

IPRC Webinar

Pediatric Delirium: Impact and Opportunities

Chani Traube, MD, FAAP, FCCM
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About Our Presenter

Chani Traube, MD, FAAP, FCCM

- Weill Cornell Medicine
- Professor of Pediatrics in the Division of Pediatric Critical Care
- Director of Clinical Research Mentoring for the Department of Pediatrics
- Chair of the National Institute of Child Health and Human Development (NICHD) Collaborative Pediatric Critical Care Research Network (CPCCRN)
- No financial disclosures

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Objectives

- 1 Establish the prevalence of delirium in seriously ill children, and its associated morbidity
- 2 Define modifiable risk factors for pediatric delirium
- 3 What about children with acquired brain injury?

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What is delirium?

Global Cerebral Dysfunction

Caused by the direct physiologic consequences of a general medical condition

- Acute onset
- Fluctuating course
- Disturbance of awareness
- Disturbance of cognition
- Reversible

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Subtypes

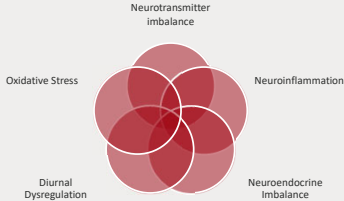
- Hyperactive**
 - Agitation, restlessness, emotional lability
- Hypoactive**
 - Apathy, decreased responsiveness
- Mixed**

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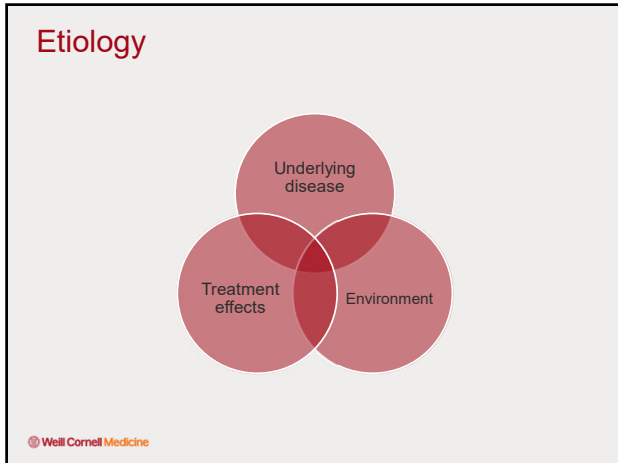
What causes delirium?

- Interruption of brain network connections
- Final common pathway: alteration in neurotransmission →
- Cognitive and behavioral changes



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Why do we care?

- Epidemic in critically ill adults
- Independent predictor of negative clinical outcomes:
 - Mortality (2-fold increase in 6-month mortality)
 - Length of stay
 - Medical costs (4-16 billion US healthcare dollars/yr)
 - Long term cognitive impairment
 - Post Intensive Care Syndrome
- 2010... pediatric literature sparse

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Evaluating our patients

It's complicated....

- Development of validated pediatric tools allows for widespread screening

An illustration of a person standing with their arms raised, surrounded by a chaotic web of blue and green lines and question marks, symbolizing the complexity of patient evaluation.

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Pediatric Confusion Assessment Method for the ICU

A flowchart detailing the pCAM-ICU assessment process. It starts with a decision point: '1 Acute Change or Fluctuating Course of Mental Status'. If 'NO', it leads to 'STOP DELIRIUM ABSENT'. If 'YES', it proceeds to '2 Inattention'. If '2' has '0-2 Errors', it leads to 'STOP DELIRIUM ABSENT'. If '> 2 Errors', it leads to '3 Altered Level of Consciousness'. If '3' is 'NO', it leads to 'DELIRIUM PRESENT'. If '3' is 'YES', it proceeds to '4 Disorganized Thinking'. If '4' has '> 1 Error', it leads to 'DELIRIUM PRESENT'. If '4' has '0-1 Error', it leads to 'DELIRIUM ABSENT'.

