

Recognition and Management of ICU Delirium

NEICS 2015

Dr Valerie Page

Watford General Hospital

What is happening in the brain?

- Oxidative stress
- Neurotransmitter imbalance
- Neuronal aging
- Inflammation
- Abnormal levels of large neutral amino acids

BRAIN trial

826 patients enrolled – median 61 years

74% delirium

79% survivors cognitive tests 3 months

75% survivors tested 12 months

Median global cognition scores 1.5 SD below
age-adjusted population mean

Similar to MCI, 40% worse than moderate TBI

Cognitive outcomes Hope-ICU

Telephone Interview of Cognitive Status

	Haloperidol	Placebo
TICS-M Median (IQR) n = 57	22 (18-27)	21 (18-24)

≤ 31 cutoff score separates MCI from normal cognition (sensitivity 71.4%)

≤ 27 score separates MCI from dementia (sensitivity 69%).

Delirium and outcome

40 year old ARDS ICU survivor college graduate

“I have been out of hospital and trying to get on with my life for the past 2 years. I have trouble with people’s names that I have worked with for years. I can’t remember where I put things at home. I can’t help my children with their homework because I can’t remember how to do simple multiplication problems.”

The delirium experience

“The rest of my stay in ICU was filled with more incidents of despair, humiliation and terror. I saw a patient stabbed to death by his wife, and two people committing suicide. I witnessed arguments, in my mind all caused by me, and the pain I felt as my lungs started to recover was all part of a plan to give me pain inducing drugs – in fact I had seen doctors laughing about it.

The day after I was extubated I found myself in the High Dependency Unit, where the sheer terror of the execution attempts began.”

Identification



Delirium – DSM V

- Disturbance in attention and awareness
- Acute onset and fluctuates
- Disturbance in cognition
- Not explained by pre-existing, established or evolving neurocognitive disorder and non-comatose patient
- Evidence for cause

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

Subsyndromal delirium

- One or more symptoms
- Not meeting full criteria
- Not progressing to delirium
- Intermediate outcomes

What does it look like?



Delirium motoric types

- Hyperactive – psychomotor agitation
- Hypoactive – psychomotor lethargy and sedation, appears quiet & co-operative BUT with inattention and disorganised thinking.
- Mixed – fluctuating hypo/hyperactive symptoms

Diagnosing delirium

Intensive Care Med
DOI 10.1007/s00134-009-1466-8

BRIEF REPORT

Peter E. Spronk
Bea Riekerk
José Hofhuis
Johannes H. Rommes

Occurrence of delirium is severely underestimated in the ICU during daily care

Received: 25 July 2008
Accepted: 16 March 2009

Abstract *Objective:* Delirium is associated with prolonged intensive

evaluated. CAM-ICU scores were obtained during 425 patient days. Considering the CAM-ICU as the

CAM-ICU

Feature 1: Acute onset of mental status changes, or Fluctuating course.

AND

Feature 2: Inattention
Squeezing hand correctly on 4 As in a
10 letter sequence

AND

Feature 3: Disorganised
thinking; 4 simple questions,
one command

OR

Feature 4: Altered level of
consciousness

CAM-ICU



Delirium Screening Checklist

- 1) Altered level of consciousness
- 2) Inattention
- 3) Disorientation
- 4) Hallucinations or delusions
- 5) Psychomotor agitation or retardation
- 6) Inappropriate speech or mood
- 7) Sleep/wake cycle disturbance
- 8) Symptom fluctuation

Delirium Screening Checklist

2. Inattention Score 1 point for:

- A. Difficulty in following commands OR
- B. Easily distracted by external stimuli OR
- C. Difficulty in shifting focus

Delirium Screening Checklist

5. Psychomotor Agitation or Retardation

Score 1 point for either:

- A. Hyperactivity requiring the use of additional sedative drugs or restraints in order to control potential danger (e.g. pulling IV lines out or hitting staff) OR
- B. Hypoactive or clinically noticeable psychomotor slowing or retardation

CAM – ICU sensitivity

- 139 acute medical oncology patients
- Psychiatric evaluation vs. CAM-ICU or ICDSC
- 36 delirious patients
- CAM-ICU 18% sensitivity
- ICDSC 47% - 62% sensitivity

Neufeld et al Psychosomatics 2013, Han et al Acad Emerg Med 2009

Delirium Triage Screen & Brief CAM

- DTS – spell LUNCH backwards
- Brief CAM – 6 months of year backwards
- 406 enrolled patients, emergency dept.
- 50 with delirium
- DTS plus bCAM – 82% sensitive, 95.8% specific

Han et al Ann Emerg Med 2013

SQID

Single question in
delirium:

Do you think has been
more confused lately?

Sensitivity 80%

Specificity 71%

Use with attention test



Rapidly Reversible, Sedation-related Delirium versus Persistent Delirium in the Intensive Care Unit

Shruti B. Patel, Jason T. Poston, Anne Pohlman, Jesse B. Hall, and John P. Kress

Department of Medicine, Section of Pulmonary and Critical Care, University of Chicago, Chicago, Illinois

Can delirium be diagnosed in sedated patients?

Patel SB. AJRCCM 2014;189:658-65

Takala J. AJRCCM 2014;189:622-24

Sedation related delirium

- 102 of 256 patients
- Paired CAM-ICU before and after SAT
- 28.9% negative after SAT
- 89% at least 1 day delirium pre vs. 77% post.
- Outcomes, same for rapidly reversible as no delirium.



