Can Goal Directed Sedation Improve Outcomes?

Yahya SHEHABI, FANZCA, FCICM, EMBA

Professor and Program Director Critical care

Monash Health and Monash University - Melbourne

School of Medicine, University New South Wales - Sydney

Disclosure and thank you

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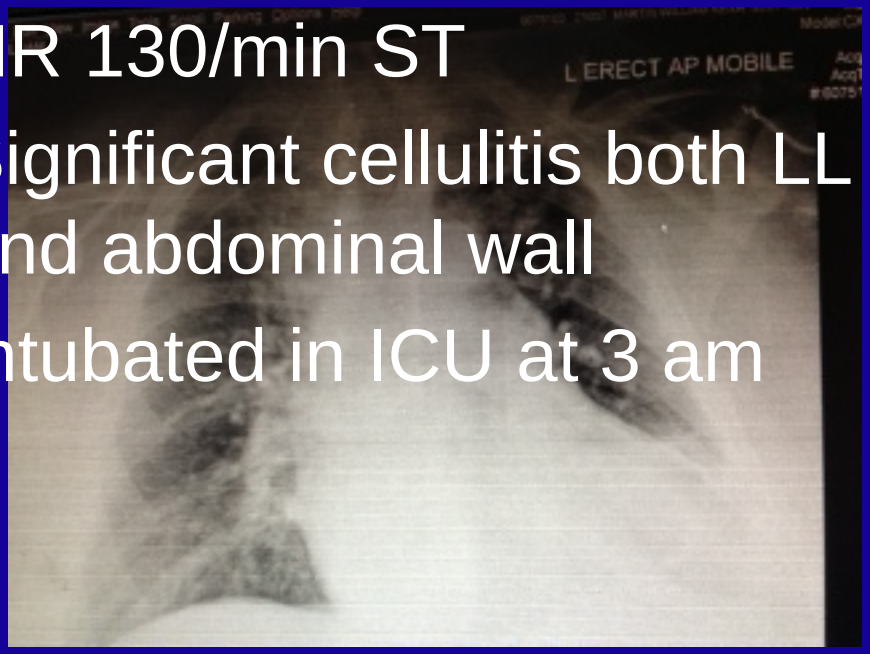
Australia 1 Sweden 1

Conventional Goals of Sedation

- Comfort through
  - Control at the bedside
  - Prevent awareness and recall
  - Prevent distress
  - Analgesia
- Facilitate necessary interventions
  - Invasive lines
  - Ventilation, suction
  - Other

Sedation in the ICU

- 63 yrs, 185 kg,
- presented severe SOB
- Temp 39.7, BP 90/55 (Norad)
- HR 130/min ST
- Significant cellulitis both LL and abdominal wall
- Intubated in ICU at 3 am

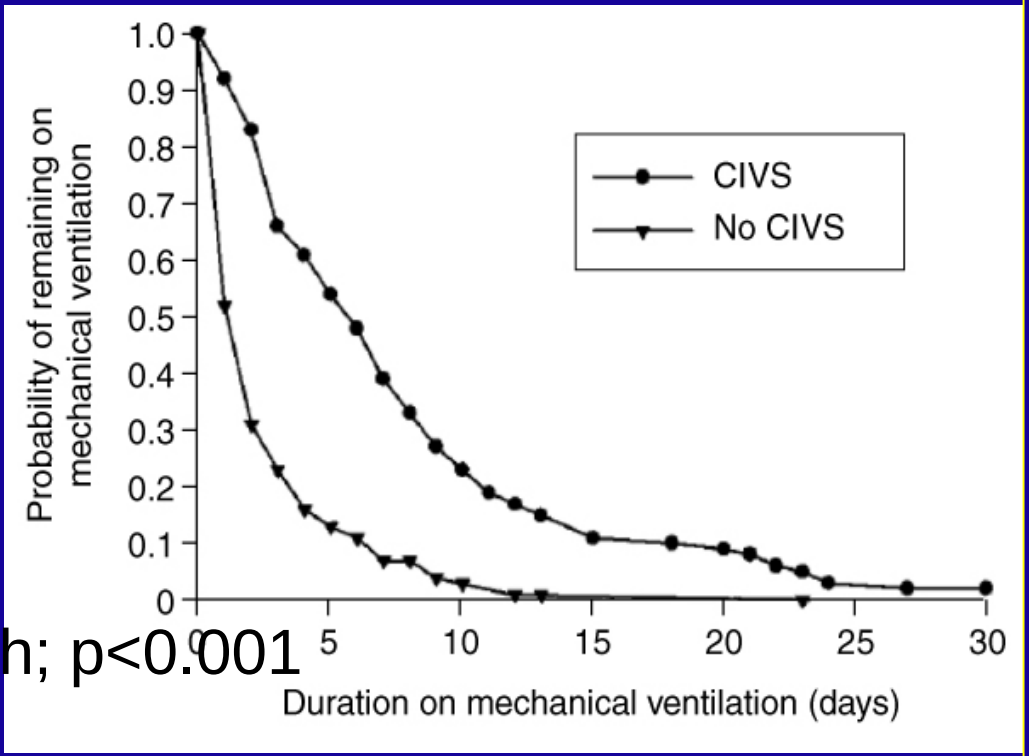


Continuous iv sedation is associated with prolongation of mechanical ventilation

Koleff Chest 1998

Single centre study
Observational study
242 total patients

93 Continuous IV sedation
64 Bolus sedation
85 No IV sedation

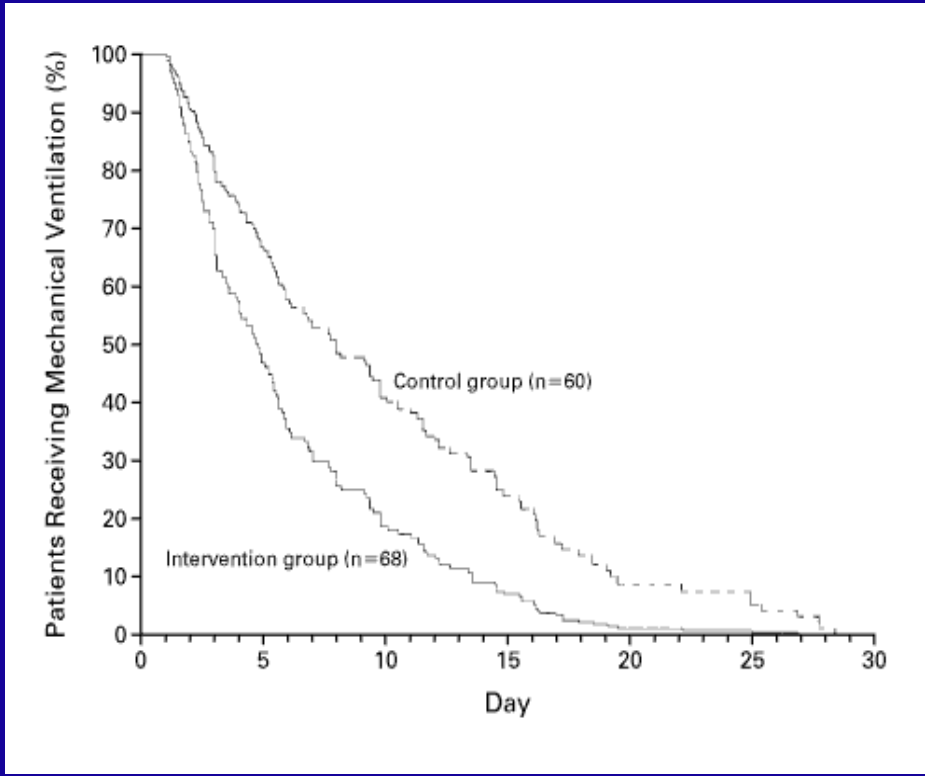


Ventilation time Crude
185±190 h vs 55.6±75.6 h; p<0.001

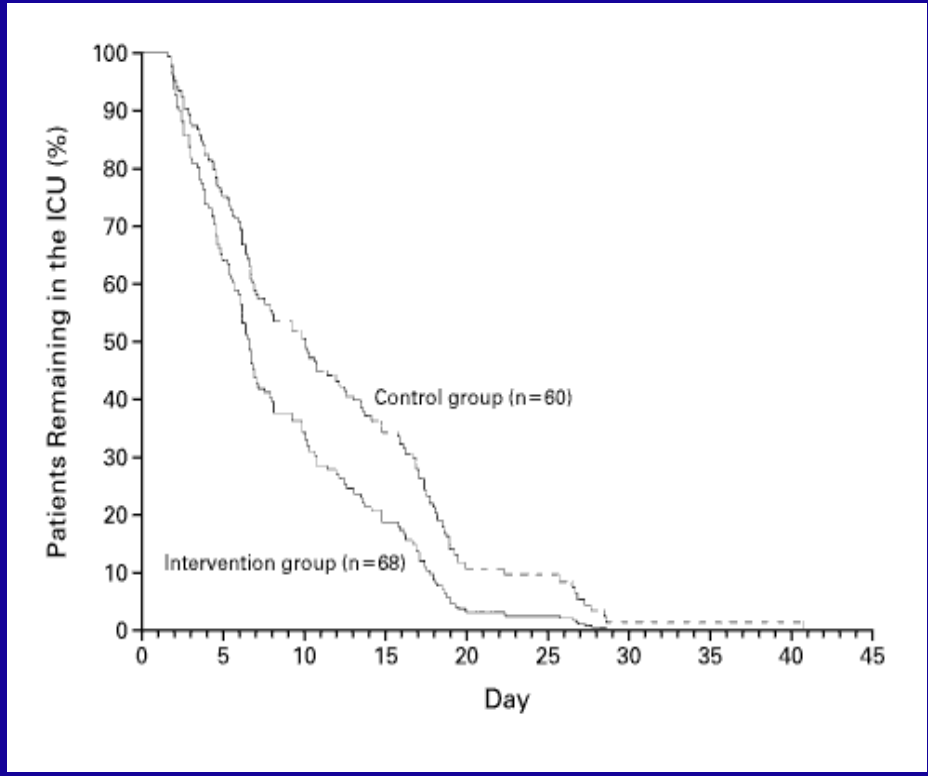
Adjusted
148 h [95% CI: 121, 175 h] vs 78.7 h [95% CI: 68.9, 88.6 h]; p<0.001

Daily Interruption of Sedative Infusions in Critically Ill Patients Undergoing Mechanical Ventilation

NEJM Volume 342:1471-1477 May 18, 2000 Number 20



Median ventilation time
7.3 days vs. 4.9 days



Median ICU length of stay
9.9 days vs. 6.4 days

DAILY INTERRUPTION OF SEDATIVE INFUSIONS IN CRITICALLY ILL PATIENTS UNDERGOING MECHANICAL VENTILATION

JOHN P. KRESS, M.D., ANNE S. POHLMAN, R.N., MICHAEL F. O'CONNOR, M.D., AND JESSE B. HALL, M.D.

We can thank Kress and coworkers for a superb study that examines approaches to care for patients receiving continuous sedative infusions in the intensive care unit. Considering the gaps in our knowledge, however, this investigation may represent not so much a call for daily wake-ups of patients undergoing mechanical ventilation as a wake-up call for practitioners in the intensive care unit to examine practices of sedation more critically. We need better methods of en-

Sedation research focus

- Reduce harm associated with deep sedation:
  - Acute brain dysfunction
  - Immobility and ICU weakness
  - Cardiovascular function
  - Tracheotomy
  - Ventilator related events
  - Depressed immunity
  - Acquired infections
  - Thromboembolism

Sedation interruption and Sedation Protocols

ONLINE FIRST

Daily Sedation Interruption in Mechanically Ventilated Critically Ill Patients Cared for With a Sedation Protocol

A Randomized Controlled Trial

Table 1. Baseline Characteristics

Characteristics	No. (%) Protocolized Sedation and Daily Interruption (n = 214)	No. (%) Protocolized Sedation (n = 209)
Mechanical ventilation, median (IQR), d	2 (1-4)	2 (1-4)
Opioid infusions		
No. (%)	184 (87)	186 (89)
Days of infusion, median (IQR)	1 (1-3)	1 (1-3)
Benzodiazepine infusions		
No. (%)	169 (81)	163 (80)
Days of infusion, median (IQR)	1 (1-3)	1 (1-3)

SLEAP study PS+DSI vs PS

Mehta et al *JAMA* Oct 2012

	PS+DI N=214	PS N=209	P value
Midazolam equivalents			
Dose /pt / day	102 (326)	82 (287)	0.04
Infusion, days	5.7 (6.4)	5.6 (5.9)	
Boluses/day	0.25 (1.1)	0.18 (0.81)	0.007
Fentanyl equivalents			
Dose / pt / day	1780 (4135)	1070 (2066)	<.0001
Infusion, days	6.4 (6.9)	6.6 (6.2)	
Boluses/day	2.2 (2.9)	1.8 (2.7)	<.0001

Key Trials of Sedative Agents

Regulatory purposes

- **3 major RCTs with nearly 1400 patients**
  - **Focused on drug A vs B**
  - **Late enrolment (up to 96 hours after ventilation)**
  - **Focused on ICU outcomes rather than patient centered long-term outcomes**
- **Sedative agents**
  - **Comparable in terms of safety and comfort**

Challenging the convention . .

