Supplementary Online Content

Bennett TD, DeWitt PE, Greene TH, et al. Functional outcome after intracranial pressure monitoring for children with severe traumatic brain injury. *JAMA Pediatr.* Published online August 28, 2017. doi:10.1001/jamapediatrics.2017.2127

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Methods

Data Sources and Probabilistic Linkage

PHIS

PHIS is a benchmarking and quality improvement database containing inpatient data from 44 U.S. children's hospitals with more than 500,000 discharges per year.[1] PHIS contains administrative data, diagnoses, and procedures as well as utilization information for pharmacy, imaging, laboratory, supply, nursing, and therapy services. These utilization data are coded using Clinical Transaction Classification (CTC) codes[2] and are grouped into 24-hour periods (days of service). PHIS data are only available to approved researchers at member hospitals. PHIS data are subjected to 175 reliability and validity checks and are accepted into the database when classified errors occur in <2% of a hospital's quarterly data.[3] Systematic data quality monitoring includes bimonthly coding consensus meetings, coding consistency reviews, and quarterly data quality reports.[4]

NTDB

The NTDB contains standardized trauma registry data from more than 3 million admissions at 900 trauma centers in the United States.[5] The NTDB contains no protected health information (PHI). The NTDB has a continuous data quality improvement process.[5]

Dataset Linkage

Briefly, we applied Markov chain Monte Carlo-augmented probabilistic linkage to records of injured children (< 18 years old at admission) in the NTDB and PHIS databases. We validated the accuracy of the linkage using identified data from a single center that submits to both databases. The linkage method is accurate for the patients in the current study: sensitivity 88%, positive predictive value (PPV) 98%, and specificity 99.99%.[6] In the context of the current dataset containing approximately 3,000 patients, a PPV of 98% suggests that as many as 60 patients might be false positive links. This is a limitation of the current dataset. False negatives in the validation linkage were found to be primarly patients who had short hospital stays (<72 hours) and were discharged home without new home care supports.[6] The original linkage was 2007-2010, and the same methods were applied to data from 2011-2012 to create the 2007-2012 cohort for this study.

Covariate Definitions

We coded the presence of "medical" complications such as cardiac arrest and seizures[7] using ICD-9-CM diagnosis codes from the PHIS file (eTable 1). For injury mechanism, injury type, and specific injury diagnoses including abuse/assault[9,10], we used ICD-9-CM diagnosis codes from the NTDB file. We categorized injury mechanism using the external cause-of-injury matrix created by the CDC (with ICD-9-CM diagnosis code 995.5 added to the child abuse/assault category) and injury type using the Barell matrix.[11,12] Injury severity score (ISS) and abbreviated injury scale (AIS) scores were generated by trauma registrars at each site (these are available in the NTDB). We defined specific intracranial hemorrhage types using the "predot" AIS codes.[13] We defined hypotension using standard Pediatric Advanced Life Support criteria based on the pre-hospital and ED vital signs present in the NTDB.[14] Drugs were identified using Clinical Transaction Classification (CTC) codes from the PHIS database.