Well Cornell Medicine Smith, et al. CCM 2011

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Cornell Assessment of Pediatric Delirium (CAPD)

Traube, et al. CCM 2014

Cornell Assessment of Pediatric Delirium (CAP-D)		*SAMPLE*				
RASS Score ____ (if -4 or -5 do not proceed)						
Please answer the following questions based on your interactions with the patient over the course of your shift:						
	Never	Rarely	Sometimes	Often	Always	Score
1. Does the child make eye contact with the caregiver?	4	3	2	1	0	2
2. Are the child's actions purposeful?				X		1
3. Is the child aware of his/her surroundings?			X			2
4. Does the child communicate needs and wants?			X			2
	Never	Rarely	Sometimes	Often	Always	Score
5. Is the child restless?				X		3
6. Is the child inconsolable?	X					0
7. Is the child underactive—very little movement while awake?	X					0
8. Does it take the child a long time to respond to interactions?		X				1
TOTAL						11

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Evaluating our patients

GUIDELINES

Clinical recommendations for pain, sedation, withdrawal and delirium assessment in critically ill infants and children: an ESPNIC position statement for healthcare professionals

Julia Harris¹, Anne-Sylvie Rametel², Monique van Dijk^{3,4}, Pavla Pitkorná^{5,6}, Jake Wollegaard⁷, Lysonne Turner⁸, Dick Tibboel⁹ and Owen Ho¹⁰

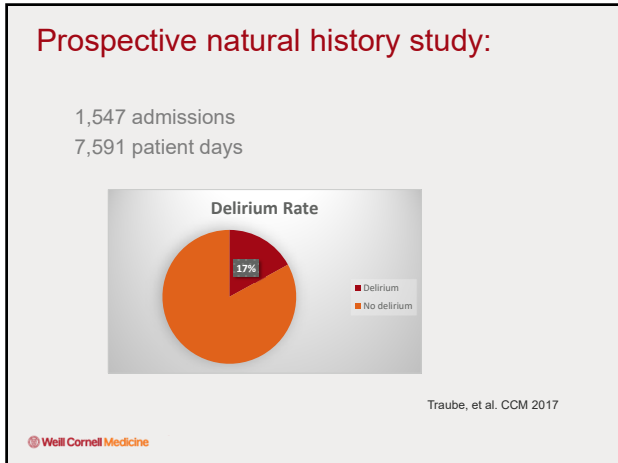
- Unit-wide screening for delirium is feasible, with quick and reliable bedside tools
- Delirium status should be assessed each shift.

Recommendation

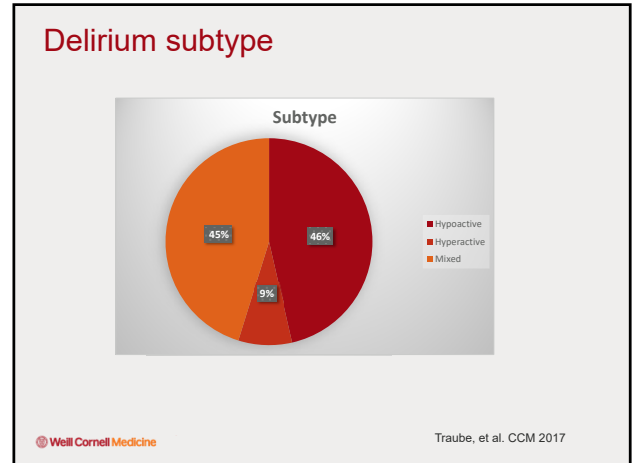
- Use CAP-D as an instrument to assess paediatric delirium (grade of recommendation = A).
- Together with the vital signs, delirium must be assessed and documented every 8-12 h (at least once per shift), 24-48 h after admission or as indicated by the delirium score of clinical condition of the child (grade of recommendation = D).

Well Cornell Medicine Harris et al. ICM. 2016

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Multivariable regression predicting delirium:

CHARACTERISTIC	ODDS_RATIO (95% CI)	p value
Age at Admission (years)	0-2 (reference)	
	>2-5	0.606 (0.389-0.936) 0.026
	>5-13	0.412 (0.260-0.646) <0.001
	>13	0.399 (0.244-0.641) <0.001
Probability of Mortality	<=0.8% (reference)	
	>0.8% & <=1.4%	1.274 (0.824-1.978) 0.277
	>1.4%	1.531 (1.016-2.318) 0.043
Developmental Delay		3.314 (2.328-4.724) <0.001
Mechanically Ventilated		1.634 (1.155-2.314) 0.006

