# Body Temperature after EMS Transport: Association with Traumatic Brain Injury Outcomes

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Abstract

**Introduction**: Low body temperatures following prehospital transport are associated with poor outcomes in patients with traumatic brain injury (TBI). However, a minimal amount is known about potential associations across a range of temperatures obtained immediately after prehospital transport. Furthermore, a minimal amount is known about the influence of body temperature on non-mortality outcomes. The purpose of this study was to assess the correlation between temperatures obtained immediately following prehospital transport and TBI outcomes across the entire range of temperatures. **Methods**: This retrospective observational study included all moderate/severe TBI cases (CDC Barell Matrix Type 1) in the pre-implementation cohort of the Excellence in Prehospital Injury Care (EPIC) TBI Study (NIH/NINDS: 1R01NS071049). Cases were compared across four cohorts of initial trauma center temperature (ITCT): <35.0°C [Very Low Temperature (VLT)]; 35.0–35.9°C [Low Temperature (LT)]; 36.0–37.9°C [Normal Temperature (NT)]; and ≥38.0°C [Elevated Temperature (ET)]. Multivariable analysis was performed adjusting for injury severity score, age, sex, race, ethnicity, blunt/penetrating trauma, and payment source. Adjusted odds ratios (aORs) with 95% confidence intervals (CI) for mortality were calculated. To evaluate non-mortality outcomes, deaths were excluded and the adjusted median increase in hospital length of stay (LOS), ICU LOS and total hospital charges were calculated for each ITCT group and compared to the NT group. **Results**: 22,925 cases were identified and cases with interfacility transfer (7361, 32%), no EMS transport (1213, 5%), missing ITCT (2083, 9%), or missing demographic data (391, 2%) were excluded. Within this study cohort the aORs for death (compared to the NT group) were 2.41 (CI: 1.83–3.17) for VLT, 1.62 (CI: 1.37–1.93) for LT, and 1.86 (CI: 1.52–3.00) for ET. Similarly, trauma center (TC) LOS, ICU LOS, and total TC charges increased in all temperature groups when compared to NT. **Conclusion**: In this large, statewide study of major TBI, both ETs and LTs immediately following prehospital transport were independently associated with higher mortality and with increased TC LOS, ICU LOS, and total TC charges. Further study is needed to identify the causes of abnormal body temperature during the prehospital interval and if in-field measures to prevent temperature variations might improve outcomes. **Key words:** hyperthermia; traumatic brain injury; hypothermia; mortality; cost

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## Introduction

In 2010, Traumatic Brain Injury (TBI) led to over 1.7 million emergency department visits, 275,000 hospitalizations, and 50,000 deaths in the United States.[1,2] The lifetime cost of TBI sustained in the year 2000 alone was estimated to be over 60 billion US dollars[3,4] with more than 2% of the US population requiring long-term assistance as a result of TBI.[5] Secondary brain injury is a major contributor to increased morbidity and mortality following TBI. Several factors have been identified as causing secondary brain injury during prehospital care including: hypotension, hypoxia, and hyperventilation.[6–17] Through multiple pathophysiological mechanisms, both elevated body temperature and low body temperature could cause secondary brain injury with resulting increases in morbidity and mortality.[18–23]

Low body temperatures in the prehospital setting have long been known to be associated with poor outcomes in general trauma patients. In this population, multiple studies have reported that body temperature <35°C is associated with a marked increase in the adjusted odds of death when compared to patients with normal body temperature.[20,22,24–26] However, the vast majority of available data on hypothermia in TBI has focused on therapeutic hypothermia as a modality to improve outcomes in the intensive care unit (ICU).[27–29]

Even less is known about the effect of elevated temperatures on TBI outcomes.[18,21,23] Patients with severe TBI are known to frequently develop idiopathic elevated temperatures ("neurogenic fever") during their hospital course. These elevated temperatures have been associated with poor outcomes and increased mortality.[30–35] Although poorly understood, it is thought that temperature abnormalities in the ICU are a result of Central Nervous System (CNS) failure to regulate temperature following injury.[36] However, these mechanisms that lead to fluctuations in body temperature during the hospital course may not be the primary cause of elevated temperatures identified on initial presentation to the ED.[19] This is more likely due to environmental exposure that occurs from the time of injury until the patient arrives at the hospital. However, a minimal amount is known about the incidence and outcomes of TBI patients who already have elevated body temperature by the end of their prehospital interval.

The purpose of the current study is to evaluate potential associations between body temperature immediately following prehospital transport and various outcomes in victims of major TBI.

