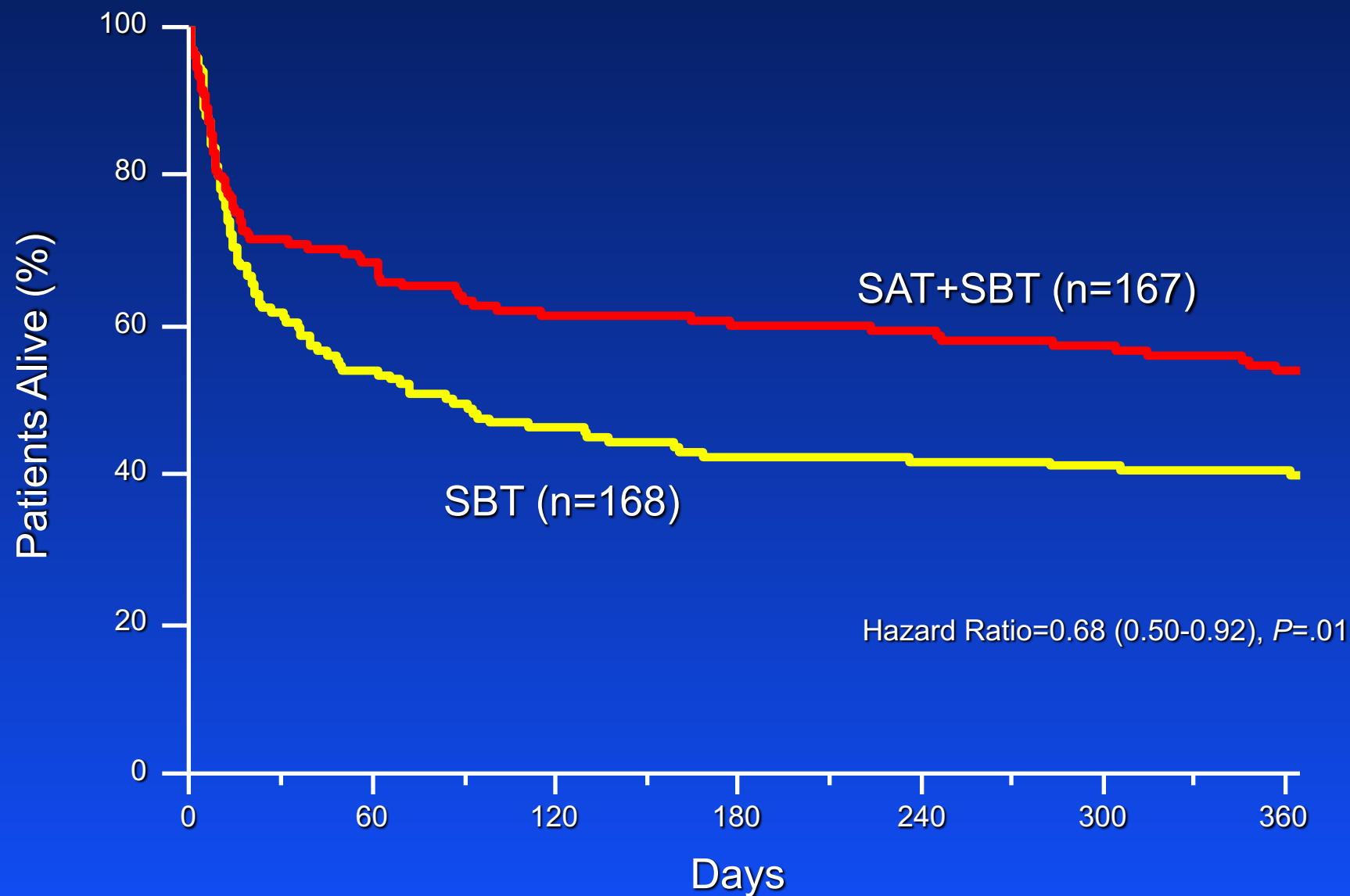
Benzodiazepines use in ABC study



Effect of Wake Up and Breathe on Coma (Daily RASS -4/-5)



Improved 1-Year Survival in ABC Trial



Static Goal or Change over
Time?

Should Definition of Light Sedation be Subjective (Patient/Family/Medical Team)?

- Ability to follow commands (sustained)
 - E.g. in Kress NEJM 2000- at least 3 of 4 objective actions: opens eyes in response to a voice, tracks investigator on request, squeezes hand, and sticks out the tongue
- Ability to communicate
 - With family, medical team, pain needs
- Ability to participate in mobilization
- Ability to participate in cognitive exercises

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



William D Schweickert, Mark C Pohlman, Anne S Pohlman, Celerina Nigos, Amy J Pawlik, Cheryl L Esbrook, Linda Spears, Megan Miller, Mietka Franczyk, Deanna Deprizio, Gregory A Schmidt, Amy Bowman, Rhonda Barr, Kathryn E McCallister, Jesse B Hall, John P Kress

Outcome	Intervention (n=49)	Control (n=50)	P
Functionally independent at discharge	29 (59%)	19 (35%)	.02
ICU delirium (days)	2.0 (0.0-6.0)	4.0 (2.0-7.0)	.03
Time in ICU with delirium (%)	33% (0-58)	57% (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% (27)	.01
Barthel Index score at discharge	75 (7.5-95)	55 (0-85)	.05
ICU-acquired paresis at discharge	15 (31%)	27 (49%)	.09
Ventilator-free days	23.5 (7.4-25.6)	21.1 (0.0-23.8)	.05
Length of stay in ICU (days)	5.9 (4.5-13.2)	7.9 (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

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How do you Summarize Sedation Level over Time?

- Number of 4 hour epochs of light vs. deep sedation
- Area under the curve approach (minimal length of time “light” per day)
 - SAT approach vs. targeted light sedation
- Sedation Index
- Plasma levels
- Objective Sedation Tools (EEG-based)

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Measures of Light Sedation and Outcomes

- Each of the threshold levels, with incorporation of time element will need to be evaluated for short and long-term outcomes
- Balanced against perceived risks- self extubation, device removal, anxiety, no other unintended consequence yet unknown