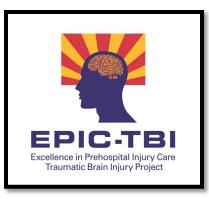
The Synergistic Effect of Prehospital Hypotension and Hypoxia in Major Traumatic Brain Injury: Profound Impact on Mortality

#### Daniel Spaite, MD Professor and Distinguished Chair of Emergency Medicine

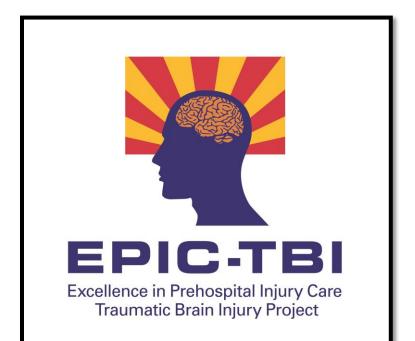






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#### Disclosure

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#### Hypotension *dramatically* increases mortality in TBI

- Chesnut RM, et al. J Trauma 1993;34:216-22.
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- Levin HS, et al. Neurosurgery 1992;31:435-43.

- Hypotension occurs *frequently* during prehospital and early in-hospital care
  - Chesnut RM, et al. J Trauma 1993;34:216-22.
  - Shutter LA, et al. Ann Emerg Med. 2008;51:S37-S8.
  - Fearnside MR, et al. Br J Neurosurg 1993;7:267-79.

#### Hypoxia dramatically increases mortality

- Chesnut, et al. J Trauma 1993;34:216-22.
- Gentleman, et al. Int Surg 1992;77:297-302.
- Silverston P. BMJ 1989;298:711-3.
- Mayer, et al. Ann Emerg Med 1985;14:1178-84.
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- Stocchetti, et al. J Trauma 1996;40:764-7.
- Fearnside, et al. Br J Neurosurg 1993;7:267-79.
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- Marmarou, et al. J Neurosurg 1991;75:S59-S66.

- Even a single hypoxic measurement dramatically increases mortality
  - Chesnut, et al. J Trauma 1993;34:216-22.
  - Jones, et al. J Neurosurg Anesthesiol 1994;6:4-14.
  - Marmarou, et al. J Neurosurg 1991;75:S59-S66.

- Hypoxia occurs *frequently* during prehospital TBI care
  - Davis DP, et al. Crit Care Med 2006;34:1202-8
  - Davis DP, et al. Prehosp Emerg Care 2007;11:1-8.
  - Stocchetti N, et al. J Trauma 1996;40:764-7.
  - Cooke RS, et al. 1995;26:395-7.
  - Davis DP, et al. J Trauma 2004;57:1-8
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- Little is known about any potential interactions between hypotension and hypoxia and their influence on outcomes
- Reasons:
  - Few studies have been large enough to evaluate the subset of patients with *both* hypotension and hypoxia
  - The approaches to management of BP and oxygenation are clinically distinct



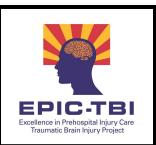
### Objective

- Among patients with major TBI cared for in a statewide trauma system:
  - To evaluate the associations between mortality and *prehospital* hypotension or hypoxia separately
  - To assess whether a hypotension/hypoxia synergistic effect exists



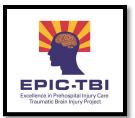
### Methods

- System setting:
  - State of Arizona
  - Over 250 Fire Departments and EMS agencies
  - Eight level 1/2 TCs
- Study setting:
  - The pre-implementation cohort of the EPIC Study:
    - Evaluation of the impact of statewide implementation of the national EMS TBI Guidelines



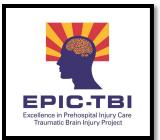
#### Methods: Data Source

- The Arizona State Trauma Registry (ASTR):
  Contains EMS and TC data on all patients taken to a Level 1/2 TCs statewide
- Data are abstracted at each TC and entered into the ASTR



#### Methods

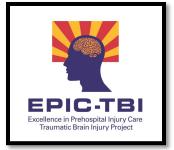
- Inclusion:
  - Four years (2008-2011)
  - All ages
  - Moderate or severe TBI:
    - CDC Barell Matrix Type 1
    - AIS-Head ≥3
- Exclusions:
  - Transfers
  - Missing EMS saturation or BP Data
- Primary Outcome: Hospital Mortality



#### Definitions

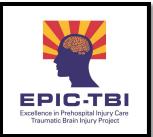
#### Hypotension:

- Age ≥10: SBP <90
- Age <10: BP <[70 + (age X 2])
- ▶ Hypoxia: O<sub>2</sub> saturation <90%



#### **Methods: Analysis**

- Logistic regression to identify associations between hypotension, hypoxia, and mortality
- Also tested for effect modification (a nonadditive relationship) between hypotension and hypoxia for mortality by including an interaction term in the final models

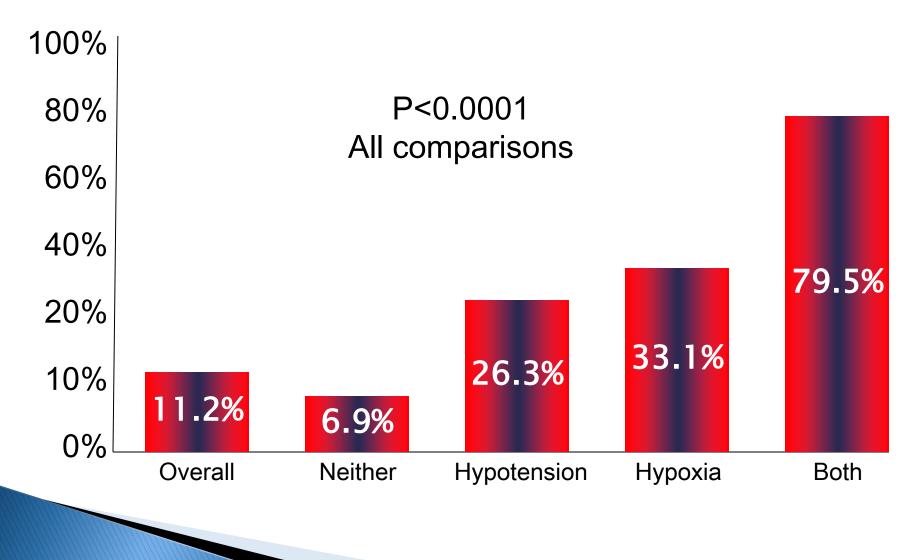


#### Results

- 9,817 cases meeting inclusion criteria,
  - 24.5% excluded for missing sat/BP data
- 7,409 cases (study group)
- Median age: 41 (IQR: 23, 58)
- 70.0% male
- Cohorts (incidence in study group):
  - Neither: 87.8%
  - Hypotension-only: 3.5%
  - Hypoxia-only: 5.8%
  - Both: 3.0%