A protocol of no sedation for critically ill patients receiving

ised trial

- Un-blinded
- Single centre
- Additional staff
- MDZ after 48 hrs
- Excluded 27 patients
- 20% cross over

ing mechanical ventilation is continuous sedation. Daily neral intesive care unit of Odense University Hospital, d to establish whether duration of mechanical ventilation erruption of sedation.

140 critically ill adult patients who were undergoing r more than 24 h. Patients were randomly assigned in a lation (20 mg/mL propofol for 48 h, 1 mg/mL midazolam group). Both groups were treated with bolus doses of ber of days without mechanical ventilation in a 28-day e care unit (from admission to 28 days) and in hospital This study is registered with ClinicalTrials.gov, number

48 h, and, as per our study design, were excluded from had significantly more days without ventilation (n=55; edation (n=58; mean 9·6 days, SD 10·0; mean difference ociated with a shorter stay in the intensive care unit (HR udied, in hospital (3·57, 1·52–9·09; p=0·0039), than was ences of accidental extubations, the need for CT or MRI um was more frequent in the intervention group than in

brain scans, or ventilator-associated pneumonia. Agitated delirium was more frequent in the intervention group than in the control group (n=11, 20% vs n=4, 7%; p=0·0400).

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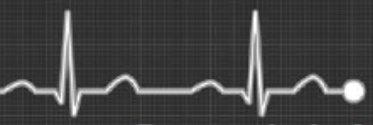
Department of Anesthesia and Intensive Care Medicine, Odense University Hospital (T Strøm MD, Prof P Toft DMSc), and Department of Biostatistics, Faculty of Health Sciences (Prof T Martinussen PhD), University of Southern Denmark, Denmark

Correspondence to:
Dr Thomas Strøm, Department of Anesthesia and Intensive Care Medicine, Odense University Hospital, University of Southern Denmark, 5000 Odense C, Denmark
t.s@dadlnet.dk

The 2013 SCCM Guidelines



Special Article

Light sedation
Analgesia first

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

Juliana Barr, MD, FCCM[1]; Gilles L. Fraser, PharmD, FCCM[2]; Kathleen Puntillo, RN, PhD, FAAN, FCCM[3]; E. Wesley Ely, MD, MPH, FACP, FCCM[4]; Céline Gélinas, RN, PhD[5]; Joseph F. Dasta, MSc, FCCM, FCCP[6]; Judy E. Davidson, DNP, RN[7]; John W. Devlin, PharmD, FCCM, FCCP[8]; John P. Kress, MD[9]; Aaron M. Joffe, DO[10]; Douglas B. Coursin, MD[11]; Daniel L. Herr, MD, MS, FCCM[12]; Avery Tung, MD[13]; Bryce R. H. Robinson, MD, FACS[14]; Dorrie K. Fontaine, PhD, RN, FAAN[15]; Michael A. Ramsay, MD[16]; Richard R. Riker, MD, FCCM[17]; Curtis N. Sessler, MD, FCCP, FCCM[18]; Brenda Pun, MSN, RN, ACNP[19]; Yoanna Skrobik, MD, FRCP[20]; Roman Jaeschke, MD[21]

Focus on delirium

- **Emerged as ICU issue after the CAM-ICU**
- Questionable relationship to:
  - Sedation depth
  - Sedative agents
- Questionable impact
  - Mortality
  - Cognitive dysfunction

The ABC (DE) approach

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 tria

Timothy D Girard, John P Kress, Barry D Fuchs, Jason W W Thomaso
Anne S Pohlman, Paul A Kinniry, James C Jackson, Angelo E Canoni
Jesse B Hall, Robert S Dittus, Gordon R Bernard, E Wesley Ely

Four centre study
1658 patients screened, 336 enrolled
MDZ and Opiates in control arm much higher
Doesn't reflect practice outside North America

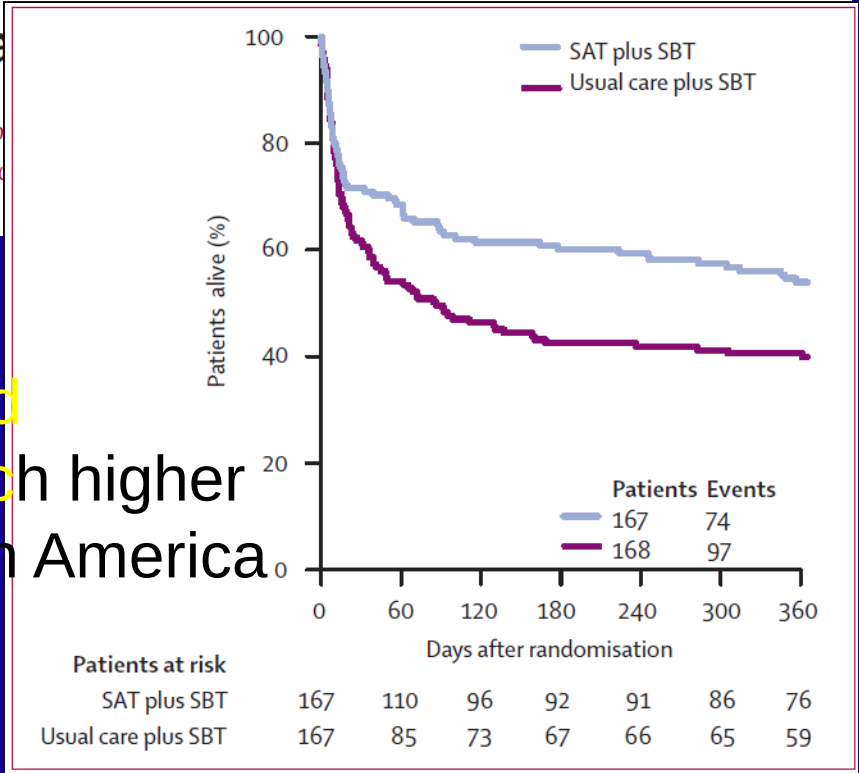


Figure 4: **Survival at 1 year**
Events indicate the number of deaths in each group in the year after enrolment.

Clinical outcomes

	Intervention group (n=167)	Control group (n=168)	p value
Ventilator-free days*			
Mean	14·7 (0·9)	11·6 (0·9)	0·02
Median	20·0 (0 to 26·0)	8·1 (0 to 24·3)	
Time to discharge (days)			
From intensive care	9·1 (5·1 to 17·8)	12·9 (6·0 to 24·2)	0·01
From hospital	14·9 (8·9 to 26·8)	19·2 (10·3 to NA)†	0·04
28-day mortality	47 (28%)	58 (35%)	0·21
1-year mortality	74 (44%)	97 (58%)	0·01
Duration of brain dysfunction (days)			
Coma	2 (0 to 4)	3 (1 to 7)	0·002
Delirium	2 (0 to 5)	2 (0 to 6)	0·50
RASS at first successful SBT	−1 (−3 to 0)	−2·5 (−4 to 0)	0·0001
Complications			
Any self-extubation	16 (10%)	6 (4%)	0·03
Self-extubation requiring reintubation‡	5 (3%)	3 (2%)	0·47
Reintubation‡	23 (14%)	21 (13%)	0·73
Tracheostomy	21 (13%)	34 (20%)	0·06

Data are mean (SD), n (%), or median (IQR). RASS=Richmond agitation-sedation scale. SAT=spontaneous awakening trial. SBT=spontaneous breathing trial. *Ventilator-free days from study day 1 to 28. †Greater than 25% of patients in the SBT group remained in the hospital at study day 28. ‡Reintubation within 48 hours of extubation.

Cognitive decline but why?

The NEW ENGLAND JOURNAL of MEDICINE

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,

Characteristic	In-Hospital Cohort (N=821)	Follow-up Cohort (N=467)
Coma		
No. of days		
Median	3	3
Interquartile range	2–6	1–5

Median (IQR) Days in Coma 3 [2-6] 3 [1-5]

Mobility after critical illness the new obsession

- NEJM case study
- 77 old following colon surgery
- 10 days on, still in
- **Poll, 94%**

  - **Minimize sedation**
  - **Institute early active and passive mobilization**
  - **Even while he is still undergoing mechanical ventilation**

ORIGINAL ARTICLE

Early Physical Medicine and Rehabilitation for Patients With Acute Respiratory Failure: A Quality Improvement Project

Dale M. Needham, MD, PhD, Radha Korupolu, MBBS, MS, Jennifer M. Zanni, PT, MSPT, Pranoti Pradhan, MBBS, MPH, Elizabeth Colantuoni, PhD, Jeffrey B. Palmer, MD, Roy G. Brower, MD, Eddy Fan, MD

Table 2: Sedation, Delirium, and Medication Outcomes

Outcome Measure	Pre-QI Period (n=27 Patients with 312 MICU Patient Days)	QI Period (n=30 Patients With 482 MICU Patient Days)	P*
Benzodiazepines			
Patients ever receiving benzodiazepines	26 (96)	22 (73)	.030
MICU days with any benzodiazepine use†	150 (50)	118 (26)	.002
Daily midazolam-equivalent dose, units (median [IQR] units)	47 (21–114)	15 (3–59)	.090
Narcotics			
Patients ever receiving narcotics	26 (96)	23 (77)	.050
MICU days with any narcotic use†	188 (62)	299 (66)	.650
Daily morphine-equivalent dose (median [IQR] units)	71 (30–180)	24 (3–120)	.010
Pain			
Daily scores (range, 0–10) (mean ± SD)‡	0.6±1.9	0.6±1.7	.790
Sedation status (daily RASS[23]) of MICU days§			
Deeply sedated (RASS −4 to −5)	129 (43)	86 (18)	<.001
Moderately sedated (RASS −2 to −3)	72 (24)	65 (14)	
Alert (RASS −1 to +1)	88 (30)	311 (67)	
Agitated (RASS +2 to +4)	8 (3)	6 (1)	
Delirium status (daily CAM-ICU[27]) of MICU days‖			
Delirious	107 (36)	125 (28)	.003
Not delirious	61 (21)	243 (53)	
Unable to assess because of deep sedation	129 (43)	86 (19)	

Original Investigation

Increased Hospital-Based Physical Rehabilitation and Information Provision After Intensive Care Unit Discharge
The RECOVER Randomized Clinical Trial

Timothy S. Walsh, MD; Lisa G. Salisbury, PhD; Judith L. Merriweather, PhD; Julia A. Boyd, PhD; David M. Griffith, MD; Guro Huby, PhD; Susanne Kean, PhD; Simon J. Mackenzie, MBChB; Ashma Krishan, MSc; Stephanie C. Lewis, PhD; Gordon D. Murray, PhD; John F. Forbes, PhD; Joel Smith, PhD; Janice E. Rattray, PhD; Alastair M. Hull, MD; Pamela Ramsay, PhD; for the RECOVER Investigators

Outcome (No. of Patients With Evaluable Data in Usual Care/Intervention Groups)	Treatment Group		Difference Scores, Mean (95% CI)	*P* Value
	Usual Care	Intervention		
RMI at 3 mo (110/118)[a]	13 (10 to 14)	13 (10 to 14)	−0.2 (−1.3 to 0.9)[b]	.71
Hospital Discharge Outcome				
Post-ICU hospital length of stay, d (119/119)[c]	10 (6 to 23)	11 (6 to 22)	0 (−2 to 2)[b]	.90
RMI (84/83)[d]	8 (5 to 10)	8 (6 to 11)	−0.7 (−1.7 to 0.4)[b]	.20
Handgrip strength, kg (82/82)[e]	15.0 (9.7 to 22.6)	14.7 (10.0 to 22.0)	1.1 (−1.3 to 3.6)[b]	.36
VAS symptom score, median (IQR) (83/80)[f]				
Breathlessness	2.8 (1.1 to 5.3)	2.5 (1.0 to 5.0)	0.2 (−0.5 to 1.0)	.49
Fatigue	5.0 (3.2 to 6.7)	5.1 (2.7 to 7.2)	0.0 (−0.9 to 0.9)	.96
Appetite	4.1 (1.7 to 6.7)	5.0 (1.9 to 7.6)	−0.4 (−1.6 to 0.4)	.33
Pain	2.6 (0.7 to 5.2)	2.3 (0.8 to 4.7)	0.0 (−0.6 to 0.8)	.89
Joint stiffness	3.6 (1.1 to 6.2)	3.3 (1.1 to 4.9)	0.5 (−0.3 to 1.5)	.21

- No difference at 3, 6 and 2 months
- Better patient satisfaction with care provided

The 2013 SCCM Guidelines

Implementation of the Pain, Agitation, and Delirium Clinical Practice Guidelines and Promoting Patient Mobility to Prevent Post-Intensive Care Syndrome

Judy E. Davidson, DNP, RN, FCCM[1]; Maurene A. Harvey, RN, MPH, MCCM[2];
Anita Bemis-Dougherty, PT, DPT, MAS[3]; James M. Smith, PT, DPT[4]; Ramona O. Hopkins, PhD[5,6]

Proposed 2 new recommendations:

- Light sedation to allow patient activities
- Promote early mobility to prevent physical deterioration and reduce delirium

Brenda Pun, MSN, RN, ACNP[19]; Yoanna Skrobik, MD, FRCP[20]; Roman Jaeschke, MD[21]

Can sedation strategies improve important outcomes?