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

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Management

- Sedation score and delirium screening
- Identify and treat precipitating factor
- Minimise impact of predisposing factors
- Pharmacological therapy

Specimen type	Blood	eGFR	30 L mL/min(> 60)
Sodium	140 mmol/L (135 - 145)		1.73m ²
Potassium	4.8 H mmol/L (3.2 - 4.5)	Protein	44 L g/L (62 - 83)
Chloride	110 mmol/L (100 - 110)	Albumin	23 L g/L (33 - 47)
Bicarb.	23 mmol/L (22 - 33)	Globulin	21 L g/L (25 - 45)
Anion Gap	9 mmol/L (4 - 13)	Bilirubin	70 C umol/L (< 20)
OSM(Calc)	295 mmol/kg(275 - 295)	CK	215 H U/L (< 10)
Glucose	9.2 H mmol/L (3.0 - 7.8)	ALP	98 U/L (40 - 110)
Fasting RR	--> (3.0 - 6.0)	Gamma GT	16 U/L (< 50)
Urea	15.0 H mmol/L (3.0 - 8.0)	ALT	125 H U/L (< 45)
Creatinine	216 H umol/L (70 - 120)	AST	215 H U/L (< 40)
Urea/Creat.	69 (40 - 100)	LD	2690 H U/L (110 - 250)
Diff: Manual	Specimen: Blood		
Hgb : 83 L	WBC : 11.4 H		
PLT : 44 L	:		
RBC : 2.72 L	HCT : 0.24 L		
GENERAL COAGULATION			
INR	1.2		
Prothrombin Time	12		
APTT	27		
Fib (derived)	8.0 H		

Risk factors

Host factors	Acute illness	Iatro/envIRON
Elderly	Severe sepsis	Sedative/analges
Co-morbidities	ARDS	Immobilisation
Pre-existing cognitive impair	MODS	TPN
Hearing/vision impairment	Drug OD or illicit drugs	Sleep deprivation
Neurological dis	Nosocomial inf.	Malnutrition
Alcohol/smoker	Met. disturbance	Anaemia

Predisposing factors?

Management – non-pharmacological

“Delirium bundle”, optimisation of risk factors

- Address visual, hearing impairment
- Orientation
- Bowels
- Familiar nurse
- Mobilisation
- Drug overhaul
- Sleep

Naughton et al. J Am Geriatr Soc 2005;53:18-23, Lundstrom et al J Am Geriatr Soc 2005;53:622-28

PROTOCOLS



Protocolised analgesia, sedation and delirium

- Tertiary Canadian ICU
- PRE: Aug 2003 – Feb 2004

Delirium assessment - ICDSC

Pain – Numeric rating Scale 0-10 rated by patient or nurse

Sedation – RASS

Skrobik et al. Anesth & Analg 2010;111:451-63

Protocol implementation

April 2004 – November 2005

- Intensivists, nurses, pharmacist group
- Standardised prescription sheets
 - Paracetamol/NSAIDs.
 - Morphine/Fentanyl
 - Propofol/Midazolam
 - Haloperidol/Olanzapine
- Portable radios and CD players
- Reorientation and reassurance routine

