



Continuous EEG Monitoring Detects More Seizures, But Does it Improve Outcomes?

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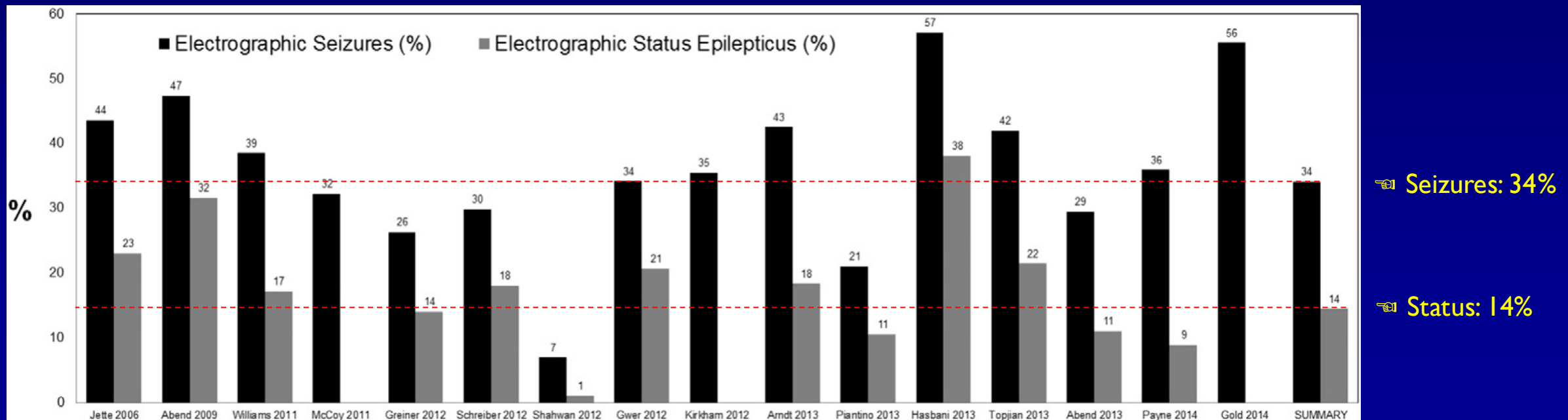
UNIVERSITY OF TORONTO
FACULTY OF MEDICINE

SickKids[®]

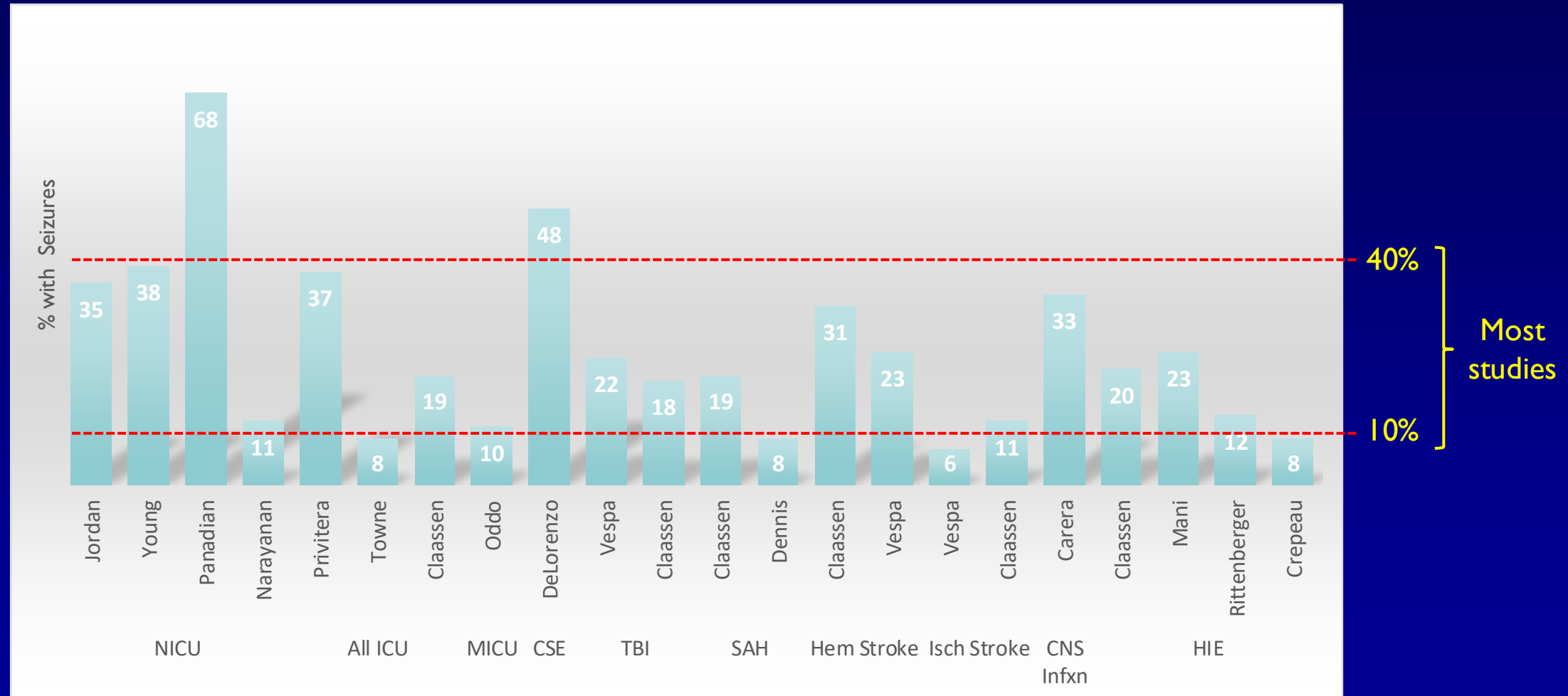
Seizures and Status Epilepticus are Common in Critically Ill Children

Cohort studies of critically ill children
undergoing clinically-indicated cEEG monitoring