Sedation in ARDS

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

High-Frequency Oscillation in Early Acute Respiratory Distress Syndrome

Niall D. Ferguson, M.D., Deborah J. Cook, M.D., Gordon H. Guyatt, M.D., Sangeeta Mehta, M.D., Lori Hand, R.R.T., Peggy Austin, C.C.R.A., Qi Zhou, Ph.D., Andrea Matte, R.R.T., Stephen D. Walter, Ph.D., Francois Lamontagne, M.D., John T. Granton, M.D., Yaseen M. Arabi, M.D., Alejandro C. Arroliga, M.D., Thomas E. Stewart, M.D., Arthur S. Slutsky, M.D., and Maureen O. Meade, M.D., for the OSCILLATE Trial Investigators and the Canadian Critical Care Trials Group*

Outcome	HFOV Group (N = 275)	Control Group (N = 273)	Relative Risk (95% CI)	P Value
Death in hospital — no. (%)	129 (47)	96 (35)	1.33 (1.09–1.64)	0.005
Death in intensive care unit — no. (%)	123 (45)	84 (31)	1.45 (1.17–1.81)	0.001
Death before day 28 — no. (%)	111 (40)	78 (29)	1.41 (1.12–1.79)	0.004
New barotrauma — no./total no. (%)*	46/256 (18)	34/259 (13)	1.37 (0.91–2.06)	0.13
New tracheostomy — no./total no. (%)†	59/273 (22)	66/267 (25)	0.87 (0.64–1.19)	0.39
Refractory hypoxemia — no. (%)	19 (7)	38 (14)	0.50 (0.29–0.84)	0.007

Sedation may be harmful in ARDS

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

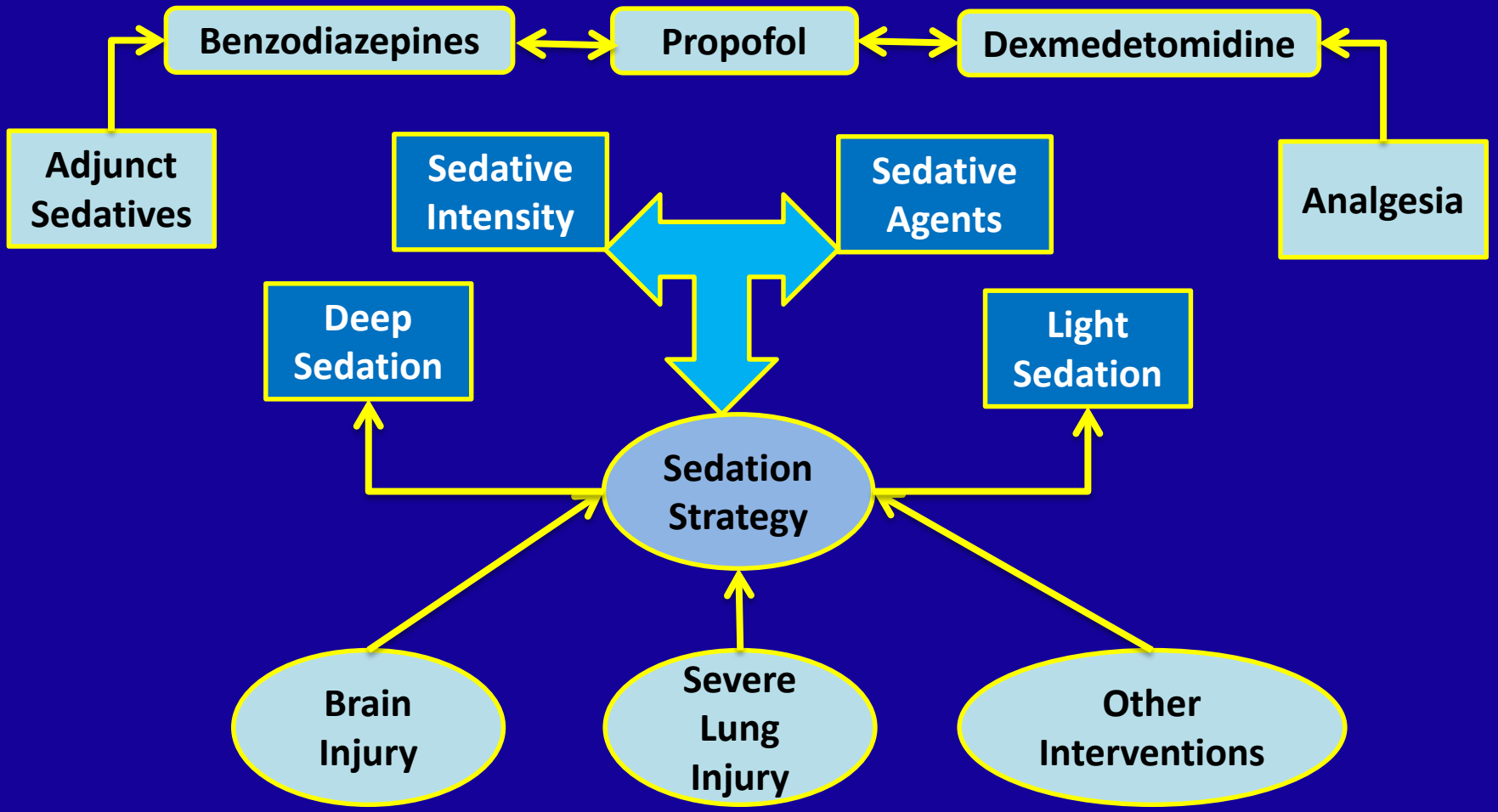
High-Frequency Oscillation in Early Acute Respiratory Distress Syndrome

Co-interventions	HFO	Control	P
Vasoactive agents	91%	84%	0.01
Neuromuscular blockers	83%	68%	0.001
Duration of vasoactive agents	2 days longer		
Duration of NM Blockers	1 day longer		
Midazolam and fentanyl duration days Med (IQR)	10(6-18	10(6-17)	0.99
Midazolam mg Med (IQR) 7 days	199(100-382)	141(68-240)	0.001
Fentanyl ugm Med (IQR) 7 days	2980 (1258-4800	2400 (1140-4430)	0.06

Different focus is needed

- Past sedation trials:
  - New concepts and novel ideas
  - Positive change in practice
  - Significant limitations
    - External validity
- Significant Knowledge and evidence gap still exists today

Sedation Strategies in Critical Illness



What Determine Sedation Strategies?

- The intensity of sedation depth
- The choice of sedative agents
- Timing of intervention
- Concomitant factors
  - Underlying critical illness
  - Pre-morbid state

Goal Directed Sedation Strategy

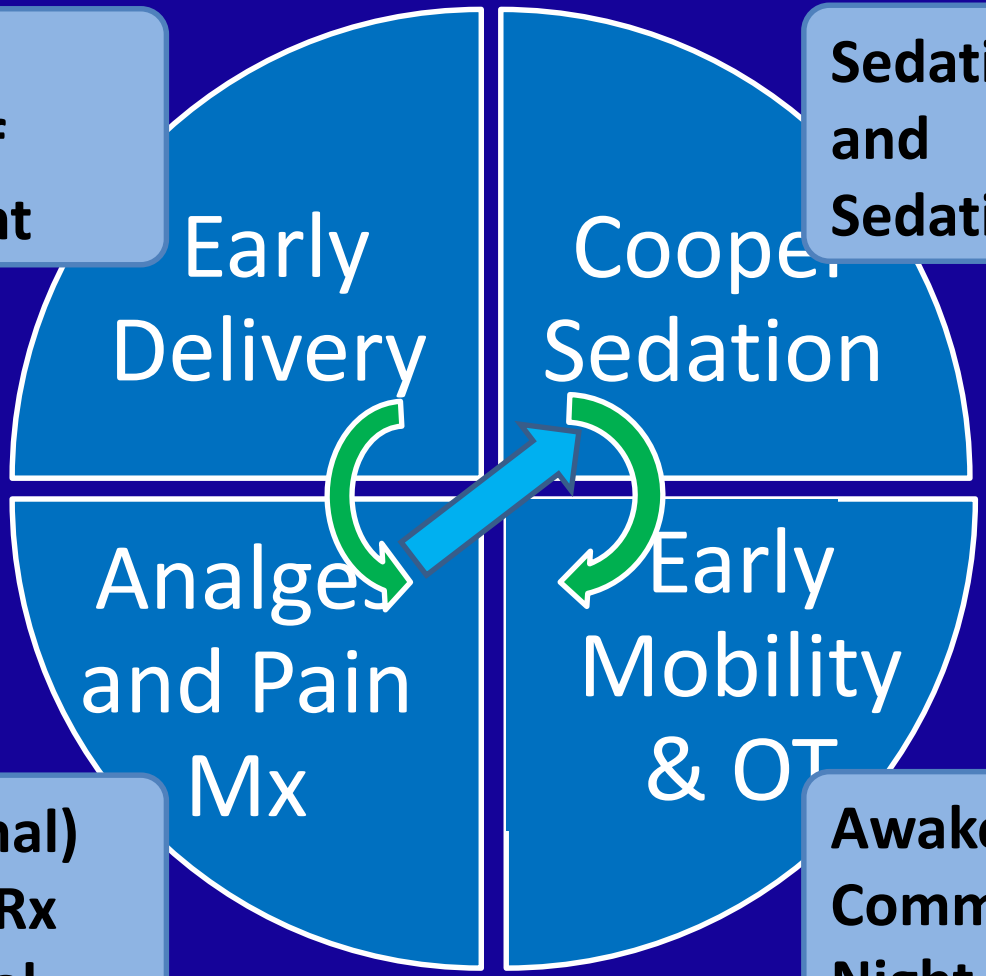
- Conventional
  - Progression from anaesthesia
    - Hypnosis / amnesia
  - Deep sedation
    - comfort
  - Conventional agents
    - Benzo, propofol
  - Short-term focus
    - Ventilation
    - Efficacy

- Goal directed
  - RCTs in critically ill patients
    - Targeted sedation
  - Light sedation
    - comfort
  - Novel agents
    - Alpha $_2$ Agonists
  - Long-term effects
    - Institutional dependency
    - Cognitive function

