Sleep no more: making sense of the ABCDEF bundle

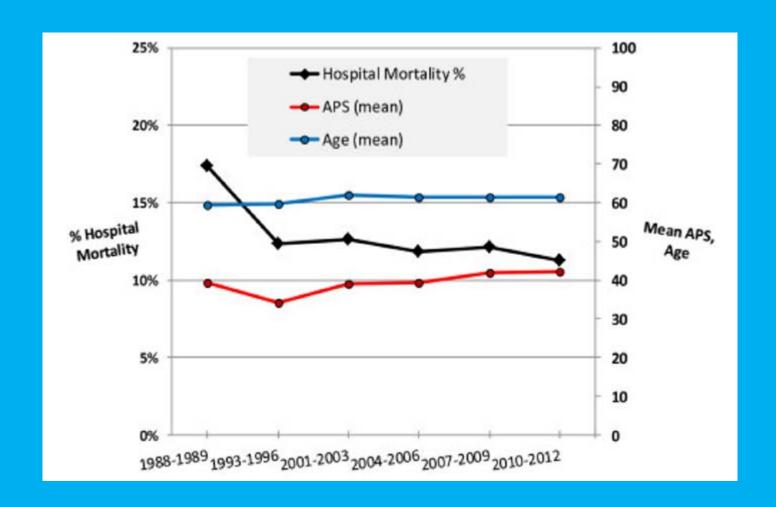
Jerry Altshuler, Pharm.D., BCPS, BCCCP Critical Care Pharmacy Coordinator Medical Intensive Care Unit The Mount Sinai Hospital



Objectives

- Describe the post-intensive care syndrome and its implications
- Explain the components of the ABCDEF bundle
- Evaluate the literature base rationalizing the ABCDEF bundle implementation
- Determine barriers and solutions to deployment of the ABCDEF bundle

Mortality Trends in the ICU



A Patient's Story

"I had septic shock 4 years ago from urosepsis and I'm in my 50s. I am writing because I have never felt like myself again. I can't think clearly, my memory has suffered. I am fatigued like never before. Before sepsis I was active, hiking, biking, rock climbing, running and now I am sedentary. This has affected every aspect of my life, I even had to leave my job as an ICU nurse because it was wearing me out"

Post Intensive Care Syndrome (PICS)

Physical Impairment

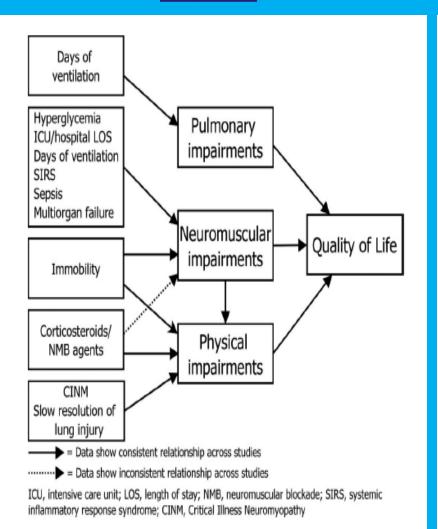
Cognitive Impairment

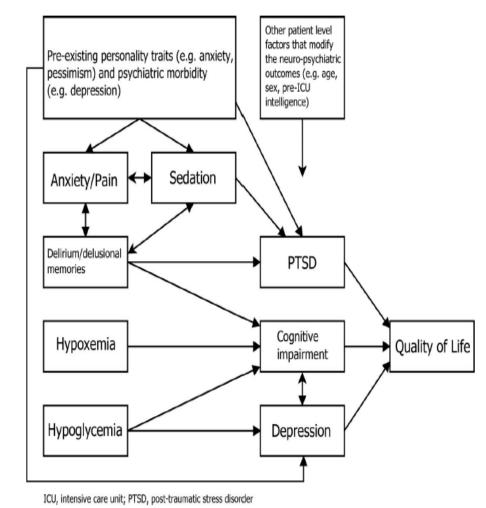
Mental Impairment

PICS Risk Factors

Physical

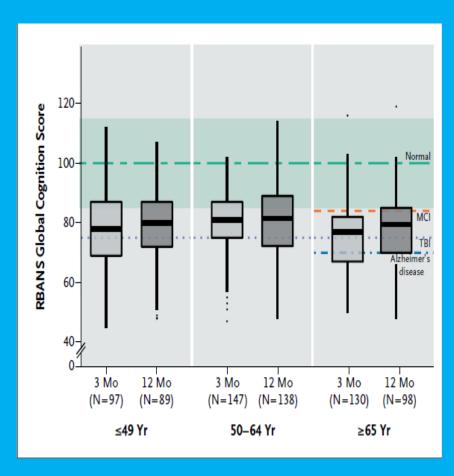
Cognitive/mental





ARDS Survivors

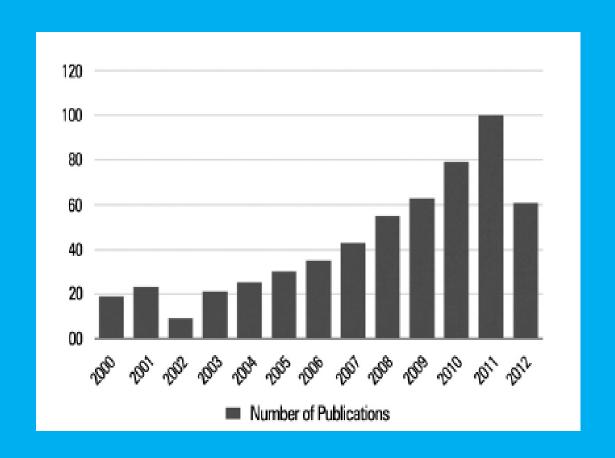
Outcome	3 Months	6 Months	12 Months
Distance walked in 6 min No. evaluated Median — m Interquartile range — m Percentage of predicted value∫	80* 281 55–454 49	78† 396 244–500 64	81; 422 277–510 66
Returned to work — no./total no. (%)¶	13/83 (16)	26/82 (32)	40/82 (49)
Returned to original work — no./total no. (%)	10/13 (77)	23/26 (88)	31/40 (78)
SF-36 score**			
Physical functioning Median (normal value) Interquartile range	35 (90) 15–58	55 (89) 30–75	60 (89) 35–85
Physical role Median (normal value) Interquartile range	0 (85) 0–0	0 (84) 0–50	25 (84) 0–100
Pain Median (normal value) Interquartile range	42 (77) 31–73	53 (77) 37–84	62 (77) 41–100
General health Median (normal value) Interquartile range	52 (78) 35–67	56 (77) 36–74	52 (77) 35–77
Vitality Median (normal value) Interquartile range	45 (69) 30–55	55 (68) 28–63	55 (68) 28–63
Social functioning Median (normal value) Interquartile range	38 (88) 19–69	63 (88) 38–88	63 (88) 38–100
Emotional role Median (normal value) Interquartile range	33 (84) 0–100	67 (84) 0–100	100 (84) 17–100
Mental health Median (normal value) Interquartile range	68 (78) 54–80	70 (78) 54–88	72 (78) 52–88