Cohort composition and cEEG Indications varied by study

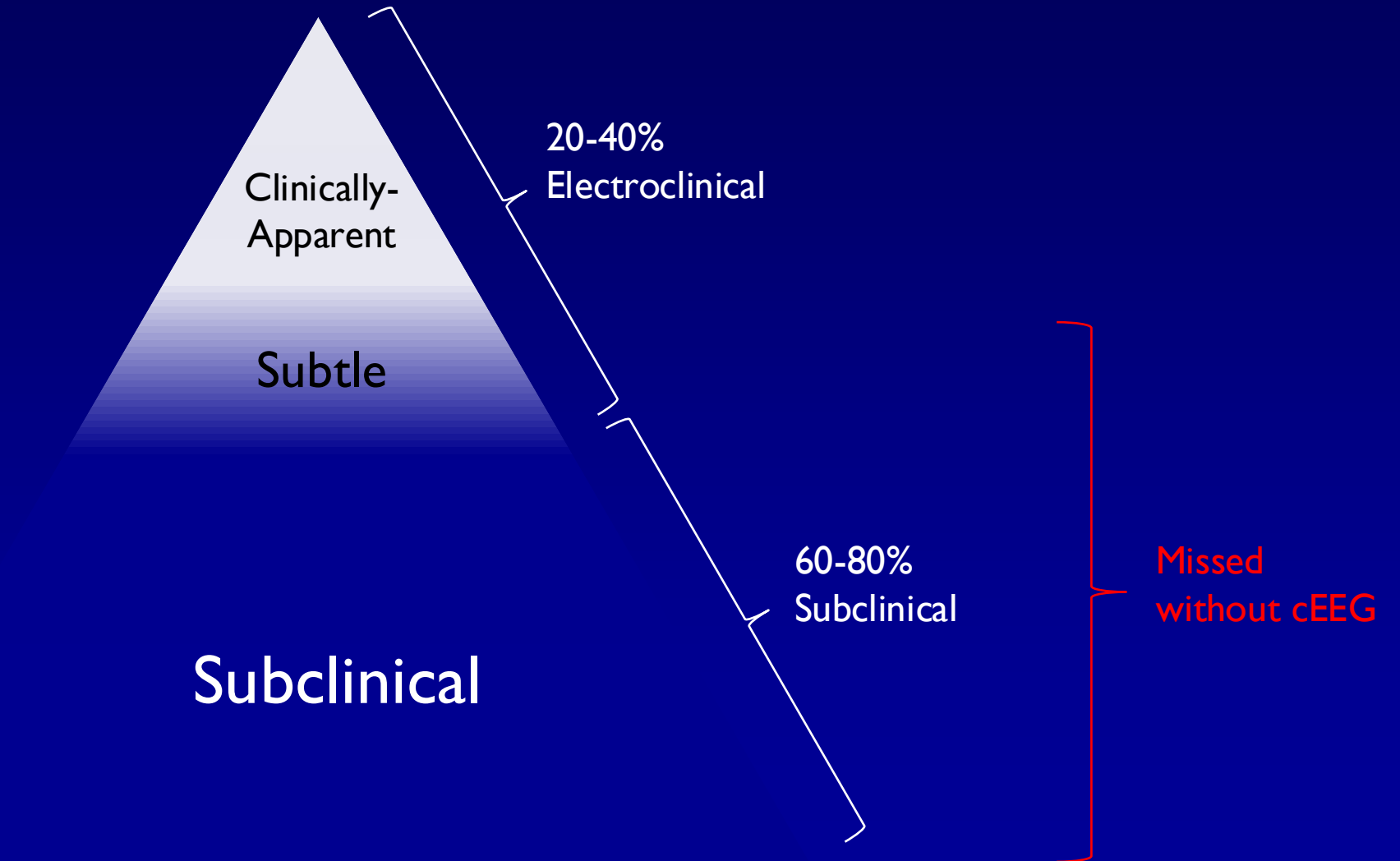


Seizures & SE Are Common in Critically Ill Adults

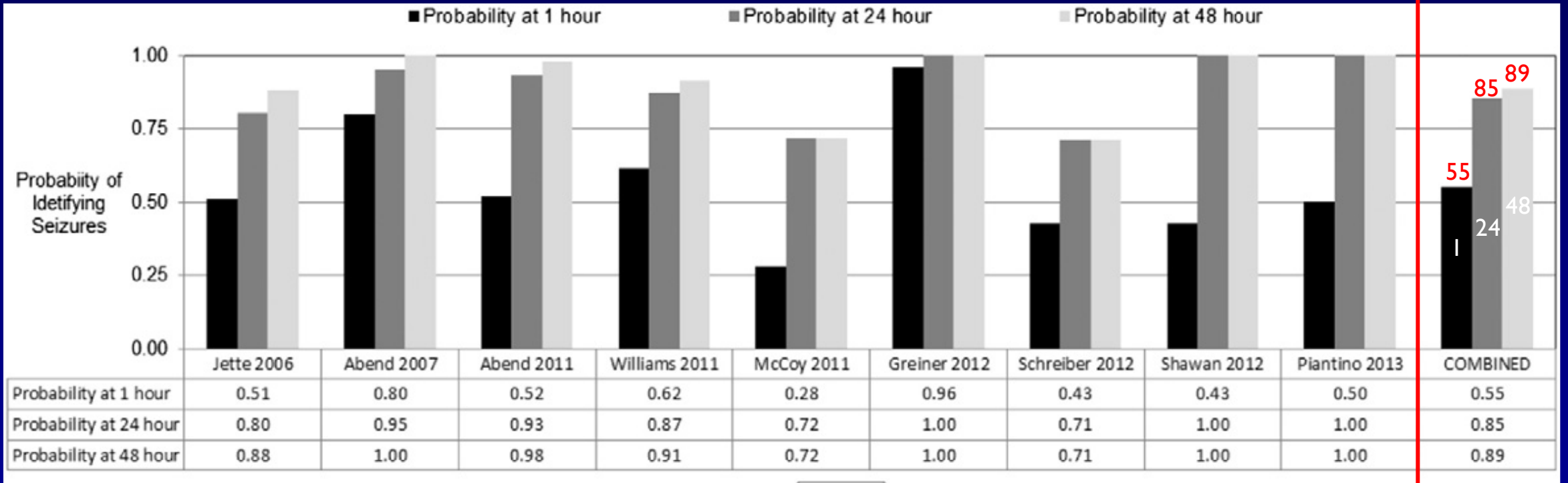


Summary courtesy of Nicholas Abend

The Majority of ICU Seizures are Subclinical



Routine EEG Misses Half of Patients with Seizures



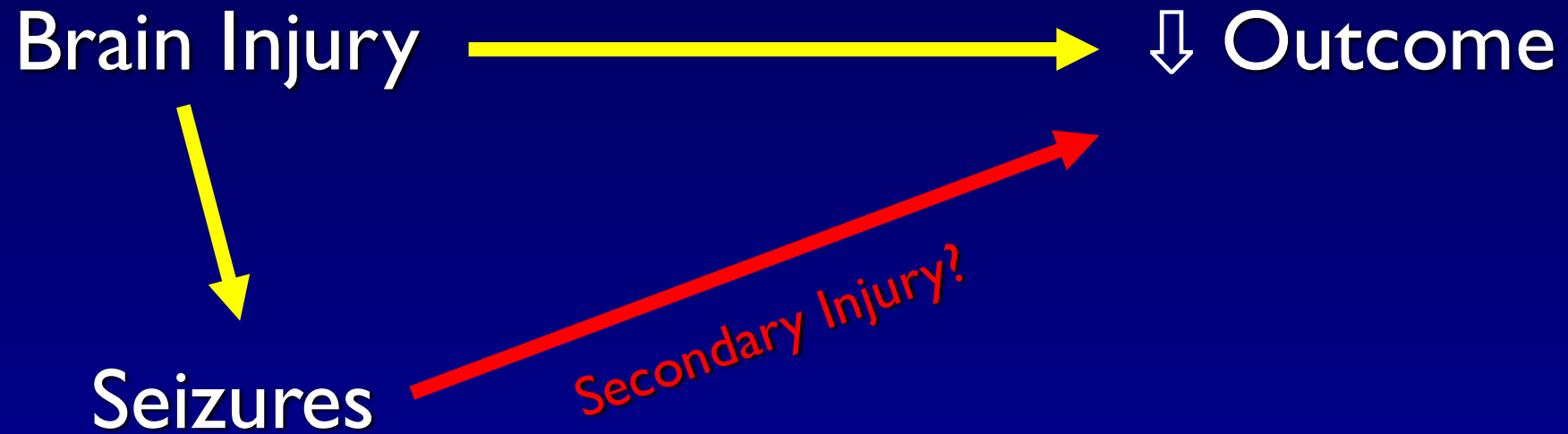
Nonconvulsive Seizures

Have Long Been Associated with Worse Outcome

- 127 adults underwent continuous EEG in ICU
- 39% had nonconvulsive seizures (49/127 patients)
 - 25 remote symptomatic etiology (stroke, seizure disorder)
 - 24 acute symptomatic etiology (MODS, HIE)
- Multivariate predictors of mortality:
 - Seizure duration (OR 1.13/hour, $p=.0057$)
 - Delay to diagnosis (OR 1.03/hour, $p=0.0351$)
 - After controlling for age, sex, seizure type, etiology

Young et al, *Neurology* 47:83-89, 1996.

Do (Subclinical) Seizures Worsen Outcome?