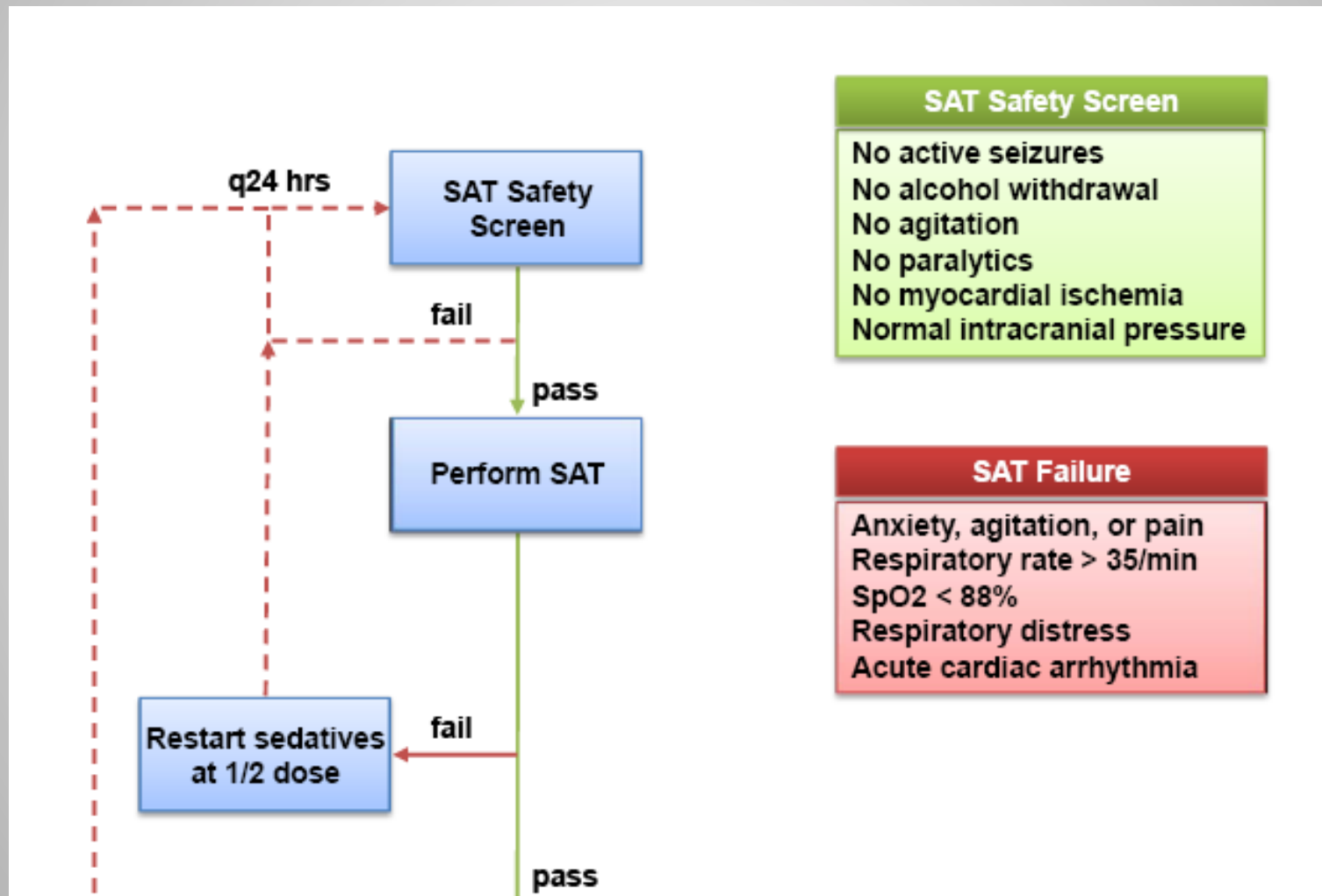
Results

- 572 PRE, 561 POST
- APACHE 17.1 vs 18.1 $p = 0.03$
- Analgesia mean NRS 1.61 vs. 1.25 significant
- Morphine equivalents 103.5mgs vs 22.3 mgs
- Delirium 34.7% vs. 34.2%
- Subsyndromal delirium 33% vs. 24.6%
- Antipsychotics given 39.4% vs. 39.7%

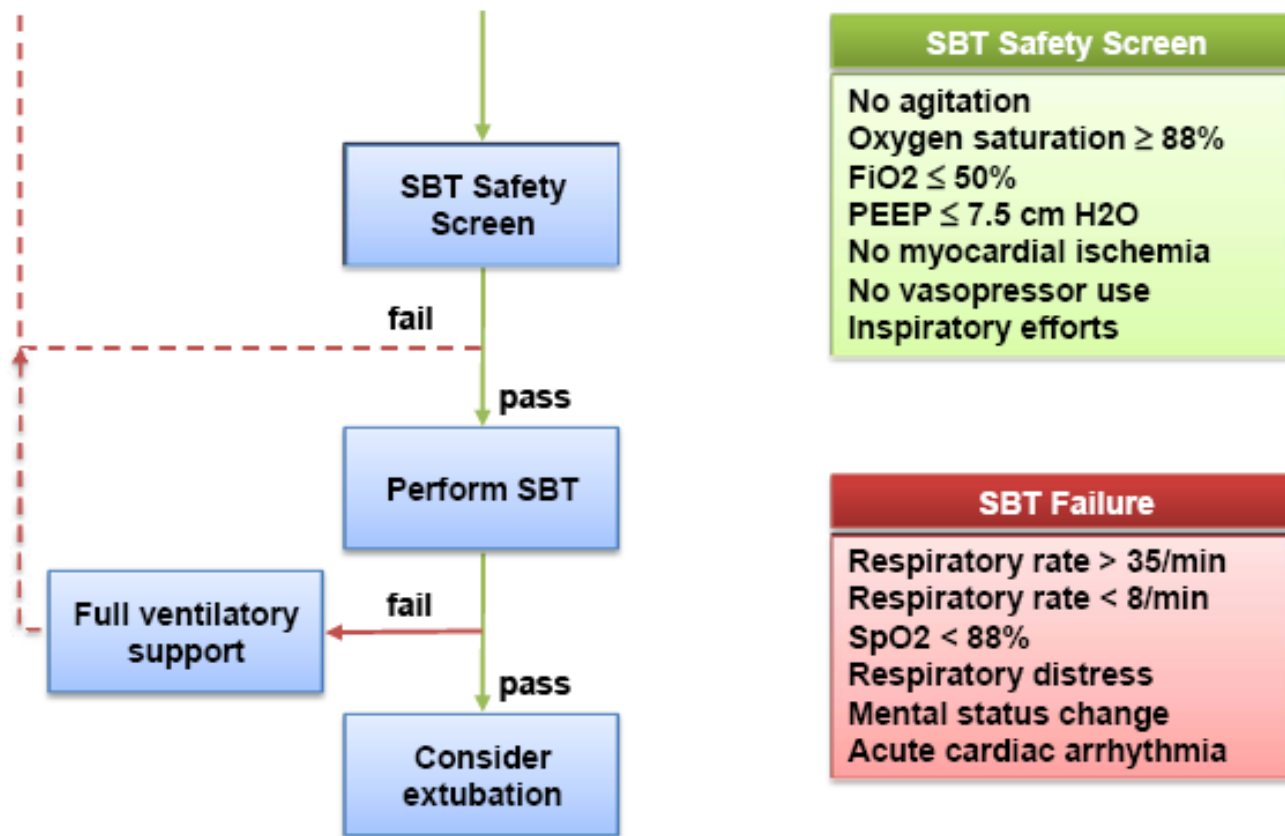
Outcomes

- Iatrogenic coma reduced from 20.5% to 8.7%
- Ventilator days 6.94 to 3.94
- Cognitively intact 31.4% to 54.8%
- Mean ICU LOS 6.32 vs. 5.35 days ($p = 0.009$)
- Return home 68.2% to 74.8% ($p = 0.049$)
- \$1000 less

Wake up



and Breathe



*Adapted from Girard TD et al. *Lancet* 2008;371:126-34

Early Mobilisation Protocol in Mechanically Ventilated Patients

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

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.

