

Pediatric Emergency Care Applied Research Network (PECARN) – *Developing Evidence & Its Implementation*

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for PECARN



Conflict of Interest

- None
- Federal funding (next page)

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Objectives

- Quick overview of PECARN – who, what, where, ...
- Review some of the output & impact on pediatric care
- Involve the participants in next steps...

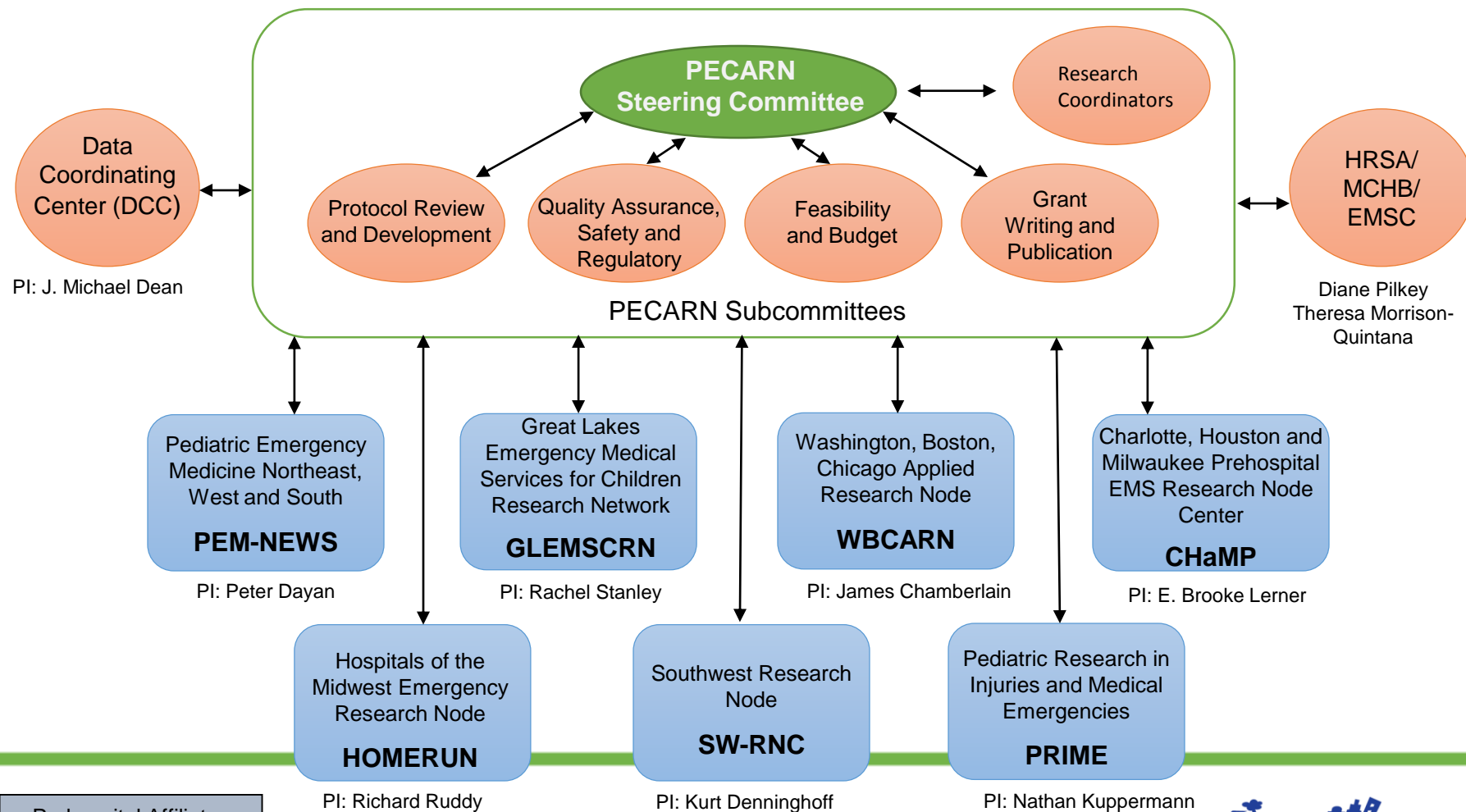
What about PEM Research Networks?

- Pediatric conditions that are high risk are rare
- 90% of children seen in non-children's hospitals for emergency visits
- Ratio of clinicians to scientists in PEM is 'high' – we love to practice
- PEM – we don't have an organ system or pediatric specific institute – low % of funding dollars for children

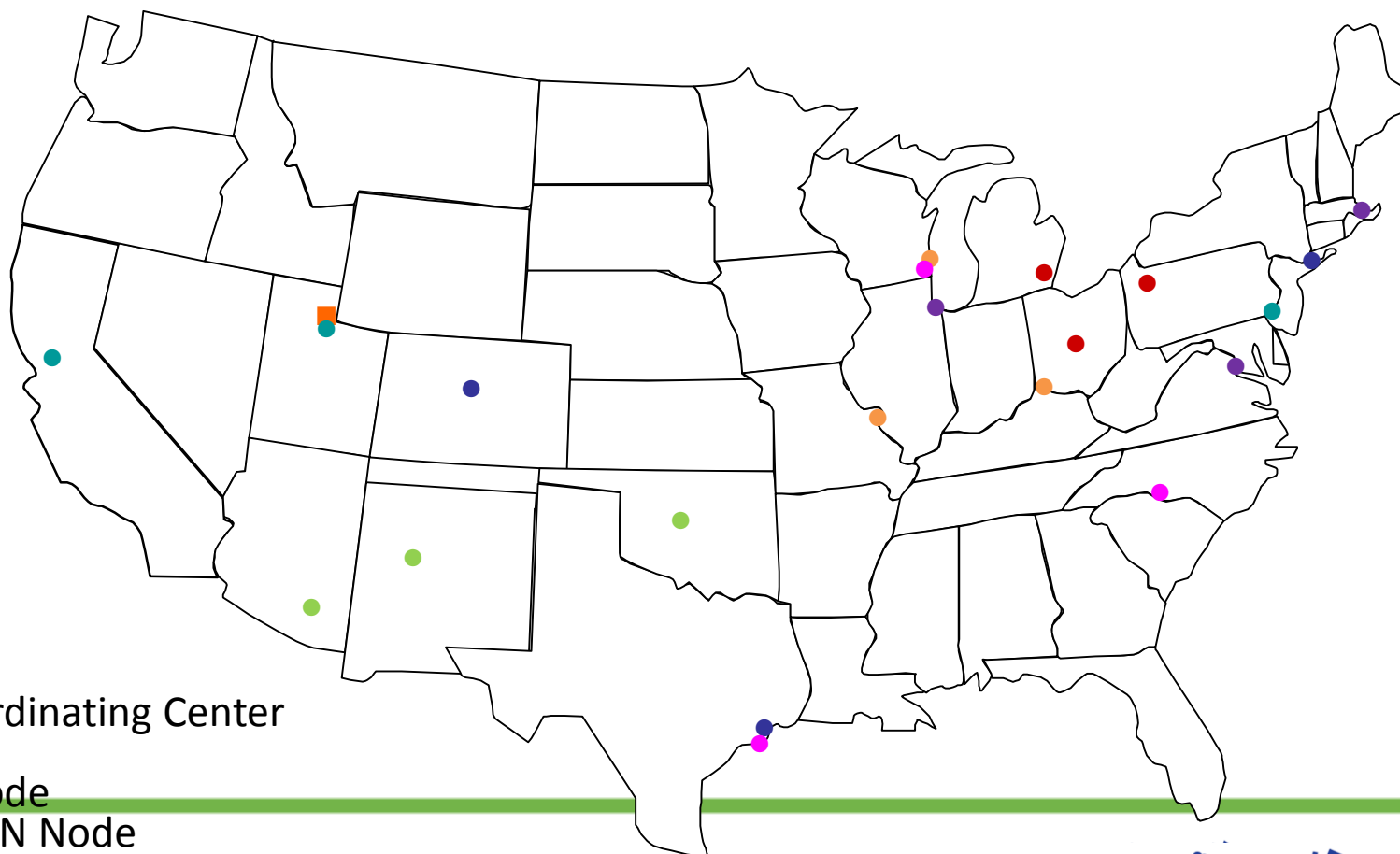
PECARN Goals

- **Develop new evidence**
- **Implement best practice across the continuum of EMSC**
- Develop next generation of EMSC researchers
- Develop & initiate prehospital funded research
- Meet performance goals – enrollment & quality

PECARN – Network Structure



The Pediatric Emergency Care Applied Research Network (PECARN) – since 2015 – Seven nodes & DCC



- = Data Coordinating Center
- = SW Node
- = PRIME Node
- = GLEMSCRN Node
- = PEM-NEWS Node
- = WBCARN Node
- = HOMERUN Node

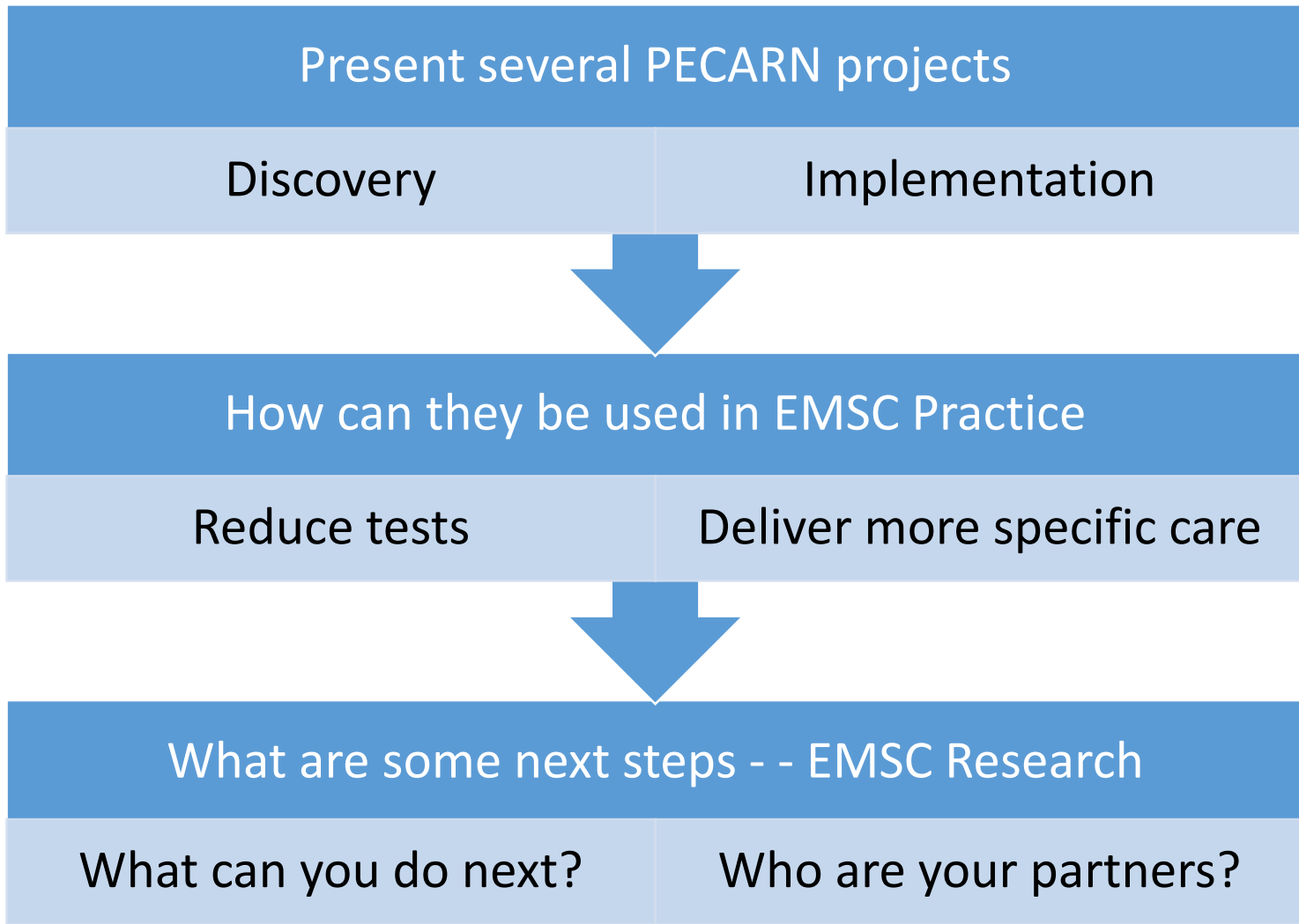
● = CHaMP Node (EMS)