Goal Directed Sedation

Implemented
Within hours of
Mechanical Vent

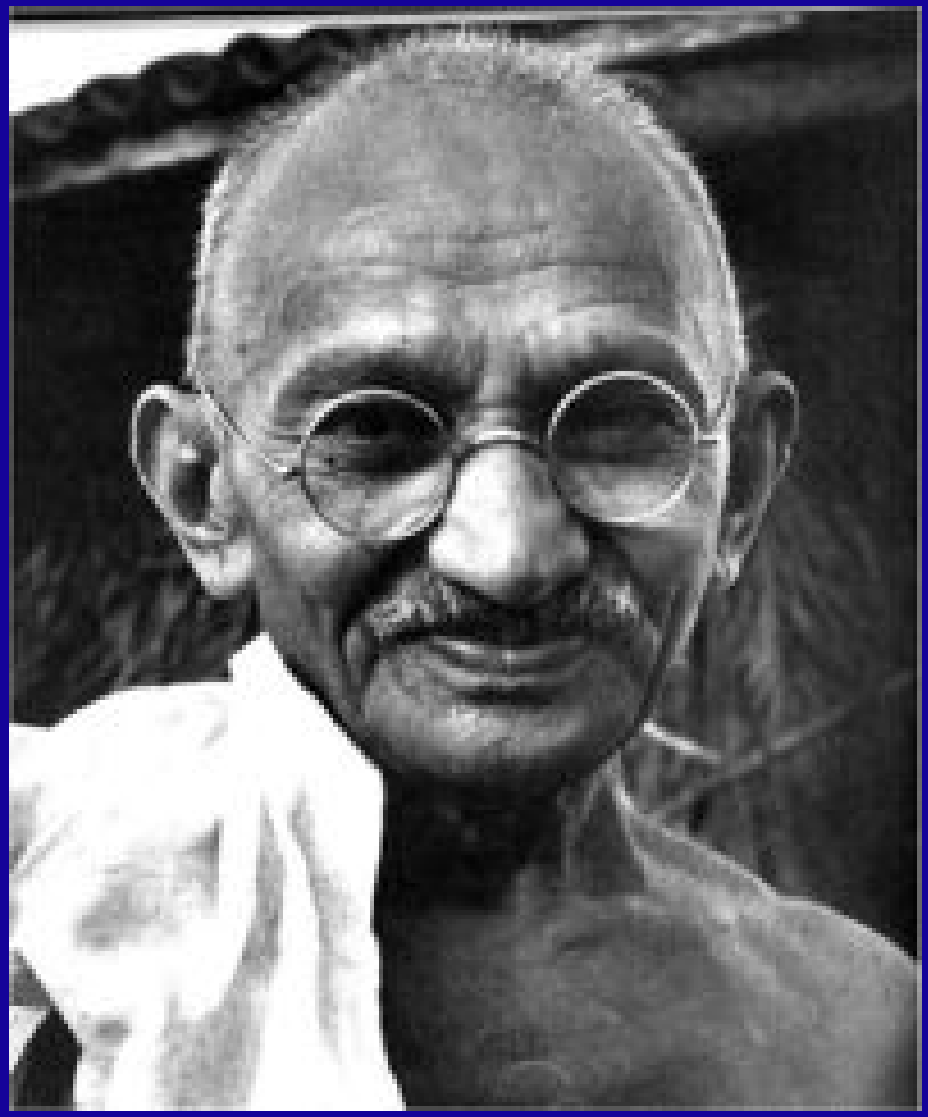
Sedative choice
and
Sedative intensity



Early opioid (Anal)
Opioid sparing Rx
Multimodal Anal

Awake and calm
Communicating
Night sleep

“The future depends on what we do today.”



Deep Sedation in Critical Illness

Intensive Care Med
DOI 10.1007/s00134-013-2830-2

ORIGINAL

Yahya Shehabi
Lucy Chan
Suhaini Kadiman
Anita Alias
Wan Nasrudin Ismail
Mohd Ali T. Ismail Tan
Tien Meng Khoo
Saedah Binti Ali
Mat Ariffin Saman
Ahmad Shaltut
Cheng Cheng Tan
Cow Yen Yong
Michael Bailey
The Sedation Practice in Intensive Care Evaluation (SPICE) Study Group investigators

Sedation depth and long-term mortality in mechanically ventilated critically ill adults: a prospective longitudi study

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 Bailey[5], Frances Bass[2], Belinda Howe[5], Colin McArthur[9], Ian M. Seppelt[10], Steve Webb[11,12], and Leonie Weisbrodt[13]; Sedation Practice in Intensive Care Evaluation (SPICE) Study Investigators and the ANZICS Clinical Trials Group*

[1]Clinical School of Medicine, University of New South Wales, Randwick, Australia; [2]Intensive Care Research, Prince of Wales Hospital, Randwick, Australia; [3]Faculty of Medicine, University of Melbourne, Melbourne, Australia; [4]Faculty of Medicine, Monash University, Melbourne, Australia; [5]Australian New Zealand Intensive Care Research Centre, School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia; [6]Intensive Care Research, Austin Hospital, Heidelberg, Australia; [7]Burns, Trauma & Critical Care Research Centre, University of Queensland, Brisbane, Queensland, Australia; [8]Australian Defence Force, Brisbane, Queensland, Australia; [9]Department of Critical Care Medicine, Auckland City Hospital, Auckland, New Zealand; [10]Department of Intensive Care Medicine, Nepean, University of Sydney, Sydney Medical School Nepean, Kingswood, Australia; [11]Intensive Care Unit, Royal Perth Hospital, Perth, Australia; [12]School of Medicine and Pharmacology and School of Population Health, University of Western Australia, Perth, Australia; [13]Sydney Nursing School, University of Sydney, Nepean Hospital, Kingswood, Australia

Rationale: Choice and intensity of early (first 48 h) sedation may affect short- and long-term outcome.
Objectives: To investigate the relationships between early sedation and time to extubation, delirium, and hospital and 180-day mortality among ventilated critically ill patients in the intensive care unit (ICU).
Methods: Multicenter (25 Australia and New Zealand hospitals) prospective longitudinal (ICU admission to 28 d) cohort study of medical/surgical patients ventilated and sedated 24 hours or more. We assessed administration of sedative agents, ventilation time, sedation depth using Richmond Agitation Sedation Scale (RASS, four hourly), delirium (daily), and hospital and 180-day mortality. We used multivariable Cox regression to quantify relationships between early deep sedation (RASS, −3 to −5) and patients' outcomes.
Measurements and Main Results: We studied 251 patients (mean age, 61.7 ± 15.9 yr; mean Acute Physiology and Chronic Health Evaluation [APACHE] II score, 20.8 ± 7.8), with 21.1% (53) hospital and 25.8% (64) 180-day mortality. Over 2,678 study days, we completed 14,736 RASS assessments. Deep sedation occurred in 191 (76.1%) patients within 4 hours of commencing ventilation and in 171 (68%) patients at 48 hours. Delirium occurred in 111 (50.7%) patients with median (interquartile range) duration of 2 (1–4) days. After

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

This is the first prospective multicentre longitudinal study of the practice of sedation in critically ill patients who were mechanically ventilated for longer than 24 hours. In addition, this manuscript contains novel data, which have primacy in identifying the quantitative relationship between early sedation depth (48 h after initiation of mechanical ventilation) and three important clinical outcomes: time to extubation, time to delirium, and hospital and 180-day mortality.

What This Study Adds to the Field

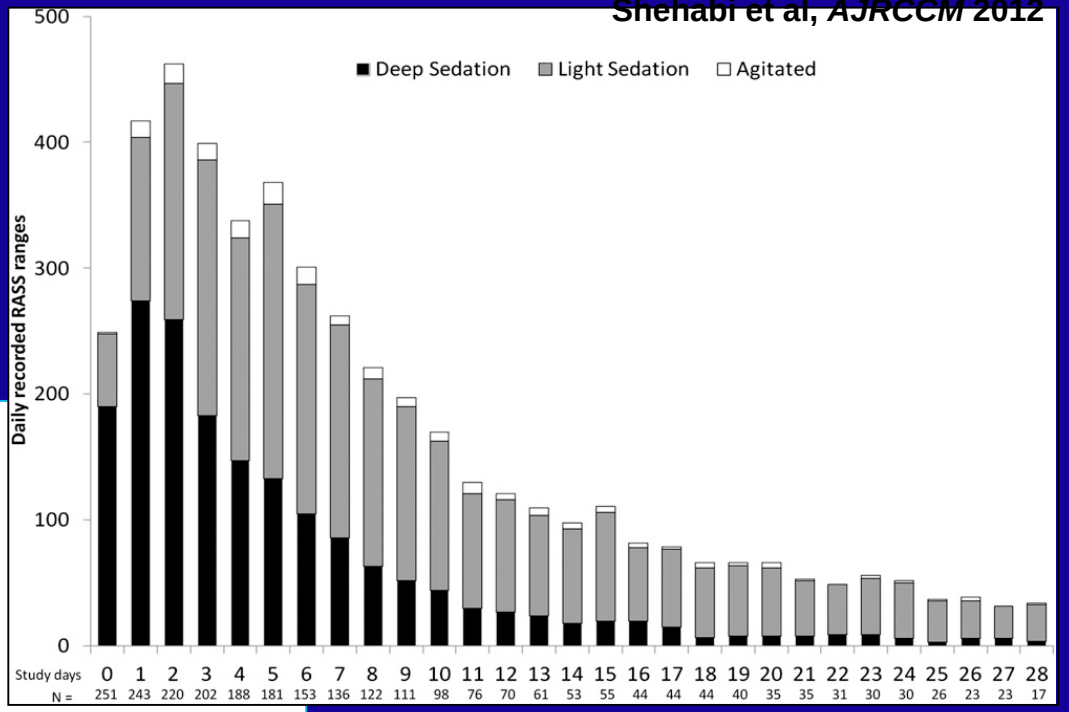
In 251 critically ill patients at multiple centers, we identified deep sedation within 4 hours of commencing ventilation as an independent negative predictor of the time to extubation, hospital death, and 180-day mortality. The early phase of ICU sedation is usually unaccounted for in randomized controlled trials due to late randomization.

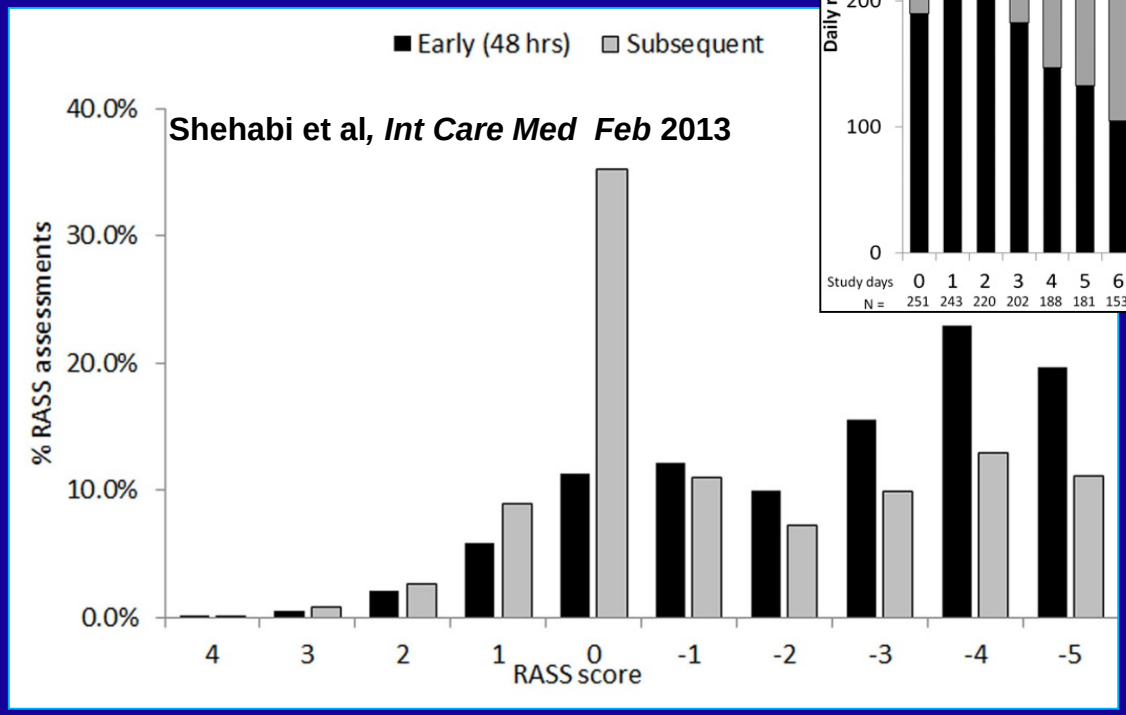
712 patients
8500 ICU days
4 countries
43 ICUs

Deep Sedation
72 hours after ventilation

- Common
- Unrecognized
- Unjustified?