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

Results

- 6 ADLS and walking 29 (59%) study group vs. 19 (35%) control group
- Shorter duration of delirium 2 days (IQR 0-6) study vs. 4 days (IQR 2-8)
- More ventilator free days 23.5 vs 21.1.
- One SAE, desaturation less than 80%
- Discontinuation of therapy 19 of 498 session

Note: Physiotherapy not routine in first 2 weeks.

Schweickert et al Lancet 2009; 373: 1874-82

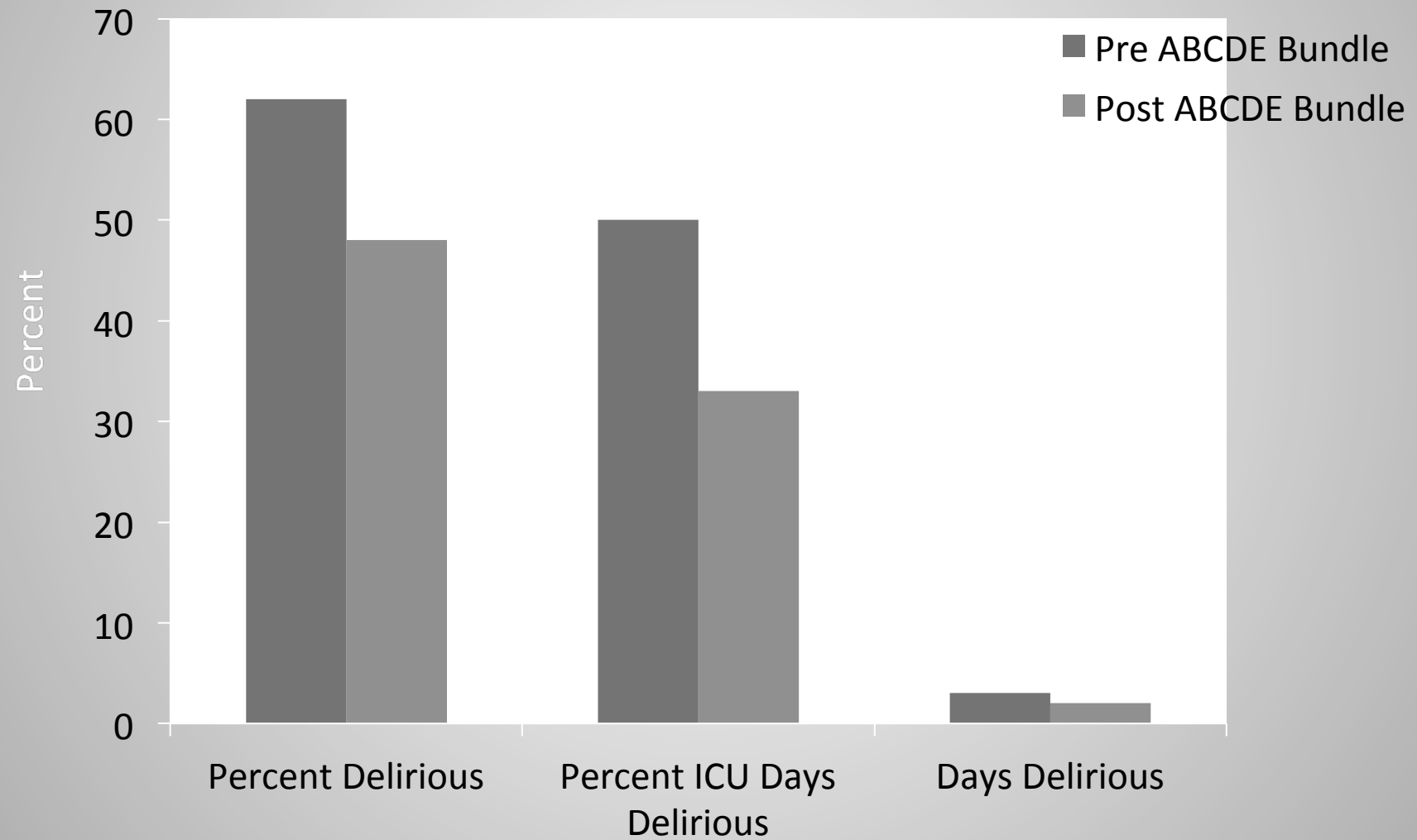
Effectiveness and Safety of the Awakening and Breathing Coordination, Delirium Monitoring/Management, and Early Exercise/Mobility Bundle

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William J. Burke, MD¹⁶

1.5 year prospective QI (before/after) study of 296 ICU patients.

Balas M, CCM 2014 epub

DELIRIUM RESULTS



Balas M CCM 2014

Drugs and delirium

- Opiate analgesics
- Benzodiazepines – choice of sedative
- Corticosteroids
- Anticholinergic load

Furosemide

Ranitidine

Digoxin

Cholinesterase inhibitors for delirium?