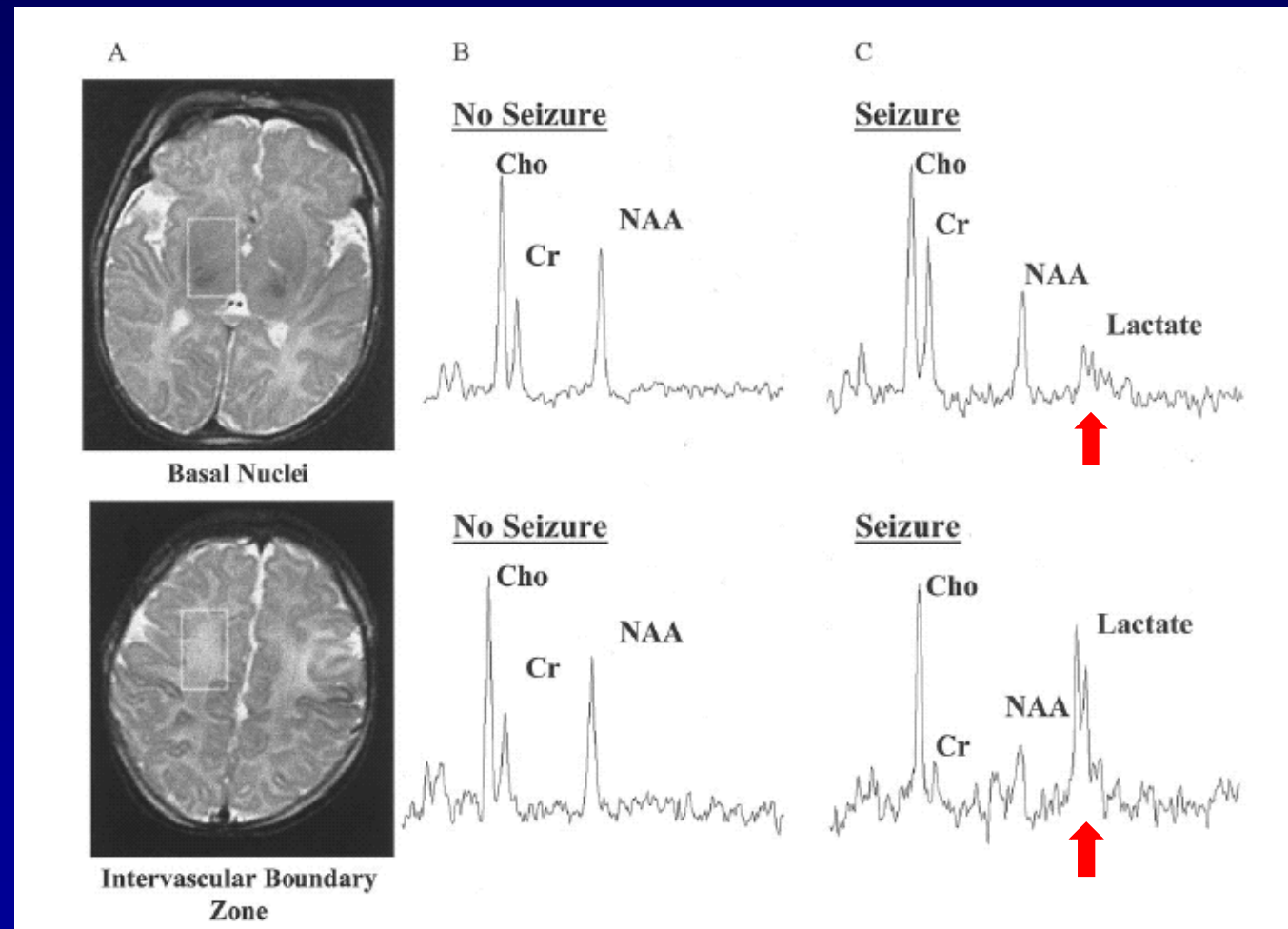
Excitotoxicity

Hypoxia-Ischemia

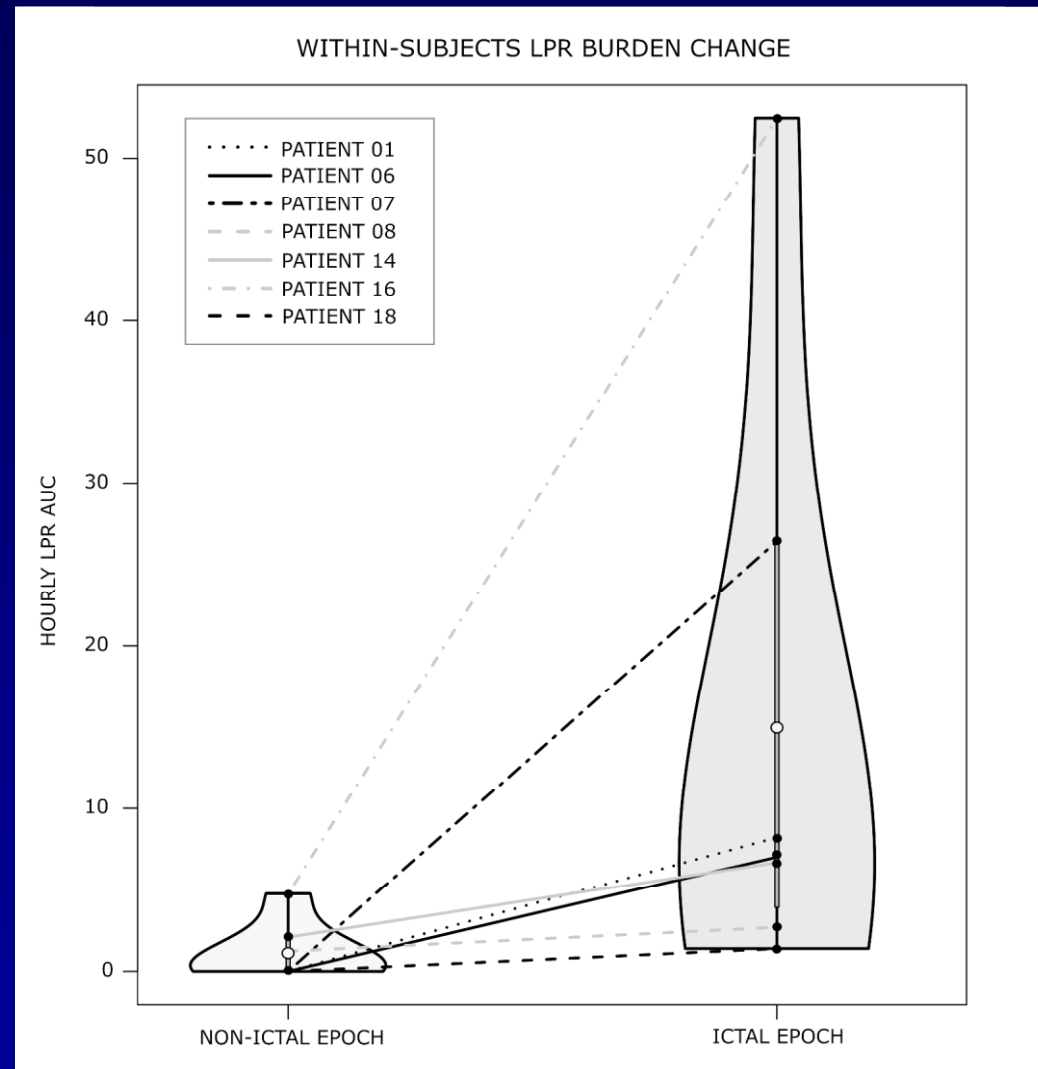
Inflammation

Evidence that Seizures have Acute Physiological Consequences

Neonatal Seizures are Independently Associated with Accumulation of Lactate



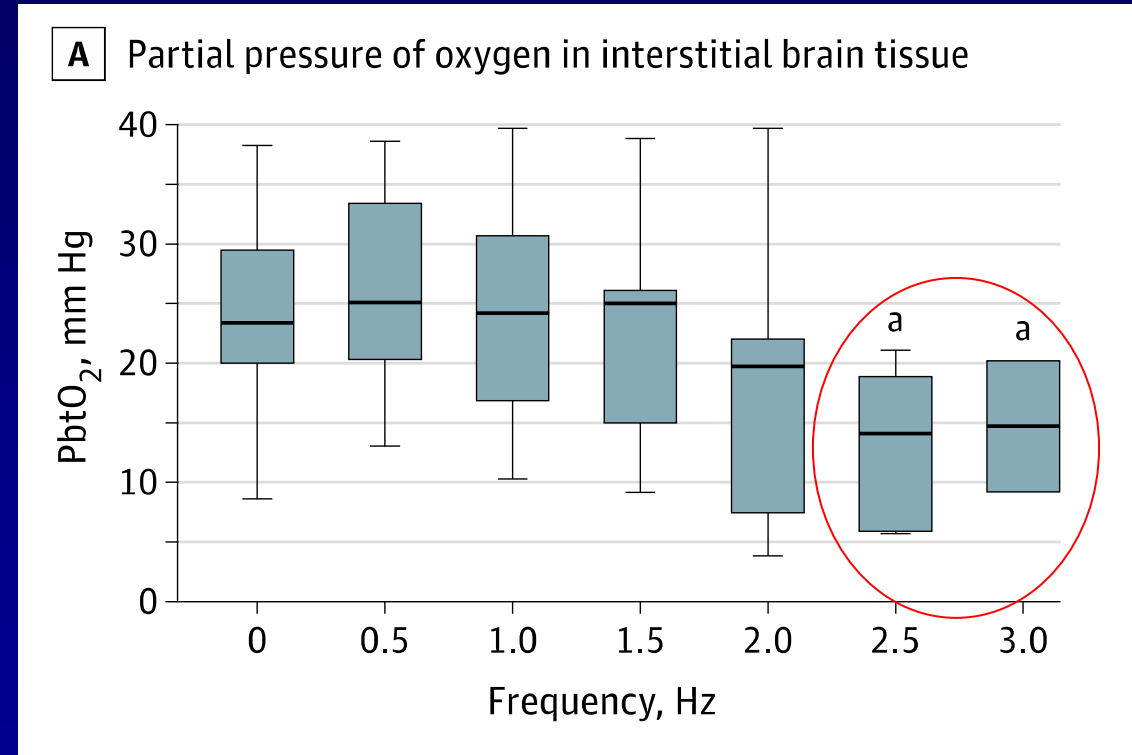
“Metabolic Crisis” Observed in Adults with Brain Trauma During Time of Seizures and Periodic Discharges



Electroencephalographic Periodic Discharges and Frequency-Dependent Brain Tissue Hypoxia in Acute Brain Injury

Jens Witsch, MD; Hans-Peter Frey, PhD; J. Michael Schmidt, PhD; Angela Velazquez, MD; Cristina M. Falo, PhD; Michael Reznik, MD; David Roh, MD; Sachin Agarwal, MD; Soojin Park, MD; E. Sander Connolly, MD; Jan Claassen, MD, PhD

- Cohort study of 90 adult patients with SAH who underwent invasive multimodality monitoring
- Increased PD frequency was associated with a stepwise increase of regional CBF, and a stepwise decrease of brain tissue oxygenation
- PDs > 2Hz demonstrated decreased brain tissue oxygenation indicative of metabolic decompensation which resembled that seen with electrographic seizures

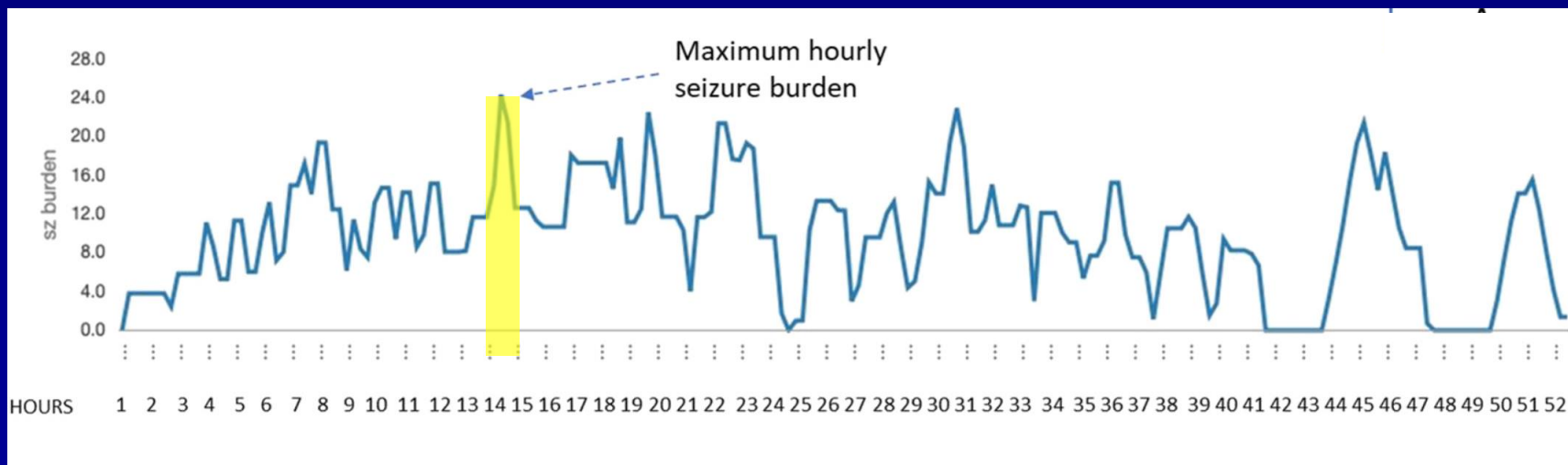


Evidence Relating Seizures to Outcome

Seizure burden is independently associated with short term outcome in critically ill children