Shehabi et al, *AJRCCM* 2012

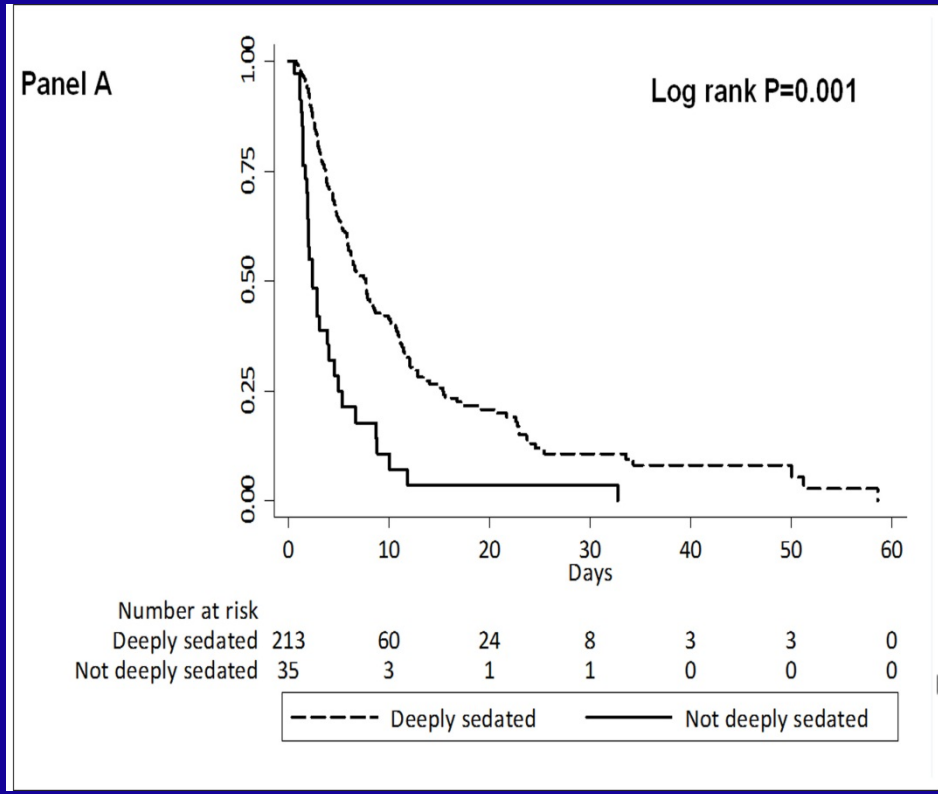




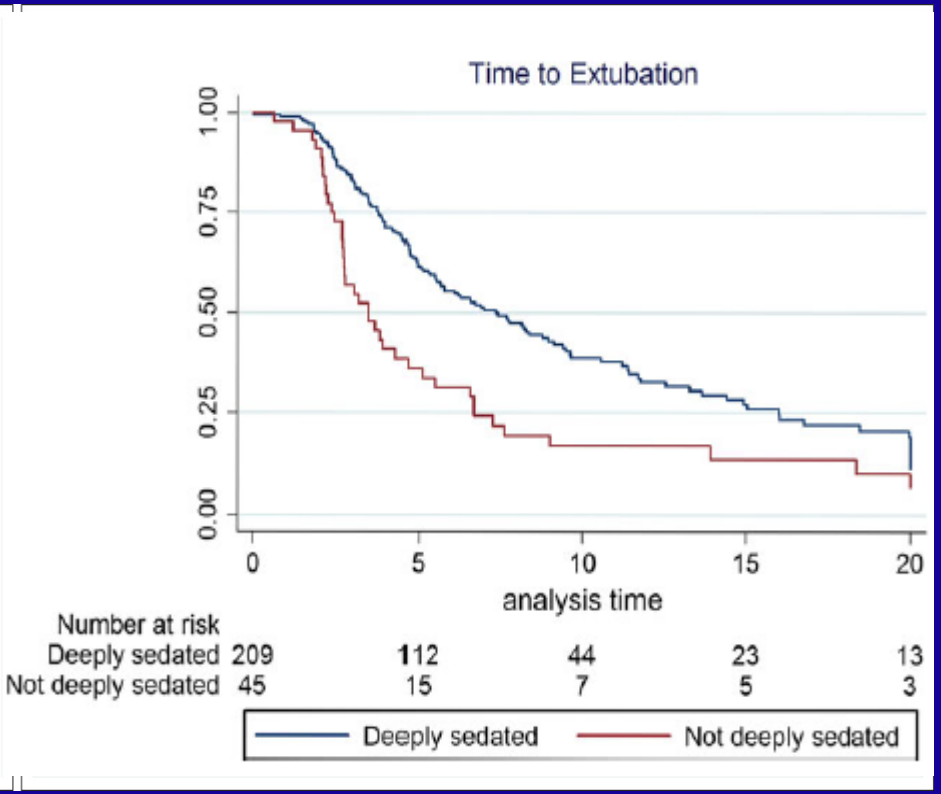
SPICE EGDS

EARLY Deep sedation may be harmful

Independently predicts time to extubation



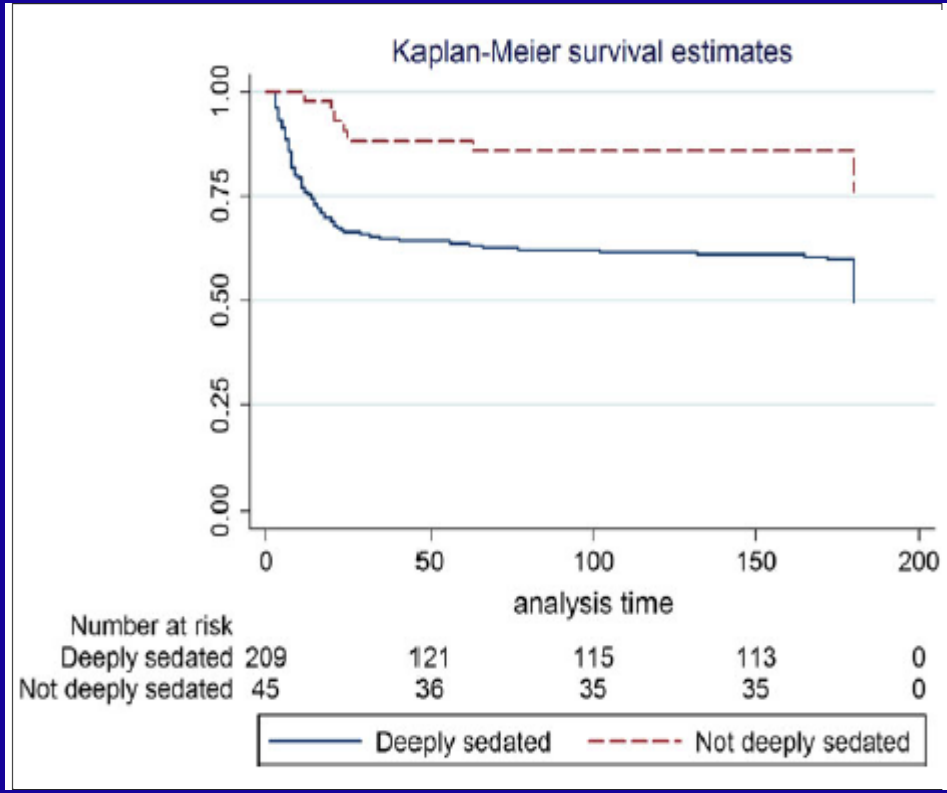
Shehabi et al, *AJRCCM* Oct 2012



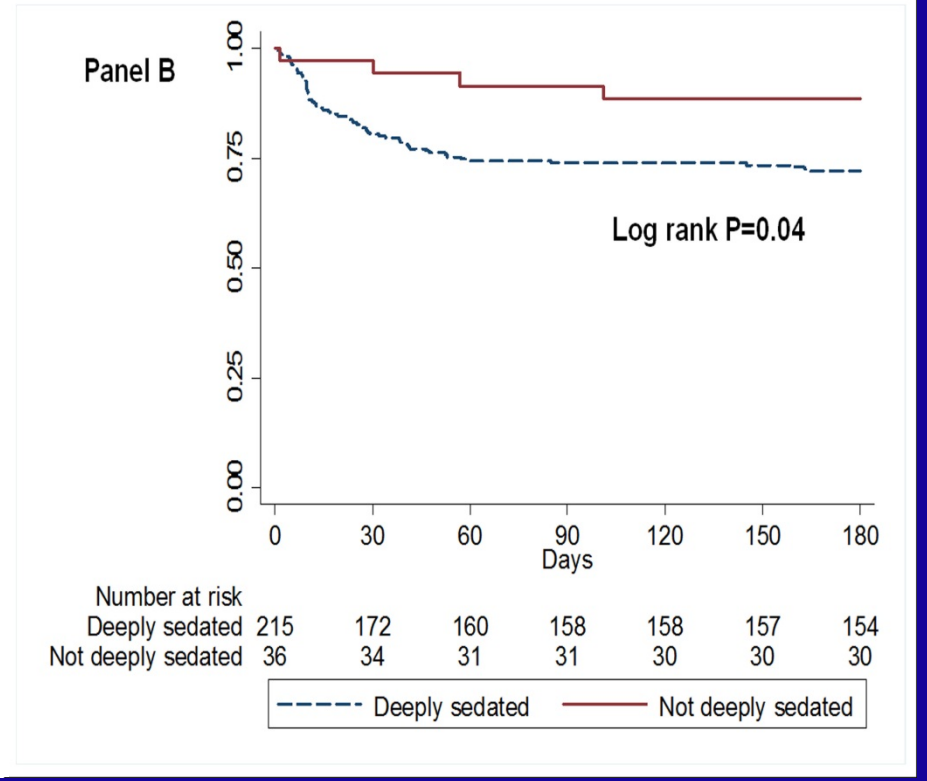
Shehabi et al, *Int Care Med Jan. 2013*

EARLY Deep sedation may be harmful

Independent predictor of 6 month mortality



Shehabi et al, *Int Care Med Jan. 2013*



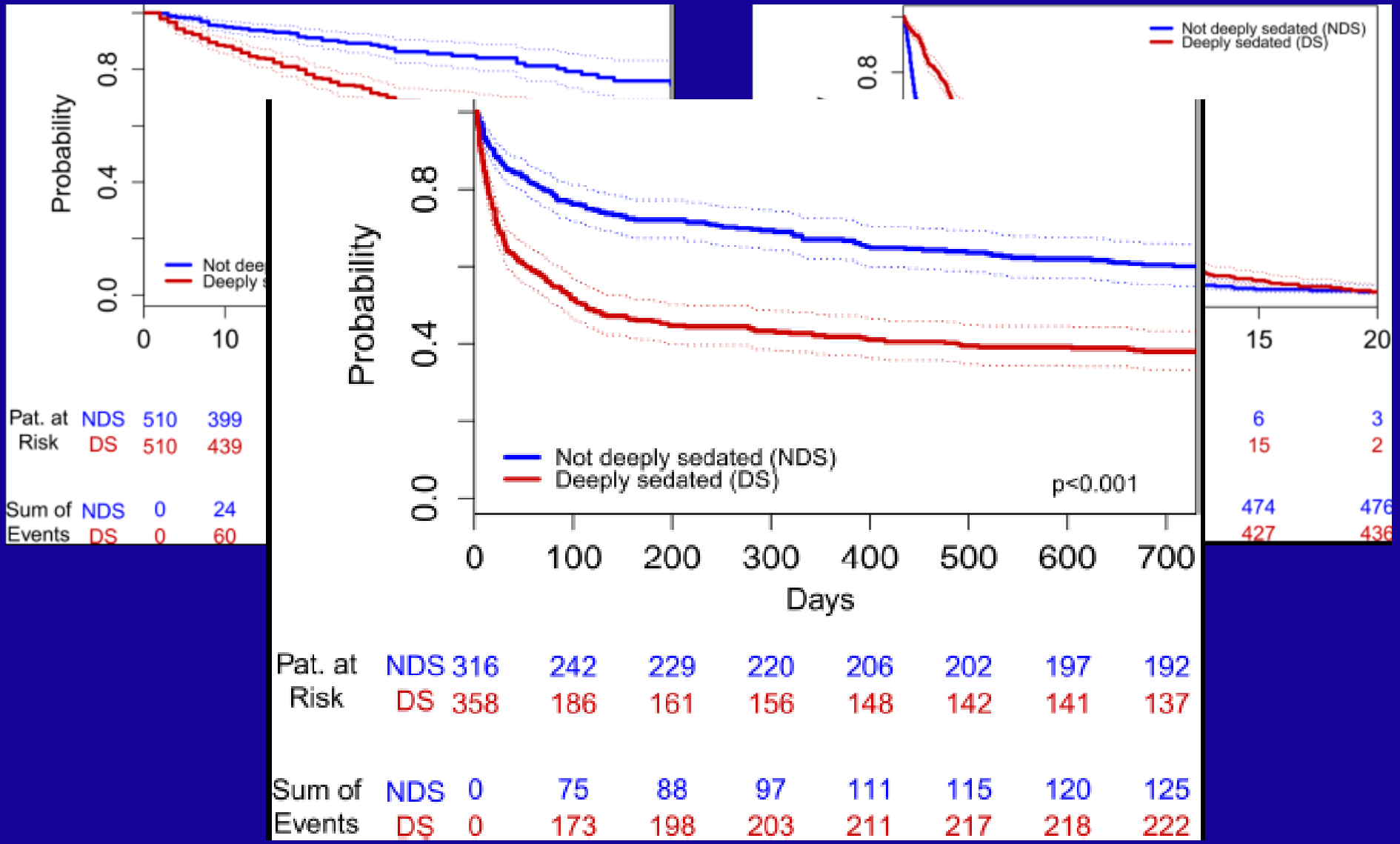
Shehabi et al, *AJRCCM* Oct 2012

Early deep sedation and 2 years survival

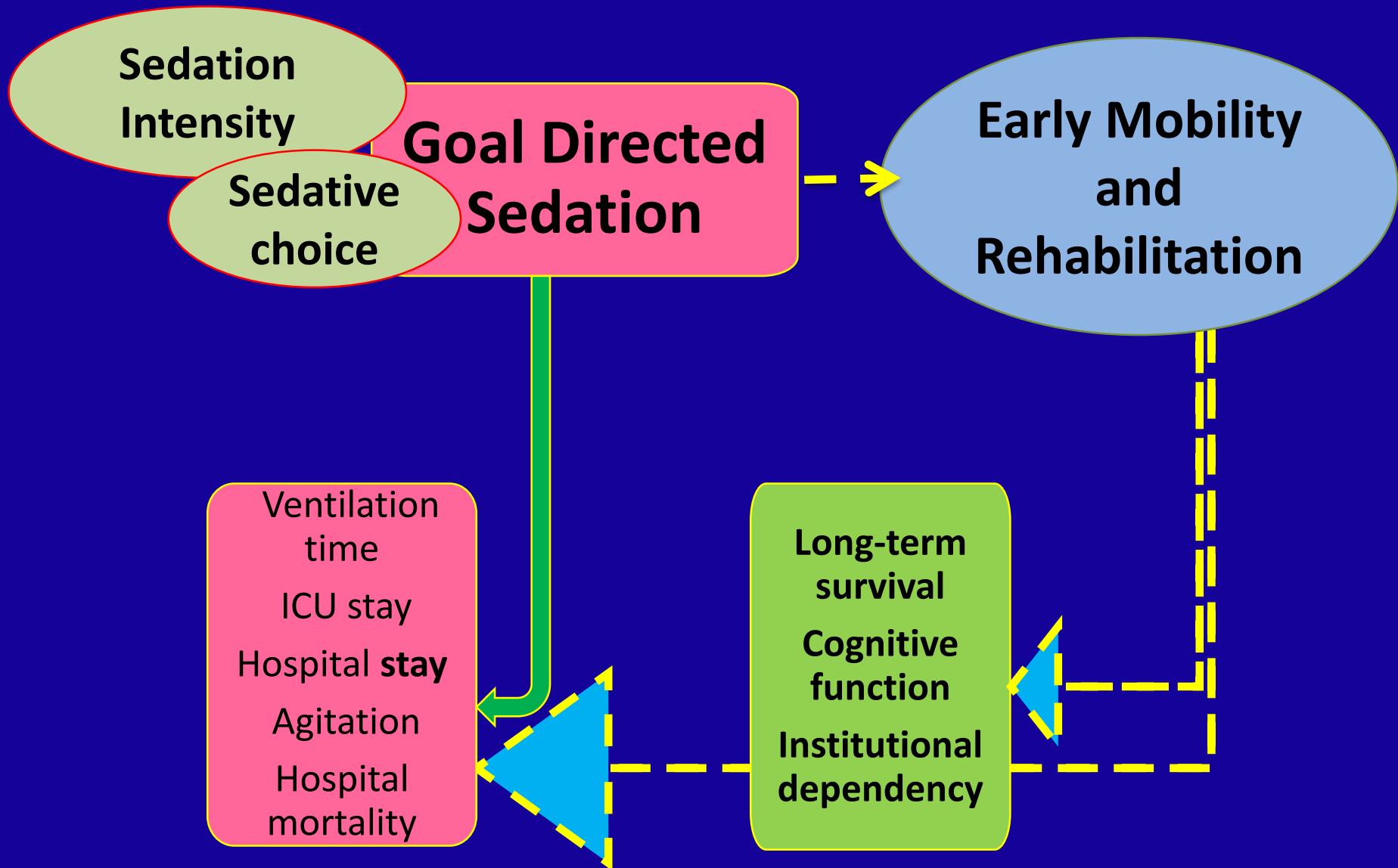
Balzer et al Crit Care 2015

- 1884 patients, matched pair analysis
- 6 years period
- Excluded neurological patients and patients who would have needed deep sedation
- Early deep sedation in 513 patients
- RASS at least every 8 hours
- Followed to 2 years for survival