The Old Way

Topic	2002 Recommendation
Pain assessment	Numeric Rating Scale
Sedation Goal	A sedation goal should be implemented
Sedation assessment	Validated sedation scale
Sedation strategy	Use of sedation protocols
Sedation selection	Lorazepam as drug of choice for most patients
Delirium risk factor	None
Delirium Prevention	None

Publication Boom



Changing Guidelines

Topic	2002 Recommendation	2013 Recommendation
Pain assessment	Numeric Rating Scale (NRS)	BPS or CPOT if NRS not assessable
Sedation Goal	A sedation goal should be implemented	Light sedation for most patients
Sedation strategy	Use of sedation protocols	Daily sedation interruption or light sedation
Sedation selection	Lorazepam as drug of choice for most patients	Non-benzodiazepines as first choice
Delirium risk factor	None	Benzodiazepines
Delirium Prevention	None	Early mobilization

BPS: behavioral pain scale CPOT: critical care pain observation tool.

The Bundle

Symptoms Pain, Agitation, Delirium Guidelines	Monitoring Tools	Care ABCDEF Bundle
Pain	Critical-Care Pain Observation Tool (CPOT) NRS Numeric Rating Scale BPS Behavioral Pain Scale	A: Assess, Prevent and Manage Pain B: Both Spontaneous
Agitation	Richmond Agitation- Sedation Scale (RASS) Sedation-Agitation Scale (SAS)	Awakening Trials (SAT) and Spontaneous Breathing Trials (SBT) C: Choice of Analgesia and Sedation D: Delirium: Assess, Prevent
Delirium	Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) Intensive Care Delirium Screening Checklist (ICDSC)	and Manage E: Early Mobility and Exercise F: Family Engagement and Empowerment

How compliant is your institution with the ABCDEF bundle?

- A. Full compliance, the entire bundle is followed
- B. Most of the bundle is followed but resources make 100% compliance challenging
- C. Some of the bundle is followed but I would like to implement more components into practice
- D. None of the bundle is currently practiced
- E. I am not sure

Pain in the ICU

Pain experienced by nearly half of all ICU patients

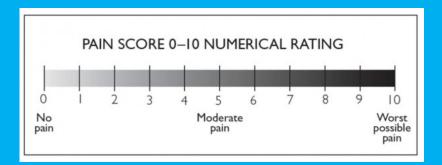
Often associated with various procedures

Associated with significant stress after ICU stay

Difficult to express and/or quantify pain

Assessing Symptoms

- Patient reported scales
 - Numerical Rating Scale
 - Visual Analog Scale



- Behavioral Pain Scales (BPS)
 - Behavioral Pain Scales (BPS)
 - Critical Care Pain Observation Tool (CPOT)
- Vital signs not reliable
 - On their own!
- Family might be helpful

BPS and CPOT

Item	Description	Score
Facial .	Relaxed	1
expression	Partially tightened	2
	Fully tightened	3
	Grimacing	4
Upper limbs	No movement	1
movement	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance	Tolerating movement	1
with mechanical ventilation	Coughing but tolerating most of the time	
	Fighting ventilator	
	Unable to control ventilation	4

Item	Description	Score
Facial .	Relaxed	0
expression	Tense	1
	Grimacing	2
Body	No movement	0
Movements	Protection	1
	Restlessness/Agitation	2
Compliance with	Tolerating ventilator or movement	0
mechanical ventilation	Coughing but tolerating	1
Or	Fighting ventilator	2
	Talking in normal tone or no sound	0
Vocalization (extubated	Sighing, moaning	1
patients)	Crying out, sobbing	2
Muscle Tension	Relaxed	0
	Tense, rigid	1
	Very tense or rigid	2

CPOT Example

CPOT



- Facial Expression: No muscle tension / relaxed
- Body Movement: None
- Muscle Tension:
 Relaxed
- O Compliance with Ventilator: Alarms not active & easy to ventilate

<u>Limitations of Behavioral Scales</u>

- Scores not proportional to patient reported
- Detect presence/lack of pain
 - Qualitative pain assessment
- Not reliable in patients unable to move or exhibit behaviors

Procedural Pain

Procedure	N (%)	Preprocedural Pain Intensity Median (IQR)	Pain Intensity During the Procedure Median (IQR)	Difference Median (IQR)	P Value*
Chest tube removal Wound drain removal Arterial line insertion Endotracheal suctioning Tracheal suctioning Peripheral intravenous insertion Peripheral blood draw Tuming Respiratory exercises Positioning Wound care Mobilization	292 (6.1) 75 (1.6) 199 (4.1) 767 (15.9) 302 (6.3) 315 (6.5) 328 (6.8) 873 (18.1) 439 (9.1) 371 (7.7) 301 (6.3) 526 (10.9)	2 (0-4) 2 (0-4) 1 (0-2.5) 1 (0-4) 1 (0-3.5) 1 (0-3) 0.5 (0-3) 1.75 (0-4) 2 (0-4) 1 (0-4) 2 (0-4) 1 (0-3)	5 (3-7) 4.5 (2-7) 4 (2-6) 4 (1-6) 4 (1-6) 3 (1-5.5) 3 (1-5) 3 (0.25-6) 3 (1-5) 3 (0-5) 3 (1-6) 2 (0-5)	2.5 (0.5-4) 2 (0-4.5) 2.75 (0-5) 1.5 (0-4) 1 (0-4) 1 (0-3) 1 (0-2.5) 1 (0-2) 1 (0-2) 0.5 (0-2) 0 (0-2)	<0.0001 <0.0001 <0.0001 <0.0001 <0.0001 <0.0001 <0.0001 <0.0001 <0.0001 <0.0001 <0.0001

"A" Summary

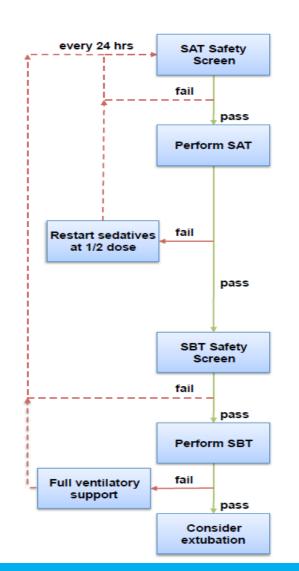
- Assess pain frequently
- Treat NRS >3, BPS >5, or CPOT>2
- Prevent pain via pre-procedural analgesia or non pharmacological therapy

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Spontaneous Awakening and Breathing