“Rivastigmine does not decrease duration of delirium and may increase mortality in critically ill patients.”

104 of 440 planned patients

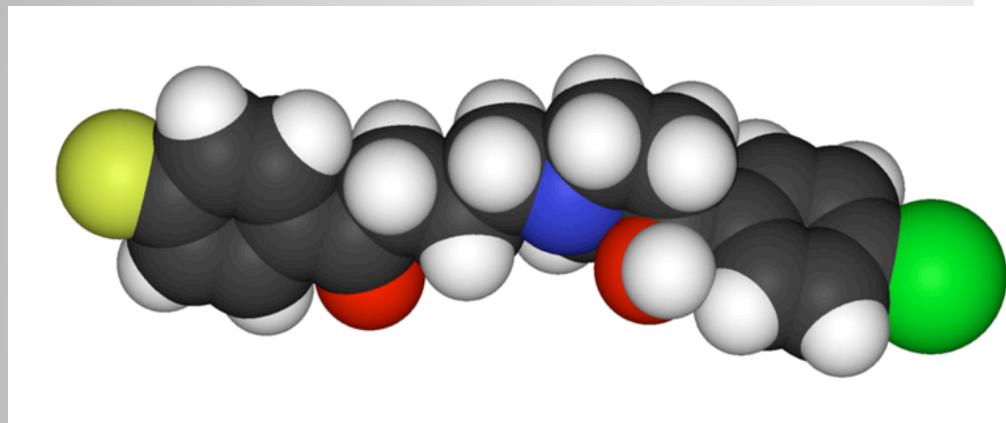
12 of 54 study gp died vs. 4 of 50 in placebo gp

Delirium duration longer and more severe
median 5 days in study gp vs. 3 in placebo gp.

Trial terminated for safety reasons.

van Eijk. Lancet 2010; 376: 1829

Haloperidol!



Hope-ICU

Delirium in the ICU: a prospective double-blind RCT of haloperidol vs. placebo

Trial intervention

- Study drug given regardless of CAM-ICU status
- Dose: 2.5 mg haloperidol or saline iv 8 hourly
- Duration: up to 14 days or until delirium resolved for 48 hours
- All study patients received a minimum of 48 hours treatment.
- Sedation standard: propofol and fentanyl