Payne et al., *Brain* 2014; 137; 1429–1438

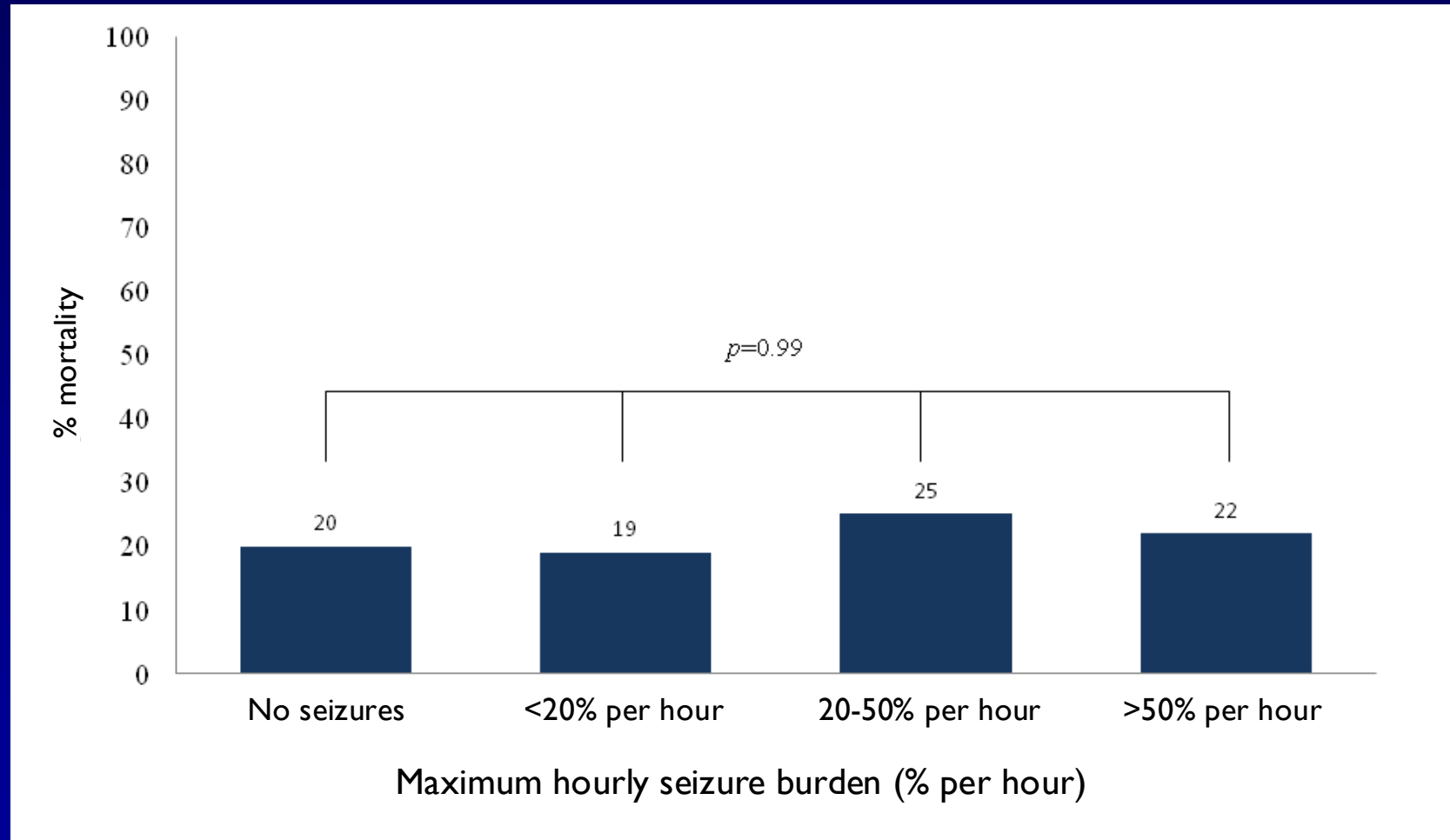
- Prospective cohort of 259 infants & children enrolled over 3 years (2009-12)
- Underwent clinical cEEG monitoring in pediatric & cardiac ICUs
- EEG analyzed to quantify each subject's **maximum hourly seizure burden**



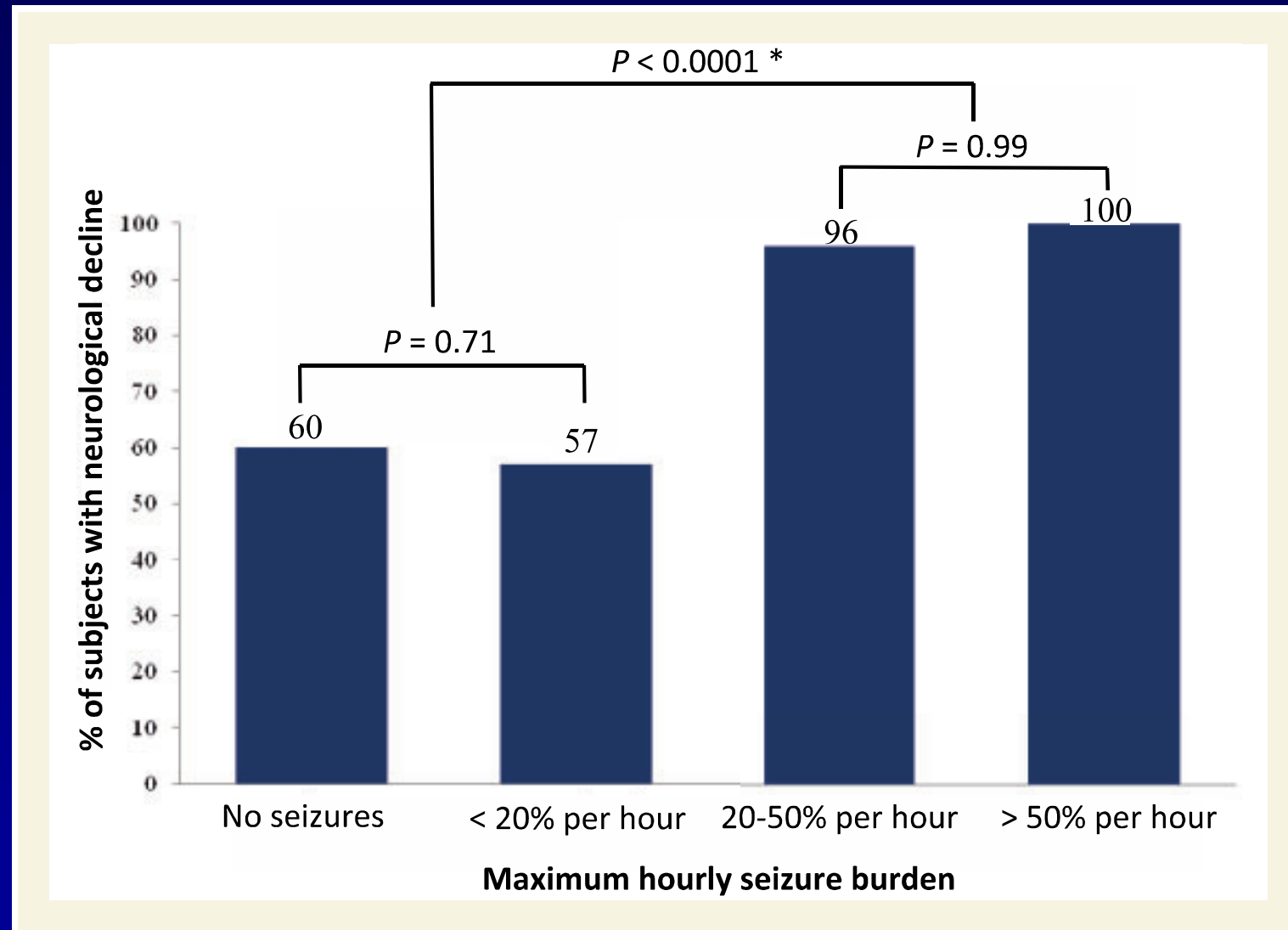
Electrographic seizures defined according to standard criteria (Chong & Hirsch 2005)