Post hoc Subgroup Analyses

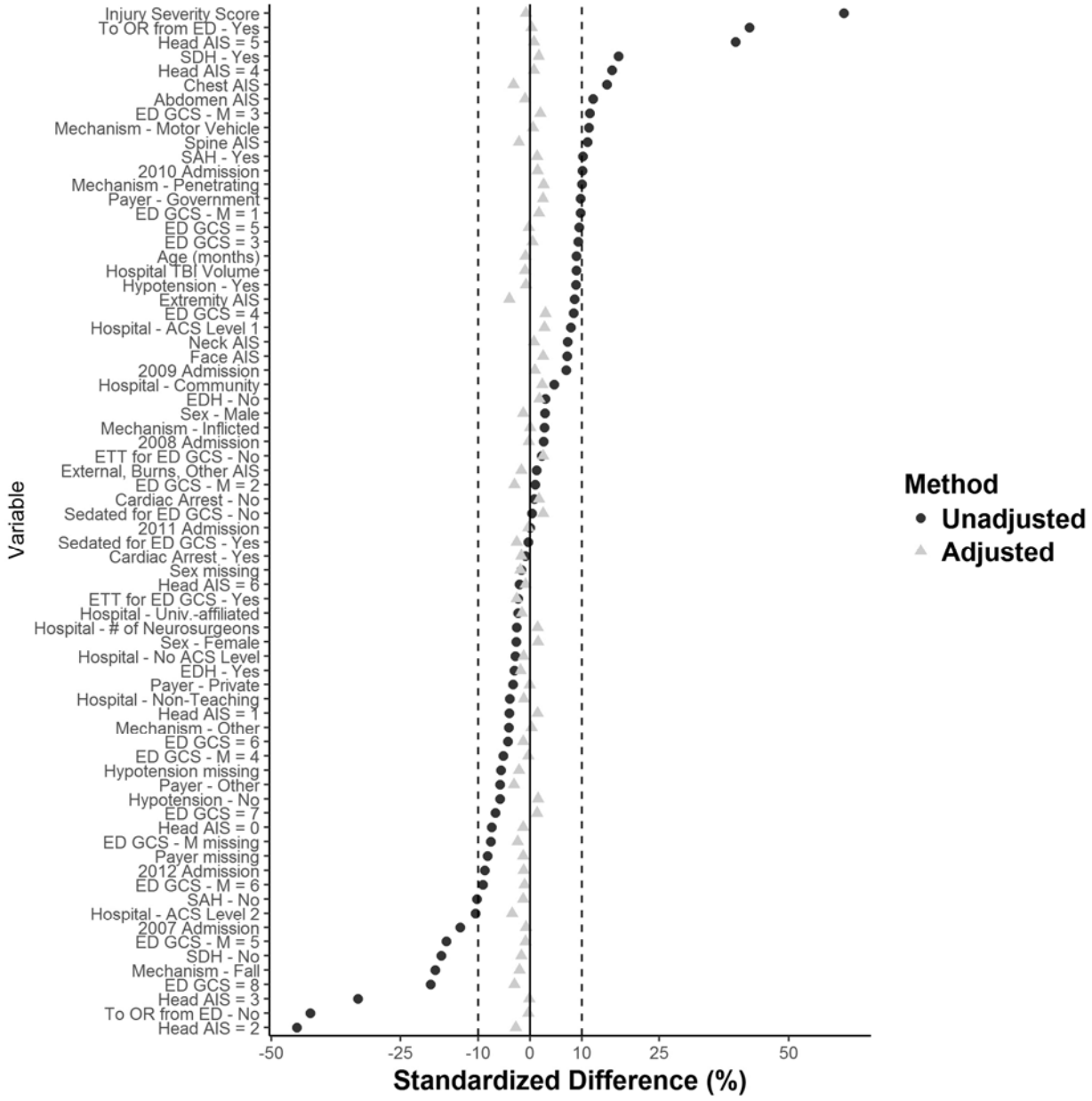
When we restricted the cohort to subjects with head AIS scores 3-5, we found that ICP monitoring was associated with worse functional survival: odds ratio 1.36 (95% CI 1.01-1.85). When we used an exposure period of 48 instead of 24 hours and restricted the cohort to those with a length of stay of at least 48 days, we also found ICP monitoring was associated with worse functional survival: OR 1.46 (95% CI 1.04-2.06). These analyses were otherwise identical to the primary analysis.

Sensitivity Analyses

We evaluated the likelihood of unmeasured confounding using the approach established by VanderWeele.[15] To do so, we considered an unmeasured confounder such as a binary variable where U = 1 represented that a patient's GCS