Trial



SAT Safety Screen

No active seizures
No alcohol withdrawal
No agitation
No paralytics
No myocardial ischemia
Normal intracranial pressure

SAT Failure

Anxiety, agitation, or pain Respiratory rate > 35/min Oxygen saturation < 88% Respiratory distress Acute cardiac arrhythmia

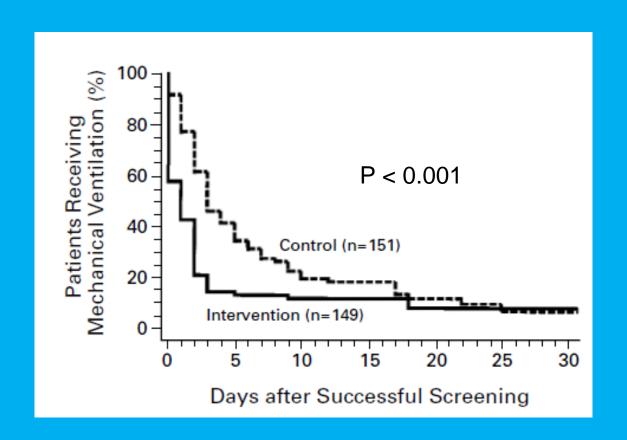
SBT Safety Screen

No agitation Oxygen saturation ≥ 88% FiO2 ≤ 50% PEEP ≤ 7.5 cm H2O No myocardial ischemia No vasopressor use Inspiratory efforts

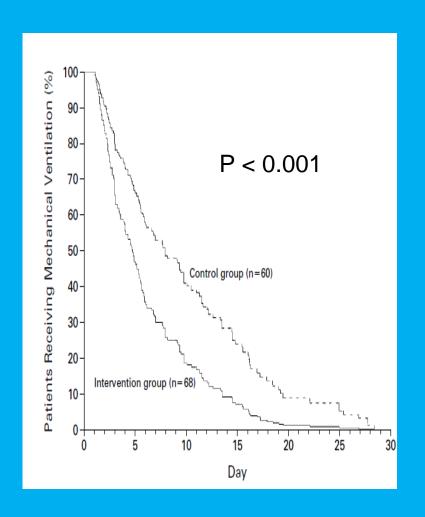
SBT Failure

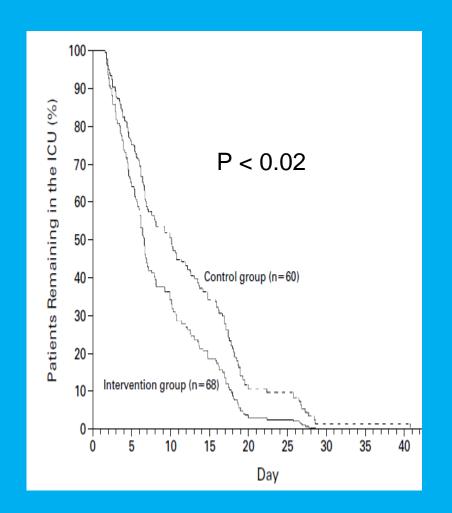
Respiratory rate > 35/min Respiratory rate < 8/min Oxygen saturation < 88% Respiratory distress Mental status change Acute cardiac arrhythmia

Spontaneous Breathing Trial

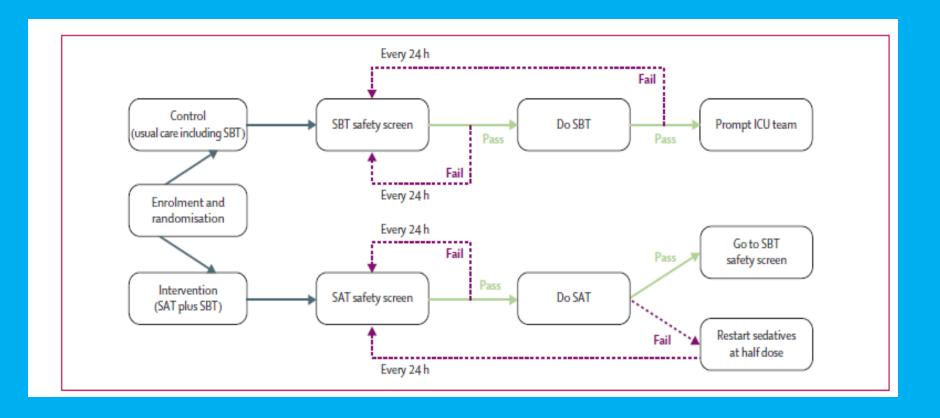


Sedation Vacation – Awakening Trial





"Wake up and Breath"



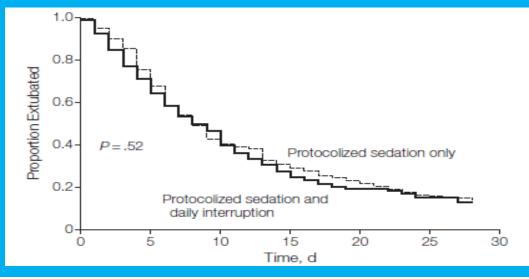
ABC

	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 (day	/s)		
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

Light Sedation

Outcome	Ramsey 1 - 2	Ramsey 3 - 4	p value
Ventilator days, mean ± SD	2.9 ± 5.0	5.5 ± 10.8	0.02
ICU length of stay, median (range)	4.0 (1–129)	5.5 (2-99)	0.03

SLEAP Trial



	Protocolized Sedation and Interruption (n = 214)	Protocolized Sedation (n = 209)	Measure of Effect, Mean Difference (95% CI)	<i>P</i> Value
Midazolam equivalents				
Total dose/patient, mg	1087 (4297) 222 (50 to 734)	1038 (4592) 237 (57 to 599)	48.4 (–804.4 to 901.2)	.91
Dose/patient/d, mg	102 (326) 8 (0 to 86)	82 (287) 0 (0 to 50)	19.23 (2.37 to 37.07)	.04
Dose/patient/d, infusion, mg	101 (325) 6 (0 to 86)	82 (287) 0 (0 to 50)	19.22 (1.92 to 36.53)	.03
Dose/patient/d, bolus, mg	0.99 (5.9) 0 (0 to 0)	0.49 (2.65) 0 (0 to 0)	0.50 (0.23 to 0.76)	<.001
Fentanyl equivalents Total dose/patient, μg	18 997 (59 928) 5286 (1512 to 16 437)	13 532 (23 219) 5936 (2056 to 15 236)	5464.6 (-3236.0 to 14 165.2)	.22
Dose/patient/d, μg	1780 (4135) 550 (50 to 1850)	1070 (2066) 260 (0 to 1400)	709.3 (522.0 to 897.7)	<.001
Dose/patient/d, infusion, μg	1664 (4070) 420 (0 to 1725)	984 (2002) 80 (0 to 1260)	679.7 (495.3 to 864.1)	<.001
Dose/patient/d bolus, μg	116 (215) 0 (0 to 100)	86 (169) 40 (0 to 150)	30.13 (19.15 to 41.11)	<.001

JAMA. 2012;308:1985-92.