Research Studies and Content Working Groups

- Registry / Core Data set
- EMSA - Prehospital Study & Working Group
- Respiratory / Asthma
- Evaluation of Trauma
- Evidence Development
- Knowledge Translation
- STI Interventions / Prevention
- Study Specific
 - Mental health screening,
 - ETOH Screening,
 - Probiotics
 - DKA
 - Febrile infants / RNA Biosignatures
 - TXA for pediatric trauma
 - Sepsis screening
 - Safety / Diagnostic errors
- Mentoring - Future investigators

Who can Submit a PECARN Proposal?

- Good ideas / concepts should be submitted through one of the 7 nodes – to a PI
- Projects can be done through nodal / non-PECARN process if small
- Formal PECARN proposals go through a ‘rigorous’ vetting from the Steering Committee - - to enhance the product



Outline for each project

Discovery / Evidence Development

- What is the aim(s) of our research project?
- What are our methods that will get us there?
- What is the result / outcome from the new discovery / evidence?


QI / Implementation Science

- What are we trying to do?
- What is our plan / change to get results?
- How we will know it helped?

Cervical Spine – Immobilization / Injury

Factors Associated With Cervical Spine Injury in Children After Blunt Trauma


Presented at the Pediatric Academic Societies annual meeting, May 2009, Baltimore, MD; and the Society of Academic Emergency Medicine annual meeting, May 2009, New Orleans, LA.

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* Participating centers and investigators are listed in the Appendix .



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 Article Info

Abstract Full Text Images References

Study objective

Cervical spine injuries in children are rare. However, immobilization and imaging for potential cervical spine injury after trauma are common and are associated with adverse effects. Risk factors for cervical spine injury have been developed to safely limit immobilization and radiography in adults, but not in children. The purpose of our study is to identify risk factors associated with cervical spine injury in children after blunt trauma.

Methods

We conducted a case-control study of children younger than 16 years, presenting after blunt trauma, and who received cervical spine radiographs at 17 hospitals in the Pediatric Emergency Care Applied Research Network (PECARN) between January 2000 and December 2004. Cases were children with cervical spine injury. We created 3 control groups of children free of cervical spine injury: (1) random controls, (2) age and mechanism of injury-matched controls, and (3) for cases receiving out-of-hospital emergency medical services (EMS), age-



Cervical Spine – Immobilization / Injury

What question this study addressed

The authors performed a case-control study and multiple logistic regression using Pediatric Emergency Care Applied Research Network (PECARN) data on children younger than 16 years to identify cervical spine injury predictors.

What this study adds to our knowledge

Using 540 cases and 1,060 controls, the authors developed an 8-risk-factor model that, when all were absent, had a sensitivity of 98% and a specificity of 26%.

8 predictors of C-Spine Injury

- Altered mental status
- Focal neurologic deficits
- Complaint of neck pain
- Torticollis
- Substantial torso injury
- Predisposing condition
- Diving mechanism
- High risk MVC

Cervical Spine – Immobilization / Injury

What next?

NIH R21 then R01 to develop and refine prediction rule for CSI in both pre-hospital and ED setting

- Immobilize less
- Image less

Decision Rules for Acute Neuroimaging after Head Trauma

Epidemiology of Pediatric Head Trauma

- Trauma the leading cause of death in children > 1 year
- Traumatic brain injury (TBI) the leading cause of death and disability due to trauma (> 70% of deaths)
- On an annual basis in the U.S., blunt head trauma in children results in:
 - 6,000 deaths
 - 60,000 hospitalizations
 - 620,000 ED visits (~50% evaluated with CT scans, use of CT increasing over the past decade, much variability in care)

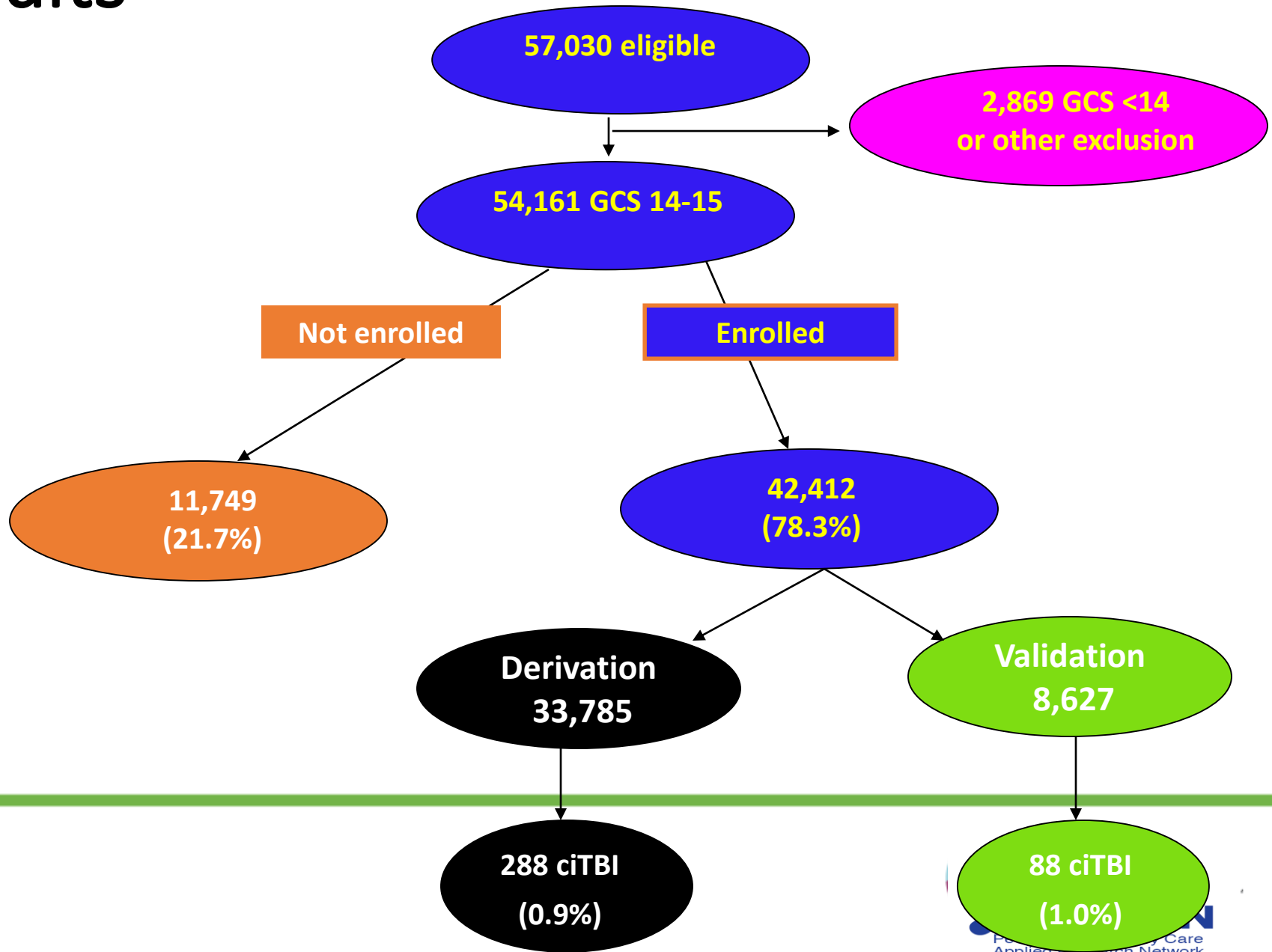
Identification of children at very low risk of clinically-important brain injuries after head trauma: a prospective cohort study

- Prospective observational study with > 40,000 children with GCS 14-15
- Derivation of low risk findings
- Validation of rule in subsequent population

The PECARN Head Injury Study

Goal: to derive a clinical decision rule to accurately identify children at near zero risk of clinically important traumatic brain injuries after blunt trauma with high accuracy and wide generalizability

Results



The PECARN TBI Rules (derived and validated)

Children are at very low risk of clinically-important traumatic brain injury (TBI) if they meet all criteria in age-specific rule:

<u>Children < 2 years</u>	<u>Children 2-18 years</u>
<ul style="list-style-type: none">1. Severe mechanism of injury2. History of LOC \geq 5 sec3. GCS = 14 or other signs of altered mental status4. Not acting normally per parent5. Palpable skull fracture6. Occipital/parietal/temporal scalp hematoma	<ul style="list-style-type: none">1. Severe mechanism of injury2. History of LOC3. GCS = 14 or other signs of altered mental status4. History of vomiting5. Severe headache in the ED6. Signs of basilar skull fracture

Recommendations for children younger than 2

A

GCS=14 or other signs of altered mental status†, or palpable skull fracture

Yes

CT recommended

13.9% of population
4.4% risk of ciTBI

No

Occipital or parietal or temporal scalp haematoma, or history of LOC ≥ 5 s, or severe mechanism of injury‡, or not acting normally per parent