### **Mortality by Cohort**

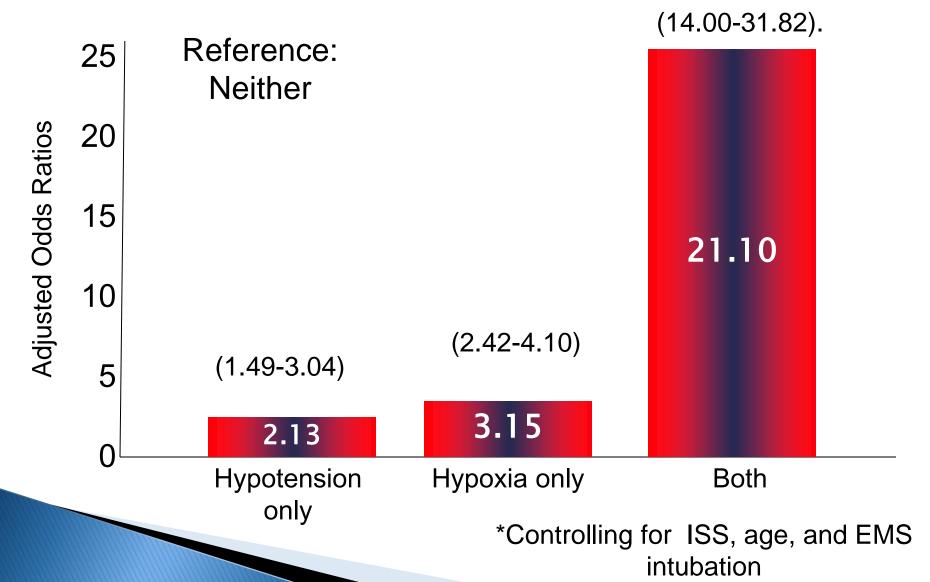


#### Results

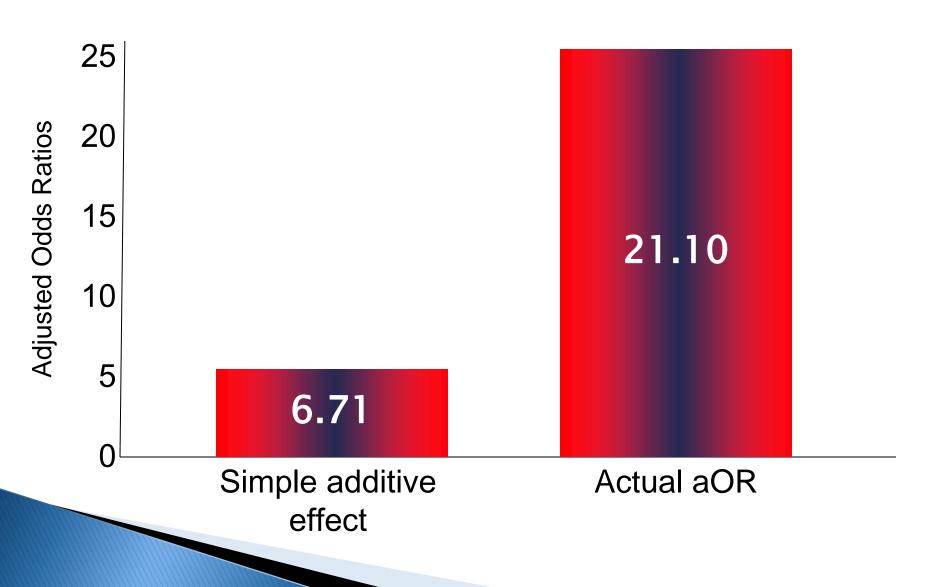
 Controlling for injury severity, age, and EMS intubation, the interaction effect ("synergy") between hypotension and hypoxia was highly significant.
 P <0.0001</li>



#### **Risk of Death: Logistic Regression**



#### **Interaction Effect**



#### Limitations

- Retrospective
- Missing prehospital sat/BP in 24.5% of cases
  - Selection bias
  - Performing Multiple Imputation for the paper
  - As EPIC matures:
    - The EMS data capture will approach 100%
    - The study will include nearly 12,000 prospective patients



### Conclusions

- In this statewide, multi-system analysis of over 7000 TBI cases:
  - 12.3% of cases had either hypotension, hypoxia, or both
  - Prehospital H/H were strongly and independently associated with mortality even after controlling for injury severity, age, and prehospital intubation.



#### Conclusions

- The aOR for *both* hypotension/hypoxia vs. *neither* is 3.1 times greater than it would be assuming a simple additive effect.
- The magnitude of this interaction effect infers a profoundly detrimental synergy between hypotension and hypoxia in causing death.



### Conclusions

Since the EMS TBI Guidelines focus on the prevention and aggressive treatment of hypotension and hypoxia, implementation of the Guidelines may significantly improve mortality in victims of major Traumatic Brain Injury.



#### Special thanks to the EPIC Partners Arizona Fire Departments and EMS Agencies



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#### Upcoming Events

 Traumatic Brain Injury (EPIC) Rollout Session Mon, 01/30/2012



#### Excellence in Prehospital Injury Care (EPIC)

#### Why is the EPIC Project important?

Each year, an estimated 1.7 million people sustain a TBI annually. Of them:

#### ° 52,000 die,

- 275,000 are hospitalized, and
- <sup>o</sup> 1.365 million, nearly 80%, are treated and released from an emergency department.

TBI is a contributing factor to a third (30.5%) of all injury-related deaths in the United States.<sup>1</sup>

There is growing evidence that the management of TBI in the early minutes after injury profoundly impacts outcome. EMS operates in the ultra-acute setting, usually providing the first care for TBI victims when treatment matters the most. Reports on implementation of evidence-based TBI treatment guidelines inside the hospital are very promising. However, no studies to date have evaluated their impact in the prehospital setting.

The EMS agencies of Arizona have already proven their ability to dramatically improve cardiac arrest survival and, thus, Arizona was selected by the National Institutes of Health to do the same with TBI.



#### Cohorts

#### Four cohorts:

- Neither hypoxia nor hypotension
- Hypoxia-only
- Hypotension-only
- Both hypoxia and hypotension



# **Results: Mortality (keeping graph in case want it for the paper/figures)**

COHORT	%	p-value
Overall	11.2	
Neither	6.9	< 0.001
Hypotension	26.3	< 0.001
Hypoxia	33.1	< 0.001
Both	79.5	< 0.001