"B" Summary

 Utilize validated sedation scales with frequent reassessment of sedation depth

 Coordinated SAT (or light sedation) and SBT can reduce mechanical ventilation, length of stay and delirium(?)

 Keep patients as awake and alert as possible, extubate when feasible

Which of the following is false regarding element "B"

- A. SAT paired with SBT can reduce time on mechanical ventilation and ICU length of stay
- B. SBT while targeting light sedation may be as effective as SAT paired with SBT
- C. SAT and SBT should only be performed after safety screens are passed
- D. Combining SAT and SBT does not generally lead to more self extubations

The Bundle

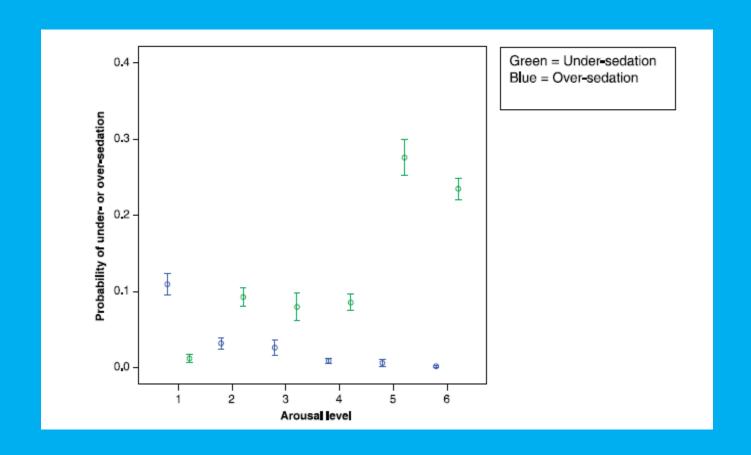
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Sedation Scales

Richmond Agitation Sedation Scale (RASS)			
4	Combative		
3	Very Agitated		
2	Agitated		
1	Restless		
0	Alert and Calm		
-1	Drowsy		
-2	Light Sedation		
-3	Moderate Sedation		
-4	Deep Sedation		
-5	Unarousable		

Sedation Agitation Scale (SAS)			
7	Dangerously agitated		
6	Very agitated		
5	Agitated		
4	Calm and cooperative		
3	Sedated		
2	Very Sedated		
1	Unarousable		

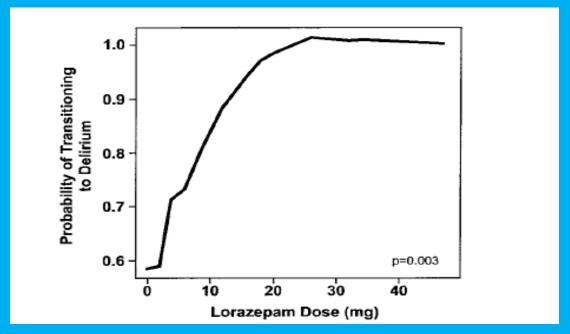
The Correct Sedation Target



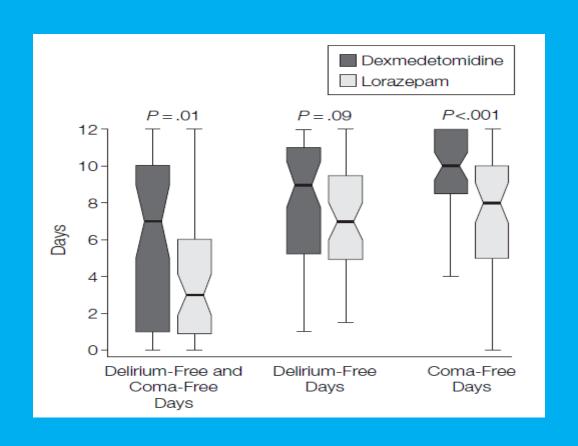
Benzodiazepine Delirium Association

Outcome	Lorazepam (n = 64)	Propofol (n = 68)	p value
Ventilator days	8.4 (4.6, 14.7)	5.8 (3.5, 10.3)	0.04
Ventilator days, survivors	9.0 (5.3, 16.8)	4.4 (3.0, 8.7)	0.006
ICU length of stay, survivors	12.7 (7.8, 19.1)	8.6 (5.0, 14.7)	0.05

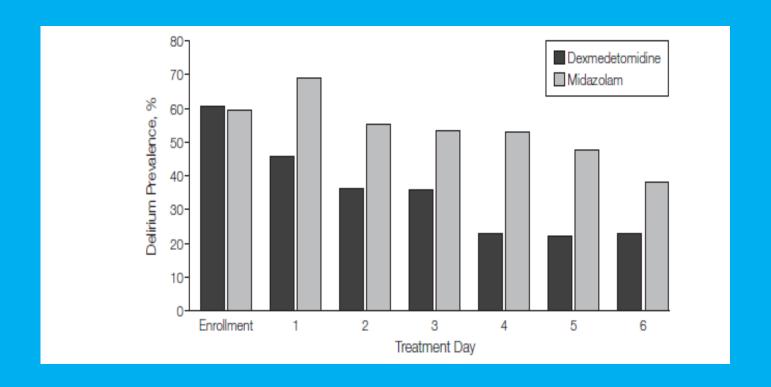
All values reported as median (IQR)