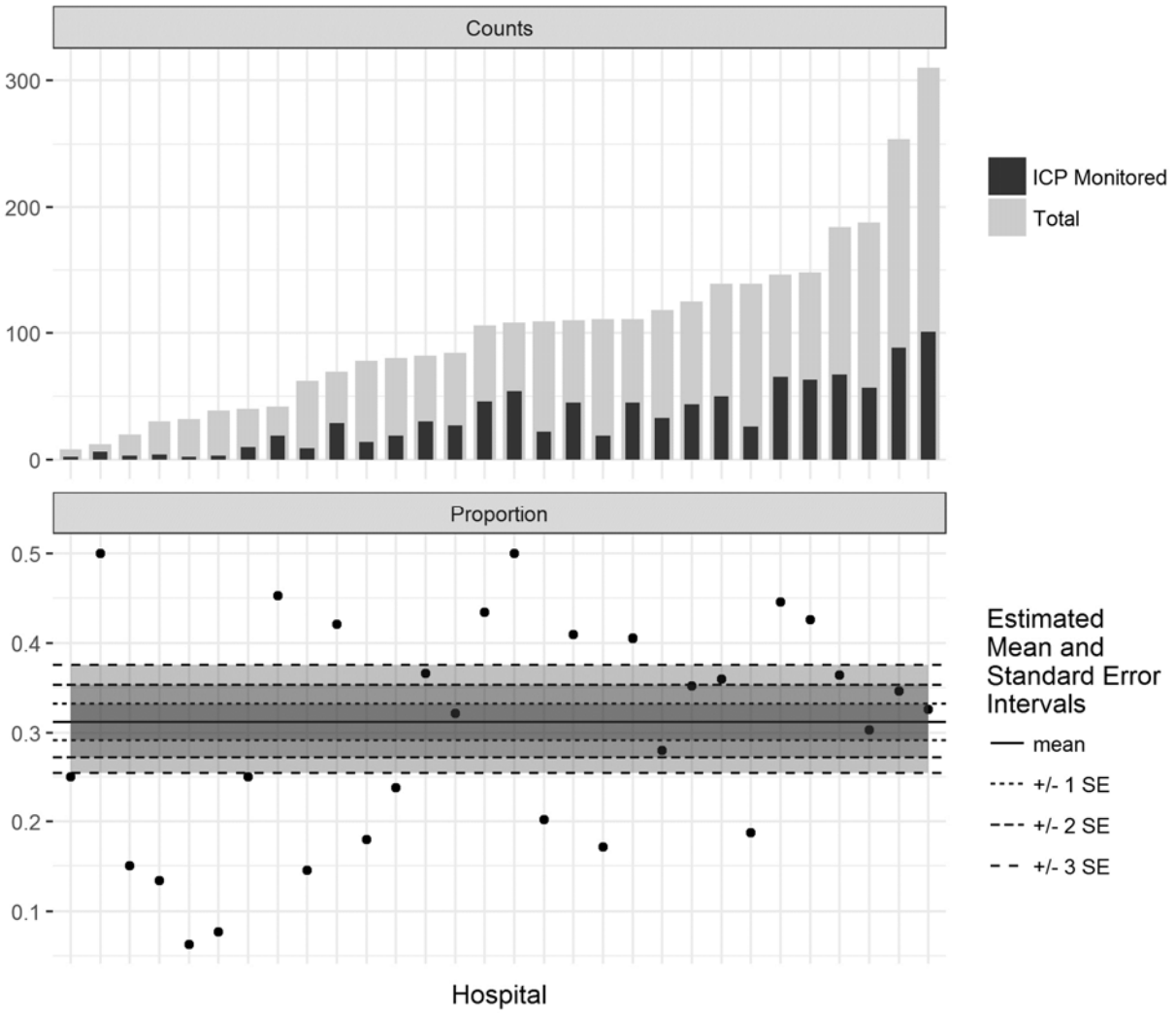
score did not improve to a certain level after all sedatives were metabolized. U = 0 would represent that a patient's GCS did improve to that level when off of sedation. The unmeasured confounder could also be a composite of neurologic exam findings. We then estimated the effect of such an unmeasured confounder across ranges of probabilities of a) bad outcome given ICP monitor placement with U = 1, b) bad outcome given ICP monitor placement with U = 0, c) U = 1 given ICP monitor placement and a matrix of covariates, and d) U = 1 given no ICP monitor placement and a matrix of covariates. See eFigure 4.

eFigure 1. Standardized Differences for Propensity Model Covariates, Before and After Propensity Weighting