Traube, et al. CCM 2017

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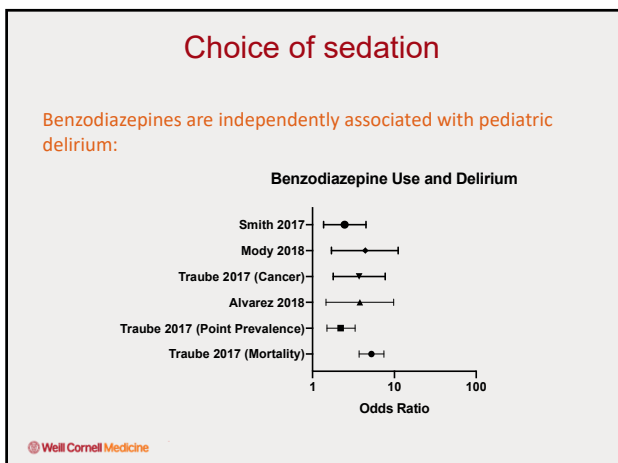
Benzodiazepines conferred 5x risk for delirium

Table 2. Multivariable Logistic Regression Analysis Predicting Ever Delirious (N=1547)

	ODDS_RATIO (95% CI)	p Value
Age at Admission (yr)	0-2 (ref)	
	>2-5	0.606 (0.389-0.936) 0.026
	>5-13	0.412 (0.260-0.646) <0.001
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	>1.4%	1.531 (1.016-2.318) 0.043
Developmental Delay		3.314 (2.328-4.724) <0.001
Ever Benzodiazepines	5.240 (3.710-7.455) <0.001	
Ever Coma	4.244 (2.684-6.783) <0.001	
Ever Anti-Cholinergics	2.169 (1.412-3.416) <0.001	
Ever Mechanically Ventilated	1.634 (1.155-2.314) 0.006	

Traube, et al. CCM 2017

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Choice of sedation

Causal inference: Benzodiazepines and Pediatric Delirium

Modi et al. Weill Cornell

- 580 subjects
- 2291 PICU days
- Transition to delirium
- Dose-response effect
- Time-dependent confounding

Mody K, et al. CCM. 2018.

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Benzodiazepines and Delirium

Temporal transition to delirium

N=1540 days

Benzodiazepines were highly and independently associated with transition from normal mental status to delirium, more than quadrupling delirium rates.

OR for delirium development after exposure to benzodiazepines is 8.7. On right, after controlling for mechanical ventilation and opiate exposure, OR is 4.4.

Mody K, et al. CCM. 2018.

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Benzodiazepines and Delirium

Dose-Dependent Transition to Delirium

n=1540 days

For every 1-log increase in benzo dose on a day with normal cognitive status, there was a 43% increase in risk for transition to delirium (OR 1.43, CI 1.3-1.6).

Mody K, et al. CCM. 2018.

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Benzodiazepines and Delirium

Marginal Structural Modeling: Pseudo-Randomization

n=2291 days

Benzos independently increase subsequent delirium risk by 333%

Confounding pathways used in weight modeling included cognitive status (delirium, coma, or normal), benzodiazepine exposure, opiate exposure, and mechanical ventilation.

Mody K, et al. CCM. 2018.

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Multi-institutional point prevalence

25 sites and 994 subjects

Pittsburgh	Nationwide Children's Hospital
Cornell	Connecticut Children's Hospital
Boston Children's	University of Washington, Seattle
Mass General	Northwestern University/Lurie/Chicago
Johns Hopkins	Al Hada Armed Forces Hospital, Saudi Arabia
CHOP	Children's Omaha
Washington University of St. Louis	University of Michigan
Duke University	Emory University
Cook Children's Hospital	Brisbane, Australia
Virginia Commonwealth	University of Wisconsin, Madison
Erasmus MC - Rotterdam	University of North Carolina
Children's Healthcare of Atlanta	
Phoenix Children's Hospital	

Traube, et al. CCM 2017

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Multi-institutional point prevalence