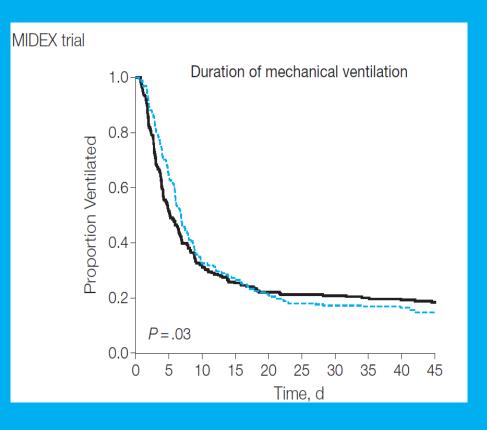
MENDS Trial

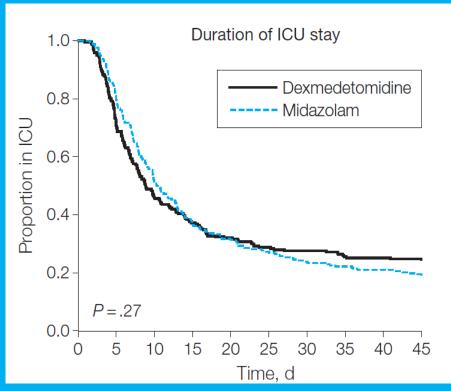


SEDCOM

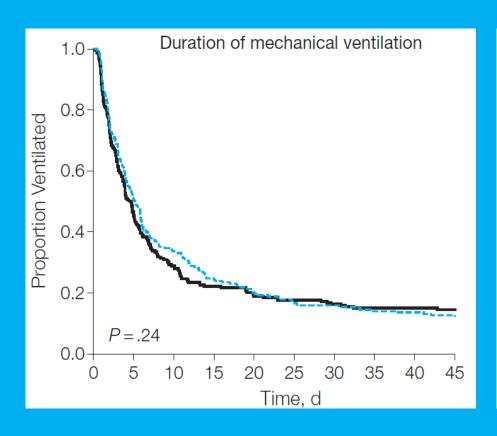


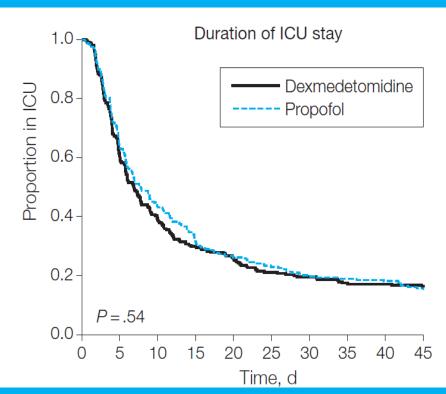
PRODEX/MIDEX





PRODEX/MIDEX



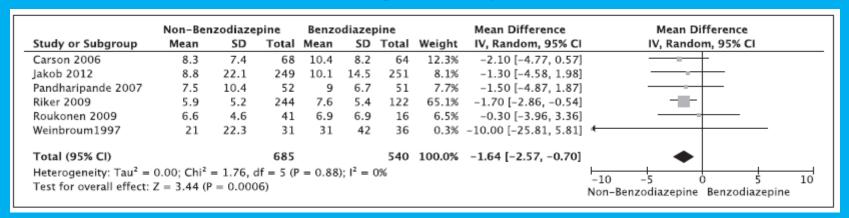


PRODEX/MIDEX

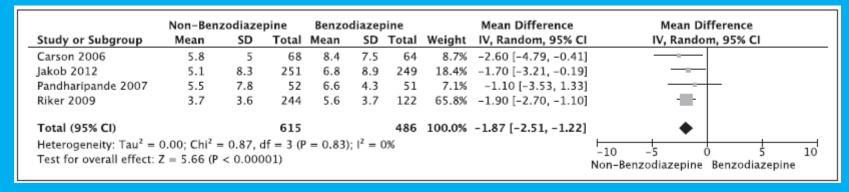
	Midex				Prodex											
	De	exmedetom	idine		Midazola	am			Dexi	medetomi	dine		Prop	ofol		
	N	(%)	Events	N	(%)	Ev	ents F	value	N	(%)	Events	N	(%)	Ever	nts P	value
CAM-ICU assessment at 48- hour follow-up																
Positive	28	(11.9)		33	(13.9)			0.393	22	(9.6)		31	(13.7	7)	().231
Negative	138	(58.7)		123	(51.7)				148	(64.9)		139	(61.	5)		
Unassessable	69	29.4		82	34.5				58	(25.4)		56	(24.8	3)		
Preferred term			Dex	medetor (N = 24'		Mic	lex Midazol (N = 25			Dex	xmedetor (N = 24		Pro	dex Propof (N = 24		
Hypertension Sinus tachycardia Hypotension			N 53 34 51	(%) (21.5) (13.8) (20.6)	events 70 46 58	N 52 54 29	(%) (20.8) (21.6) (11.6)	events 74 89 51	P value 0.913 0.025 0.007	52 48 32	(%) (21.1) (19.5) (13.0)	events 62 85 38	N 37 28 33	(%) (15.0) (11.3) (13.4)	events 40 46 41	P value 0.08 0.013
Atrial fibrillation Agitation Bradycardia			33 39 35	(13.4) (15.8) (14.2)	42 44 47	42 41 13	(16.8) (16.4) (5.2)	68 44 16	0.317 0.903 < 0.001	30 19 32	(12.2) (7.7) (13.0)	38 20 51	35 29 25	(14.2) (11.7) (10.1)	45 33 33	0.595 0.171 0.328

The Benzodiazepine Problem

ICU Length of Stay



Duration of Mechanical Ventilation



Analgo-Sedation

Utilize opioids to treat pain before administering sedatives

Attain analgesia and sedation from single drug

Avoid sedative related adverse events

 Inappropriate for pharmacologic paralysis, increased ICP, alcohol/benzodiazepine withdrawal

"No Sedation Protocol"

	No sedation (n=55)	Sedation (n=58)	p value
Days without mechanical ventilation (from intubation to day 28)	13-8 (11-0); 18-0 (0-24-1)	9-6 (10-0); 6-9 (0-20-5)	0.0191*†
Length of stay (days)			
Intensive care unit	13-1 (5-7)‡	22.8 (11.7)‡	0.0316*§
Hospital	34 (17-65)	58 (33-85)	0.0039*∫¶
Mortality			
Intensive care unit	12 (22%)	22 (38%)	0.06
Hospital	20 (36%)	27 (47%)	0.27
Drug doses (mg/kg)			
Propofol (per h of infusion)**	0 (0-0-515)	0.773 (0.154-1.648)	0.0001
Midazolam (per h of infusion)	0 (0-0)	0.0034 (0-0.0240)	<0.0001
Morphine (per h of mechanical ventilation)	0.0048 (0.0014-0.0111)	0.0045 (0.0020-0.0064)	0.39
Haloperidol (per day of mechanical ventilation)	0 (0-0-0145)	0 (0-0)	0.0140
Tracheostomy	16 (29%)	17 (29%)	0.98
Ventilator-associated pneumonia	6 (11%)	7 (12%)	0.85

"C" Summary

- Assess pain and level of sedation frequently
- Manage pain before using sedatives
- Consider non-opioid analgesics to decrease opioid requirement
- Consider neuropathic pain specific pharmacotherapy
- Consider non-benzodiazepine based sedation when necessary

Which of the following is true regarding sedation pharmacotherapy?