# METHODS

## Study Design

This study is a retrospective observational analysis of data contained in the Arizona State Trauma Registry (ASTR) and the Excellence in Prehospital Injury Care (EPIC) TBI database. The ASTR database contains information on all trauma patients cared for at level 1 trauma centers (TCs) in Arizona (total of 8 TCs) and was matched with prehospital data for participating EMS agencies transporting patients to one of the TCs. More than 90% of TBI patients in Arizona were cared for by agencies participating in the EPIC project. The details of the EPIC Study, a statewide, before/after, controlled evaluation of the impact of implementing the EMS TBI treatment guidelines (NIH/NINDS: 1R01NS071049; ClinicalTrials.gov: #NCT01339702), have been reported in detail elsewhere.[37]

## Data Validity Efforts

The ASTR data validation tool, developed collaboratively by Arizona Department of Health Services (ADHS) staff and the trauma registry software vendor significantly increases the ASTR data quality. More than 800 data checks are performed per record for the full data set. Data checks include warning flags for blank fields, invalid entries, date and time errors, and other data logic errors. The Data and Quality Assurance (DQA) staff within ADHS run validation reports and the results are sent to the reporting hospitals so that the data can be updated, confirmed, and resubmitted to the ASTR with changes. The DQA section also performs statewide inter-rater reliability testing as a quality assurance tool to continuously improve on trauma data entry standardization and data reliability.

## Study Population and Setting

Cases of moderate/severe ("major") TBI in the State of Arizona, occurring between January 1, 2007 and December 31, 2012 were identified using the ASTR/EPIC database. In the EPIC Study, major TBI is defined as those patients with physical trauma who have trauma center diagnosis(es) consistent with TBI (either isolated or multisystem trauma that includes TBI) and meet at least one of the following definitions for moderate or severe TBI: a) Centers for Disease Control (CDC) Barell Matrix-Type 1; b) Head Region Severity Score (International Classification of Diseases-ICD-9) $\geq$3; and/or c) Abbreviated Injury Scale (AIS)-Head Region Severity Score $\geq$3.[37] Cases were excluded if temperature on arrival to the TC was not recorded, temperature was recorded after a transfer from a non-TC to a TC, or if other important risk adjusters were missing. The included patients were cared for by more than 100 different EMS agencies. We are not aware of any attempt to specifically detect, prevent, or treat temperature abnormalities in the prehospital setting.

## Human Subjects Review

The necessary regulatory approvals for EPIC have been obtained from the Arizona Department of Health Services (ADHS) and the State Attorney General. The University of Arizona Institutional Review Board and the ADHS Human Subjects Review Board have approved the project and publication of de-identified data.[37]

## Statistical Analysis

All cases of major TBI in the EPIC/ASTR data set were evaluated. Those with an interfacility transfer and those without a documented ITCT or missing important risk adjusters (e.g., race, ISS, payment source) were excluded. The unadjusted association between the continuous variable ITCT and mortality was first evaluated using a Lowess smoothing function, with the outcome transformed to logits (log odds), in order to assess whether body temperature was linearly related to the outcome in the logit, a key requirement for continuous variables in logistic regression. Fractional polynomial regression was used to find a transformation for ITCT as a continuous variable for logistic regression to satisfy the requirement of linearity in the logit. ITCT was also categorized using the following four commonly-used clinical cutoffs for abnormal body temperatures: very low temperatures (<35.0°C), low temperatures (35.0–35.9°C), normal temperatures (36.0–37.9°C), and elevated temperatures (≥38.0°C). Non-mortality outcomes were evaluated utilizing the sub-group of patients who survived. A severity-adjusted analysis (outlined in the following section) was then used to compare mortality and non-morality outcomes among the four temperature-defined groups.

## Measurements and Key Outcomes

The outcomes for this study were in-hospital mortality following the initial injury and other commonly reported non-mortality outcomes: TC length-of-stay, intensive care unit (ICU) length of stay, and total TC charges in US Dollars ($).

## Analysis

A multivariable risk adjustment analysis was performed comparing mortality between the very low temperature, low temperature, and elevated temperature groups to that of the cases with normal temperature. The covariates for the severity adjusted analysis were chosen a priori, based on the known or suspected relationship (either directly or as a potential confounder) to the main outcome variable, mortality, and accounted for: injury severity scale (ISS), age, sex, race, ethnicity, trauma type (blunt vs. penetrating), and payment source (private, public, self, other) as describe elsewhere.[37] The results of the logistic regression model are reported as adjusted odds ratios (aOR) with 95% Confidence Intervals (CI) for mortality among each group when compared to those in the NT group. Median regression was used to model the severity adjusted median difference in non-mortality outcomes between the very low temperature, low temperature, and elevated temperature groups to those cases with normal temperature after adjusting for ISS, age, sex, and trauma type. Statistical analyses were conducted using SAS v9.3 (SAS Institute, Inc., Cary, NC) and Stata v14 (StataCorp LP, College Station, TX).