Yes

Observation versus CT on the basis of other clinical factors including:

- Physician experience
- Multiple versus isolated§ findings
- Worsening symptoms or signs after emergency department observation
- Age < 3 months
- Parental preference

32.9% of population
0.9% risk of ciTBI

No

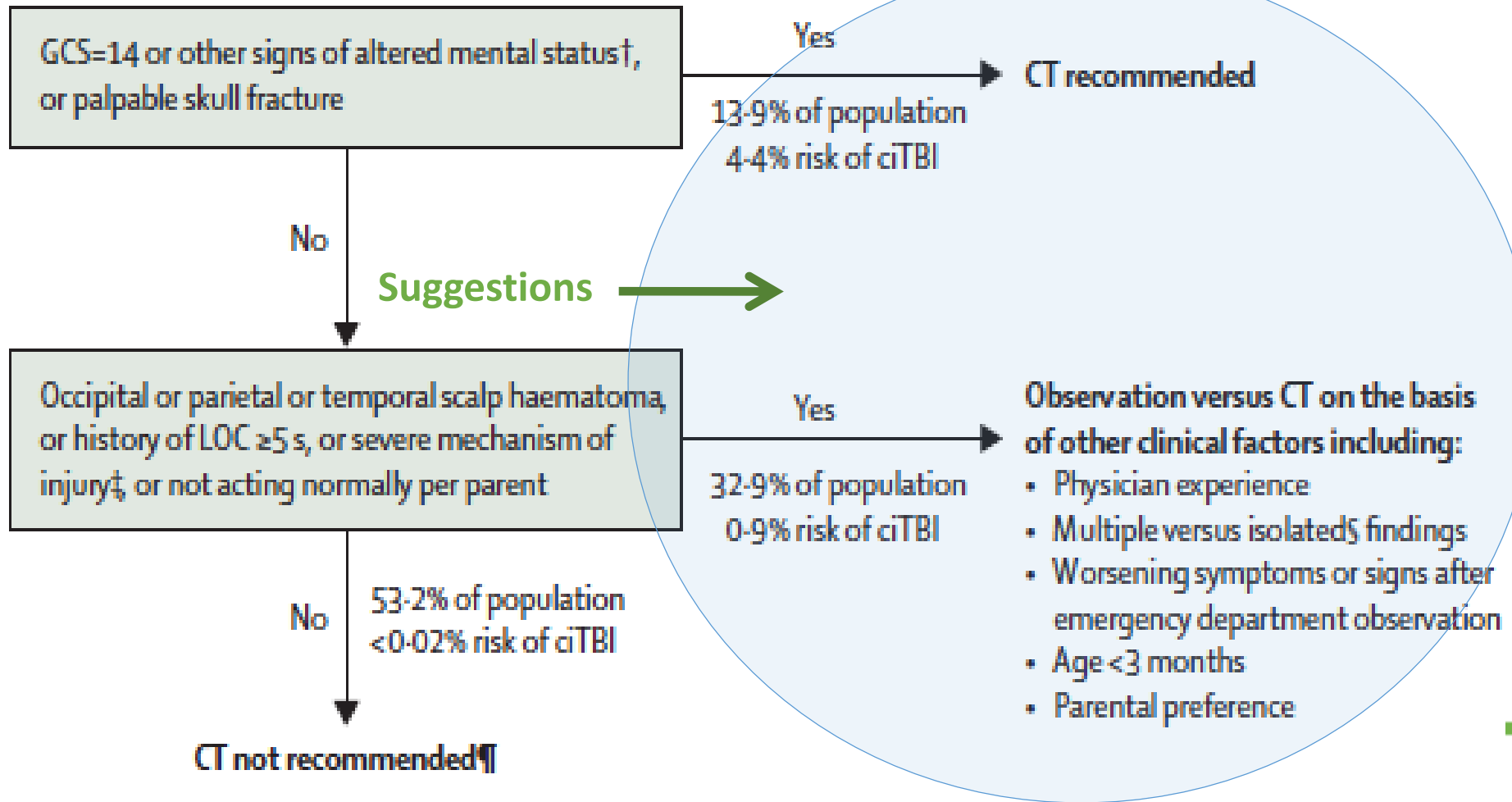
53.2% of population
< 0.02% risk of ciTBI

CT not recommended¶

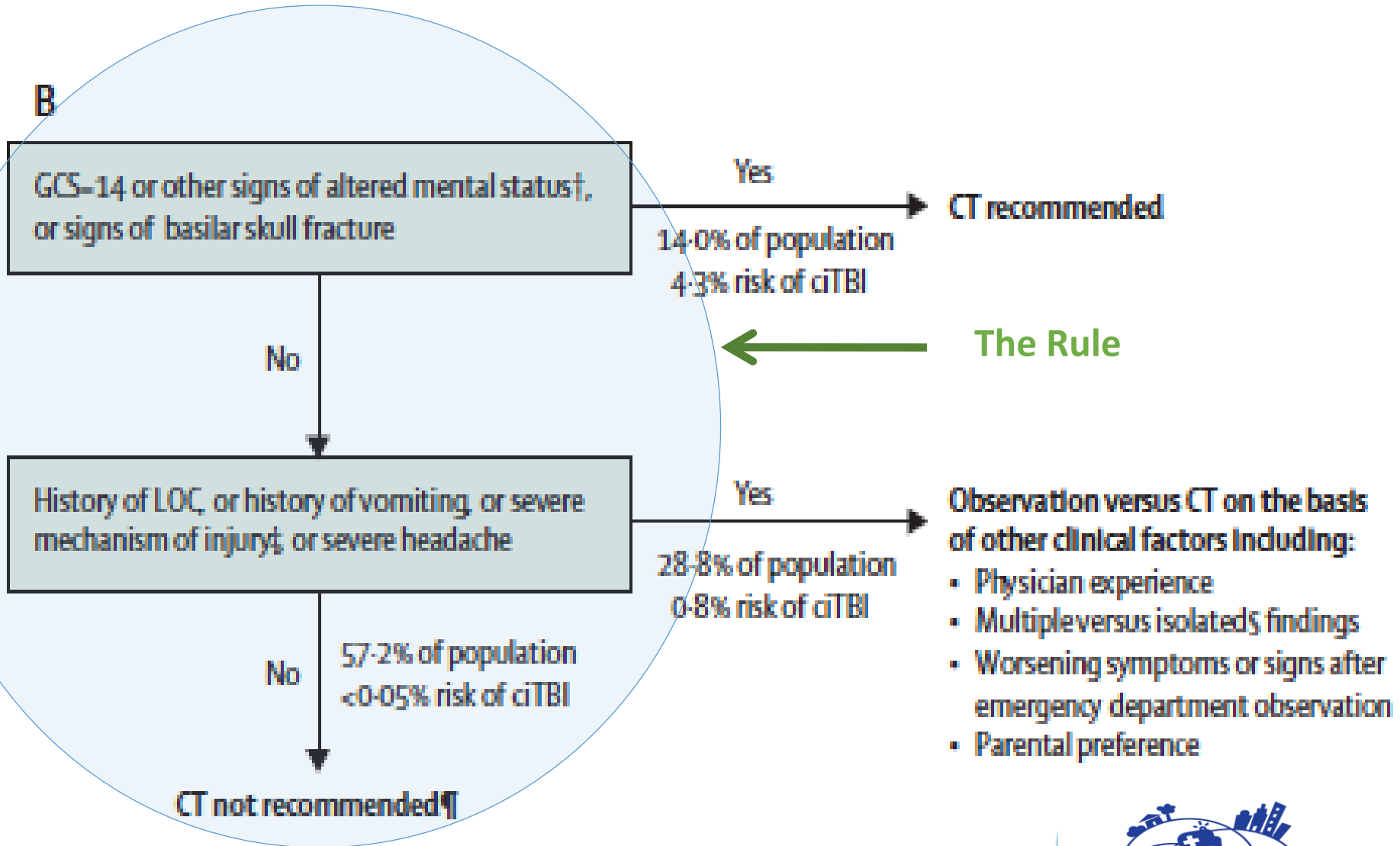
The Rule

Recommendations for children younger than 2

A

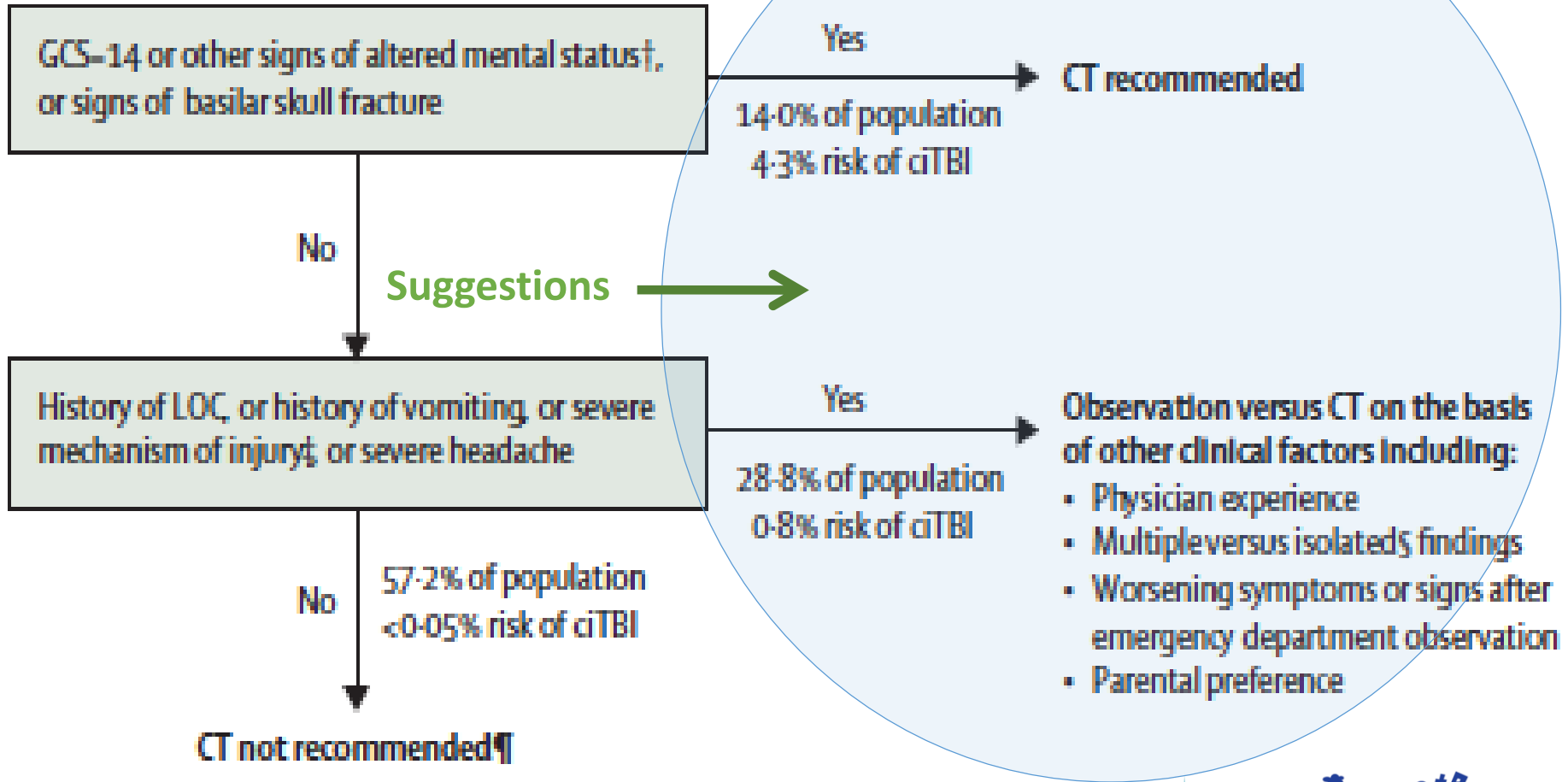


Recommendations for children 2 years and older



Recommendations for children 2 years and older

B





Identification of children at very low risk of clinically-important brain injuries after head trauma: a prospective cohort study