- Outcome: PCPC score at baseline compared to hospital discharge

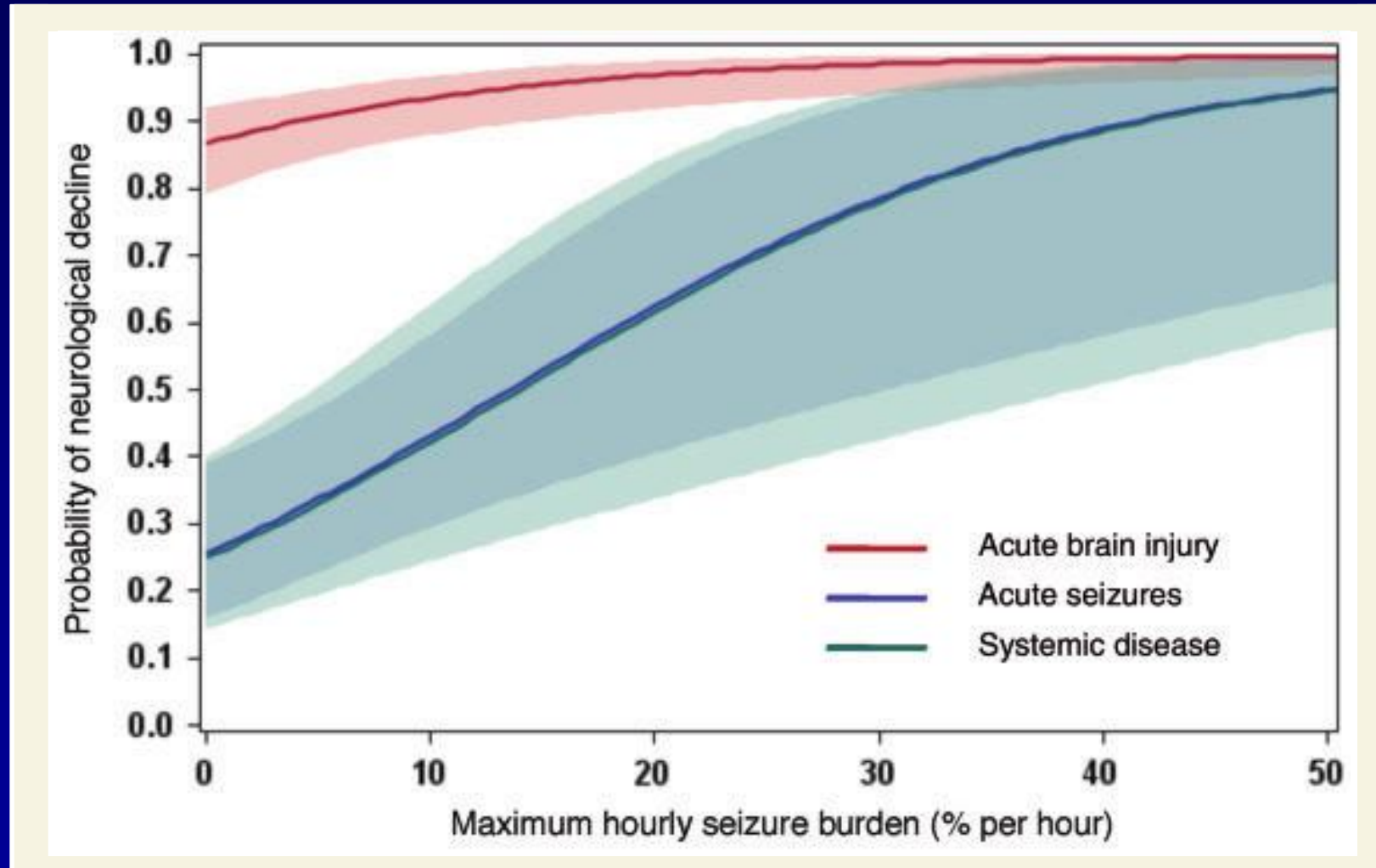
Seizure Burden was Not Associated With Mortality



Seizure Burden $\geq 20\%$ per hour (12 minutes) was associated with neurological decline



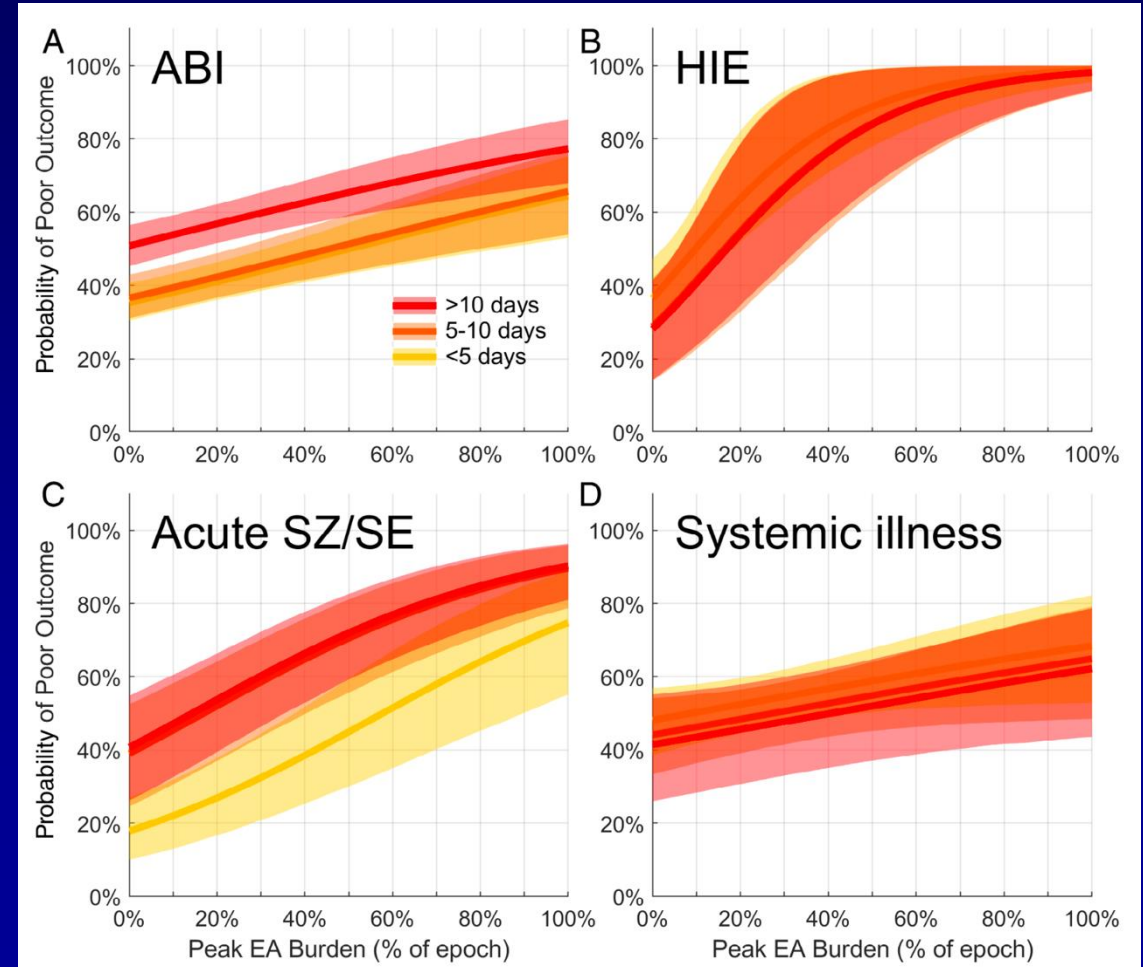
Probability of neurological decline rose with increasing seizure burden across all diagnostic categories



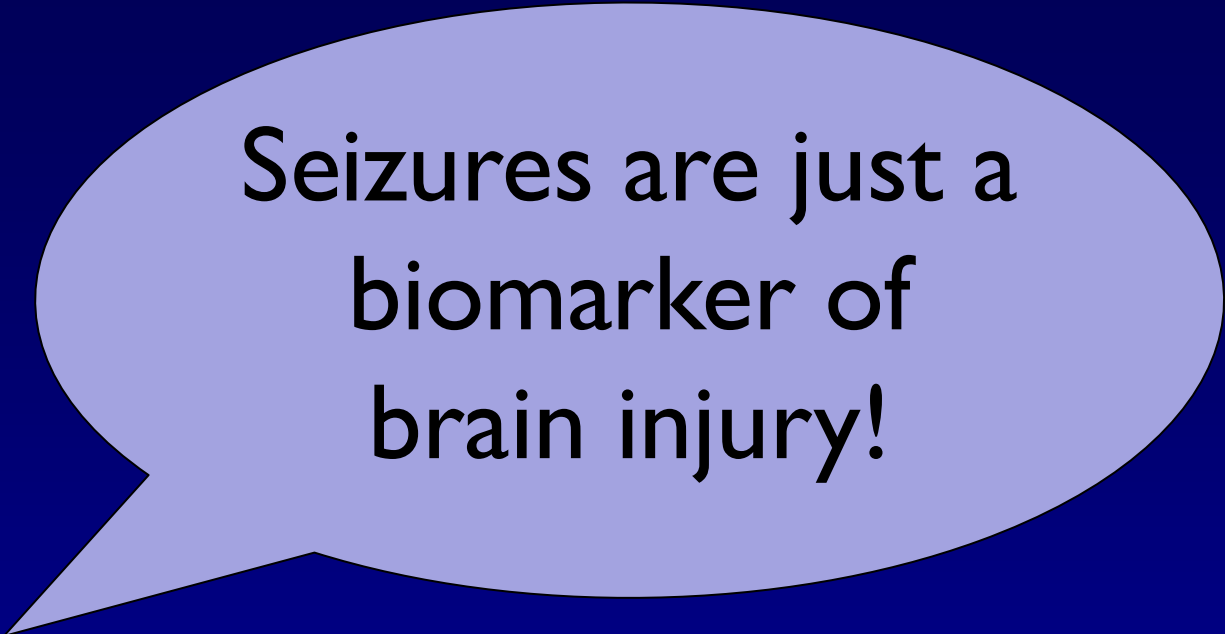
Automated Annotation of Epileptiform Burden and Its Association with Outcomes

Zafar SF et al., Ann Neurol. 2021

- 1,967 adult neurologic, medical, and surgical patients, with >16 h cEEG
- AI quantification of “epileptiform activity” (EA) burden including:
 - Seizures, LPDs, GPDs, LRDA, GRDA
- Multivariable model adjusting for age, gender, GCS, history of acute brain injury or epilepsy, cardiac arrest or seizure on presentation, and admission diagnosis
- Maximum 12-hour EA burden independently correlated with outcome: $mRS \geq 5$



stratified based on interval between the last EEG and discharge



Seizures are just a
biomarker of
brain injury!



