A New Frontier in Critical Care: Saving the Injured Brain

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Disclosures: ICU Physician Vanderbilt
- Abbott, Hospira, Orion
- NIH and VA U.S. Federal Funding
- Author of PAD Guidelines of SCCM 2013
SAG Guidelines for sustained use of sedatives and analgesics in the critically ill adult

Jacobi, CCM 2002
Dr. Swenson explained, "I'll tell you the truth. What I have discovered...is not what I expected. It is something greater, much more ambitious than anything we had hoped for...in science: Never be so focused on what you are looking for that you overlook the thing you actually find."

Ann Patchett - 2011, State of Wonder
Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit

Juliana Barr, MD, FCCM; Gilles L. Fraser, PharmD, FCCM; Kathleen Puntillo, RN, PhD, FAAN, FCCM; E. Wesley Ely, MD, MPH, FACP, FCCM; Céline Gélinas, RN, PhD; Joseph F. Dasta, MSc, FCCM, FCCP; Judy E. Davidson, DNP, RN; John W. Devlin, PharmD, FCCM, FCCP; John P. Kress, MD; Aaron M. Joffe, DO; Douglas B. Coursin, MD; Daniel L. Herr, MD, MS, FCCM; Avery Tung, MD; Bryce R. H. Robinson, MD, FACS; Dorrie K. Fontaine, PhD, RN, FAAN; Michael A. Ramsay, MD; Richard R. Riker, MD, FCCM; Curtis N. Sessler, MD, FCCP, FCCM; Brenda Pun, MSN, RN, ACNP; Yoanna Skrobik, MD, FRCP; Roman Jaeschke, MD

Barr J et al, CCM 2013;41:263-306
Articles on Delirium in ICU
(MeSh or Text headings in English)

Number of Articles

Year


Morandi et al, Intensive Care Med 2008
Delirium Prevention and Safety: Starting with the ABCDEF’s

It is essential to consider delirium management in the broader picture of ICU patient care as a major piece of the current guidelines for Pain, Agitation, and Delirium (PAD) of the Society of Critical Care Medicine (SCCM). Advancements in research and technology are resulting in higher acuity and increased complexity of care, which is resulting in drastic increases in workload and demands on staff. More than ever, there is a great need to develop simpler ways of implementing safer and better care into practice for our sickest patients.

The ABCDEF bundle is one way to align and coordinate care, which includes specific focus on delirium as a component of the overall care patients receive including sedation and pain medications, breathing machines, and mobilization.

What are the components of the ABCDEF bundle?
50-70% Cognitively Impaired

Jackson *AJRCCM* 2010; 182: 183
Girard *Crit Care Med* 2010; 38: 1513
60-80% Functionally Impaired
ICU Survivorship

Iwashyna  *Annals of Int Med* 2010; 153:204-5
After 5 months I felt better and returned to work but was fired 10 weeks later... it didn't surprise me because I was struggling terribly. I couldn't organize my work; committed many errors in documentation; frequently lost things; forgot meetings, and did not manage my time well.

http://www.icudelirium.org/testimonials.html
When I returned to work, the work I did before seemed foreign and unfamiliar. I became isolated and excluded from everyone. No one wanted to be around me. My wife of more than 36 years told me that I was just “feeling sorry” for myself, and I just needed to get on with my life. I nearly ended my life a few times. Then after five years of this hell, Oct 2 2013 CBS News ran a report about people just like me. From that report I found your website. I cried for long time; it has changed my wife’s opinion about me. For the first time in the past five years, I think believe I have a future.

http://www.icudelirium.org/testimonials.html
Cognitive Impairment: Sepsis

Before Sepsis

-3 years
-1 year

After Sepsis

+1 year
+3 years

% survivors cognitively impaired

Mild Cognitive Impairment
Moderate/Severe Cog Impairment

Iwashyna T, JAMA 2010;304:1787-1794

p<0.001
Delirium as a Predictor of Mortality in Mechanically Ventilated Patients in the Intensive Care Unit
Delirium Duration & Mortality