Delirium Prevalence

■ Delirium ■ Coma ■ Delirium-Free

Traube, et al. CCM 2017

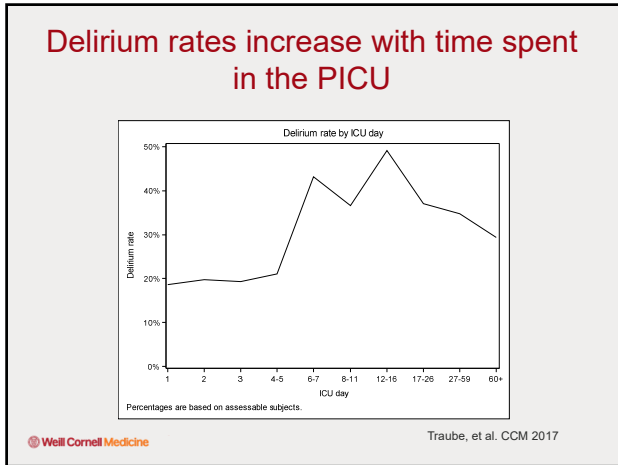
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Multi-institutional point prevalence

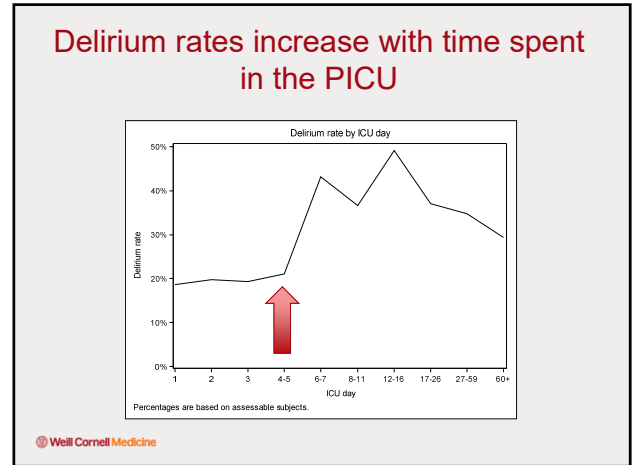
Variable	Adjusted odds ratios	
	(95% CI)	
Age > 2 years	0.7 (0.5, 1.0)	
Physical restraints	4.0 (2.0, 7.7)	
Mechanical ventilation	1.7 (1.1, 2.7)	
Narcotics	2.3 (1.5, 3.5)	
Benzodiazepines	2.2 (1.5, 3.3)	
Antiepileptics	2.9 (1.8, 4.8)	
General anesthesia	0.4 (0.3, 0.8)	
Vasopressors	2.4 (1.5, 3.8)	

Traube, et al. CCM 2017

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- ### Delirium in Other Pediatric Populations
- Cardiac (~50%)
 - Cancer (~17%)
 - Stem Cell Transplant (~35%)
 - NICU (~22%)
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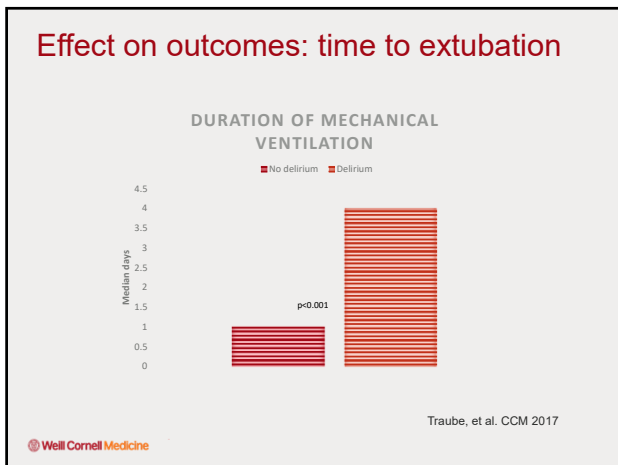
Effect on outcomes: length of stay

Multivariable Linear Regression Analysis Predicting PICU length of stay (N=1547)

Characteristic	Relative Days (95% CI)	p Value
Probability of Mortality		
<=0.8%	reference	
>0.8% & <=1.4%	1.022 (0.946-1.103)	0.585
>1.4%	1.313 (1.214-1.419)	<0.001
Ever Mechanically Ventilated	1.224 (1.146-1.308)	<0.001
Ever Delirious	2.309 (2.116-2.518)	<0.001

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Effect on outcomes: duration of delirium