You need to do a
Randomized
Controlled Trial!

Effect of Treatment of Subclinical Neonatal Seizures Detected With aEEG: Randomized, Controlled Trial

Van Rooij et al, Pediatrics, 2010

- 42 infants with moderate-severe HIE randomized to
 - Group A: treatment of clinical + subclinical seizures
 - Group B: treatment of clinical seizures only
- Seizures measured by amplitude-integrated EEG
 - aEEG display was concealed in group B
- Outcome: MRI injury severity at day 4-10
- Power analysis: sample size of 130 infants required

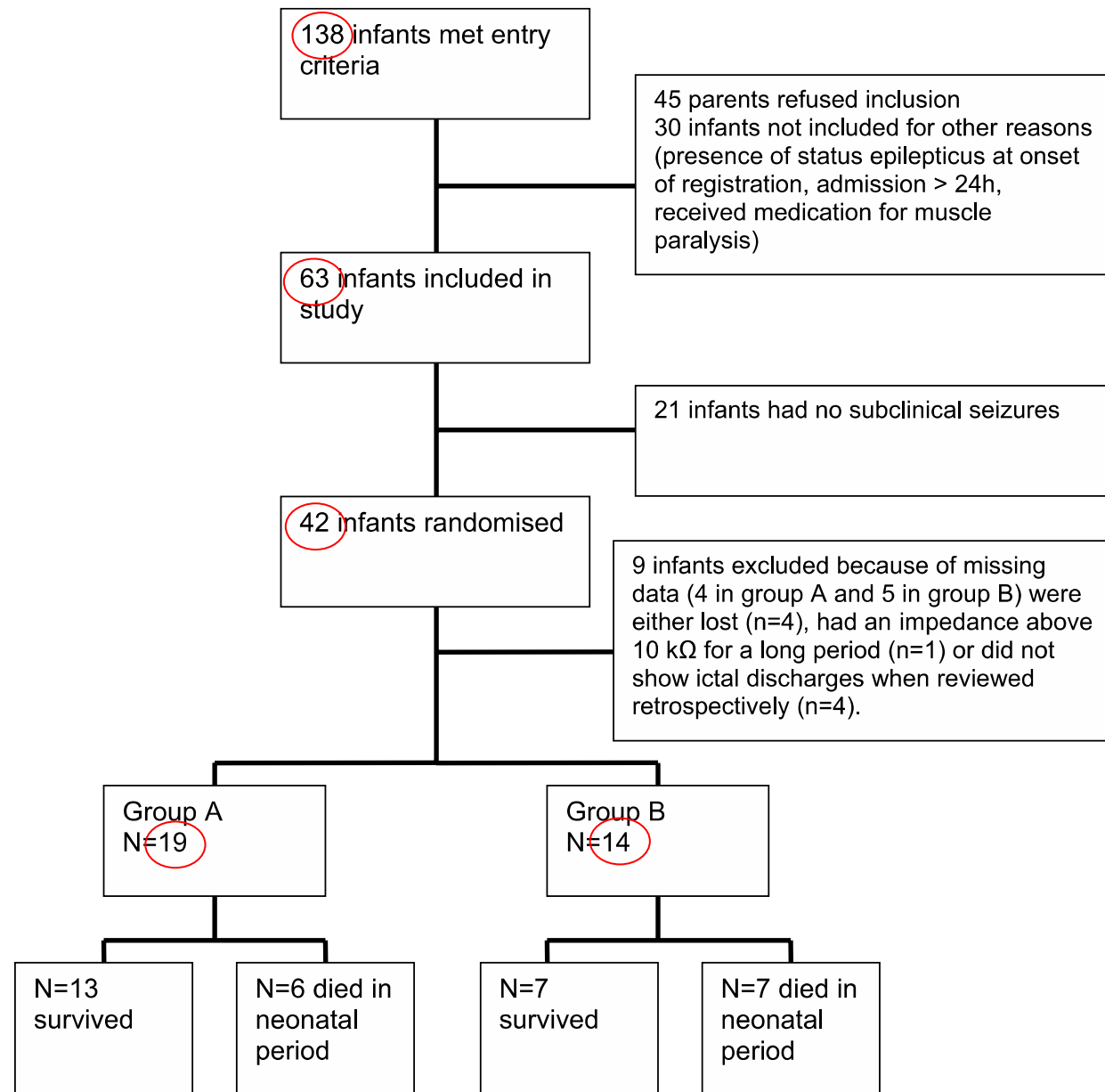
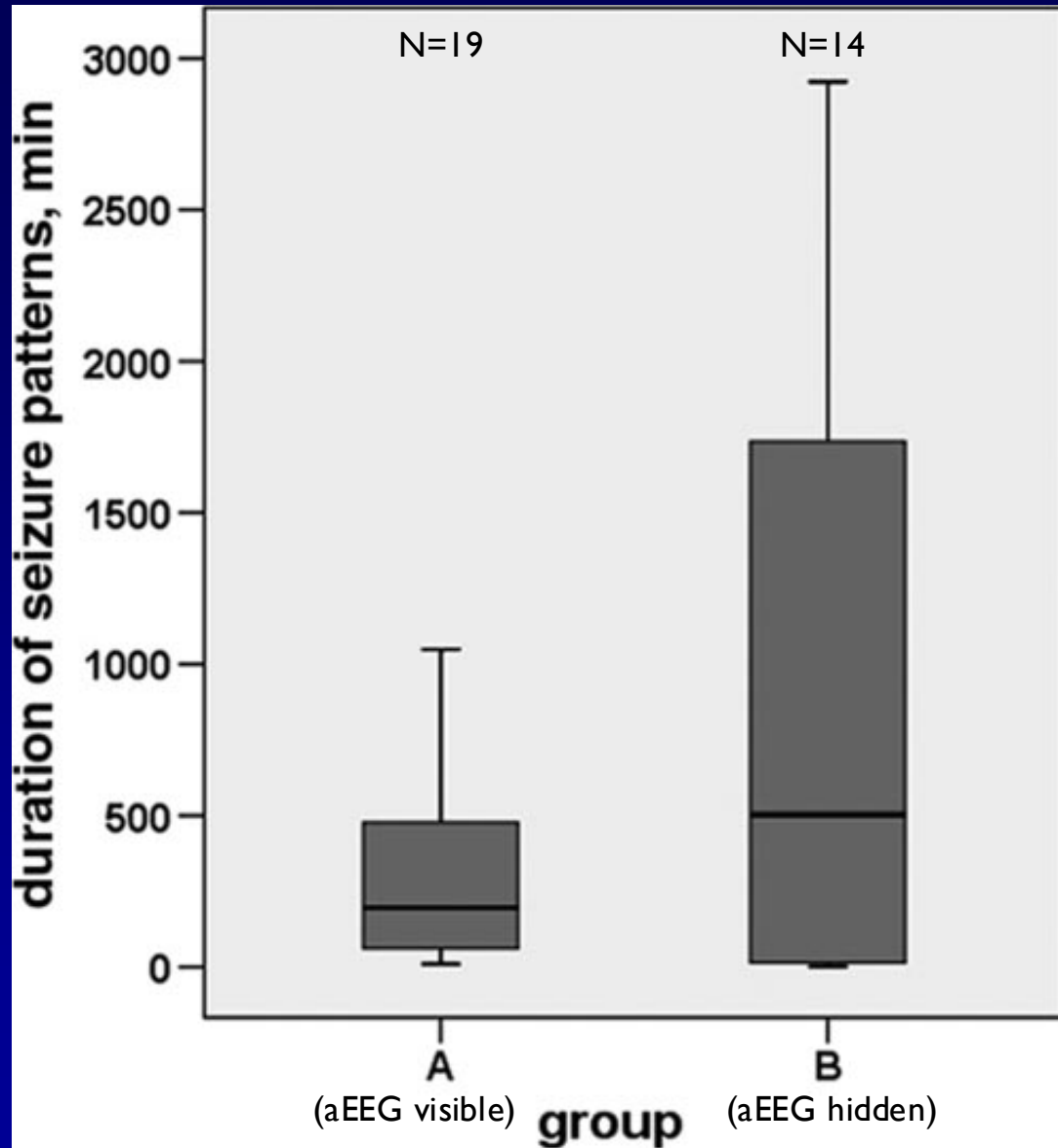


FIGURE 1
Flow diagram of inclusion.



- Trend to lower electrographic seizure duration in aEEG visible group
- Seizure burden can actually be reduced with EEG-guided therapy
- No significant difference in MRI injury severity between treatment groups
- In combined cohort, longer seizure duration was associated with worse MRI brain injury

Better Seizure Detection



Better Seizure Therapy



↓ Seizure Burden



Underpowered



Continuous vs Routine Electroencephalogram in Critically Ill Adults With Altered Consciousness and No Recent Seizure

A Multicenter Randomized Clinical Trial

Andrea C. Rossetti, MD; Kaspar Schindler, MD, PhD; Raoul Sutter, MD; Stephan Rüegg, MD; Frédéric Zubler, MD, PhD; Jani Novy, MD, PhD; Mauro Oddo, MD; Loane Warpelin-Decrausaz, PhD; Vincent Alvarez, MD

JAMA Neurol 2020

Better Seizure Detection



Better Seizure Therapy?