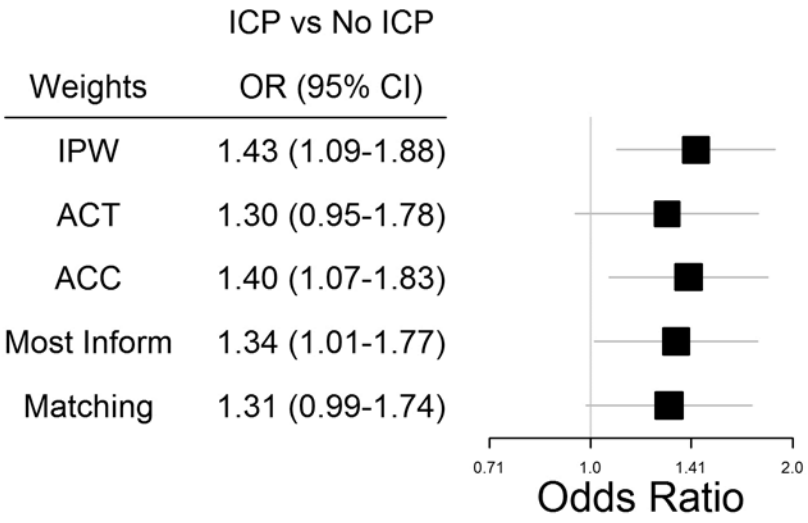
eFigure 1 Legend: All standardized differences are < 10% after propensity weighting.

eFigure 2. ICP Monitoring Rates by Hospital



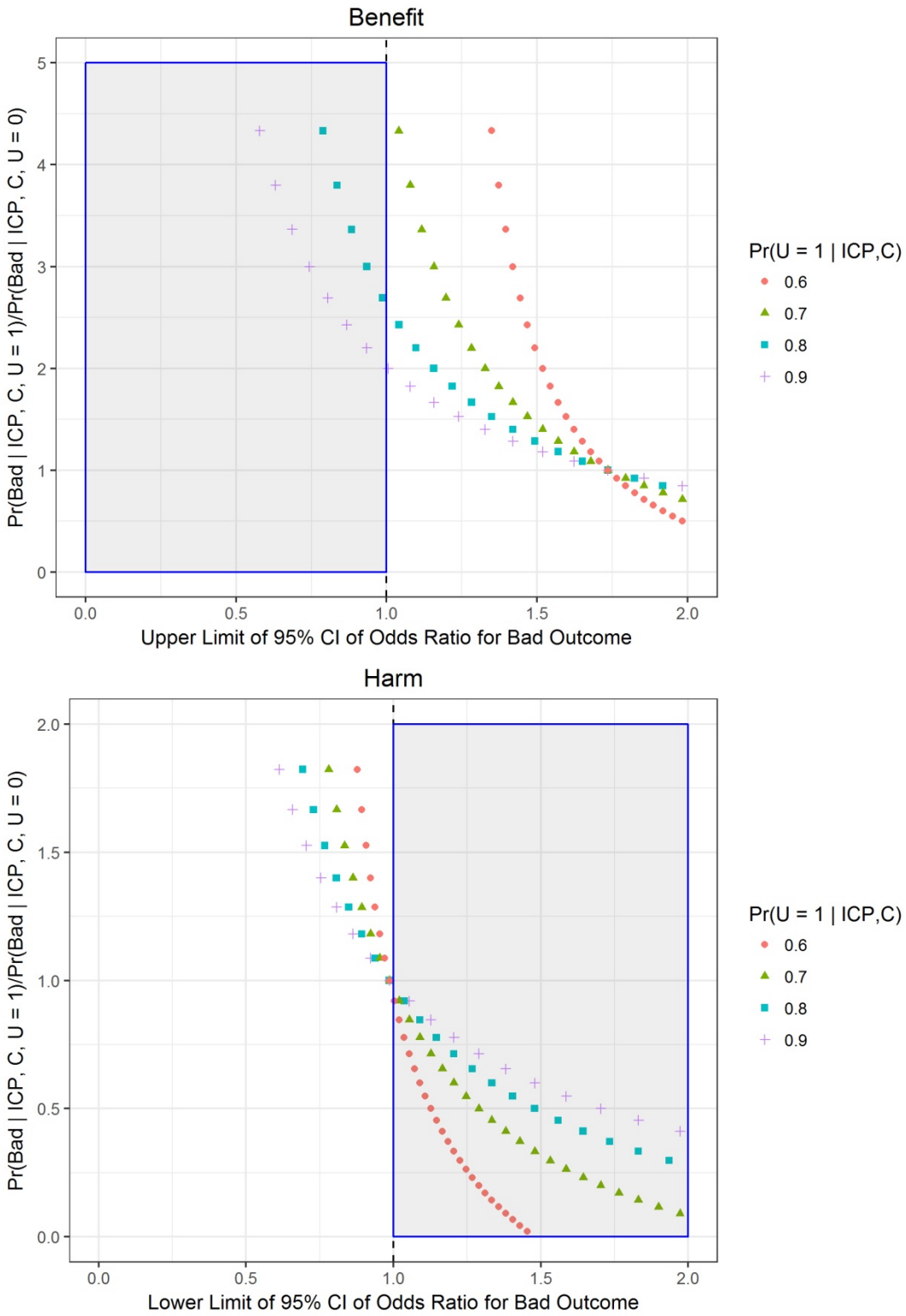
eFigure 2 Legend: ICP = intracranial pressure; SE = standard error. The upper panel shows raw counts of patients and patients with ICP monitoring by hospital. The lower panel shows the proportion of patients at each hospital who received ICP monitoring. The mean shown is the proportion of patients in the entire cohort who received ICP monitoring. A generalized estimating equations model with a binary outcome (ICP monitor yes/no), exchangeable correlation structure, and clustering by hospital was used to generate the standard errors shown.