Nathan Kuppermann, James F Holmes, Peter S Dayan, John D Hoyle, Jr, Shireen M Atabaki, Richard Holubkov, Frances M Nadel, David Monroe, Rachel M Stanley, Dominic A Borgialli, Mohamed K Badawy, Jeff E Schunk, Kimberly S Quayle, Prashant Mahajan, Richard Lichenstein, Kathleen A Lillis, Michael G Tunik, Elizabeth S Jacobs, James M Callahan, Marc H Gorelick, Todd F Glass, Lois K Lee, Michael C Bachman, Arthur Cooper, Elizabeth C Powell, Michael J Gerardi, Craig A Melville, J Paul Muizelaar, David H Wisner, Sally Jo Zuspan, J Michael Dean, Sandra L Wootton-Gorges, for the Pediatric Emergency Care Applied Research Network (PECARN)*

Summary

Lancet 2009; 374: 1160–70

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See Comment page 1127

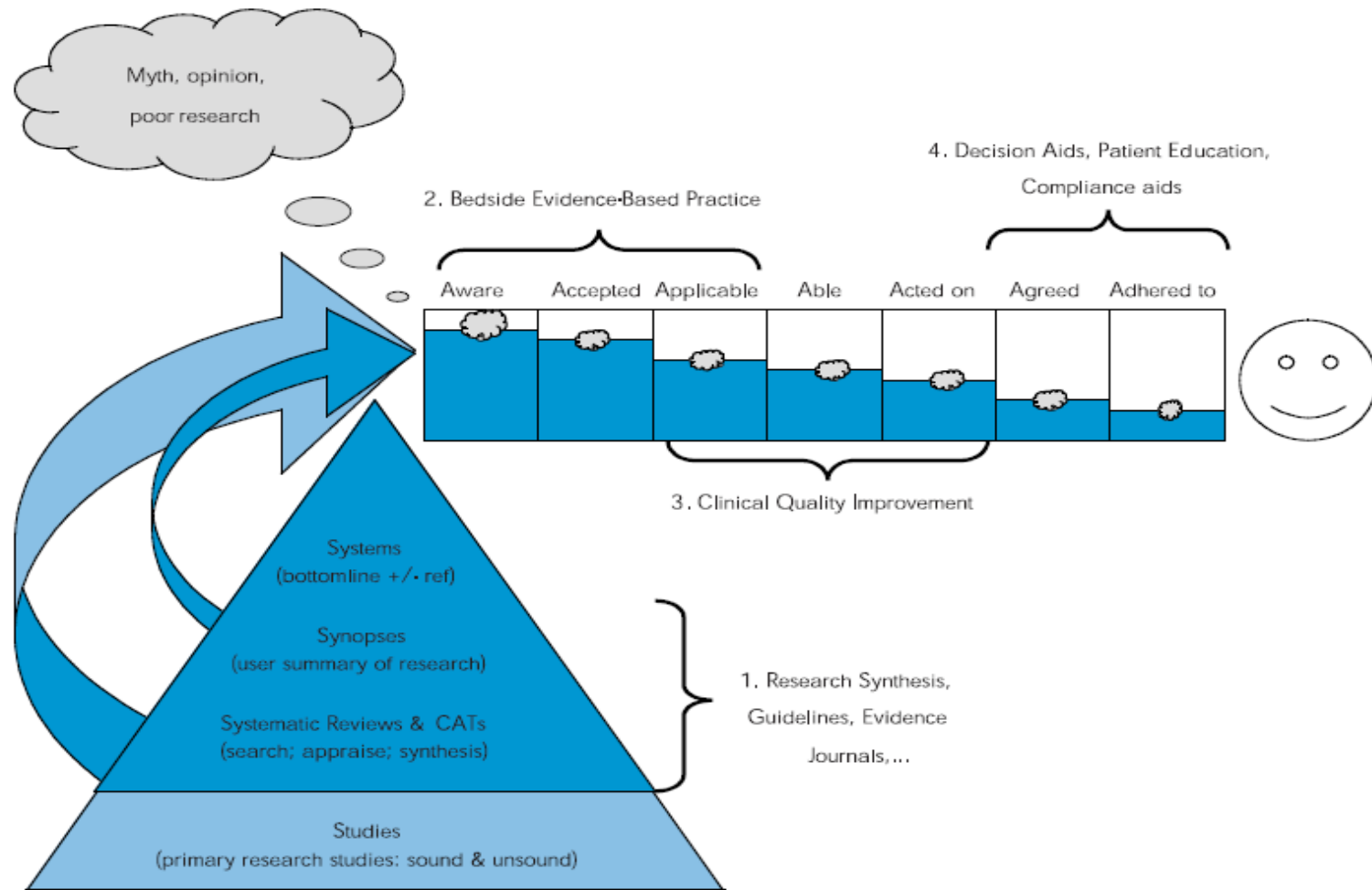
*Members listed at end of paper

Background CT imaging of head-injured children has risks of radiation-induced malignancy. Our aim was to identify children at very low risk of clinically-important traumatic brain injuries (ciTBI) for whom CT might be unnecessary.

Methods We enrolled patients younger than 18 years presenting within 24 h of head trauma with Glasgow Coma Scale scores of 14–15 in 25 North American emergency departments. We derived and validated age-specific prediction rules for ciTBI (death from traumatic brain injury, neurosurgery, intubation >24 h, or hospital admission \geq 2 nights).

How to get clinicians to use the prediction rules?

Knowledge Translation Pipeline



The research-to-practice pipeline. New research, of varying soundness, is added to the expanding pool and enters practice both directly or is reviewed, summarised, and systematised (delay) before entering practice, with leakage occurring at each of several stages between awareness and patient outcome. Different knowledge translation disciplines focus on different parts of the pipeline (1-4).

Glasziou and Haynes, 2005

Challenges to Knowledge Translation using Computerized Algorithms

The human brain

Shankar Vedantam (author of “*The Hidden Brain*” and NPR social science correspondent) and Berkeley Dietvorst (Wharton doctoral student)

- Even though algorithms typically outperform humans, we are distrustful of algorithms
- People fail to use algorithms even when they see it outperform humans
- Humans fear machines (“algorithmic aversion”)

Translating Research into Practice

What PECARN is doing...

Use of Traumatic Brain Injury Prediction Rules With Clinical Decision Support

Peter S. Dayen, MD, MSc,^a Dustin W. Ballard, MD, MBE,^{a,c} Eric Tham, MD,^a Jeff M. Hoffman, MD,^a Marguerite Swicklik, MSN, RN,^a Sara J. Deskyne, MPH,^a Braline A. Alessandrini, MD, MSCE,^a Leah Tzimenatos, MD,^{a,c} Lalit Bajaj, MD, MPH,^a David R. Vinson, MD,^{c,d} Dustin G. Mark, MD,^a Steve R. Offerman, MD,^a Un K. Chettipally, MD, MPH,^{a,c} Marilyn D. Petersen, MBE,^a Molly H. Schaeffer, MSc,^a Jun Wang, MS,^a T. Charles Gasper, PhD,^a Howard S. Goldberg, MD,^{a,c} Robert W. Grundmeier, MD,^a Nathan Kuppermann, MD, MPH,^{a,d} for the Pediatric Emergency Care Applied Research Network (PECARN), Clinical Research on Emergency Services and Treatment (CREST) Network, and Partners Healthcare Traumatic Brain Injury-Knowledge Translation Study Group

OBJECTIVES: We determined whether implementing the Pediatric Emergency Care Applied Research Network (PECARN) traumatic brain injury (TBI) prediction rules and providing risks of clinically important TBIs (ciTBIs) with computerized clinical decision support (CDS) reduces computed tomography (CT) use for children with minor head trauma.

METHODS: Nonrandomized trial with concurrent controls at 5 pediatric emergency departments (PEDs) and 8 general EDs (GEDs) between November 2011 and June 2014. Patients were <18 years old with minor blunt head trauma. Intervention sites received CDS with CT recommendations and risks of ciTBI, both for patients at very low risk of ciTBI (no Pediatric Emergency Care Applied Research Network rule factors) and those not at very low risk. The primary outcome was the rate of CT, analyzed by site, controlling for time trend.

RESULTS: We analyzed 16 635 intervention and 2394 control patients. Adjusted for time trends, CT rates decreased significantly ($P < .05$) but modestly (2.3%–3.7%) at 2 of 4 intervention PEDs for children at very low risk. The other 2 PEDs had small (0.8%–1.5%) nonsignificant decreases. CT rates did not decrease consistently at the intervention GEDs, with low baseline CT rates (2.1%–4.0%) in those at very low risk. The control PED had little change in CT use in similar children (from 1.6% to 2.9%); the control GED showed a decrease in the CT rate (from 7.1% to 2.6%). For all children with minor head trauma, intervention sites had small decreases in CT rates (1.7%–6.2%).

CONCLUSIONS: The implementation of TBI prediction rules and provision of risks of ciTBIs by using CDS was associated with modest, safe, but variable decreases in CT use. However, some secular trends were also noted.

abstract

Pediatrics 2017



Specific Aims

1. To develop and pilot test a computer-based data collection and recommendation system to implement the PECARN TBI prediction rules.
2. To assess whether this system decreases the number of (unnecessary) head CTs in the ED in children at very low risk of important brain injuries.