<table>
<thead>
<tr>
<th>Days of Delirium</th>
<th>Relative Hazard of Death (HR)</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 vs 1</td>
<td>1.7</td>
<td>1.27-2.29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>0 vs 2</td>
<td>2.69</td>
<td>1.58-4.57</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>0 vs 3</td>
<td>3.73</td>
<td>1.92-7.23</td>
<td>&lt;0.001</td>
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</tbody>
</table>

Shehabi Y, et al. CCM 2010; 38:2311–2318
Bringing to light Risk factors And Incidence of Neuropsychological dysfunction in ICU survivors
Long-Term Cognitive Impairment after Critical Illness


ABSTRACT

BACKGROUND
Survivors of critical illness often have a prolonged and disabling form of cognitive impairment that remains inadequately characterized.
Delirium and Brain Atrophy

(A) 46 year old, no delirium      (B) 42 year old, 12 days of delirium

Gunther M et al. CCM 2012;40:2022-32
The Picture of Dementia Following ICU Care

A

<table>
<thead>
<tr>
<th>RBANS Global Cognitive Score</th>
<th>&lt;65 Years</th>
<th>&gt;=65 Years</th>
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<tbody>
<tr>
<td>N</td>
<td>244</td>
<td>130</td>
</tr>
<tr>
<td>3 Months</td>
<td>227</td>
<td>98</td>
</tr>
<tr>
<td>12 Months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Legend:
- Normal
- MCI
- TBI
- AD

N=244 for 3 Months, N=227 for 12 Months, N=130 for 3 Months, N=98 for 12 Months.
Delirium and Executive Function
<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Monitoring</th>
<th>Management</th>
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</thead>
<tbody>
<tr>
<td>Pain</td>
<td>BPS</td>
<td>$\text{SaO}_2$</td>
</tr>
<tr>
<td>Agitation</td>
<td>RASS</td>
<td>$\text{SBT}$</td>
</tr>
<tr>
<td>Delirium</td>
<td>CAM-ICU</td>
<td>$\text{Ca}^2$</td>
</tr>
</tbody>
</table>

**Airplane Draft**

**ICU Liberation - 3 Columns**
ICU PAD Guidelines

ABCDEF Bundle Checklist*

• A – Assess, Prevent and Manage Pain
• B – Both SATs and SBTs
• C – Choice of Sedation
• D – Delirium: Assess, Prevent and Manage
• E – Early Mobility and Exercise
• F – Family Engagement and Empowerment

*www.icudelirium.org
*www.iculiberation.org
ABCDEF Bundle Objectives

- Optimize pain management.
- Break the cycle of deep sedation and prolonged mechanical ventilation.
- Reduce the incidence, duration of ICU delirium.
- Improve short, long-term ICU patient outcomes.
- Reduce health care costs!

Morandi et al Curr Opin Crit Care 2011;17:43-9
Vasilevskis et al Crit Care Med 2010;38:S683-91
Zaal et al, ICM 2013;39:481-88
Colombo et al, Minerva Anest 1012;78:1026-33
Liberated...?
Liberated...
Liberated...texting while on vent
Liberated...
ventilated patient and nurse “talking”
SCCM’s ICU Liberation Collaborative 2015-2017

West

Midwest/Northeast

Southeast

VANDERBILT UNIVERSITY MEDICAL CENTER
New Order Set: Benzodiazepine Use

**Median dose - Lorazepam equivalents (mg)**

Adjusted Ratio of Medians: 0.71 (95% CI: -1.31, -0.10)

Dale CR & Treggiari M, Ann ATS 2014;11:367-74
Probability of Delirium over Time

Adjusted OR of delirium: 0.67 (95% CI: 0.49, 0.91)

Dale CR & Treggiari M, Ann ATS 2014;11:367-74
Effectiveness and Safety of the Awakening and Breathing Coordination, Delirium Monitoring/Management, and Early Exercise/Mobility Bundle