- A. Propofol and benzodiazepines appear to be associated with similar time on mechanical ventilation
- B. Propofol and benzodiazepines appear to be associated with similar rates of delirium
- C. Dexmedetomidine has not been shown to be associated with less delirium than propofol
- D. Dexmedetomidine has not been shown to be associated with less delirium than benzodiazepines

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Delirium

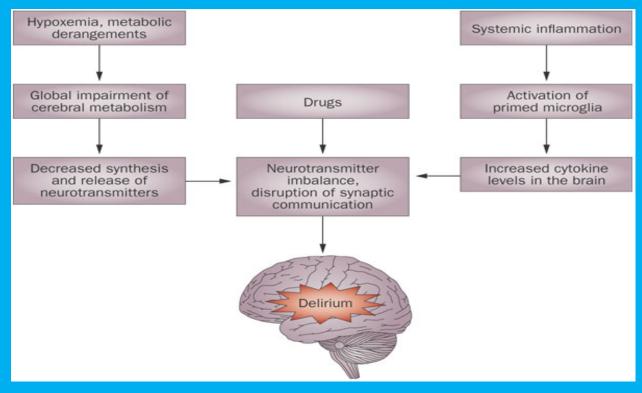
 Disturbance of consciousness and cognition developing acutely and fluctuating

Occurs in up to 80% of ICU patients

Costs \$4 - \$16 billion in the United States annually

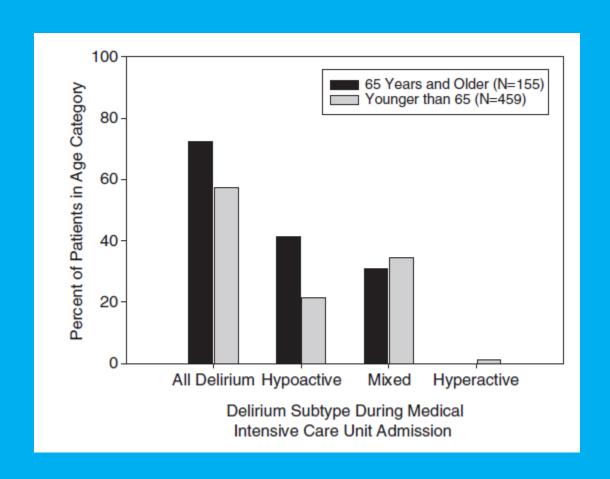
Associated with increased mortality

Delirium Risk Factors

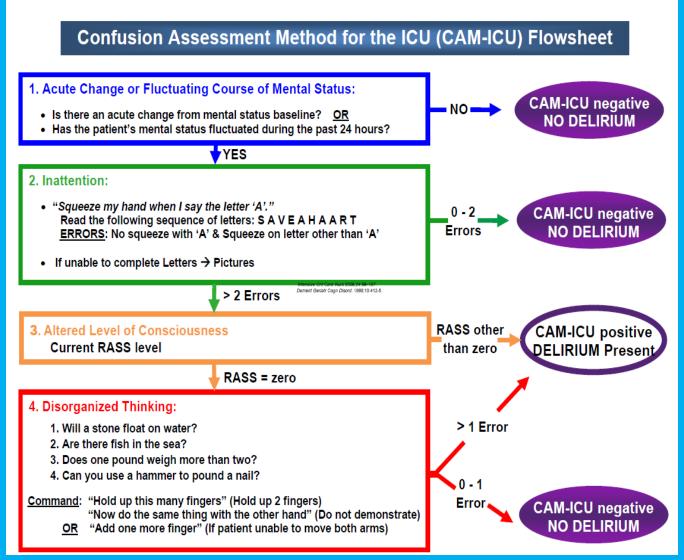


Pharmacological	Non-Pharmacological
Antimicrobials	Pain
Benzodiazepines	Sepsis
Corticosteroids	Metabolic derangement
Anticholinergics	CNS infection
Opioids	Renal Failure

Delirium Types



Assessment - CAM-ICU



Intensive Care Delirium Screening Checklist - ICDSC

- Altered level of consciousness
- Inattention
- Disorientation
- Hallucination, delusion, or psychosis
- Psychomotor agitation
- Inappropriate speech or mood
- Sleep/wake cycle disturbances
- Symptom fluctuation

- 1 point per domain
- > 4 = delirium

Delirium Pharmacotherapy

Study	Details	N	Findings
Skrobik 2004	RCT, haloperidol vs olanzapine	73	No difference in delirium severity over 5 days
HOPE- ICU	RCT, Haloperidol vs placebo	141	No difference time spent in delirium
Devlin 2010	RCT, Quetiapine vs placebo	36	Faster delirium resolution 1.0 vs. 4.5 days p =.001 less time spent in delirium 36 vs. 120 p =.006
MIND trial	RCT, haloperidol vs ziprasidone vs placebo	101	No difference in days alive without delirium
Michaud 2016	Retrospective cohort, quetiapine vs placebo for hypoactive delirium	113	Duration of hypoactive delirium shorter (1.5 vs 2.0 days, p=0.04)

Management and Prevention

- Avoid deliriogenic medications
- Pain Management
- Manage Constipation?
- Reorientation
- Non pharmacologic sleep enhancement?
- Consider atypical antipsychotics to reduce duration of delirium
- Avoid pharmacological prophylaxis

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Delirium	Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) Intensive Care Delirium Screening Checklist (ICDSC)	and Manage E: Early Mobility and Exercise F: Family Engagement and Empowerment