Blunt Head Trauma Assessment

☐ **Blunt Head Trauma Assessment (skip any question if unable to determine answer)**

Blunt head trauma?
 ☐ No
 ☒ Yes - less than 24 hours ago
 ☐ Yes - more than 24 hours ago

Loss of consciousness?
 ☐ No
 ☐ Yes - less than 5 seconds
 ☐ Yes - 5 seconds up to one minute
 ☐ Yes - 1 minute or longer
 ☐ Yes - duration unclear

Vomiting since injury?
 ☐ No
 ☐ Once
 ☐ Twice
 ☐ Three or more times

Acting normally per caregiver?
 ☐ Yes
 ☐ No

Severe mechanism of injury?
 ☐ No
 ☐ Yes

Current headache?
 ☐ No
 ☐ Mild
 ☐ Moderate

Other signs of altered mental status?
 ☐ No
 ☐ Yes

Temporal, parietal, or occipital scalp hematoma?
 ☐ No
 ☐ Yes

☐ **GCS**

Eye Opening

Verbal Response

Motor Response

Total GCS

Other signs of altered mental status?
 ☐ No
 ☐ Yes

Row Information:
 Other signs of altered mental status defined as any of the following:

- Agitation
- Somnolence
- Repetitive questioning
- Slow response to verbal communication

Temporal, parietal, or

Decision Support: Patient < 2 years who meets rule

♥ Traumatic Brain Injury Risk: Child less than 2 years

RECOMMENDATION: A head CT is not recommended for this patient based on the absence of any of the [PECARN prediction rule](#) variables.

Risk Estimate: The risk of [clinically-important traumatic brain injury](#) for patients less than 2 years is < 1/5000

Importantly, the PECARN rules were based on attending initial evaluations (not based on subsequent evaluations over time).

The age-specific PECARN rule findings documented are:

Loss of consciousness?:	No
Acting normally per caregiver?:	Yes
Mechanism of injury?:	Mild
Total Glasgow Coma Scale score:	15
Other signs of altered mental status?:	No
Scalp hematoma?:	None
Palpable skull fracture or unclear on the basis of swelling or distortion of the scalp?:	No

If the above clinical findings are incorrect, please revise.

Note: The PECARN prediction rules do not apply to patients with: bleeding diatheses, ventricular (e.g. "VP") shunts, known brain tumors, or pre-existing neurological disorders complicating your clinical assessment.

[Click here to view the PECARN prediction rule manuscript \(Lancet\)](#)

↩ Click to provide a revised risk assessment

CT rates in patients with minor blunt head trauma at very low risk of clinically-important TBI (N=7,482) at intervention EDs before and after implementation of CDS (*adjusted for time trends*)

EDs	Months Before CDS*	Months After CDS*	CT rate before CDS	CT rate after CDS	Unadjusted Odds Ratio	Adjusted Odds Ratio (95% CI)**	P value**
Intervention PED 1	13.1	10.1	52/963 (5.4%)	22/705 (3.1%)	0.56	0.56 (0.34 , 0.94)	0.03
Intervention PED 2	14.2	12.0	18/434 (4.1%)	7/264 (2.7%)	0.63	0.60 (0.25 , 1.47)	0.3
Intervention PED 3	13.2	10.1	65/809 (8.0%)	39/898 (4.3%)	0.52	0.49 (0.32 , 0.74)	<.001
Intervention PED 4	9.6	15.7	22/158 (13.9%)	42/319 (13.2%)	0.94	0.66 (0.24 , 1.87)	0.4
Intervention GED 1	15.7	12.3	7/341 (2.1%)	10/391 (2.6%)	1.25	1.25 (0.47 , 3.33)	0.7
Intervention GED 2	15.7	12.3	15/556 (2.7%)	23/521 (4.4%)	1.67	1.78 (0.92 , 3.47)	0.09
Intervention GED 3	15.6	12.3	3/88 (3.4%)	3/165 (1.8%)	0.52	0.52 (0.07 , 3.91)	0.7
Intervention GED 4	15.6	12.3	12/303 (4.0%)	16/567 (2.8%)	0.70	3.30 (0.60 , 22.08)***	0.2
All Intervention EDs	.	.	194/3,652 (5.3%)	162/3,830 (4.2%)	0.79	0.72 (0.53 , 0.99)	0.04
Control PED†	†	†	6/378 (1.6%)	12/418 (2.9%)	1.83	1.85 (0.69 , 4.98)	0.2
Control GED†	†	†	22/311 (7.1%)	10/385 (2.6%)	0.38	0.35 (0.16 , 0.75)	0.007

CT rates in all patients with minor blunt head trauma
(N=16,635) at intervention EDs before and after CDS (*adjusted
for time trends*)

EDs	CT Rate Before CDS	CT Rate After CDS	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)*	P value
Intervention PED 1	474/2,366 (20.0%)	275/1,673 (16.4%)	0.79 (0.67, 0.93)	0.78 (0.67 , 0.92)	0.004
Intervention PED 2	187/1,438 (13.0%)	117/1,036 (11.3%)	0.85 (0.67, 1.09)	0.84(0.66 , 1.07)	0.2
Intervention PED 3	389/1,930 (20.2%)	273/1,912 (14.3%)	0.66 (0.56, 0.78)	0.66 (0.56 , 0.78)	<.001
Intervention PED 4	288/596 (48.3%)	447/1,002 (44.6%)	0.86 (0.70, 1.06)	0.86 (0.70 , 1.05)	0.1
Intervention GED 1	68/535 (12.7%)	53/550 (9.6%)	0.73 (0.50, 1.07)	0.73 (0.50 , 1.07)	0.1
Intervention GED 2	177/1,056 (16.8%)	100/830 (12.0%)	0.68 (0.52, 0.89)	0.80 (0.48 , 1.36)	0.4
Intervention GED 3	25/167 (15.0%)	29/249 (11.6%)	0.75 (0.42, 1.33)	0.74 (0.41 , 1.31)	0.3
Intervention GED 4	81/480 (16.9%)	87/815 (10.7%)	0.59 (0.42, 0.82)	0.93 (0.50 , 1.72)	0.8
All Intervention EDs	1,689/8,568 (19.7%)	1,381/8,067 (17.1%)	0.84 (0.78, 0.91)	0.91 (0.86, 0.97)	0.002
Control PED [†]	90/638 (14.1%)	86/688 (12.5%)	0.87 (0.63, 1.19)	0.86 (0.63, 1.18)	0.3
Control GED [†]	81/521 (15.5%)	63/547 (11.5%)	0.71 (0.50, 1.01)	0.71 (0.50, 1.02)	0.06

CT rates in patients with minor blunt head trauma who were not at very low risk for ciTBI by PECARN TBI prediction rule criteria (N=7,117) at intervention EDs before and after CDS (*adjusted for time trends*)

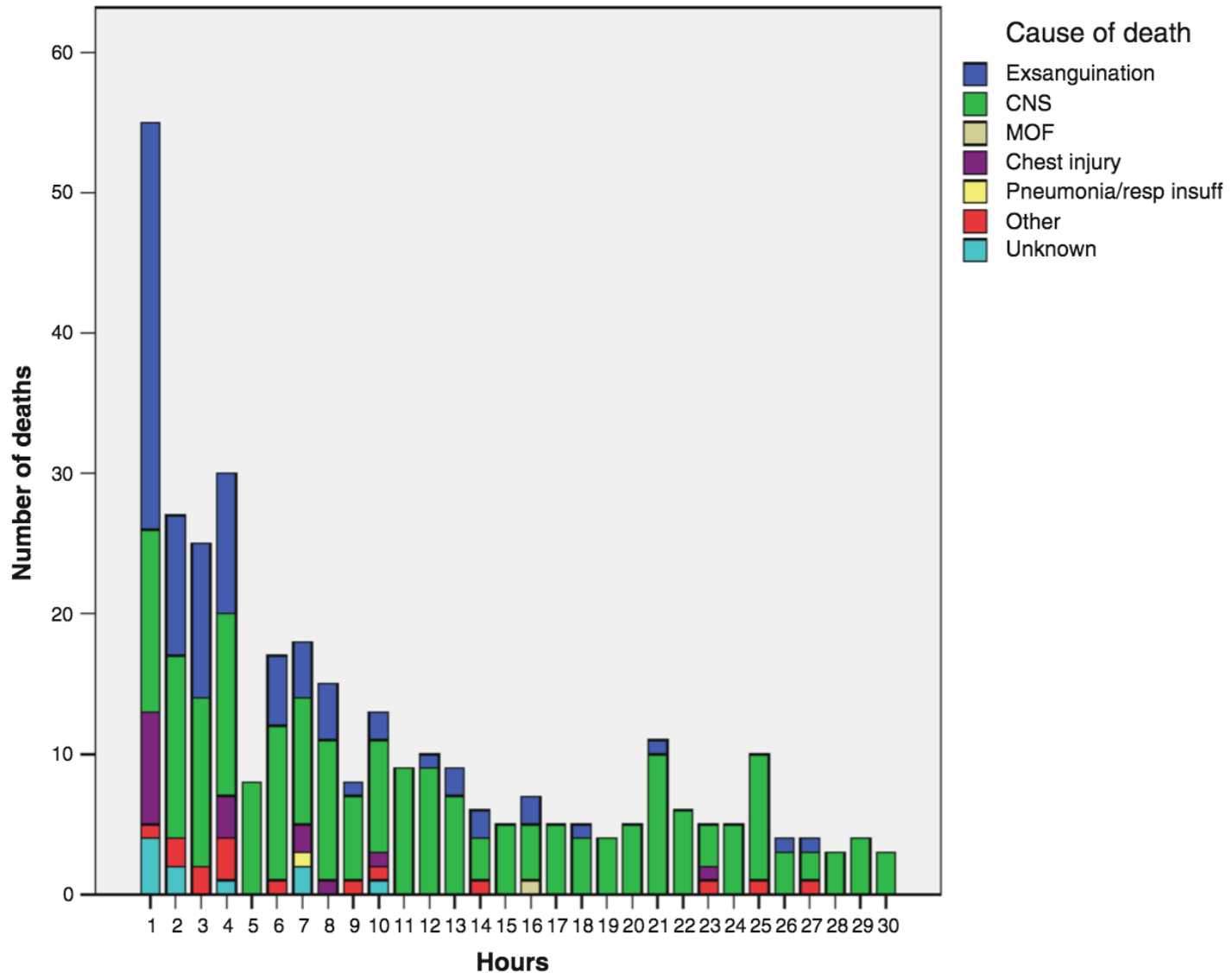
EDs	CT Rate Before CDS	CT Rate After CDS	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)*	P value*
Intervention PED 1	405/1,206 (33.6%)	241/790 (30.5%)	0.87 (0.72, 1.05)	0.87 (0.72 , 1.05)	0.2
Intervention PED 2	154/657 (23.4%)	94/444 (21.2%)	0.88 (0.66, 1.17)	0.88 (0.66 , 1.17)	0.4
Intervention PED 3	295/890 (33.1%)	223/818 (27.3%)	0.76 (0.61, 0.93)	1.36 (0.87 , 2.13)	0.2
Intervention PED 4	249/362 (68.8%)	380/586 (64.8%)	0.84 (0.63, 1.11)	1.15 (0.65 , 2.05)	0.6
Intervention GED 1	59/154 (38.3%)	41/131 (31.3%)	0.73 (0.45, 1.20)	0.73 (0.45 , 1.21)	0.2
Intervention GED 2	154/372 (41.4%)	76/236 (32.2%)	0.67 (0.48, 0.95)	0.68 (0.48 , 0.96)	0.03
Intervention GED 3	21/66 (31.8%)	25/70 (35.7%)	1.19 (0.58, 2.43)	1.20 (0.58 , 2.44)	0.6
Intervention GED 4	66/139 (47.5%)	70/196 (35.7%)	0.61 (0.39, 0.96)	0.64 (0.41 , 1.00)	0.05
All intervention EDs	1,403/3,846 (36.5%)	1,150/3,271 (35.2%)	0.94 (0.86, 1.04)	1.03 (0.91 , 1.17)	0.6
Control PED	84/230 (36.5%)	70/223 (31.4%)	0.80 (0.54, 1.17)	0.79 (0.53, 1.18)	0.2
Control GED	58/157 (36.9%)	52/117 (44.4%)	1.37 (0.84, 2.22)	1.35 (0.82, 2.21)	0.2