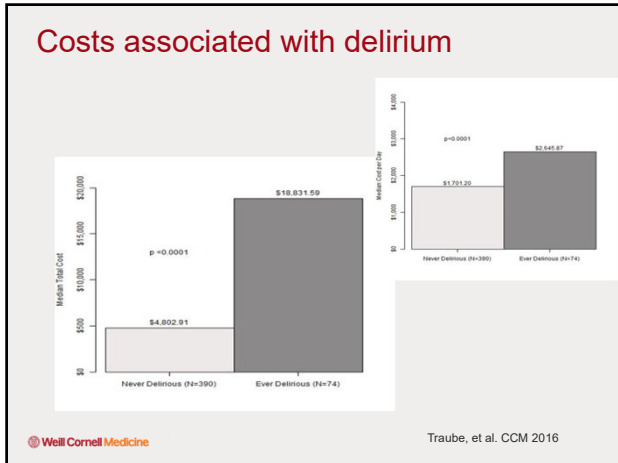
TABLE 3. Severity of Illness and Outcome Measures of Patients Without Delirium, With Mild Delirium (< 24 Hr), and With Severe Delirium (> 24 hr)

Outcome Parameter	No Delirium (Group 0)	Mild Delirium (Group 1)	Severe Delirium (Group 2)	p
n (%)	32 (34.4)	30 (32.8)	31 (33.3)	
Pediatric Index of Mortality 2	1.21 ± 1.06	1.27 ± 0.84	1.41 ± 0.68	Not significant
Mechanical ventilation on the PICU (hr)	9.0 ± 18.7	29.7 ± 39.8	69.0 ± 74.5	<0.001
Time to first analysis* (d)	1.0 ± 1.0	2.0 ± 1.9	3.7 ± 3.2	<0.001
Length of stay* (d)	10.6 ± 7.3	13.5 ± 7.1	21.8 ± 19.7	0.043
Level of care (NRPULS)	3.0 ± 0.3	2.9 ± 0.3	3.3 ± 0.4	<0.001

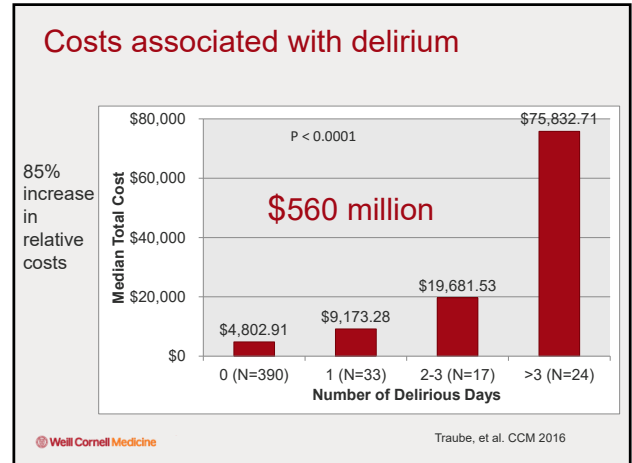
*Delirium on average commenced when Richmond Agitation and Sedation Score > -3.
 *Confidence for Pediatric Index of Mortality 2, duration of mechanical ventilation, and time to first assessment.
 Values are expressed as mean ± SD.