Michele C. Balas, PhD, RN, APRN-NP, CCRN\textsuperscript{1}; Eduard E. Vasilevskis, MD, MPH\textsuperscript{2,3,4}; Keith M. Olsen, PharmD, FCCP, FCCM\textsuperscript{5,6}; Kendra K. Schmid, PhD\textsuperscript{7}; Valerie Shostrom, MS\textsuperscript{7}; Marlene Z. Cohen, PhD, RN, FAAN\textsuperscript{8}; Gregory Peitz, PharmD, BCPS\textsuperscript{5,6}; David E. Gannon, MD, FACP, FCCP\textsuperscript{9}; Joseph Sisson, MD\textsuperscript{9}; James Sullivan, MD\textsuperscript{10}; Joseph C. Stothert, MD, PhD, FCCM, FACS\textsuperscript{11}; Julie Lazure, BSN, RN\textsuperscript{12}; Suzanne L. Nuss, PhD, RN\textsuperscript{13}; Randeep S. Jawa, MD, FACS, FCCM\textsuperscript{11}; Frank Freihaut, RRT\textsuperscript{14}; E. Wesley Ely, MD, MPH, FCCM\textsuperscript{3,4,15}; William J. Burke, MD\textsuperscript{16}

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

Balas M, CCM 2013;42:1024-36
VENTILATOR FREE DAY RESULTS

- Pre ABCDE Bundle
- Post ABCDE Bundle

$p = 0.04$

Days

Ventilator Free Days-28 Day

Balas M, CCM 2013;42:1024-36
DELIRIUM RESULTS

Balas M, CCM 2013;42:1024-36
Early Mobility

- Pre ABCDE Bundle
- Post ABCDE Bundle

OOB ICU: p=0.005
OOB MV: p=0.07
OOB Non-MV: p=0.005

Balas M, CCM 2013;42:1024-36
28 DAY MORTALITY RESULTS

ICU Total Hospital

Pre ABCDE Bundle Post ABCDE Bundle

p=0.04

p=0.07

Balas M, CCM 2013;42:1024-36
ADJUSTED ANALYSIS

• Controlling for age, sex, mechanical ventilation, APACH II score, Charlson Comorbidity Index

• Delirium anytime - OR 0.55 (0.33-0.93); p=0.03

• OOB anytime in ICU - OR 2.11 (1.30-3.45); p=0.003

Balas M, CCM 2013;42:1024-36
### Hopkins QI Project = Reduced Delirium via less benzodiazepines and more mobility

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Pre-QI (n=27)</th>
<th>Post-QI (n=30)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days with any benzodiazepine use**</td>
<td>150 (50%)</td>
<td>118 (26%)</td>
<td>.002</td>
</tr>
<tr>
<td>Days alert (RASS -1 to +1)</td>
<td>88 (30%)</td>
<td>311 (67%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>PT/OT in MICU</td>
<td>19 (70%)</td>
<td>28 (93%)</td>
<td>.040</td>
</tr>
<tr>
<td>Number of PT/OT treatments in ICU</td>
<td>1 (0-3)</td>
<td>7 (3-15)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Days without delirium</td>
<td>61 (21%)</td>
<td>243 (53%)</td>
<td>.003</td>
</tr>
<tr>
<td>Days of delirium in ICU</td>
<td>107 (36%)</td>
<td>125 (28%)</td>
<td></td>
</tr>
<tr>
<td>Days of Coma</td>
<td>129 (43%)</td>
<td>86 (19%)</td>
<td></td>
</tr>
</tbody>
</table>

** Benzodiazepine dose (median midazolam eq) from 47mg down to 15 mg/day

Needham DM Arch Phys Med Rehabil 2010; 91:536-542
IHI’s and CDC’s Rethinking Critical Care: Implementing Change Using Bundle Approach

Qualitative descriptions of IHI’s and CDC’s collaboratives between 2011 and 2014.

**Conclusion:** Changing critical care practices requires an interprofessional approach addressing cultural, psychological, and practical issues.