# Results

The EPIC TBI database contained 22,925 cases of major TBI, out of which 11,877 (51.8%) were included in the study. Of the 22,925 cases identified 2,083 (9.1%) were excluded due to missing ITCT data. An additional 7,361 (32.1%) cases were excluded because they were interfacility transfers and 1213 (5.3%) due to transport by private vehicle. An additional 391 (1.7%) cases were excluded either due to missing information on race, ISS, or payment source leaving 11,877 cases included in this study. The demographic data for the study population stratified by ITCT group are shown in Table 1. Most cases (70.1%) were men and median age was 39 years. The majority (58.6%) had an ISS >15 and had a blunt mechanism of injury (95.6%). Patients excluded due to missing ITCT were more likely to be seriously injured (79.9% with an ISS > 15) and less likely to have blunt injury (85.6%).

Figure 1 shows the plot of ITCT versus the unadjusted log odds (logit) of death using a Lowess smoothing function, which suggests a non-linear relationship between ITCT and the outcome in the logit scale. Fractional polynomial regression failed to find an adequate transformation of the continuous variable that was linearly associated with the log odds of death, a key requirement of logistic regression. Thus, ITCT categorized into 4 categories, based on commonly used clinical definitions of body temperature abnormalities, was used for all analyses.

Table 1. Study population demographic data

| | Initial Trauma Center Temperature | | | | |
|---|---|---|---|---|---|
| | <35°C | 35–35.9°C | 36–37.9°C | ≥38°C | Total TBI |
| **Total Patients** | 473 (4.0%) | 2,256 (19.0%) | 8,971 (75.5%) | 177 (1.5%) | 11,877 |
| **Male** | 350 (73.9%) | 1,581 (70.0%) | 6,266 (69.8%) | 134 (75.7%) | 8,331 (70.1%) |
| **Age in Years (Q1-Q3)** | 36 (22–54) | 39 (22–58) | 39 (22–57) | 37 (20–55) | 39 (22–57) |
| **Race** | | | | | |
| **Hispanic** | 74 (15.6%) | 532 (23.5%) | 2,189 (24.4%) | 48 (27.1%) | 2,843 (23.9%) |
| **White** | 305 (64.4%) | 1419 (62.8%) | 5,555 (61.9%) | 101 (57.0%) | 7,380 (62.1%) |
| **Other** | 94 (19.8%) | 305 (13.5%) | 1,227 (13.6%) | 28 (15.8%) | 1,654 (13.9%) |
| **Injury Severity Score (ISS) > 15** | 407 (86.0%) | 1,655 (73.3%) | 4,763 (53.0%) | 136 (76.8%) | 6,961 (58.6%) |
| **Payer** | | | | | |
| **Public Insurance** | 219 (46.3.%) | 1,095 (48.5%) | 4,092 (45.6%) | 79 (44.6%) | 5,485 (46.2%) |
| **Private Insurance** | 162 (34.2%) | 786 (34.8%) | 3,294 (36.7%) | 65 (36.7%) | 4,307 (%36.3) |
| **Other Insurance** | 92 (19.4%) | 375 (16.6%) | 1,585 (17.6%) | 33 (18.6%) | 2,085 (17.6%) |
| **Blunt Trauma** | 423 (89.4%) | 2,110 (93.5%) | 8,658 (96.5%) | 167 (94.3%) | 1,1358 (95.6%) |
| **Mortality** | 147 (31.0%) | 365 (16.1%) | 565 (6.2%) | 32 (18.0%) | 1,109 (9.3%) |

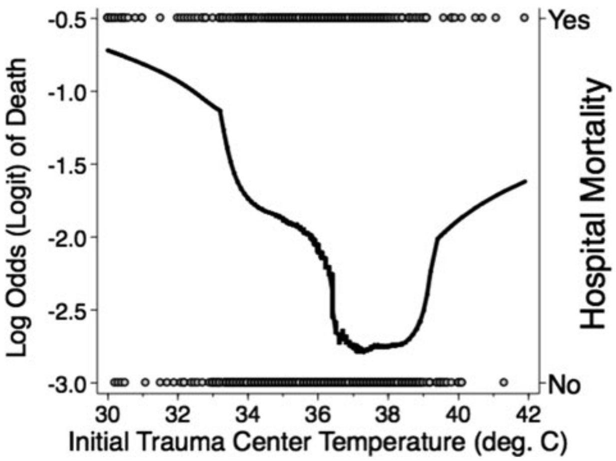


FIGURE 1. Lowess smoothing function for unadjusted mortality versus initial trauma center temperature.