↓ Seizure Burden ?

- Pragmatic multicenter trial that randomized 402 patients with impaired consciousness 1:1 to **routine EEG** (2x30 min) vs. **cEEG** for 30-48 hours
- **Mortality** (49%) and CPC at 6 months did not differ between groups
- **mRS evolution** at 6 months was better in the rEEG group than the cEEG group
- Considerations
 - Excluded patients with recent seizures or status epilepticus – likely to have high seizure burden
 - When seizures were detected in routine EEG group, they could be converted to cEEG (n=5)
 - cEEG was reported at least 2-3 times per day – potential for delay to treatment
 - Seizures were detected in only 4% in rEEG group and 16% in cEEG group – underpowered
 - ASMs were modified in 21% of routine EEG group vs. 39% of cEEG group
 - Seizure burden was not reported in either the routine EEG or cEEG groups



Efficacy of delivery of care with Tele-continuous EEG in critically ill patients: a multicenter randomized controlled trial (Tele-cRCT study) study

Limotai et al. *Critical Care*, 2025

- Randomized 254 critically ill patients aged ≥ 15 years at risk for developing NCS in 8 regional hospitals across Thailand to either a cEEG (≥ 24 h) or routine EEG (30 min) with centralized remote EEG interpretation
- Enrolment challenges due to COVID-19 (desired sample size was 648 participants)
- NCS/NCSE was detected more commonly in cEEG (22%) than rEEG arm (14%)
- No between-group difference in mRS or mortality up to 12 months
- cEEG group was more likely to receive ASM / anaesthetic therapy
- Impact of cEEG on seizure burden?

Better Seizure Detection



Better Seizure Therapy



↓ Seizure Burden ?

Treating Rhythmic and Periodic EEG Patterns in Comatose Survivors of Cardiac Arrest

B.J. Ruijter, H.M. Keijzer, M.C. Tjepkema-Cloostermans, M.J. Blans, A. Beishuizen, S.C. Tromp, E. Scholten, J. Horn, A.-F. van Rootselaar, M.M. Admiraal, W.M. van den Bergh, J.-W.J. Elting, N.A. Foudraine, F.H.M. Kornips, V.H.J.M. van Kranen-Mastenbroek, R.P.W. Rouhl, E.C. Thomeer, W. Moudrous, F.A.P. Nijhuis, S.J. Booij, C.W.E. Hoedemaekers, J. Doorduyn, F.S. Taccone, J. van der Palen, M.J.A.M. van Putten, and J. Hofmeijer, for the TELSTAR Investigators*

VIEWPOINT

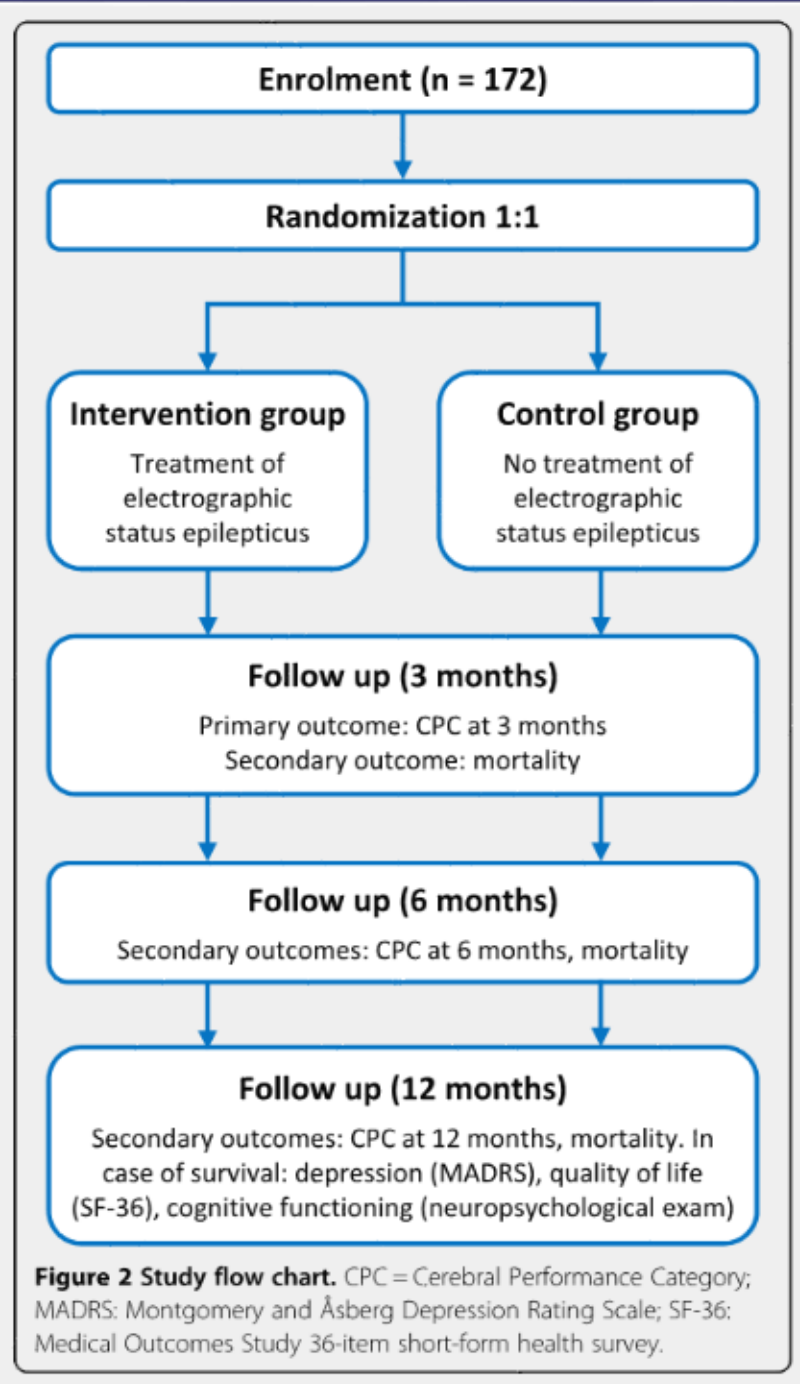
Epileptiform Electrographic Patterns After Cardiac Arrest Give Up or Treat?

Andrea O. Rossetti, MD, FAES; Sarah Benghanem, MD, PhD

JAMA Neurology Published online November 11, 2024

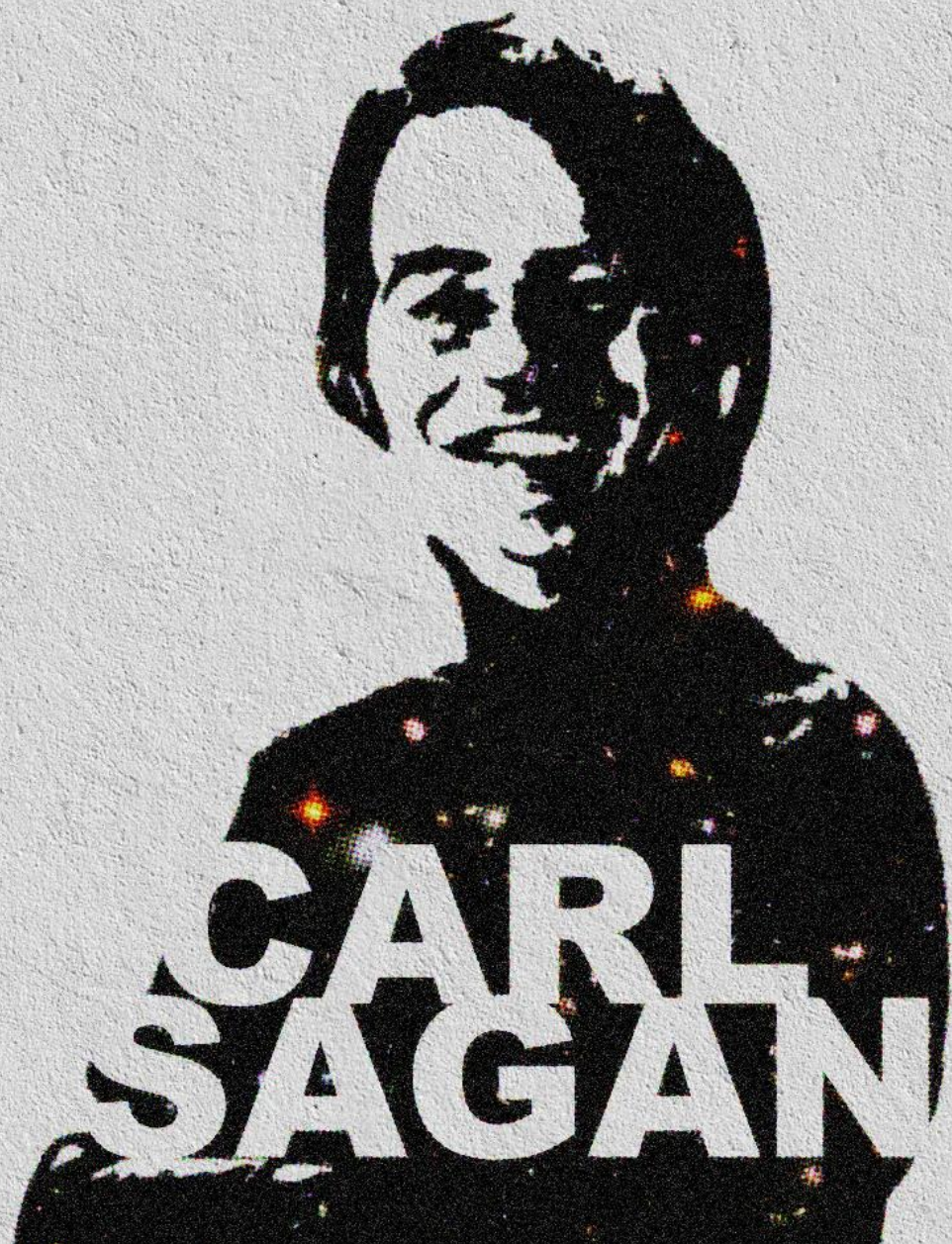
Prespecified subgroup analysis among 36 patients with electrographic seizures or evolving, rhythmic EEG patterns