**Key Take Home Points:**
1. Test changes on a small scale
2. Feed back data regularly and provide ongoing education
3. Build will through seeing the work in action

Klompas M, AJRCCM 2015;191:292-301
CDC’s Wake Up and Breathe Collaborative

- 20 ICUs: 12 full collaborative
- 5,164 consecutive MV days
- Opt-out SATs and SBTs
- 3x-4x increase in completion
- 35% less VAE risk/MV episode
- 65% less IVAC risk/MV episode
- 8 “surveillance only” ICUs had no improvements

Klompas M, AJRCCM 2015;191:292-301
Wake Up and Breathe in Indiana

• N=702 MICU/SICU patients
• Implemented paired SATs/SBTs
• Avg RASS was 1 level more arousable (p<0.0001)
• Prevalence of delirium down 11% (66.7% to 55.3%, p=0.06)
• Combined delirium/coma down by 6% (p=0.01)
Keystone’s ABCDE Bundle Collaborative

- 51 hospitals in Michigan’s Keystone ICU initiative
- Those implementing SATs + delirium screening were **3.5x more likely** to exercise ventilated pts
- Incomplete or non-sequential bundle implementation yielded lower success rates
- Authors wrote: “another layer of evidence that for the ABCDEs, the whole is greater than sum of the parts”

Miller, Hyzy, Iwashyna, Ann ATS, epub May 2015
SAT + SBT = 4 day shorter ICU/hosp LOS

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 trial

ABC Trial: One-Year Survival

NNT=7

Sedation Interruption in SLEAP

Mehta S, JAMA 2012;308:1985-92
## Benzodiazepine Use in Trials *

<table>
<thead>
<tr>
<th>Study</th>
<th>Control</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kress NEJM 2000</td>
<td>90 mg/day</td>
<td>53 mg/day</td>
</tr>
<tr>
<td>Girard ABC Lancet 2007</td>
<td>84 mg/day</td>
<td>54 mg/day</td>
</tr>
<tr>
<td>Mehta SLEAP JAMA 2012</td>
<td>82 mg/day</td>
<td>102 mg/day</td>
</tr>
<tr>
<td>OSCILLATE NEJM 2013</td>
<td>141 mg/day</td>
<td>199 mg/day</td>
</tr>
</tbody>
</table>

* All values converted and expressed as **mean** midazolam dose per patient, **median** for ABC study were 8 mg and 5 mg, respectively
From Canadian Authors of SLEAP…
n=712 and 3,620 patient-days

“We found that nearly all patients were managed with continuous-infusion opioids and sedatives. We also found that actual practice was different from what we expected because the available clinical tools – such as protocols and assessment scales – were not necessarily applied at the bedside.”

Burry LD, Can J Anesth May 2014 epub
Data collected 2008-2009
SPICE Study – first 48 hours
mean 50 mg/d benzos

Shehabi AJRCCM 2012;186:724-31
No Sedation: ICU Length of Stay

ICU stay reduced by 9.7 days

2013 PAD Guidelines:

“We suggest that sedation strategies using non-benzodiazepines (propofol or dexmedetomidine) may be preferred over sedation with benzodiazepines (midazolam or lorazepam)”

Grade 2B Recommendation

Crit Care Med. 2013;41:263-308
Buffalos to Beer to Brain Cells
Cliff the mailman and philosopher

Cliff: “Well you see, Norm, it's like this . . A herd of buffalo can only move as fast as the slowest buffalo. And when the herd is hunted, it is the slowest and weakest ones at the back that are killed first. This natural selection is good for the herd as a whole, because the general speed and health of the whole group keeps improving by the regular killing of the weakest members.”
Buffalos to Beer to Brain Cells

“In much the same way, Norm, the human brain can only operate as fast as the slowest brain cells. Now, as we know, excessive intake of alcohol kills brain cells. But naturally, it attacks the slowest and weakest brain cells first. In this way, regular consumption of beer eliminates the weaker cells, making the brain a faster and more efficient machine. And that, Norm, is why you always feel smarter after a few beers.”

sitcom **CHEERS**
Daily Risk of Delirium in MENDS

Daily Risk of Delirium in SEDCOM

Riker, et al. JAMA 2009;301:489-499
Pain, Agitation, and Delirium Are Interrelated