Torso trauma is the second leading cause of death from trauma and hemorrhage is the leading etiology

Trauma is the leading cause of morbidity and mortality in children in the US

Rank	<1	1-4	5-9	10-14	15-24
1	Congenital Anomalies 5,107	Unintentional Injury 1,394	Unintentional Injury 758	Unintentional Injury 885	Unintentional Injury 12,341
2	Short Gestation 4,148	Congenital Anomalies 507	Malignant Neoplasms 439	Malignant Neoplasms 477	Homicide 4,678
3	SIDS 2,063	Homicide 385	Congenital Anomalies 163	Suicide 267	Suicide 4,600
4	Maternal Pregnancy Comp. 1,561	Malignant Neoplasms 346	Homicide 111	Homicide 150	Malignant Neoplasms 1,604
5	Unintentional Injury 1,110	Heart Disease 159	Heart Disease 68	Congenital Anomalies 135	Heart Disease 1,028
6	Placenta Cord. Membranes 1,030	Influenza & Pneumonia 91	Chronic Low Respiratory Disease 60	Heart Disease 117	Congenital Anomalies 412
7	Bacterial Sepsis 583	Septicemia 62	Cerebro-vascular 47	Chronic Low Respiratory Disease 73	Cerebro-vascular 190
8	Respiratory Distress 514	Benign Neoplasms 59	Benign Neoplasms 37	Benign Neoplasms 45	Influenza & Pneumonia 181
9	Circulatory System Disease 507	Perinatal Period 52	Influenza & Pneumonia 37	Cerebro-vascular 43	Diabetes Mellitus 165
10	Necrotizing Enterocolitis 472	Chronic Low Respiratory Disease 51	Septicemia 32	Septicemia 35	Complicated Pregnancy 163

In the initial 24 hours after injury, hemorrhage is the leading cause of death



There are no drug treatments for injured children to improve outcomes

Tranexamic Acid (TXA)

- Antifibrinolytic agent
- FDA approved for hemophilia and menorrhagia
- Most frequently used for pediatric and adult surgery
- Inexpensive
- Safe

RESEARCH

REVIEW

European Journal of Cardio-Thoracic Surgery 42 (2012) 781–786
doi:10.1093/ejcts/ezs127 Advance Access publication 24 April 2012

The NEW ENGLAND JOURNAL of MEDICINE

Effi

ORIGINAL ARTICLE

Day **Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial**

WOMAN Trial Collaborators*

Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial

*CRASH-2 trial collaborators**

- 20,000+ adults with significant hemorrhage
- Randomized to TXA or placebo
- All-cause mortality: TXA 1463 [14.5%] vs. Placebo 1613 [16.0%], NNT = 67
- No increase in adverse events

VIEWPOINT

Tranexamic acid in pediatric trauma: why not?

Suzanne Beno^{1*}, Alun D Ackery², Jeannie Callum³ and Sandro Rizoli²

The PREDICT DELPHI STUDY:

Establishing the Research Priorities of Paediatric Emergency Medicine Physicians in Australia and New Zealand

9
(5.02)

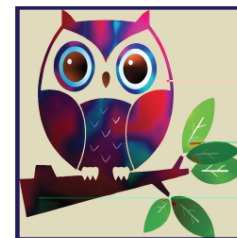
In paediatric patients who sustain blunt trauma with haemodynamic instability, does early tranexamic acid 15mg/kg compared to placebo improve mortality and reduce morbidity?



PERUKI

What are the Research Priorities of Paediatric Emergency Medicine (PEM) Clinicians in the United Kingdom & Ireland? - an International Survey

¹S Hartshorn, ²C Bevan, ³F Cleugh, ⁴M Lyttle, ³I Maconochie, ^{5,6}R O'Sullivan



PERUKI

5

In paediatric major trauma patients with major haemorrhage does IV tranexamic acid compared to no treatment reduce mortality and morbidity?

TiC-TøC

Traumatic Injury Clinical Trial Evaluating
Tranexamic Acid in Children

Can we improve the identification & management of occult depression in teenagers?

Grant Number: 5U01MH104311-02 REVISED
FAIN: U01MH104311

Principal Investigator(s):

David A. Brent, MD
JACQUELINE M GRUPP-PHELAN, MD
CHERYL A KING (contact), PHD

Emergency Department Screen for Teens at Risk for
Suicide
(ED-STARS)
PECARN Protocol Number 033

Pediatric Emergency Care Applied Research Network
National Institute of Mental Health (NIMH)



Screening of Teens for Mental Health / Depression

Prioritizing Research to Reduce Youth Suicide and Suicidal Behavior

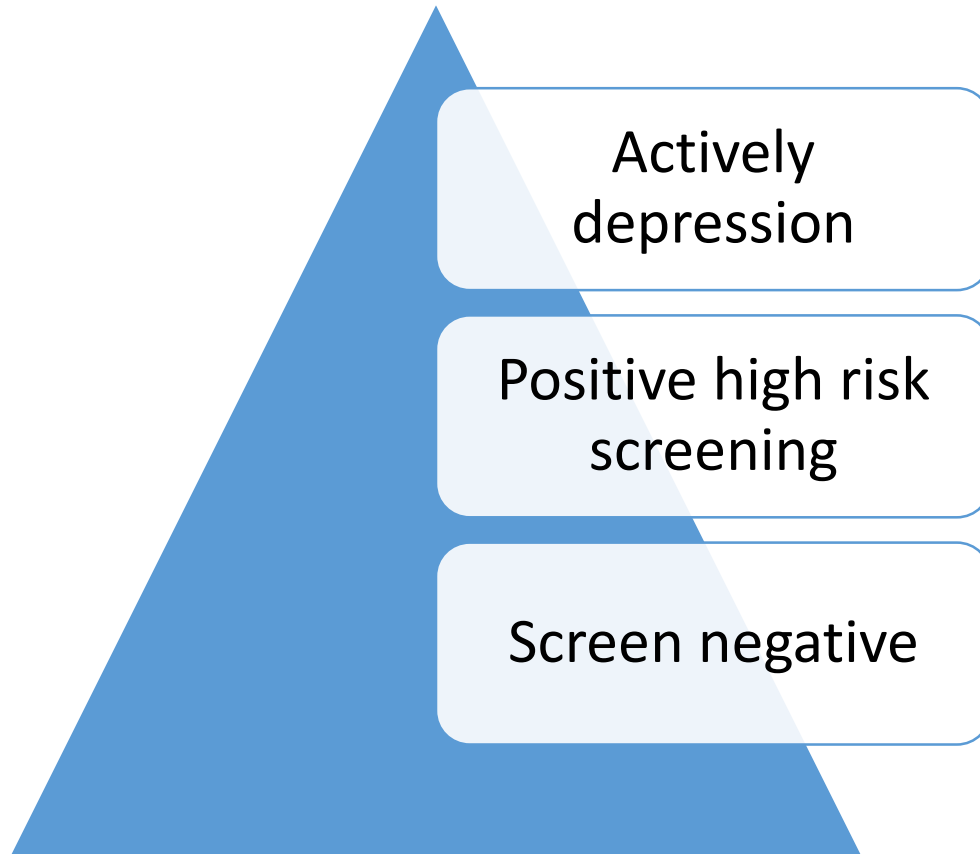
Jeffrey A. Bridge, PhD, Lisa M. Horowitz, PhD, MPH, Cynthia A. Fontanella, PhD, Jackie Grupp-Phelan, MD, MPH, John V. Campo, MD

The goal of the National Action Alliance for Suicide Prevention is to reduce suicide and suicide attempts in the U.S. by 40% in the next decade. In this paper, a public health approach is applied to suicide prevention to illustrate how reductions in youth suicide and suicidal behavior might be achieved by prioritizing research in two areas: (1) increasing access to primary care-based behavioral health interventions for depressed youth and (2) improving continuity of care for youth who present to emergency departments after a suicide attempt. Finally, some scientific, clinical, and methodologic breakthroughs needed to achieve rapid, substantial, and sustained reductions in youth suicide and suicidal behavior are discussed.

(Am J Prev Med 2014;47(3S2):S229–S234) © 2014 American Journal of Preventive Medicine



Depression management in EDs



ED STARS - -

Specific Aim 1. To develop an optimal suicide risk screen for youth presenting to the emergency department (ED). We will develop a personalized, computerized adaptive screen (CAS) and compare its psychometric properties (e.g., sensitivity, specificity, positive and negative predictive value) for predicting one or more suicide attempts to those of the Ask Suicide-Screening Questions (ASQ).

Specific Aim 2. To develop and validate a parsimonious CAS algorithm for risk stratification of youth to “high risk for suicide attempt” (high probability), “at risk” (need for mental health referral but no high risk) and “low risk” (low probability, no need for mental health referral) groups.

Aim 1 and 2 data is complete with 7000 patients enrolled at multiple PECARN sites.

ED Stars

Specific Aim 3. To validate the CAS personalized suicide risk screen prospectively, examining its sensitivity and specificity for the 3-month prediction of suicide attempts.

Specific Aim 4. To determine if the IAT adds incrementally to the prediction of suicide attempts above and beyond CAS and ASQ scores.