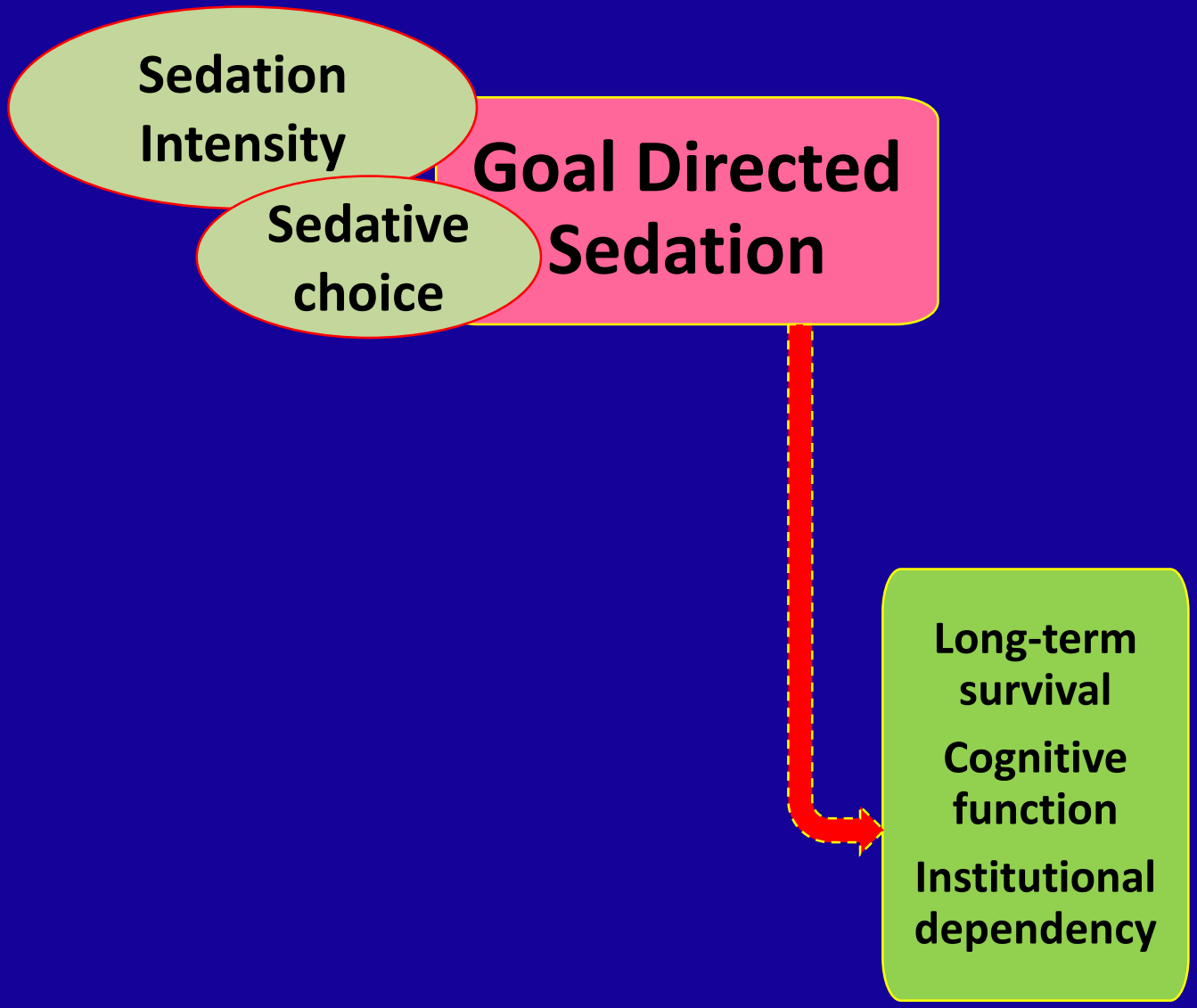
Time to extubation and mortality



A new framework sedation in critical illness



A new framework sedation in critical illness



Is Early Deep Sedation Modifiable?

EGDS – ANZ Pilot RCT

Crit Care Med Aug 2013

Early Goal-Directed Sedation Versus Standard Sedation in Mechanically Ventilated Critically Ill Patients: A Pilot Study*

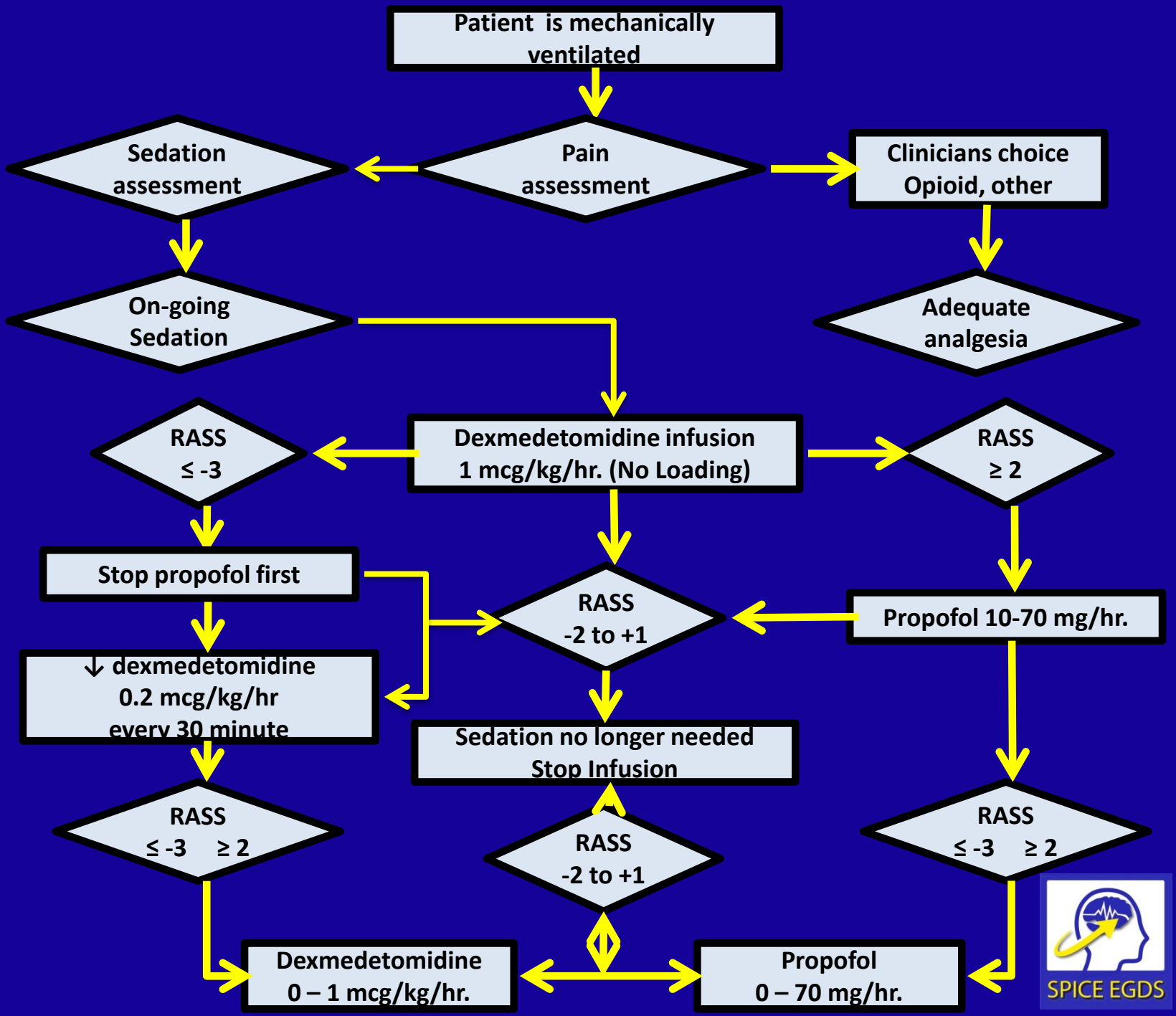
Yahya Shehabi, FCICM, FANZCA, EMBA[1,2,3]; Rinaldo Bellomo, MD, FCICM, FRACP[2,3]; Michael C. Reade, MBBS, MPH, DPhil, FCICM[4]; Michael Bailey, PhD[3]; Frances Bass, RN, BN, GDipICU[5]; Belinda Howe, RN, BN[3]; Colin McArthur, FANZCA, FCICM[3,6]; Lynne Murray, FAIMS[3]; Ian M. Seppelt, MBBS, FANZCA, FCICM[7]; Steve Webb, MPH, PhD, FCICM[3,8]; Leonie Weisbrodt, RN, BN, MN(Hons)[9]; for the Sedation Practice in Intensive Care Evaluation (SPICE) Study Investigators and the Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group