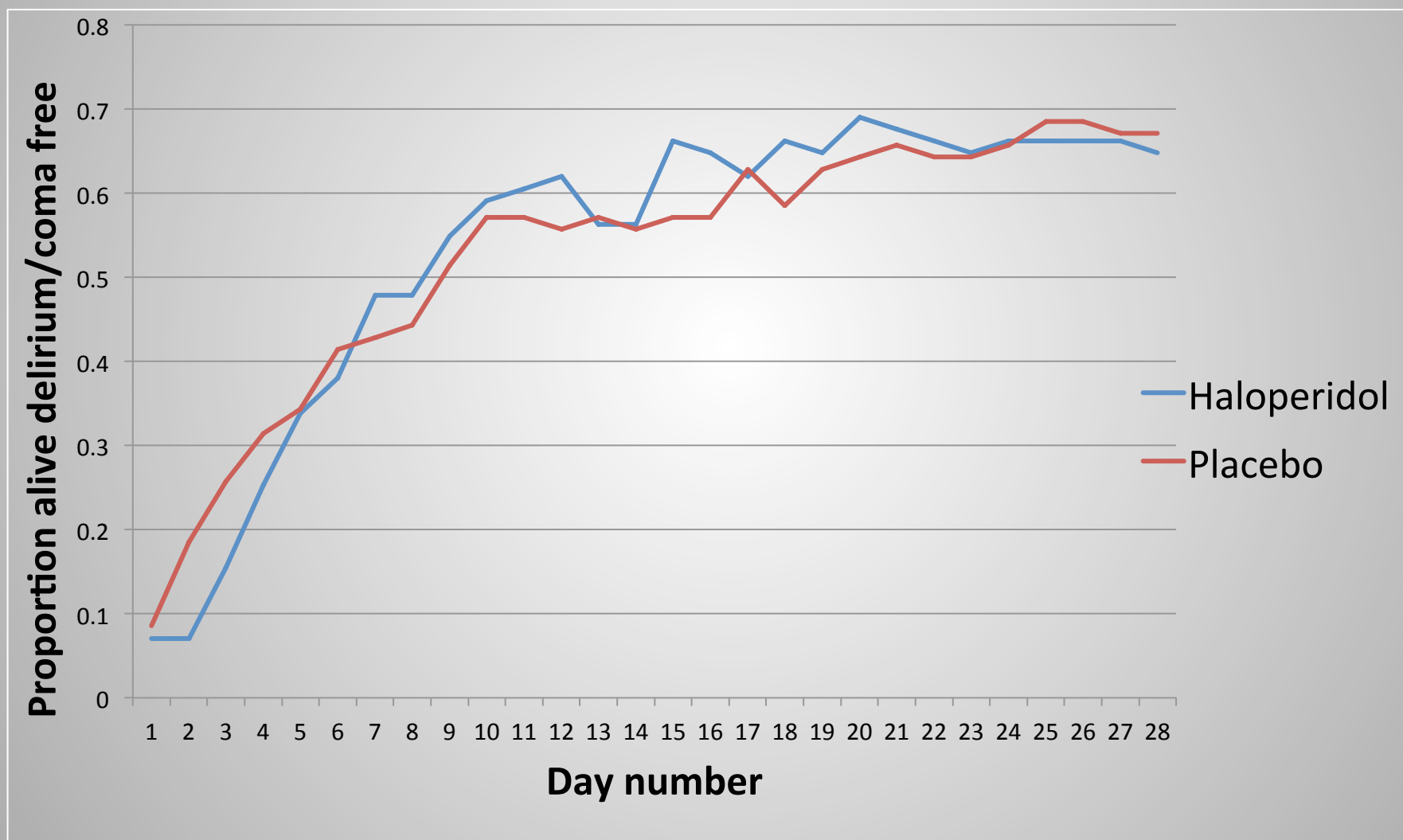
Patient characteristics

	Haloperidol n=71	Placebo n=70
Age mean (SD)	67.9 (16.5)	68.7 (14.88)
Male n (%)	37 (45.6%)	44 (54.3%)
Medical patient n (%)	42 (59%)	49 (70%)
Surgical patient n (%)	29 (41%)	21 (30%)
Sepsis no/total (%)	25/52 (48%)	27/52 (52%)
APACHE score mean (SD)	19.8 (6.2)	19.7 (6.9)
No. doses of study drug	13.5 (8-21)	14.5 (7-24)

Results

	Haloperidol	Placebo	Statistics
Delirium-free/coma-free in 14 days median (IQR)	5 (0-10)	6 (0-11)	p=0.55
Days in coma 14 days median (IQR)	1.2 (2.14)	1.2 (1.9)	p=0.99
Days in delirium 14 days median (IQR)	5 (2-8)	5 (1-8)	p=0.99

Resolution of delirium over time



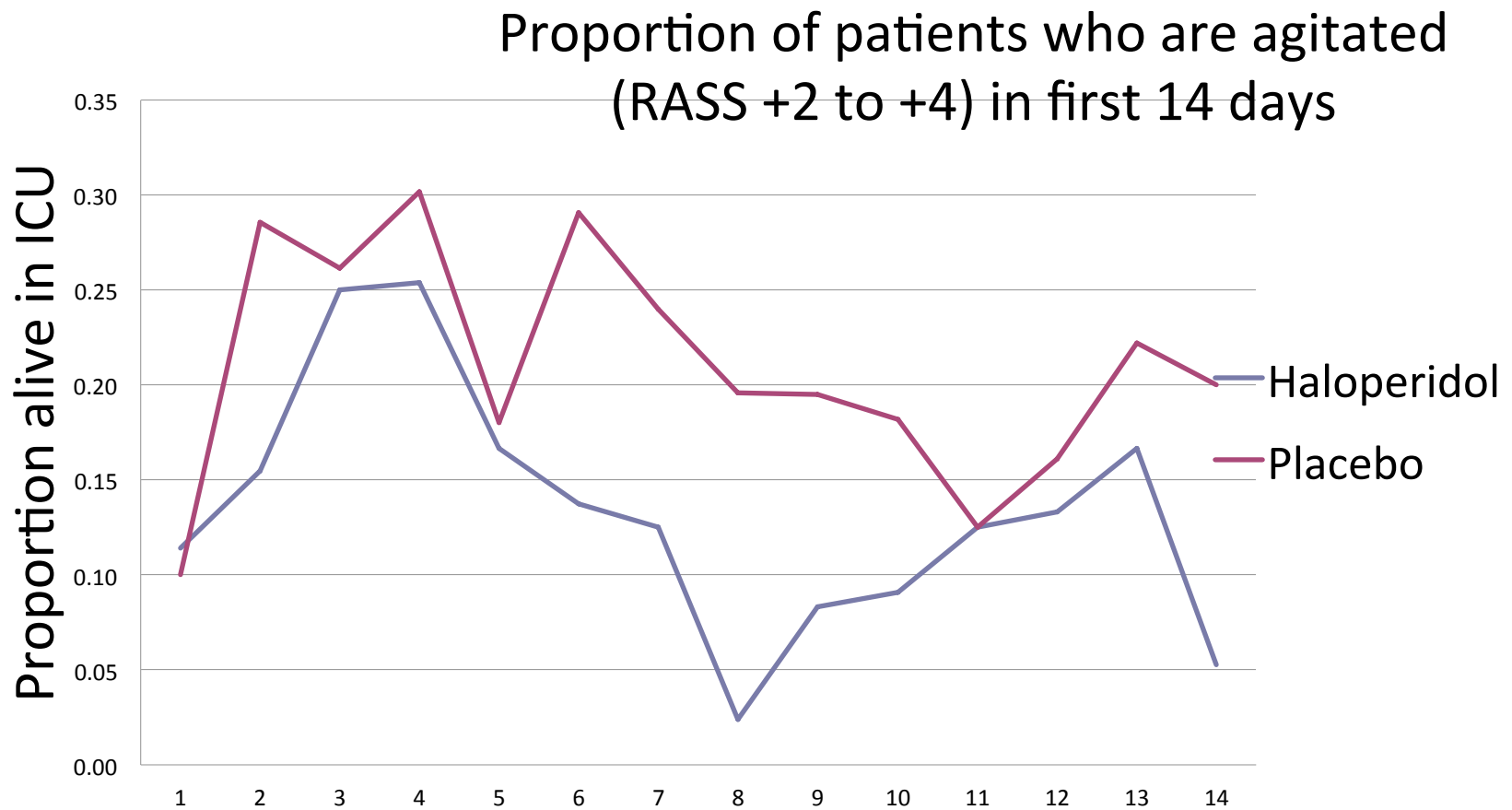
Secondary outcomes

	Haloperidol	Placebo	Statistics
Ventilator-free days 14 days n(%)	7 (0-11)	4 (0-11)	p=0.67
Mortality at 28 days n(%)	20 (28.2%)	19 (27.1%)	RR 1.04 (0.16,0.96)
Length ICU stay (days)	11 (9.5)	12.4 (10.8)	p=0.47