Aim 3 and 4 begun in July – enrolling high risk and low risk patients to validate the CAS and if the IAT adds to prediction of attempts

What is the best treatment for ED / Prehospital management of status epilepticus after failure of benzodiazepine?

- Which secondary antiepileptic is most effective?
- Which is safer?



Funded through NINDS



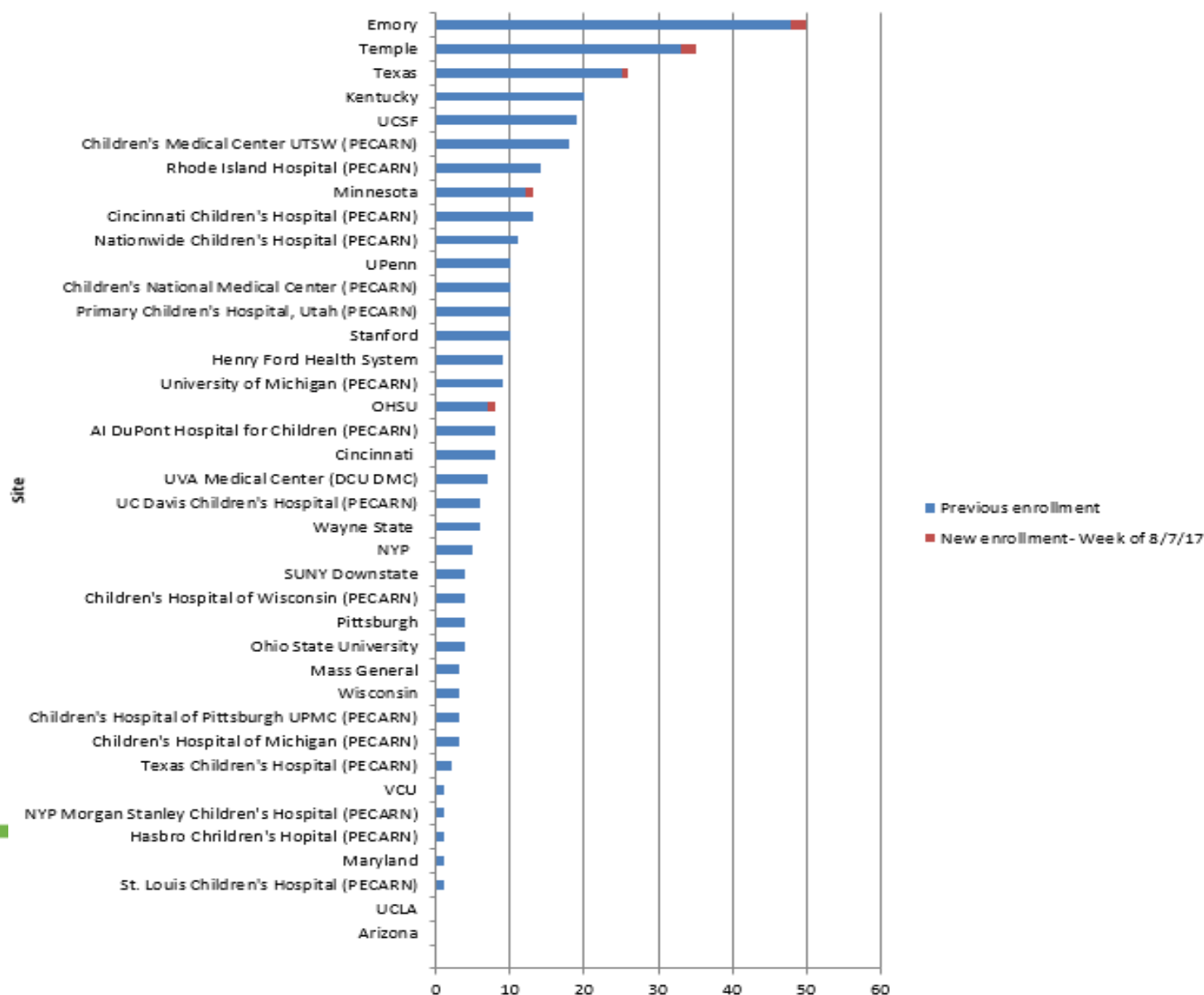
ESETT – Established Status Epilepticus Treatment Trial

- Partnership with neurology, general EM and PEM
- Life threatening and time sensitive condition - - use of EFIC (exception from informed consent)
- Currently enrolling with pediatric enrollment ahead of schedule
- Randomization to one of three therapies – valproic acid, fosphenytoin, levetiracetam
- Study procedures – complete in 1 hour

Funded through NINDS



ESETT Enrollment Status: August 7 - 13, 2017



Febrile infants - Background

- 20 - 35 % of urban pediatric emergency department (ED) visits are for fever
- ~ 500,000 ED visits in the U.S. for infants 60 days or younger are for fever
- Many more to clinics and offices

How can we better manage febrile infants (<2 months of age)

- Identification of etiology to improve management
- Reduce health services use in low risk infants
- Reduce admission for young infants who can be managed at home

Newer data about UA and UTI in infants 0-2 months old with temp $\geq 38^{\circ}\text{C}$

Urinary tract infections in 7-9%

- ◆ Sensitivity of UA $\sim 85\text{-}95\%$
- ◆ Dipstick (LE) only slightly less sensitive than full UA
 - *Lack of inflammation likely asymptomatic bacteruria*
- ◆ Urine concentration matters (3 vs 6 WBC/HPF)
- ◆ UA sensitivity close to 100% in bacteremic UTIs

Newer data about WBC thresholds and IBI

- Much data suggest that the peripheral WBC at either end of the spectrum is **not** a good screen for bacteremia/bacterial meningitis (*Bonsu 2003*)

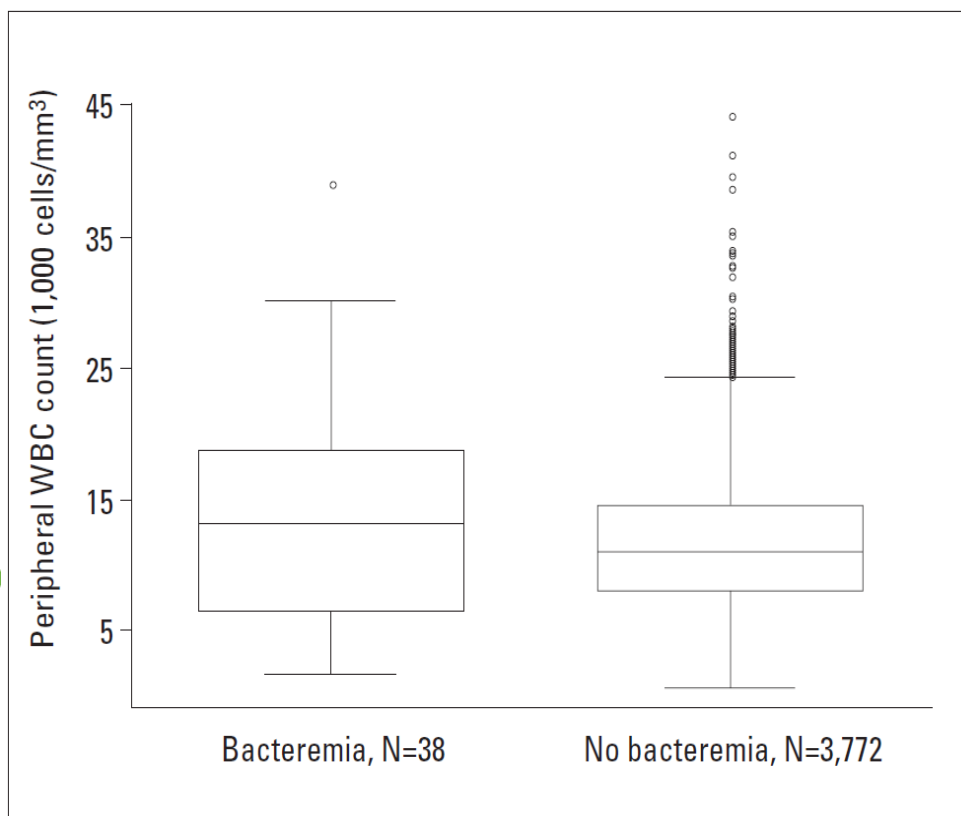


Table 1.

Test sensitivity and specificity at various thresholds of the total peripheral WBC count among febrile infants aged 0 to 89 days.

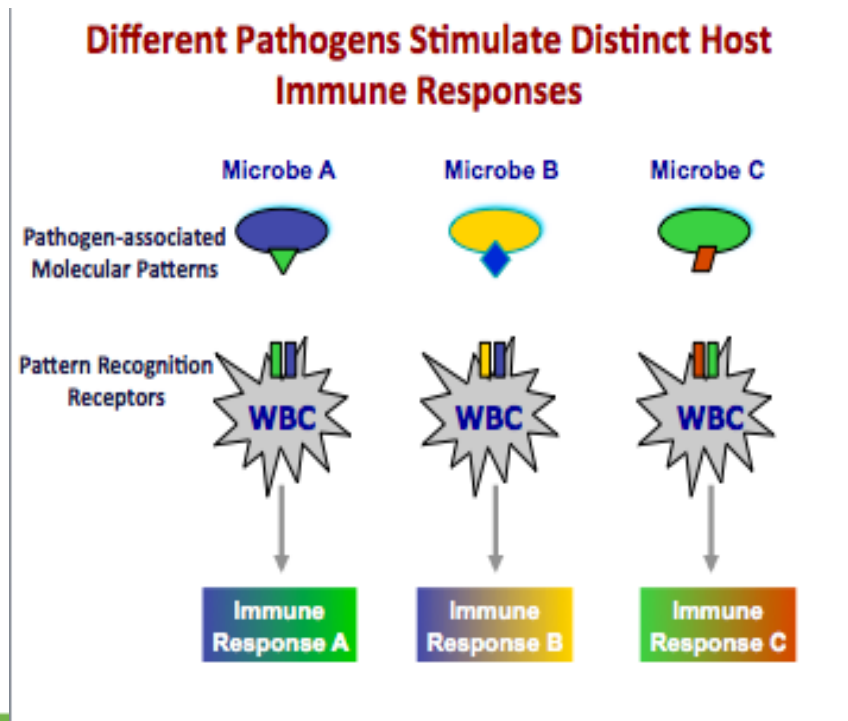
WBC Cutoff (1,000s/mm ³)	Bacteremia (N=38)	Sensitivity, %* (95% CI)	No Bacteremia (N=3,772)	Specificity, %* (95% CI)
≥5	30	79 (63–90)	201	5 (4–6)
≥10	23	61 (43–76)	1,581	42 (40–44)
≥15	17	45 (29–62)	2,928	78 (76–79)
≥20	9	24 (11–40)	3,517	93 (92–94)
≥25	5	13 (4–28)	3,700	98 (97–99)
≥30	2	5 (1–2)	3,758	99 (99–100)
<5 or ≥15	25	66 (49–80)	2,727	72 (71–74)
<5 or ≥20	17	45 (29–62)	3,316	88 (87–89)

*Sensitivity is the number of bacteremic infants with test results above the WBC count cutoff (or within the appropriate interval). Specificity is the number of nonbacteremic infants with test results below the WBC count cutoff (or outside the appropriate interval).