Early Goal Directed Sedation A Process of Care

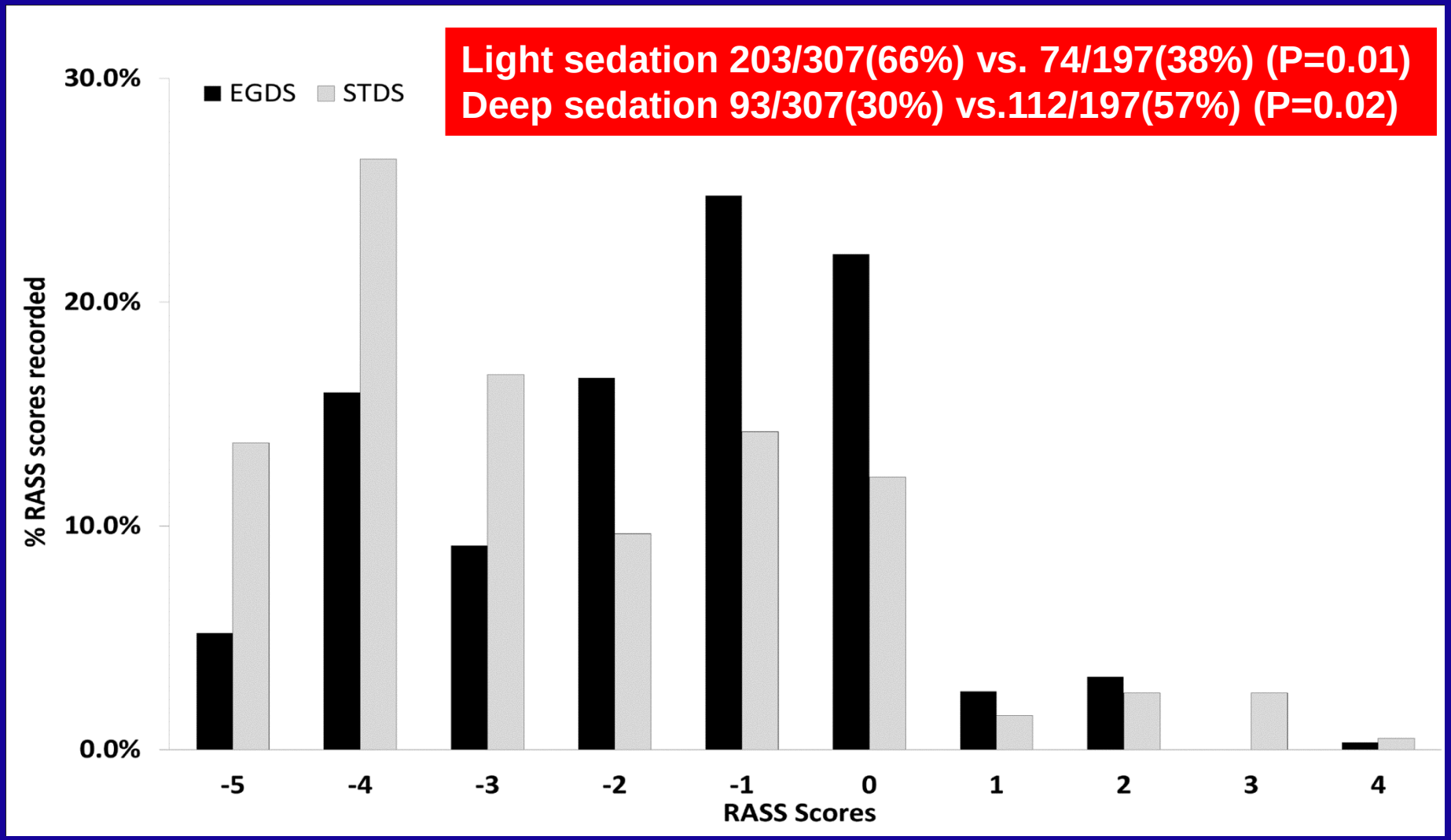
- EGDS is a **combination strategy**:

  - **Early** commencement of sedative intervention
  - Effective **analgesia**
  - Utilizing **dexmedetomidine** as a primary sedative agent
    - Rousable sedation and reduced overall sedation depth
    - Facilitate wakefulness and ventilation weaning
    - Reduce overall sedative and opioid load
  - Targeted **light sedation** RASS -2 to +1.
  - Avoiding and **minimizing benzodiazepines**

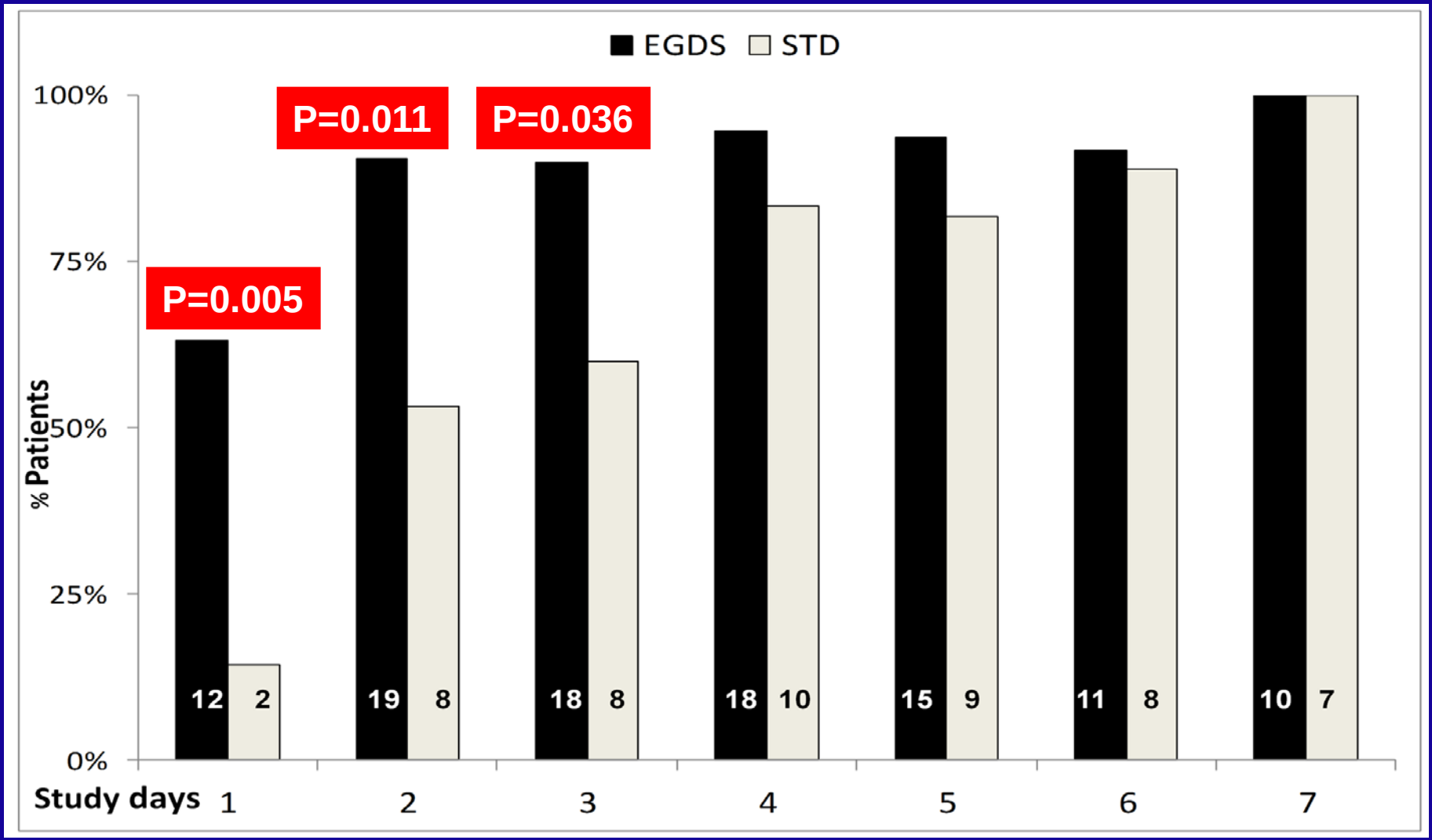
EGDS detailed Algorithm



Time spent in light sedation first 48 hours



Patients achieving light sedation during the first 7 study days



EGDS Pilots Main outcomes

	EGDS Combined ANZ + Malaysia			EGDS Malaysian Main OUTCOMES		
Clinical outcome	EGDS N=52	STDS N=45	P value	EGDS N=31	STDS N=29	P value
Time to randomization hrs. Median [IQR]	2.1 (0.21-5.5)	1.1 (0.5-4.65)	0.56	2.17 (0.17-6)]	1.5 (0.5-5.33)	0.72
RASS --2 to +1 first 48 h % Light sedation range	71% 517/732	51% 312/606	<0.0001	74% 314/425	58% 238/409	<0.0001
RASS -3 to -5 first 48 h % Deep sedation range	26% 187/732	46% 278/606	<0.0001	22% 94/425	41% 166/409	<0.0001
% ICU days with –ve Delirium	55%	40%	0.0005	52%	37%	0.002
Physical restraints % (n)	15% (8)	42% (19)	0.003	7 (23%)	14 (48%)	0.037
Ventilation time Med (IQR) hrs	61.8 (43.5 -100.5)	65.0 (44-125.1)	0.47	53.17 (41.5-90.2)	71.8 (46.3-137)	0.13
ICU Length of Stay Med (IQR) D	4.3 (2.76-8.63)	5.04 (3.5-9.35)	0.37	3.55 (2.25-6.14)	4.84 (3.8-9.35)	0.07
Hospital Length of Stay Med (IQR) Days	11.7 (7.3-28.85)	14.57 (8.5-26.8)	0.62	11.16 (6.9-15.89)	14.04 (8.94-24.8)	0.18
Hospital mortality N (%)	7 (13%)	5 (11%)	0.73	4 (13%)	4 (14%)	1.0