Open label antipsychotics

Drug	Haloperidol (n=71)	Placebo (n=70)	Difference
Haloperidol			
Patients treated	6	15	RR=0.39 (0.16,0.96)
Total dose	1.0 (4.05)	1.7 (4.4)	p= 0.32
Olanzapine			
Patients treated	4	6	
Total dose	0.4 (2.0)	3.1 (15.4)	p= 0.15
Any antipsychotic	8 (11%)	18 (25%)	RR=0.44 (0.2,0.94)

Agitation



PAD guidelines - antipsychotics

We provide no recommendation for using a pharmacologic delirium prevention protocol in adult ICU patients, as no compelling data demonstrate that this reduces the incidence or duration of delirium in these patients (low/very low).

There is no published evidence that treatment with haloperidol reduces the duration of delirium in adult ICU patients (No Evidence).

Atypical antipsychotics may reduce the duration of delirium in adult ICU patients (low/very low recommendation).

Anti-inflammatory intervention

- Evidence for neuroinflammation in delirium
- Statins anti-inflammatory actions - suppress up-regulation of toll receptors, reduce TNF- α , IL-1 β , MCP-1, leucocyte adhesion molecules
- Animal studies demonstrate improved post-operative cognitive function with statins.
- Prospective cohort study Watford demonstrate decrease daily risk delirium with daily statin use.

Statins and delirium

- Prospective cohort study
- August 2011 to February 2012
- Consecutive ICU admissions
- 319 patients no statins vs. 151 patients statins
- Daily CAM-ICU assessment

Results – Preadmission statins

	Statins	No Statins	p
Age (years, SD)	63 (19)	77 (11)	< 0.01
Sex (Male, %)	165 (52%)	86 (57%)	0.51
APACHE II (SD)	17 (7)	18 (7)	0.32
ICU LOS (days, IQR)	5 (3-8)	4 (2-7)	0.07
ICU Mortality (%)	63 (20)	27 (18)	0.32
Delirium free (days, IQR)	3 (1-5)	2 (1-5)	0.81

Daily statin and less risk of delirium

	OR	(95% CI)	P
Statin	1.93	(1.12 to 3.36)	0.02
Age	1.01	(0.99 to 1.04)	0.31
APACHE	0.78	(0.73 to 0.84)	<0.01

Daily risk of delirium following statin administration,
N = 375, Person days = 2267

MoDUS

– Modifying Delirium Using Simvastatin

Hypothesis

Treatment with enteral Simvastatin 80mg once daily for a maximum of 28 days will increase the number of delirium/coma free days in mechanically ventilated patients at high risk of delirium

Trial

- 142 mechanically ventilated patients
- 80 mgs simvastatin daily for 28 days or until discharge
- Primary outcome delirium/coma free days at 14 days
- Secondary outcomes cognitive function at 6 months, LOS, mortality, cost effectiveness

Patients

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Welcome to your preview of The Times

My nightmare in hospital

David Aaronovitch
Last updated at 5:45PM, November 12 2011

David Aaronovitch explains how routine keyhole surgery led to a terrifying bout of 'ICU psychosis' during which he thought he was going mad

On Sunday, September 4, I woke up to find that I was no longer mad. It was 2pm, my two brothers were sitting on either side of my hospital bed, my wife between them, the sun was slanting in through the window behind me and the horror that had dominated my life for nearly a week had evaporated. But I will never forget those days and nights of terror and delusion, and will never think about madness in the same way again.