eFigure 3. Choice of Matching Weights Did Not Affect Primary Analysis



eFigure 3 Legend: ICP = intracranial pressure; OR = odds ratio; IPW = inverse probability weighting; ACT = absolute causal effect in the treated; ACC = absolute causal effect in the control; "Most Inform" = Causal effect in the population for which the study sample is most informative. An OR > 1 reflects worse outcomes with ICP monitoring.

eFigure 4. Sensitivity Analyses for Robustness to Unmeasured Confounding



eFigure 4 Legend: Pr = probability; ICP = intracranial pressure; C = a subject's vector of covariates; "Bad" = Bad (Primary) Outcome; U = Unmeasured binary confounder (see text); CI = confidence interval; In the upper panel, points to the left of the vertical

dashed line represent scenarios consistent with a statistically significant benefit associated with ICP monitoring. In the lower panel, points to the right of the vertical dashed line represent scenarios consistent with a statistically significant harm associated with ICP monitoring. See text and eMethods for details.

eTable 1. Variable Definitions

Diagnosis	PHIS ICD-9-CM codes		NTDB ICD-9-CM codes		CTC codes
Seizure	345.x, 780.3, 780.33, or 780.39				
Cardiac arrest	427.5x				
Abuse/Assault			E960.0, E961-E968, 995.50, 995.54, 995.55, or 995.59		
Procedure					
ICP monitoring	01.10, 01.31, or 02.21	OR	01.10, 01.31, or 02.21	OR	255551
Craniotomy or Craniectomy	01.24, 01.25, 01.31, 01.59, 02.11, or 02.12				
New Gastrostomy Tube	43.11 or 43.19		43.11 or 43.19		
New Tracheostomy			31.29 or 31.1x		
Injury	**predot AIS codes**				
EDH	140630, 140632, 140634, or 140636				
SAH	140684				
SDH	140650, 140652, 140654, or 140656				

PHIS = Pediatric Health Information Systems. ICD-9-CM = International Classification of Diseases, 9th revision, Clinical Modification. NTDB = National Trauma Data Bank. CTC = Clinical Transaction Classification. AIS = Abbreviated Injury Scale. EDH = Epidural hematoma. SAH = Subarachnoid hemorrhage. SDH = Subdural hematoma.

eTable 2. Propensity Model Covariates

Demographics/Events	Injuries/Exam	Hospital
Age	ISS	ACS level
Gender	9 AIS scores	Teaching
Insurance	EDH	Number of neurosurgeons
Admission Year	ED GCS	Volume
Mechanism	ED GCS-Motor	
EMS or ED Hypotension	ED GCS (sedated)	
Cardiac Arrest	ED GCS (ETT)	
to OR from ED		

ISS = injury severity score; ACS = American College of Surgeons; AIS = worst abbreviated injury scale scores for each of 9 body regions; EDH = epidural hematoma; EMS = Emergency Medical Services: pre-hospital care; ED = Emergency Department; GCS = Glasgow Coma Scale; sedated = sedated at time of ED GCS assessment; ETT = intubated at time of ED GCS assessment. OR = operating room.