Early Mobility and Exercise



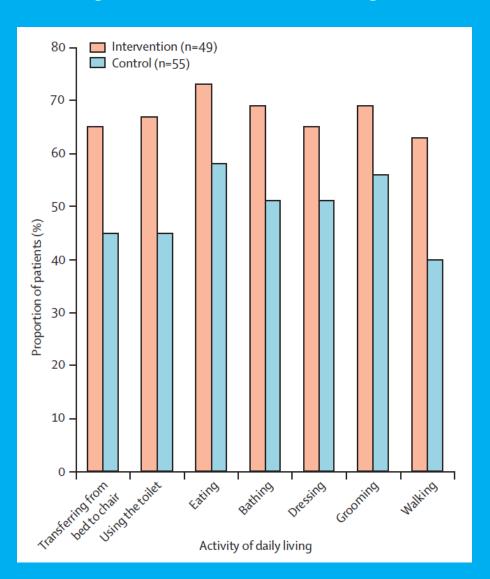




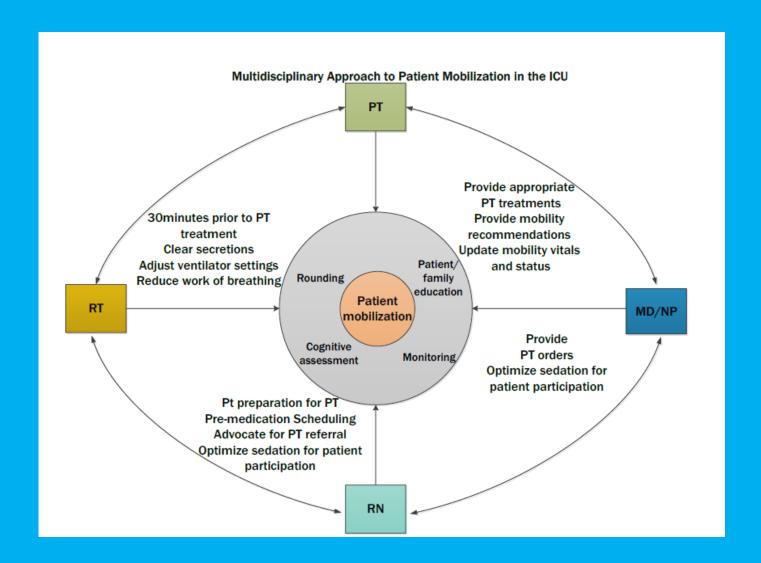
Early Mobility

	Intervention (n=49)	Control (n=55)	p value
Return to independent functional status at hospital discharge	29 (59%)	19 (35%)	0.02
ICU delirium (days)	2.0 (0.0-6.0)	4.0 (2.0-7.0)	0.03
Time in ICU with delirium (%)	33% (0–58)	57% (33-69)	0.02
Hospital delirium (days)	2.0 (0.0-6.0)	4.0 (2.0-8.0)	0.02
Hospital days with delirium (%)	28% (26)	41% (27)	0.01
Barthel Index score at hospital discharge	75 (7·5–95)	55 (0-85)	0.05
ICU-acquired paresis at hospital discharge	15 (31%)	27 (49%)	0.09
Ventilator-free days*	23.5 (7.4–25.6)	21.1 (0.0-23.8)	0.05
Duration of mechanical ventilation (days)	3.4 (2.3-7.3)	6.1 (4.0-9.6)	0.02
Duration of mechanical ventilation, survivors (days)	3.7 (2.3–7.7)	5.6 (3.4-8.4)	0.19
Duration of mechanical ventilation, non-survivors (days)	2.5 (2.4–5.5)	9.5 (5.9–14.1)	0.04
Length of stay in ICU (days)	5.9 (4.5–13.2)	7-9 (6-1-12-9)	0.08
Length of stay in hospital (days)	13.5 (8.0-23.1)	12.9 (8.9–19.8)	0.93
Hospital mortality	9 (18%)	14 (25%)	0.53

Early Mobility and Quality of Life



Mobilizing as a Team Effort



Early Mobility and Exercise Summary

- Mobility is responsibility of the entire team
- Wide spectrum of activities patients can do
 - In bed: Passive range of motion, turning side to side, sitting on side of bed
 - Out of bed: Standing at bedside, sitting in chair, walking
- Early mobility is effective in
 - Decreasing delirium incidence
 - Improving capacity for physical functioning
 - Decreasing time spent on mechanical ventilation

The Bundle

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Family Engagement

Most recent addition to bundle

Focus on emphasizing "patient and family-centered care"

Keep family members present and engaged in care

Family Presence

- Approximately 90% of US ICUs had restrictive visitation policies in 2008-2009 Survey
 - Average of 2.8 limitations
- Concept of an "Open" ICU
 - Open visitation policies
 - Daily meetings with family
 - Participation in rounds?
 - Participation in CPR?
- Patient and Family benefits

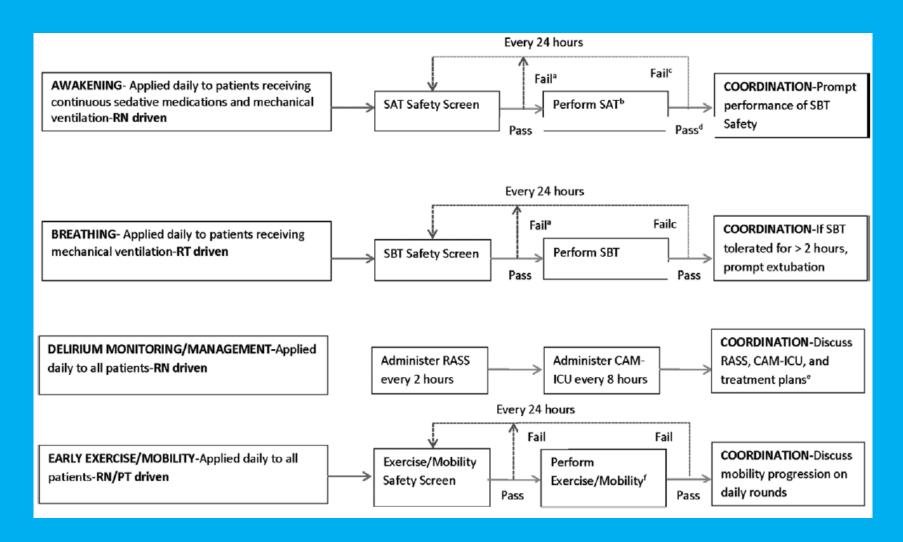
Family Presence During CPR

Variable	Intervention Group (N = 233)	Control Group (N = 242)	P Value†	Family Member Present (N=289)	Family Member Absent (N=186)	P Value†
IES score — median (interquartile range)‡	22 (12–33)	24 (13–35)	0.26	21 (11–32)	26 (15–36)	0.007
Presence of PTSD-related symptoms — no. (%)∫	64 (27)	90 (37)	0.01	78 (27)	76 (41)	0.01
HADS score — median (interquartile range) \P	10 (6–16)	11 (6–19)	0.44	9 (5–16)	12 (7–19)	0.02
Symptoms of anxiety — no./total no. (%)	34/230 (15)	55/239 (23)	< 0.001	46/287 (16)	43/182 (24)	<0.001
Symptoms of depression — no./total no. (%)∥	39/230 (17)	50/239 (21)	0.13	42/287 (15)	47/182 (26)	0.009
Saw a psychologist after resuscitation of the patient — no./total no. (%)	20/232 (9)	18/242 (7)	0.83	25/289 (9)	13/185 (7)	0.23
Received newly prescribed psychotropic drugs after resuscitation of the patient — no./ total no. (%)	64/230 (28)	77/238 (32)	0.22	72/287 (25)	69/181 (38)	<0.001
Made a suicide attempt after resuscitation of the patient — no./total no. (%)	2/227 (1)	3/238 (1)	_	5/285 (2)	0/180	_
Survival						
Return of spontaneous circulation — no.		94 (27)	58 (25)	0.59	
Survival to hospital admission — no. (%)			63 (18)	36 (16)	0.42
Survival to day 28 — no. (%)			11 (3)	9 (4)	0.64

The Bundle

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Putting it all Together – Balas 2014