David Aaronovitch, photographed last month
Mark Harrison

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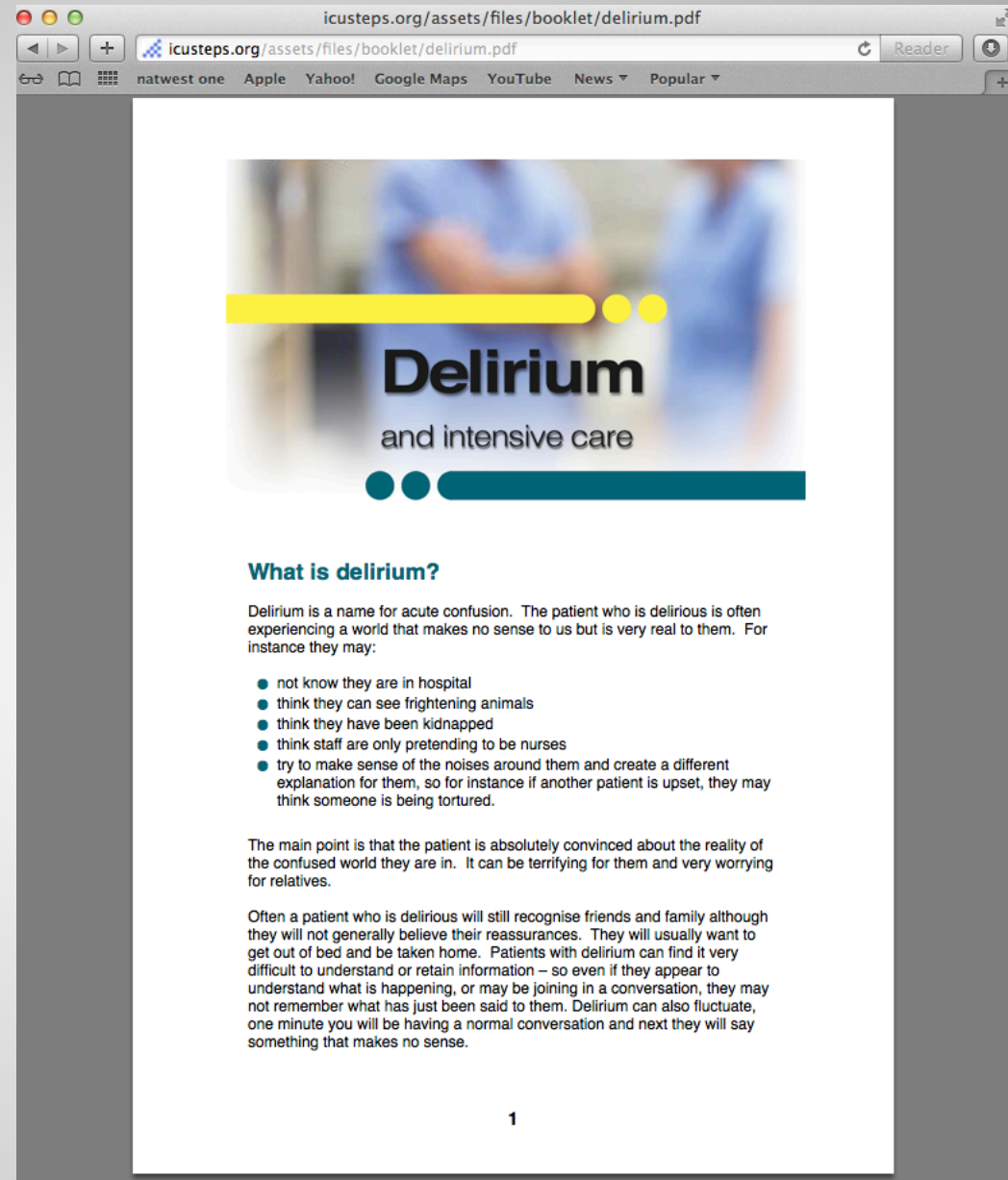
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Combating Delirium in ICU Patients

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Home

Posted on August 5, 2008 in [delirium news](#) by admin

Delirium is one of the unresolved challenges to healthcare.

Delirium is a serious acute medical condition; its been called a medical emergency. It results in such serious adverse outcomes for so many patients – including death – that in any other condition it would have clinicians searching for information with the same fervour given to cancer or HIV.

Delirium? Isn't that what the BBC are so good at portraying in Dickens adaptations? The heroine tosses and turns, glowing with perspiration mumbling the name of the worthy man she is destined to end up with or the less than worthy die loving. Yes the diagnostic features of delirium are clearly present, but understand most delirium is a quiet confusion not agitation.

Delirium in ITU?

Delirium is the commonest neuropsychiatric condition in hospital, 15% to 25% on general medical wards, up to 60% on surgical wards – critical care 80% in the sickest ventilated patient. Hang on; I am losing some of you. There are no 2 ways about it. Yes there is (and always has been) a currently grossly under diagnosed condition in your ITU that will influence whether the patient lives or dies regardless of APC, vasopressin or low-volume ventilation. It can be diagnosed in 2 minutes in an easy to apply, non-invasive test with no equipment needed. You in the "I just don't believe it" camp can huff and puff; here is the website that tells it how it is.

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- Professor Danny McAuley, Queens University, Belfast
- Drs Tim Alce & Annalisa Casarin Research Fellows
- Xiao Bei Zhao RN
- Dr Neil Soni, Imperial College, London
- Watford ICU staff
- Intensive Care Foundation
- Warwick Clinical Trials Unit

Remifentanyl

- Opioid
- Given by infusion
- Metabolised by non-specific esterases
- Ultra-short half-life
- Compared with fentanyl 3.2 vs. 47.3 minutes

Remifentanyl reduces the incidence of post-operative delirium

376 matched pairs fentanyl vs. remifentanyl

Nursing Delirium Screening Scale

Delirium in PACU 12.2% vs 7.7%

Delirium 1st post-op day 5.8% vs. 1.9%

Post-operative stay 16.2 +/- 14.2 vs. 6.6 +/- 8.7 days

Dexmedetomidine

- High α_2 –adrenoreceptor affinity
- Sedative and Analgesic
- Not GABAergic
- No anticholinergic effects
- Not suitable for deep sedation
- Loading dose NOT recommended

Dexmedetomidine

- In open label study n=90 elective cardiac surgery less delirium 3% comp propofol 50% and midazolam 50%
- NNT 2.1
- MENDS vs. midazolam less delirium, more time at targeted sedation.

Maldonado 2009; 50: 206-17, Pandharipande 2007; 298: 2644-53

Dexmedetomidine

- MIDEX and PRODEX 44 centres 9 countries
- Non-inferiority study.
- No meaningful delirium monitoring
- Ventilator days shorter vs. midazolam $p=0.03$
not vs. propofol $p=0.24$
- LOS and mortality similar.
- More hypotension and bradycardia comp.
midazolam