eTable 3. Demographic and Hospital Characteristics

Variable, n (%) unless shown	No ICP, n = 2,082	ICP, n = 1,002	SMD (%)
Demographics			
Age (months), median (IQR)	81 (27, 147)	90 (32, 156)	8.76
Female	768 (37)	360 (36)	2.52
Admission Year			17.66
2007	284 (14)	98 (10)	
2008	396 (19)	198 (20)	
2009	343 (16)	188 (19)	
2010	339 (16)	202 (20)	
2011	323 (16)	159 (16)	
2012	397 (19)	157 (16)	
Insurance Status			10.60
Government	1,035 (50)	539 (54)	
Private Insurance	697 (33)	325 (32)	
Other	261 (13)	109 (11)	
Missing	89 (4)	29 (3)	
Hospital ACS Certification			11.89
None	695 (33)	317 (32)	
Level 1	1,238 (59)	638 (64)	
Level 2	149 (7)	47 (5)	
Hospital Volume			8.94
0 - 10 per year	174 (8)	49 (5)	
11 - 20 per year	836 (40)	392 (39)	
21 - 30 per year	449 (22)	248 (25)	
> 30 per year	623 (30)	313 (31)	
Hospital Neurosurgeons			2.24
0 - 3	817 (39)	415 (41)	
4 - 5	1,157 (56)	562 (56)	
6 - 10	108 (5)	25 (2)	
Hospital Teaching Status			6.13
University Hospital	1,724 (83)	821 (82)	
Community Hospital	273 (13)	148 (15)	
Non-Teaching	85 (4)	33 (3)	

The standardized mean differences (SMDs) shown are prior to propensity weighting. ICP = intracranial pressure; IQR = interquartile range; ACS = American College of Surgeons. When calculating the SMD's, age, hospital volume, and the number of neurosurgeons were treated as continuous variables. All other variables were considered categorical.

eTable 4. Injury Characteristics

Variable, n (%) unless shown	No ICP, n = 2,082	ICP, n = 1,002	SMD (%)
Injury Mechanism			21.45
Motor Vehicle	859 (41)	477 (48)	
Abuse/Assault	452 (22)	223 (22)	
Fall	349 (17)	107 (11)	
Penetrating	11 (1)	14 (1)	
Other	411 (20)	181 (18)	
Injury Severity Score (ISS)			58.52
median (IQR)	18 (11, 26)	26 (20, 34)	
mean (SD)	20 ± 12	27 ± 11	
minimum	0	0	
maximum	75	75	
Intracranial Hemorrhages			
EDH	151 (7)	66 (7)	2.62
SDH	410 (20)	258 (26)	14.49
SAH	279 (13)	172 (17)	10.48
Worst Head AIS score			
0	137 (7)	51 (5)	
1	14 (1)	4 (0)	
2	269 (13)	16 (2)	
3	310 (15)	53 (5)	
4	1,102 (53)	616 (61)	
5	244 (12)	260 (26)	
6	6 (0)	2 (0)	
ED GCS score			22.33
3	1,300 (62)	670 (67)	
4	75 (4)	50 (5)	
5	71 (3)	51 (5)	
6	238 (11)	104 (10)	
7	195 (9)	77 (8)	
8	203 (10)	50 (5)	
ED GCS-Motor score			23.08
1	1,357 (65)	699 (70)	
2	95 (5)	44 (4)	
3	85 (4)	66 (7)	
4	316 (15)	137 (14)	
5	168 (8)	43 (4)	
6	28 (1)	5 (0)	
missing	33 (2)	8 (1)	
ED GCS measurement			

Intubated	1,517 (73)	719 (72)	2.47
Sedated	1,061 (51)	508 (51)	0.52
Disposition from ED			
OR	118 (6)	160 (16)	
ICU	1,780 (85)	749 (75)	
Floor	67 (3)	42 (4)	
Other/Missing	117 (6)	51 (5)	

The standardized mean differences (SMDs) shown are prior to propensity weighting. ICP = intracranial pressure; ISS = injury severity score; IQR = interquartile range; EDH = epidural hematoma; SDH = subdural hematoma; SAH = subarachnoid hemorrhage; AIS = abbreviated injury scale; ED = Emergency Department; GCS = Glasgow Coma Scale; OR = operating room; ICU = intensive care unit. When calculating the SMD's, ISS and the AIS variables were treated as continuous variables. All other variables were considered categorical.

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