The Next Frontier

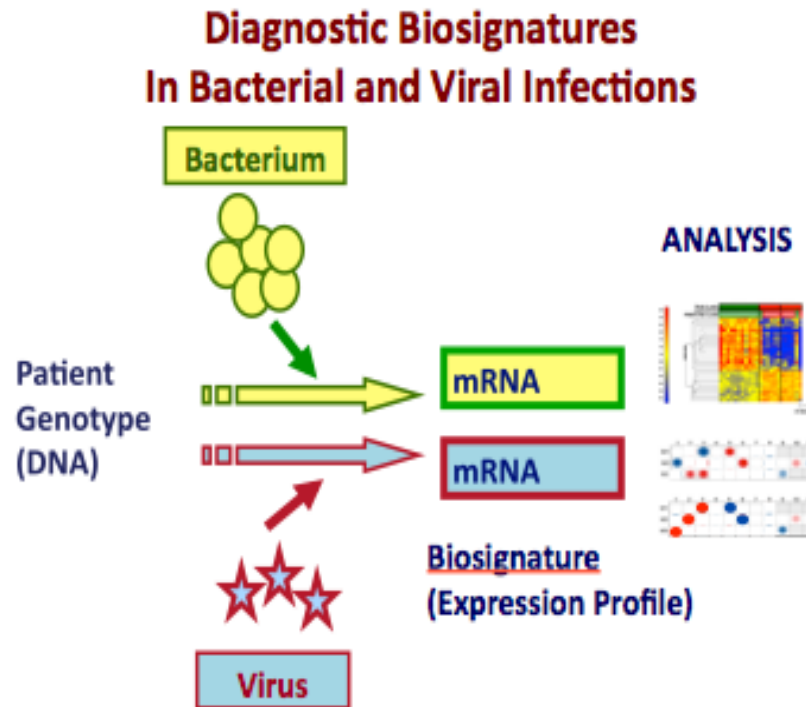
RNA Transcription Biosignatures

Alternative to pathogen identification:
Measure the host response to infection by measuring gene



The Next Frontier

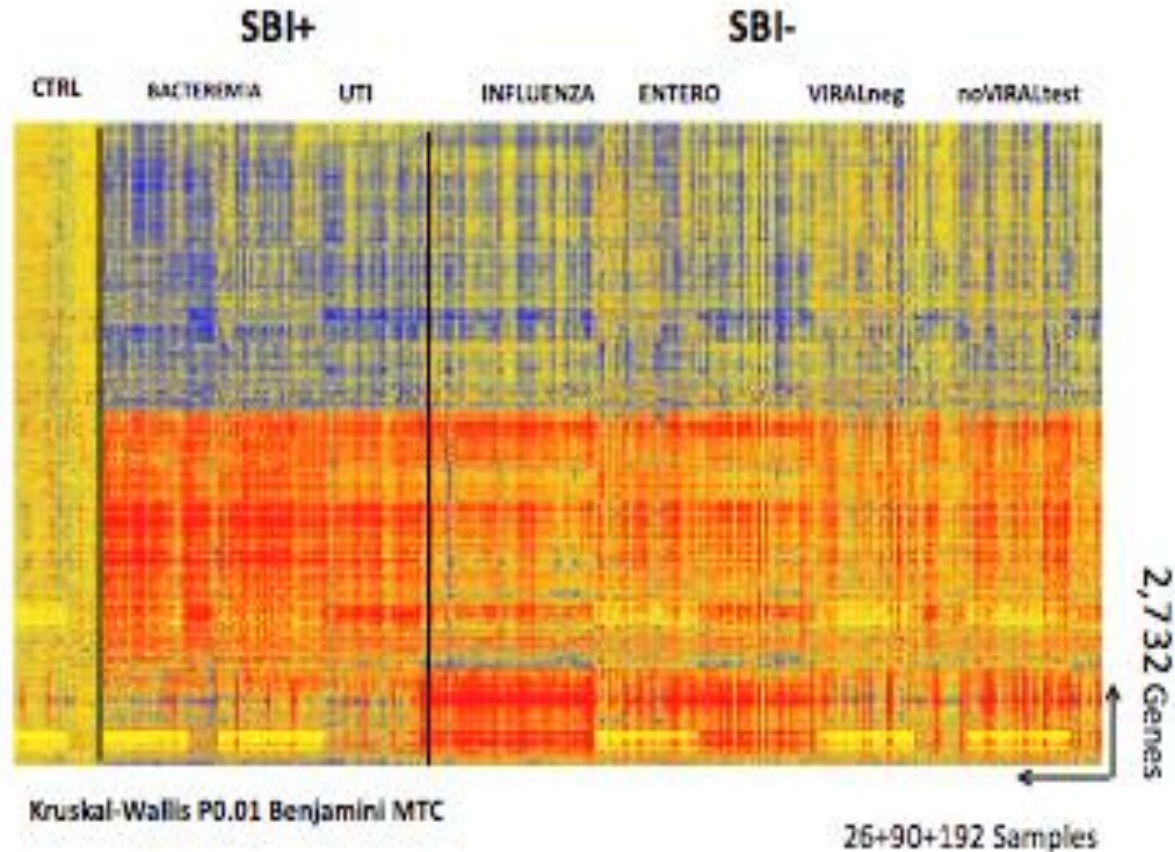
RNA Transcription Biosignatures



The Next Frontier

RNA Transcription Biosignatures

RNA Biosignatures in SBI + and SBI - Infants



Association of RNA Biosignatures With Bacterial Infections in Febrile Infants Aged 60 Days or Younger

Prashant Mahajan, MD, MPH, MBA; Nathan Kunnermann, MD, MPH; Asuncion Mejias, MD, PhD; Nicolas Suarez, PhD;

Damien Chaussabel, PhD; T. Charles C

Atabaki, MD, MPH; Jonathan E. Benn

Lorin Browne, DO; Daniel M. Cohen, M

Richard Greenberg, MD; John D. Hoyl

Jared Muenzer, MD; Lise E. Nigrovic, I

Richard M. Ruddy, MD; Mary Saunden

Octavio Ramilo, MD; for the Pediatric

Key Points

Question Can the host response measured by RNA biosignatures distinguish young febrile infants with and without bacterial infections?

Findings In this prospective observational study of 279 febrile infants 60 days or younger, 66 classifier genes distinguished infants with and without bacterial infections with 87% sensitivity and 89% specificity. Ten classifier genes distinguished infants with bacteremia from those without bacterial infections with 94% sensitivity and 95% specificity.

Meaning In this preliminary study, host RNA biosignatures accurately distinguished febrile infants 60 days or younger with and without bacterial infections.

A.

MD;

, MD;

, PhD;

BA;

JAMA. 2016;316(8):846-857. doi:10.1001/jama.2016.9207



Diabetic ketoacidosis and cerebral injury: *Do fluids make a difference?*

DKA - epidemiology

- 64% of all deaths in children with diabetes are associated with DKA
- Of pediatric deaths due to diabetes, 83-97% are caused by DKA
- 62-63% of DKA-related deaths in children are the result of cerebral injury/edema

What causes cerebral injury in DKA? (traditional view)

- Cerebral edema occurs in a small minority of DKA episodes (~1%)
- Edema and increased ICP in these patients leads to cerebral injury
- Variations in DKA treatment likely play an important role in causing cerebral edema, particularly when DKA treatment leads to a rapid decline in osmolality

The fluid controversy

What has spooked us, and motivated us

The fluid controversy

What has spooked us, and motivated us

- ◆ Case series of 40 children with DKA and CE:
 - “Only 4 of 40 cases occurred at fluid intakes less than or equal to 4.0 L/m²/day” (*J Pediatr* 1988)

The fluid controversy

What has spooked us, and motivated us

Editorial:

“Emergency resuscitation should not be given unless shock ... If emergency phase needed, aliquots of 5-10 cc/kg **brain swelling during treatment of severe DKA is a tragedy that now may be prevented**”

(J Pediatr 1988)

The fluid controversy

What has spooked us, and motivated us

Letter to the editor:

“To state that brain swelling during treatment of severe DKA is a tragedy that now may be prevented is unsubstantiated and **does little else than give plaintiff’s attorneys the rope with which to try to hang pediatricians who will have an unfortunate encounter with this complication** Until basic research defines the pathophysiology of CE during DKA **and randomized prospective clinical studies** ...we are all guessing about how this elephant looks.” (*J Pediatr* 1989)



FLuid therapies Under Investigation in DKA: “the FLUID trial”

Funded by grant 1R01HD062417-01 from the Eunice Kennedy Shriver NICHD.

PECARN is supported by the Health Resources and Services Administration (HRSA), Maternal and Child Health Bureau (MCHB), Emergency Medical Services for Children (EMSC) through the following grants:

U03MC00008, U03MC00003, U03MC22684, U03MC00007, U03MC00001 , U03MC22685, U03MC00006



Objective

To determine the impact of IV fluid infusion rate and sodium content on neurological and neurocognitive outcomes of DKA in children

Methods

Overview and Patient Selection

- Prospective, multi-center, 2 x 2 factorial design RCT of IV fluid treatment for DKA
 - 13 PECARN hospitals
 - 2011-2017
- Inclusion criteria
 - Age 0 - 18 years
 - DKA
 - serum glucose > 300 mg/dL, venous pH < 7.25 or serum bicarbonate < 15mmol/L

PECARN Studies

- New / Pending – PED SCREEN, Pain management in fractures (comp effectiveness), C-spine validation, R03 – Disparities in ED
STI screening, Setting a PEM Nursing Research Agenda
- Planning Grants – Asthma – IV Magnesium, Antimicrobial Stewardship, Steroids – school based asthma program, HUS from STEC

Pending Pre-Hospital Studies

- Does prehospital asthma therapy reduce ED Admits or Length of Stay (and resource use)?
- Does prehospital identification for possible sepsis improve sepsis pathway use & outcomes?
- Role of simulation & deliberate practice in high risk procedures / critically ill or injured children

Summary

- High impact pediatric illnesses & trauma – multi-center discovery work & implementation of best practice
- Involves 18 Pediatric EDs and 9 prehospital care agencies across diverse population
- Improves the ED based research at each institution
- Continues to look for partnerships across content experts from EMSC experts & others

Questions?

Thank you -