Sedative and Analgesic Agents

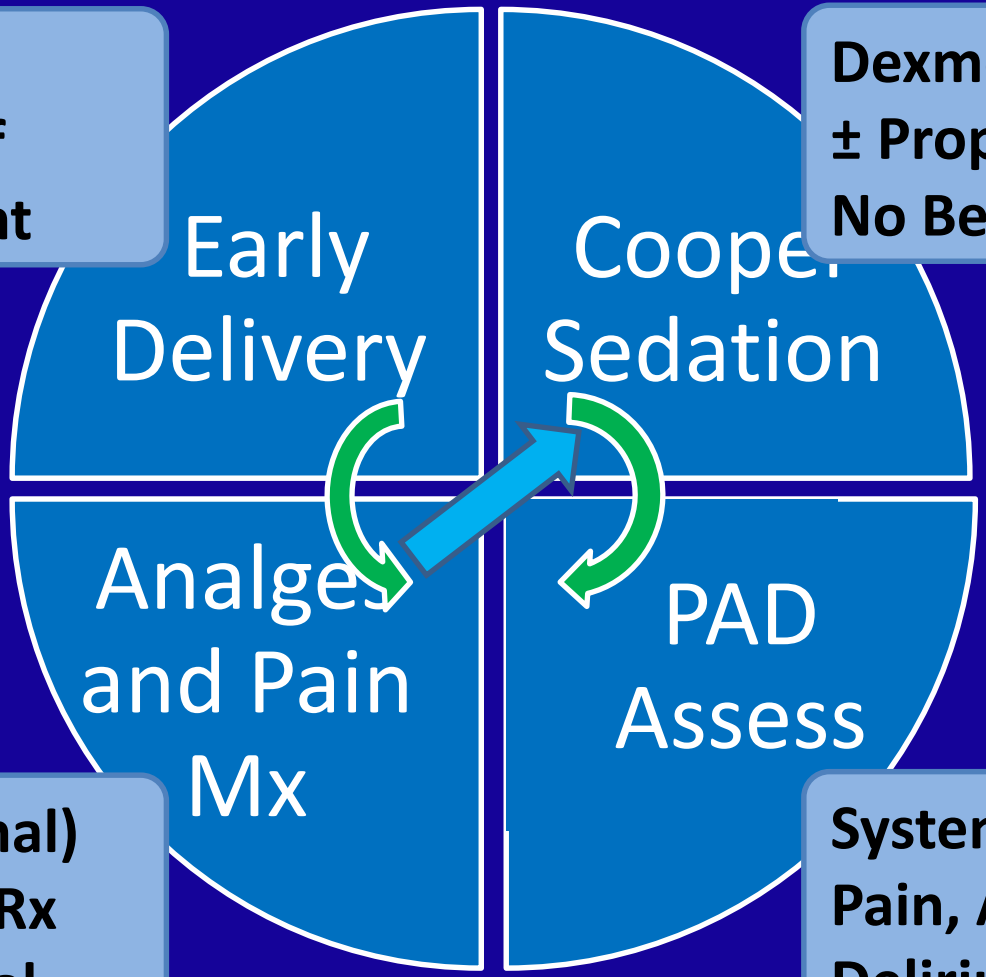
Drugs given Median {IQR] per patient	EGDS N=52	STDS N=45	%. Rx EGDS vs. STDS	P value
Dexmedetomidine ug	1559 # (490-3660)	799 (260-1338)	98% vs 4%	<0.0001 0.34 #
Time on Dexmed D	3 (2-5)	0[0-0]		<0.0001
Midazolam mg	4.5 # (2-9)	56 (36.5-123)	19% vs 80%	0.036 <0.0001#
Time on Midazolam D	0 [0-0]	2 (2-3)		<0.0001
Propofol mg	535 # (150-1200)	2150 (880-4630)	42% vs 47%	0.65 0.06 #
Time on Propofol D	1.23 (2.15)	1.42 (2.03)		0.65
Morphine mg	131.5 # (24-279)	110 (21-199)	27% vs 51%	0.014 0.40#
Fentanyl ug	420 # (140-1000)	1340 (512.5-1950)	58% vs 62%	0.65 0.019 #

Early Goal Directed Sedation

- Novel way to achieve GDS Early
- In pilot trials:
  - Delivered within 2 hours of ventilation
  - Effective, safe and practical at the bedside
  - Reversed early deep sedation
  - Reduced use of opioids, Benzos and propofol
  - Reduced the use of physical restraints
  - Increased delirium free days

Early Goal Directed Sedation

Implemented
Within hours of
Mechanical Vent



Dexmedetomidine
± Propofol
No Benzo

Early opioid (Anal)
Opioid sparing Rx
Multimodal Anal

Systematic and freq
Pain, Agitation and
Delirium assess

Can Early Goal Directed Sedation improves Outcome?

- Critical illness trajectory is determined early
  - Early deep sedation is
    - unjustified
    - lead to long-term harm
  - Delayed physical and occupational interventions little impact
  - Family centered care should commence early
- Plausible that EGDS can impact drivers of long-term outcomes positively
  - Deliver a holistic approach to ICU sedation

I was given EGDS and … …

Sedation Practice in Intensive Care Evaluation

- SPICE I:
  - Identify current standard care
  - Identify drivers of poor patients outcomes
  - Identify modifiable elements associated with poor outcomes
- SPICE II:
  - Identify aspects of “sedation practice” that may improve outcome
  - Test the feasibility of possible intervention/s in a pilot multi-centre study in ANZ intensive care units

–SPICE III

- Identify components of “sedation strategy” that is likely to improve long-term outcomes
- Scientifically test this “combination” against current practice

Early Goal Directed Sedation vs. Standard Care Sedation

Sedation Practices in Intensive Care Evaluation:

SPICE III: A Prospective Multicentre Randomised Controlled Trial of

Early Goal Directed Sedation Compared with Standard Care in Mechanically Ventilated Patients in Intensive Care

anzic research centre

ANZICS Clinical Trials Group

SPICE EGDS

THE PRINCE OF WALES HOSPITAL

SCIENTIA MANU ET MENTE

Hypothesis

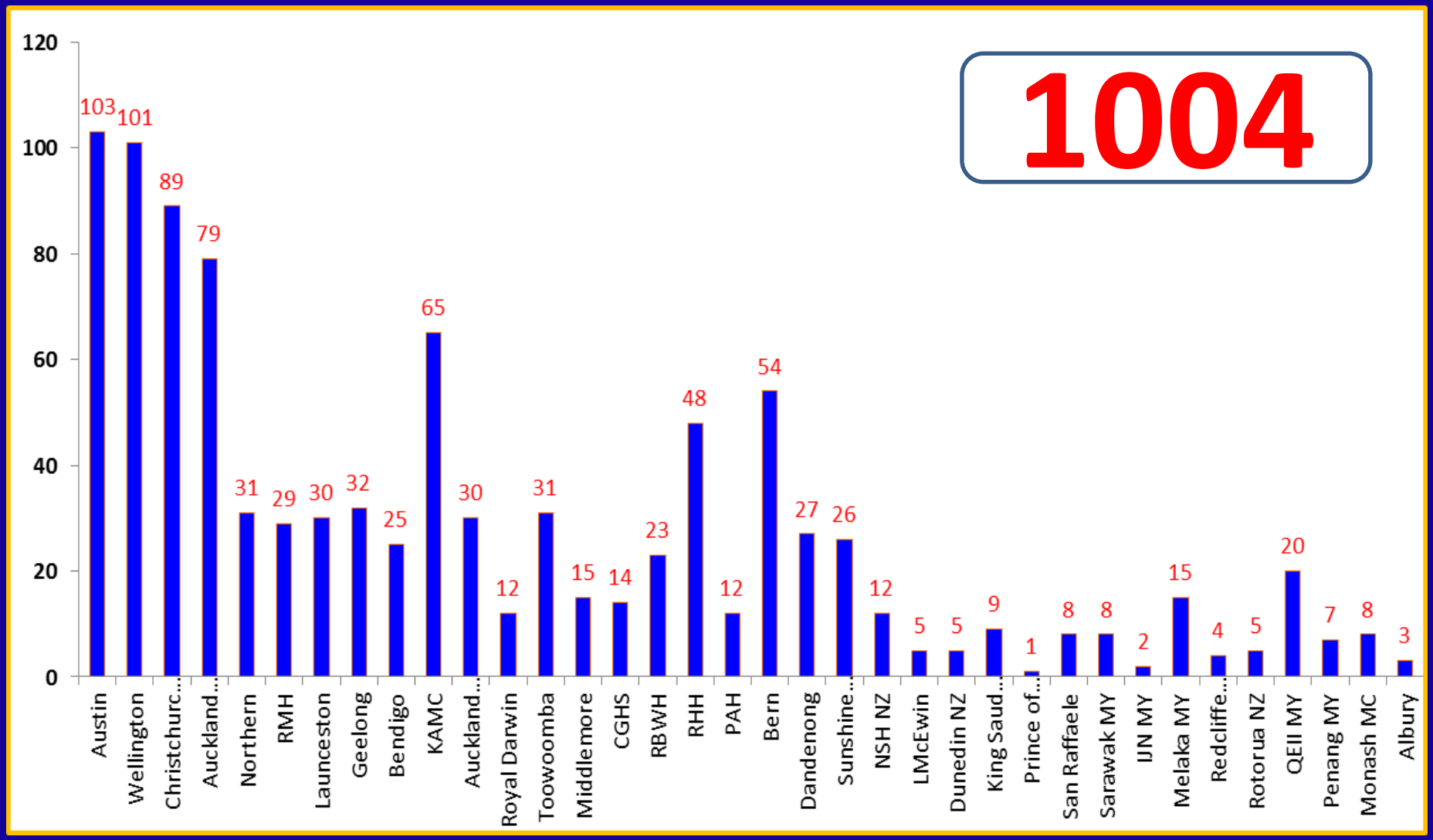
Early Goal-Directed Sedation (EGDS), compared to standard sedation practice,

reduces 90-day all-cause mortality in critically ill patients who require mechanical ventilation

Study Aim

- To investigate the clinical effectiveness of an Early Goal Directed Sedation Strategy on
  - 90 day All-Cause mortality
  - Cognitive function at 180 days
  - Institutional dependency at 180 days

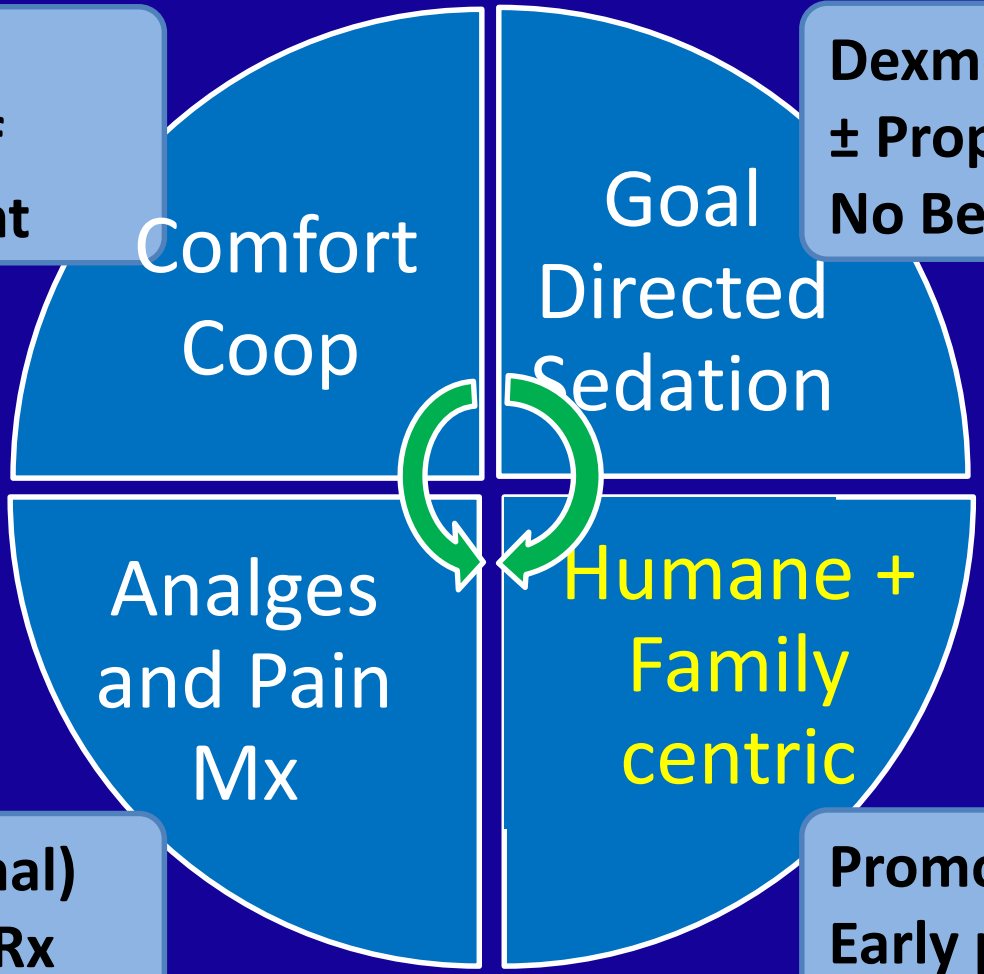
SPICE III is a global agenda



Early Goal Directed Sedation within a holistic appraoch

Implemented
Within hours of
Mechanical Vent

Dexmedetomidine
± Propofol
No Benzo



Early opioid (Anal)
Opioid sparing Rx
Multimodal Anal

Promote sleep and
Early physical rehab
Family focused

Summation

- Sedation practice is evolving rapidly
  - Light sedation and analgesia first paradigm
  - Benzo minimization
- Goals of sedation are changing
- Goal Directed (defined) Sedation
  - Sedation intensity and choice of sedative agents
  - Multimodal pain Mx and
  - Define goals early, adjusted frequently

Can Early Goal Directed Sedation Improves Outcome? YES

"We are here to put our dent in the universe. Otherwise why else even be here?"

Steve Jobs

Thank you

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ANZICS Clinical Trials Group

ANCORA IMPARO

SPICE EGDS

THE PRINCE OF WALES HOSPITAL

SCIENTIA

MANU ET MENTE