Cardinal Symptoms of Delirium and Coma

AROUSABLE TO VOICE
- Acute mental status change
- Fluctuating mental status
- Inattention
- Disorganized thinking
- Hallucinations, Delusions, Illusions
- Altered level of consciousness

UNAROUSABLE TO VOICE
- COMA

Delirium in Mechanically Ventilated Patients

Validity and Reliability of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)
Ely EW, JAMA 2003;289:2983-91

Monitoring Sedation Status Over Time in ICU Patients
Reliability and Validity of the Richmond Agitation-Sedation Scale (RASS)
The Iconic Picture of Early Mobility

- Point prevalence study in Germany showed <10% walking
- “Yes ‘n How many deaths will it take, Till he knows that too many people have died?” Dylan, Times They Are A-Changin’

Needham DM, JAMA 2008;300:1685-90
Nydahl P et al, CCM 2014;42:1178-1186
Clemmer T, CCM 2014;42:1308-09
Mobilization = Less Delirium

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention (n=49)</th>
<th>Control (n=55)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU/Hosp Delirium Days</td>
<td>2 days</td>
<td>4 days</td>
<td>0.03</td>
</tr>
<tr>
<td>Time in ICU with Delirium</td>
<td>33%</td>
<td>57%</td>
<td>0.02</td>
</tr>
<tr>
<td>Time in Hosp. with Delirium</td>
<td>28%</td>
<td>41%</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Schweickert et al, Lancet 2009;373:1874-82
Minimum Criteria for Consulting PT/OT and Initiating Early Exercise

M – Myocardial Stability
• No evidence of active myocardial ischemia
• Stable heart rate and cardiac rhythm

O – Oxygenation adequate on
• $FIO_2 \leq 0.6$
• PEEP $\leq 10$ cm H$_2$O.

V – Vasopressor(s) Minimal
• No increase dose of any vasopressor infusion for at least 2 hours*

E – Engages to Voice
• Patient response to verbal stimulation (RASS $\geq -3$)
Mobilizing the Brain with Sudoku & Scrabble
Excellence

Aristotle: “We are what we repeatedly do. Excellence is not an act, but a habit”

Jiro Dreams of Sushi - Tokyo
# ICU Delirium & Cognitive Impairment Study Group: local members

<table>
<thead>
<tr>
<th>Pratik Pandharipande</th>
<th>Carla Sevin</th>
<th>Brett Norman</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jim Jackson</td>
<td>Leanne Boehm</td>
<td>Jack Schnelle</td>
</tr>
<tr>
<td>Jin Han</td>
<td>Christin Rowan</td>
<td>Sandra Simmons</td>
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<tr>
<td>Ed Vasilevskis</td>
<td>Cayce Strength</td>
<td>Stephan Heckers</td>
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<tr>
<td>Chris Hughes</td>
<td>Brenda Pun</td>
<td>Cathy Fuchs</td>
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<td>Tim Girard</td>
<td>Aimee Hoskins</td>
<td>Heidi Smith</td>
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<tr>
<td>Wes Ely</td>
<td>Amy Kiehl</td>
<td>Jennifer Thompson</td>
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<tr>
<td>Lorraine Ware</td>
<td>Rob Gould</td>
<td>Rameela Chandrasekhar</td>
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<td>Gordon Bernard</td>
<td>Carrie Jones</td>
<td>Angie Williams</td>
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<td>Bob Dittus</td>
<td>Erin Holm</td>
<td>Nate Brummel</td>
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<tr>
<td>Ted Speroff</td>
<td>Mayur Patel</td>
<td>Maddie Morrell</td>
</tr>
<tr>
<td>Mike Stein</td>
<td>Mariu Carlo</td>
<td>Kwame Frimpong</td>
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<tr>
<td>Sunil Geevarghese</td>
<td>Jo Ellen Wilson</td>
<td>Joanna Stollings</td>
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<td>Melinda Buntin</td>
<td>John Graves</td>
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<td></td>
<td>Bill Pojedinec</td>
<td>Brennan McNeil</td>
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