Well Cornell Medicine Meyburg, et al. CCM 2017

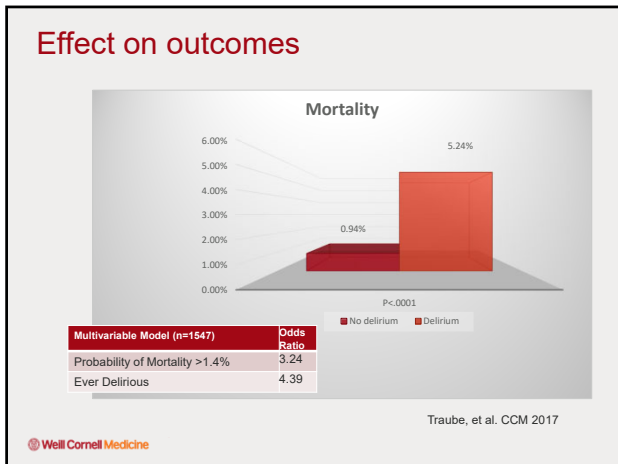
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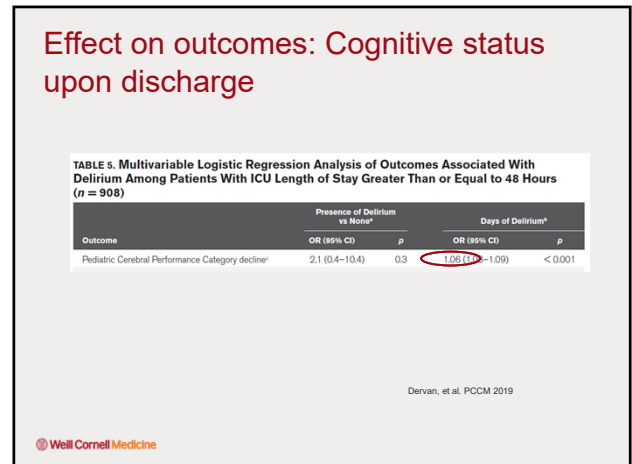
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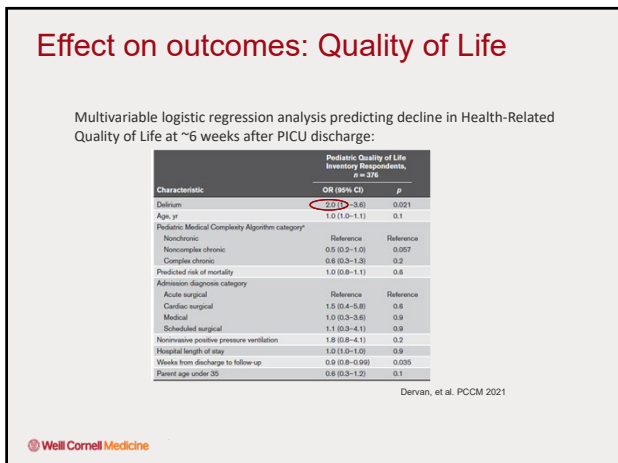
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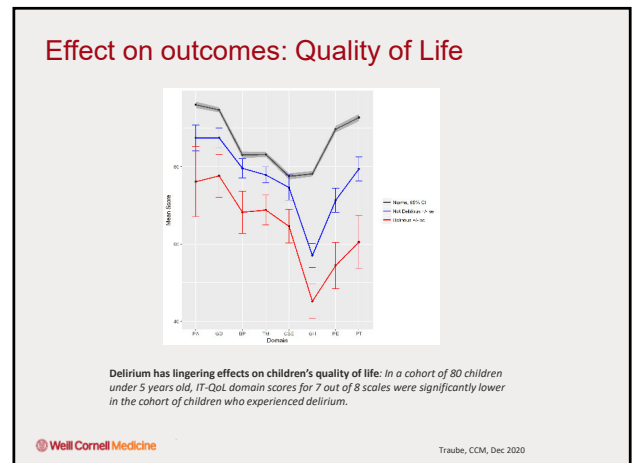
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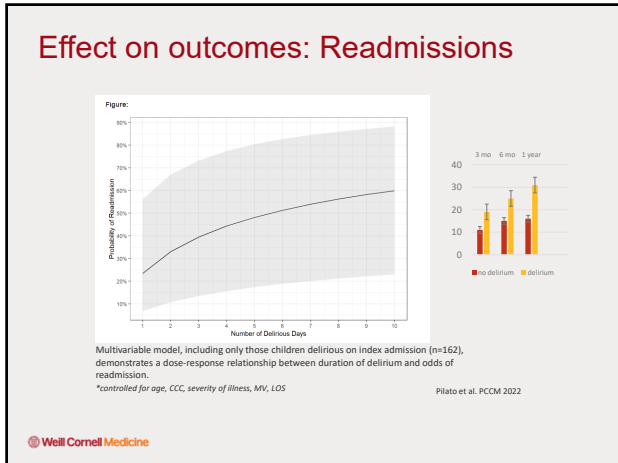
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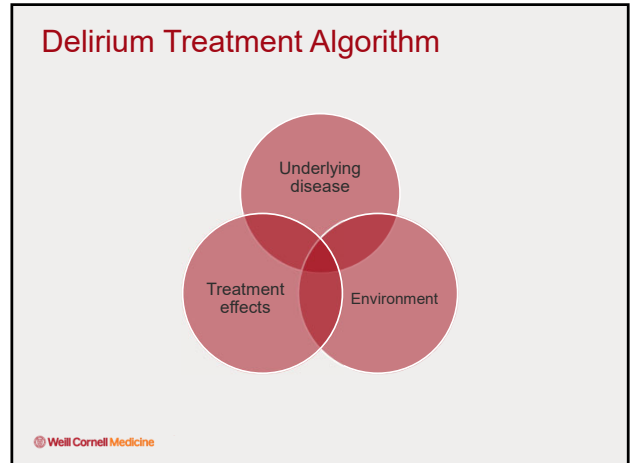
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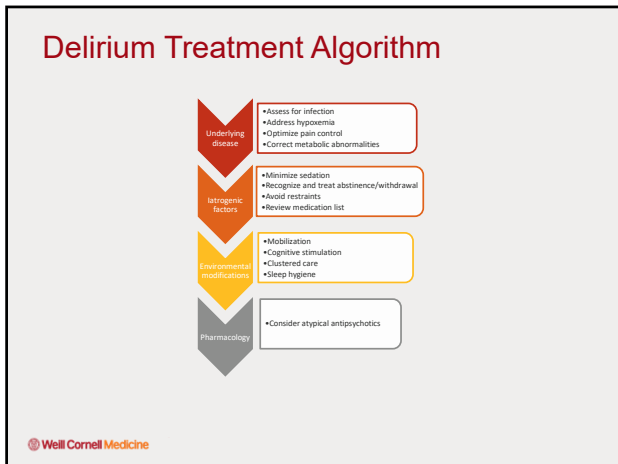
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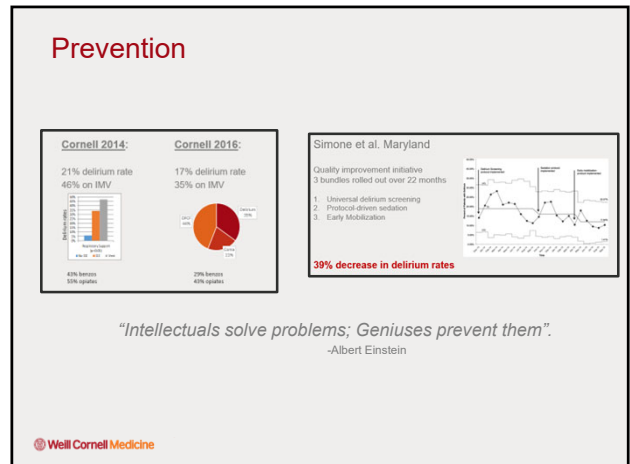
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Recognizing delirium has measurable effects