- Favourable outcome seen in
 - 6/20 (30%) of patients randomized to pharmacologic treatment group
 - 0/16 patients randomized to standard care
- **TELSTAR 2** trial planned on a selected cohort of cardiac arrest patients with electrographic seizures and less malignant EEG background patterns



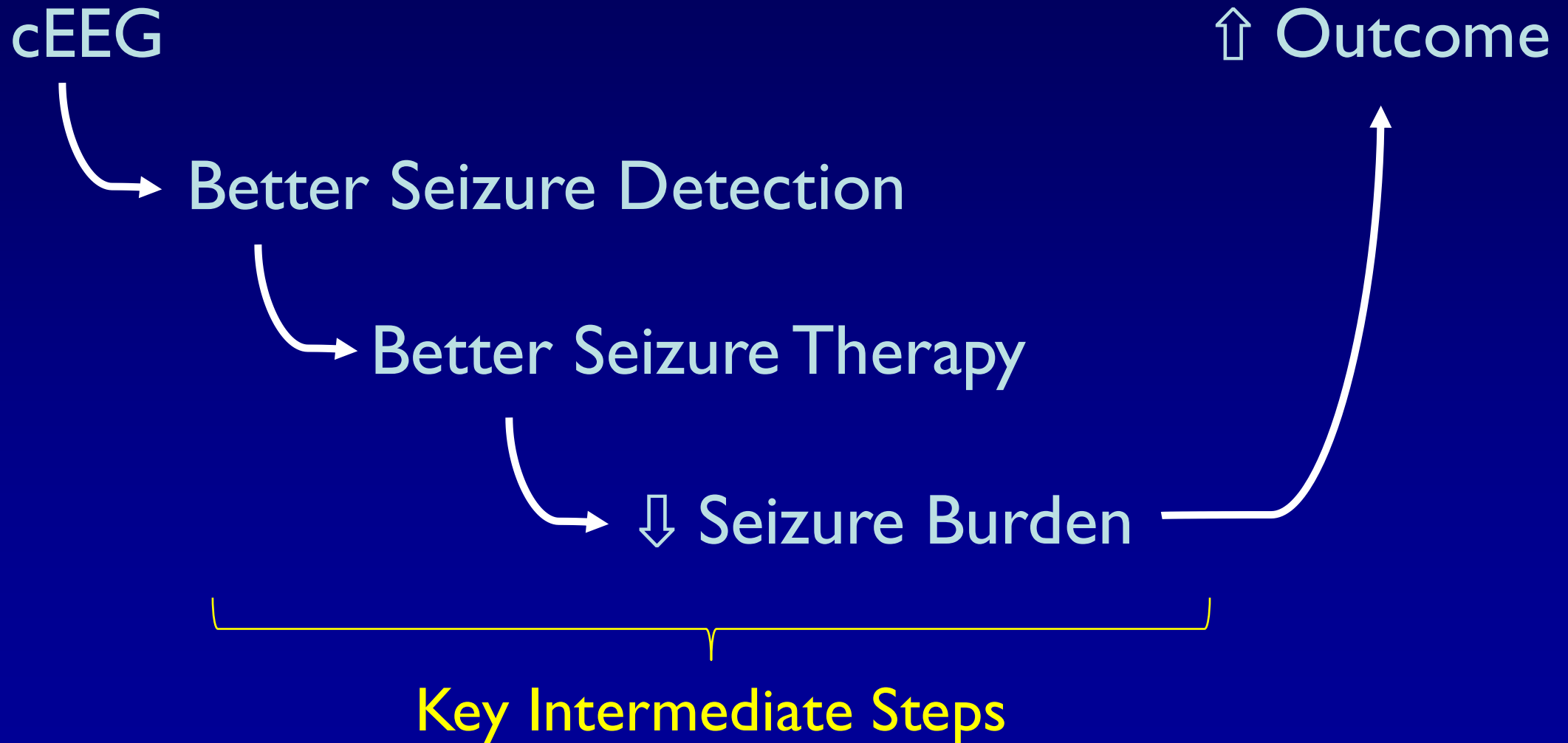
So, where does that leave us?

**ABSENCE
OF
EVIDENCE
IS NOT
EVIDENCE
OF
ABSENCE**

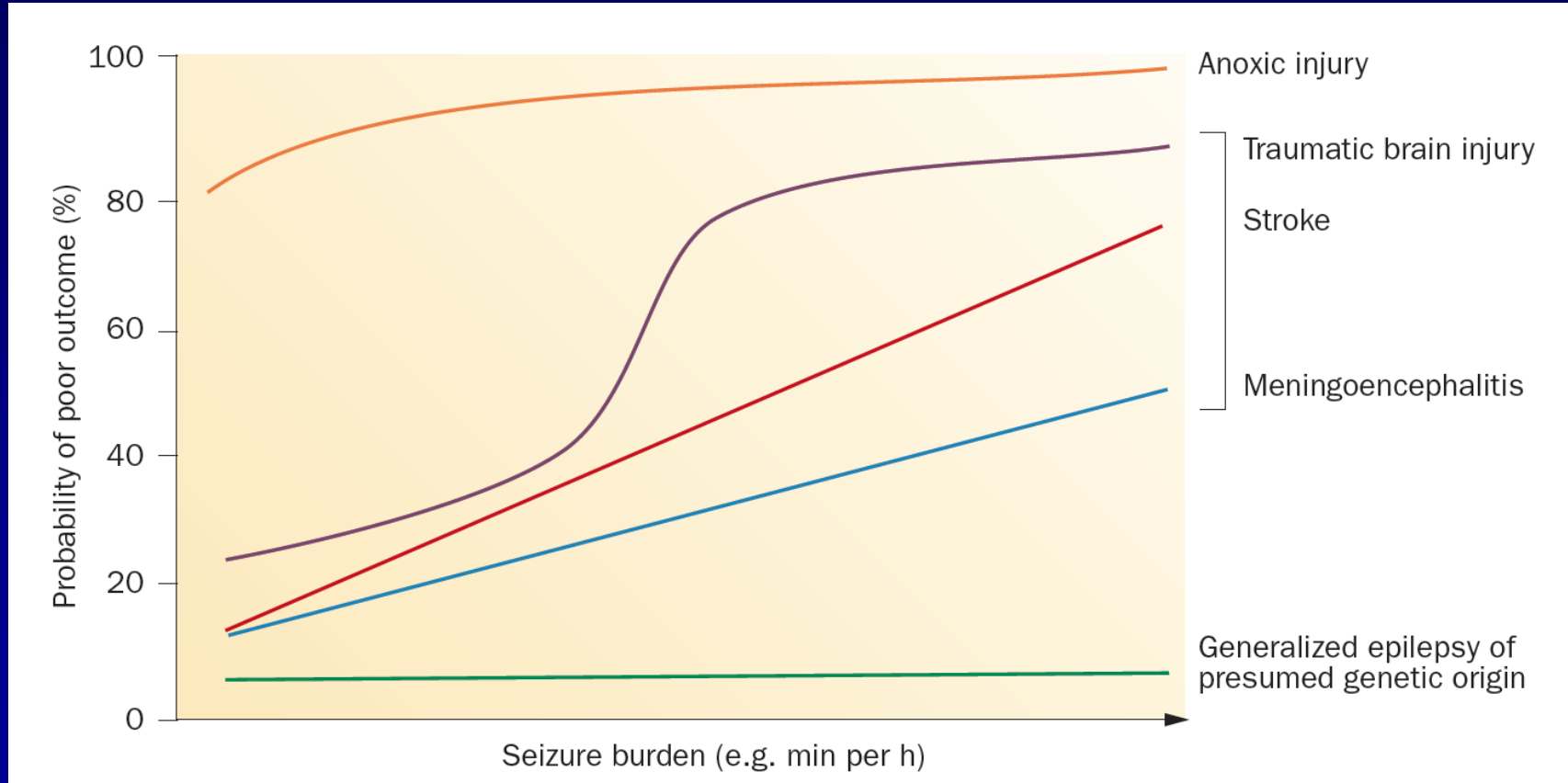


**CARL
SAGAN**

cEEG is Necessary but Not Sufficient



Potential Deleterious Effects of Seizures Likely Depend on Underlying Etiology



Summary

- Seizures are common in critically ill patients with acute encephalopathy
- Most seizures are subclinical
- Association between seizure burden and outcome is consistent
 - Even after adjusting for etiology, illness severity, ASM exposure
- But causal link between seizure burden and outcome has not been established
- cEEG monitoring is required for optimal management of seizures in the ICU
- cEEG monitoring is not sufficient to improve outcomes – needs to be coupled to improvements in seizure management
- Question remains which patients may benefit from improved seizure detection and successful reduction in seizure burden in order to improve their outcomes