Bundle Efficacy Evaluation

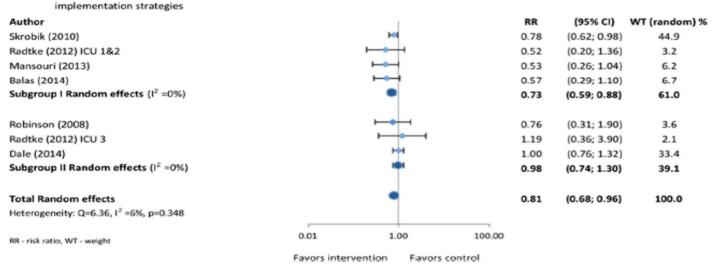
ABCDE Bundle Component Outcome	Pre-ABCDE Bundle (n = 146)	Post-ABCDE Bundle (n = 150)	Unadjusted <i>p</i>	Adjusted Odds Ratio	Adjusted p
Awakening and breathing coordinationa					
Ventilator-free days ^a					
Mean (sp)	15 (11.4)	18 (10.6)			
Median (IQR)	21 (0-25)	24 (7-26)	0.04		
Delirium monitoring/management					
Delirium anytime, n (%)	91 (62.3)	73 (48.7)	0.02	0.55 ^b (0.33-0.93)	0.03
Early exercise/mobility					
Mobilized out of bed anytime in ICU, n (%)	70 (48)	99 (66.0)	0.002	2.11 ^b (1.30-3.45)	0.003
28-day mortality ^c					
Hospital mortality (ICU and post-ICU), n (%)	29 (19.9)	17 (11.3)	0.04	0.56 ^b (0.28-1.10)	0.09
ICU mortality, <i>n</i> (%)	24 (16.4)	14 (9.3)	0.07		
Time to discharge ^d (d)					
From ICU, median (IQR)	5 (3, 8)	4 (3, 5)	0.21	1.16° (0.89-1.50)	0.27
From hospital, median (IQR)	13 (9, 15)	11 (9, 13)	0.99	1.01 (0.77-1.31)	0.96

Bundle Components and Efficacy

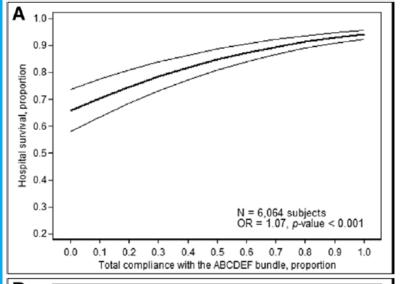
C Length of Stay after implementation in studies using PAD or ABCDE (n=4) with high (I) versus low (II) number of implementation strategies

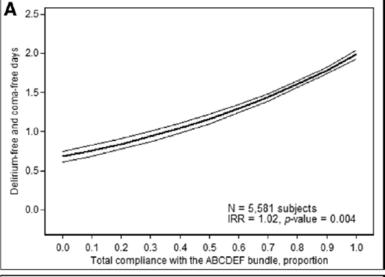
implementation strat	egies			
Author	WMD	(95% CI)	Weight (%)	
Skrobik (2010)	-0.97	(-1.82; -0.12)	42.9	⊢
Radtke (2012) ICU1&2	-2.00	(-2.88; -1.12)	39.5	
Mansouri (2013)	-6.35	(-9.50; -3.20)	6.9	
Balas(2014)	0.40	(-1.61; 2.41)	7.6	-
Subgroup I	-1.67	(-2.46; -0.88)	96.9	⊢
Radtke (2012) ICU3	-2.00	(-4.11; 0.11)	3.1	
Subgroup II	-2.00	(-4.03; 0.03)	3.1	—
Overall	-1.71	(-2.45; -0.98)	100.0	⊢ ♠⊣
			_	
WMD - Weighted mean differ	rence, CI - confid	dence interval	-12.0	-10.0 -8.0 -6.0 -4.0 -2.0 0.0 2.0 4.0
				Favors intervention Favors control

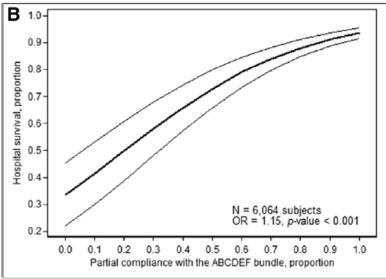
Risk ratio of mortality after implementation in studies using PAD or ABCDE (n=6) with high (I) versus low (II) number of implementation strategies

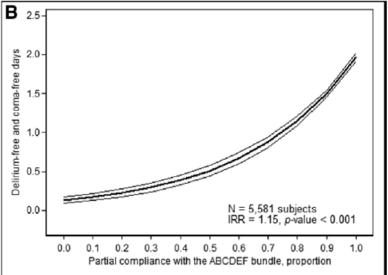


Multi-Center Bundle Assessment

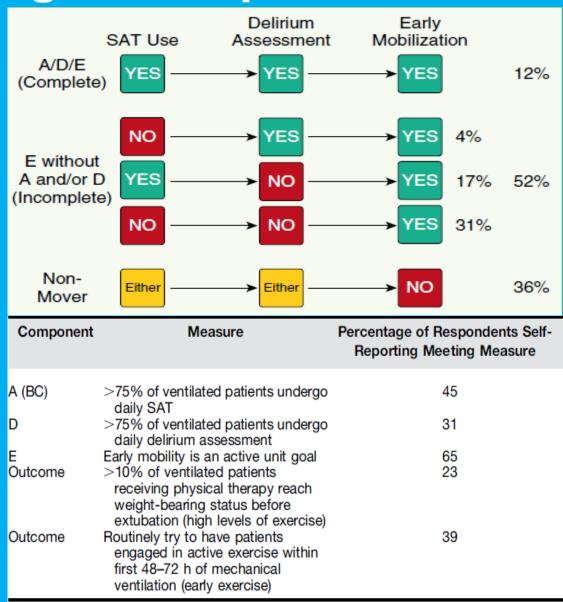








Challenges to Implementation



2017 World Wide Bundle Implementation

- 1521 respondents
 - 47 countries
- 57% bundle implementation
 - Varying degrees of compliance

Component	Compliance	
A - Pain assessment	83% Compliance	
B - Spontaneous Awakening/breathing trials	66%/67%	
C - Choice of drugs	BZD minimization - 90%	
E – Early mobility	Recommended often 31% mobility team	
F – Family	67 % "family involved" 35% 24/7 open unit	

Specific Challenges

Patient-related barriers	Clinician-related barriers	Protocol-related barriers	ICU contextual barriers
Lack of patient cooperation	Safety of tubes, catheters, and wires	Learning curve	Lack of leadership/manag ement
Patient instability and patient safety concerns	Lack of conceptual agreement with guidelines	Lack of clarity as to who is responsible	Lack of inter- professional team support and training/expertise
Patient status issues	Perception that rest equals healing	Unavailable or cumbersome to use protocols	Physical environment, equipment, and resources

Conclusion

- While ICU care is constantly improving, the PICS continues to be an important problem
- The ABCDEF bundle utilizes several evidence based strategies to emphasize the patient-centered experience
- Compliance with the bundle can improve various ICU related outcomes and improve quality of life
- Widespread implementation has been challenging with several barriers identified

Sleep no more: making sense of the ABCDEF bundle

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