- Delirium is a common and under-recognized problem in seriously ill children.
- Detecting and treating pediatric delirium may improve short- and long-term outcomes.

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What about delirium after an acute brain injury?

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Rehab and Delirium: Critical Questions

- Delirium is likely a frequent complication after acquired brain injury
- Delirium can be difficult to assess after acquired brain injury
- How does delirium overlap with Post Traumatic Confusional State?
- Can we differentiate between static encephalopathy (new post-injury baseline) and superimposed delirium?
- Does it matter?

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Rehab and Delirium: Study Objectives

- Determine feasibility of delirium screening
- Describe prevalence of positive screens
- Explore longitudinal trends in CAPD scores, to discriminate between static encephalopathy and gradual improvement
- Explore prognostic significance of delirium in ABI

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Rehab and Delirium: Study Design

- Prospective cohort study
- Pediatric inpatient rehabilitation unit
- Consecutive ABI admissions
- Intervention: all children screened for delirium twice daily throughout their rehab stay

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Rehab and Delirium: Feasibility

- CAPD implemented in EMR in 2019
- **Compliance since has been 97.6%!!!**

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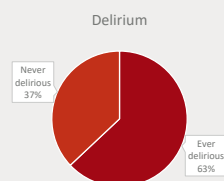
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Rehab and Delirium: Results

N=150 subjects; 15,314 delirium screens

Median age 11.8 years (~7-15)

29% of screens were positive



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Rehab and Delirium: Longitudinal Trends

Two raters independently identified three primary patterns:

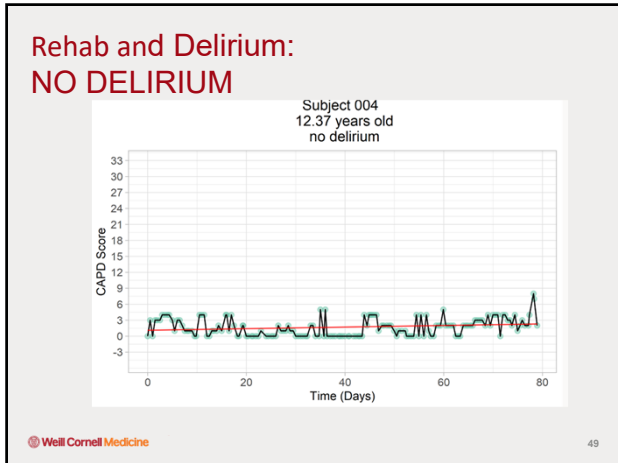
- No delirium (51%)
- Delirium improving over time (36%)
- Static encephalopathy (13%)

(In 10 kids, episodic delirium noted but no clear trend detected)

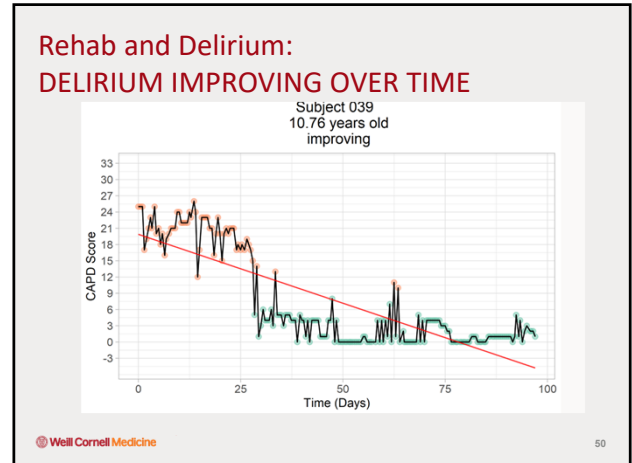
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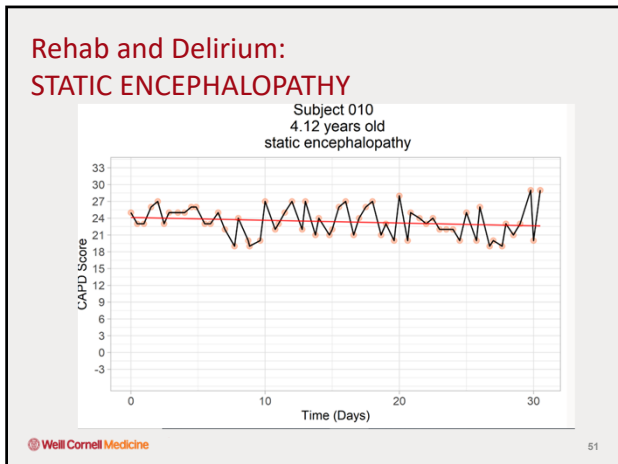
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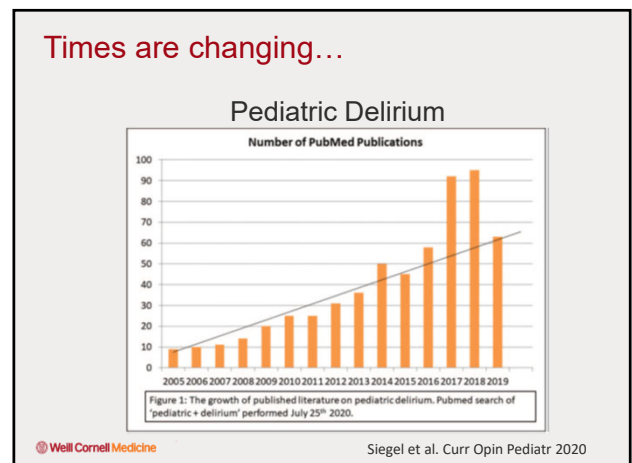
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- ### Rehab and Delirium: Conclusions
- Delirium occurs frequently in children with ABI during inpatient rehabilitation
 - Routine delirium screening facilitates early detection and intervention that may maximize functional outcomes
 - Longitudinal screening allows for differentiation of children with varying patterns of recovery.
 - » Future research can use group-based trajectory modeling to identify distinct patterns that may predict outcomes.
 - » Delirium on admission may predict cognitive status upon discharge.
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- ### Rehab and Delirium: NEXT STEPS
- Multi-institutional point prevalence PILOT study
 - » Feasibility
 - » Prevalence
 - Large scale longitudinal study of delirium in children with ABI in acute rehab setting
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