TABLE 3. Non-mortality adjusted median regression analysis

| Temperature | Median Hospital LOS (95% CI) | Median ICU LOS (95% CI) | Median Hospital Charges (95% CI) |
|---|---|---|---|
| ≥ 38°C | 2.38 (1.94–2.81) | 1.29 (1.18–1.40) | $42,714 (36,853–48,574) |
| 36–37.9°C | Referent | Referent | Referent |
| 35–35.9°C | 1.07 (0.94–1.21) | 0.41 (0.38–0.45) | $11,599 (9,846–13,352) |
| < 35°C | 2.84 (2.52–3.13) | 1.29 (1.22–1.37) | $37,135 (33,214–41,055) |

Values reported represent the adjusted increase in LOS or hospital charges with (95% Confidence Intervals) in each group when compared to the median value for the 36–37.9°C group.

The normal temperature group accounted for 75.5% ($n$ = 8,971) of the total study population, while there were 2,256 (19.0%) in the low temperature group, 473 (4.0%) in very low temperature group, and 177 (1.5%) in the elevated temperature group. Injury severity scores were higher in the elevated temperature, low temperature and very low temperature groups than in the normal temperature group. These differences were even more striking in patients with an ISS ≥ 25. The very low temperature group had more penetrating trauma (11.6%) cases compared to the other groups. The overall mortality in our study population was 9.3% ($n$ = 1,109). The crude mortality for each group is shown in Table 2. There was a significant increase in crude mortality across all temperature groups when compared to the normal temperature group ($p < 0.0001$).

The crude and adjusted odds of mortality in each group are shown in Table 2. The adjusted odds of mortality differed significantly in the very low temperature (aOR 2.41, 95% CI 1.83–3.17), low temperature (aOR 1.62, 95% CI 1.37–1.93), and elevated temperature (aOR 1.86, 95% CI 1.15–3.00) group as compared to the normal temperature group.

After excluding deaths, the association between ITCTs and crude non-mortality outcomes were calculated and are illustrated in Figure 2. This figure demonstrates the median hospital length of stay, ICU length of stay, and total hospital charges across all temperature groups. The median regression analysis provides the adjusted increases in median hospital length of stay, ICU length of stay, and TC total charges in all three groups compared with the normal temperature group (Table 3). All three groups had a significant increase in hospital length of stay and ICU length of stay compared to the normal temperature group (p values < 0.0001).

TABLE 2. Crude and adjusted odds of mortality when temperature on arrival to a trauma center is above or below normal

| Temperature | Mortality $n$/N (%) | Crude OR (95% CI) | Adjusted OR (95% CI) |
|---|---|---|---|
| >38°C | 32/177 (18.0) | 3.28 (2.21–4.86) | 1.86 (1.15–3.00) |
| 36.0–37.9°C | 565/8971 (6.2) | Referent | Referent |
| 35–35.9°C | 365/2256 (9.5) | 2.87 (2.49–3.30) | 1.62 (1.37–1.93) |
| <35°C | 147/473 (31.0) | 6.70 (5.42–8.29) | 2.41 (1.83–3.17) |

## DISCUSSION

The negative impact of secondary insults on TBI outcome is well known. For example, hypoxia,[9,10,12,17,38] hypotension,[9,12,16,17,38] and hyperventilation (in intubated patients)[14,15,38–40] are all associated with at least a doubling of mortality. While in-hospital fever is strongly associated with the risk of death,[31–33,36] a minimal amount is known regarding the impact of high temperatures occurring at the time of hospital arrival.

We found a significant association between abnormal initial trauma center temperature and poor outcomes in victims of major TBI. Since the temperatures were the initial ones obtained at the hospital, they likely reflect abnormalities that occurred during the prehospital interval. Although the association between hypothermia at the time of hospital arrival and increased mortality following TBI has been reported,[20,22,24,41,42] we believe this is the first study to demonstrate this association across the entire range of presenting temperatures. Our findings show that increased body temperature occurring during the prehospital interval has an associated increased risk that is similar to the other the commonly-reported secondary insults (i.e., hypoxia, hypotension, and hyperventilation). In addition to the mortality findings, we identified a strong association between abnormal ITCTs and non-mortality outcomes with statistically significant increases in hospital

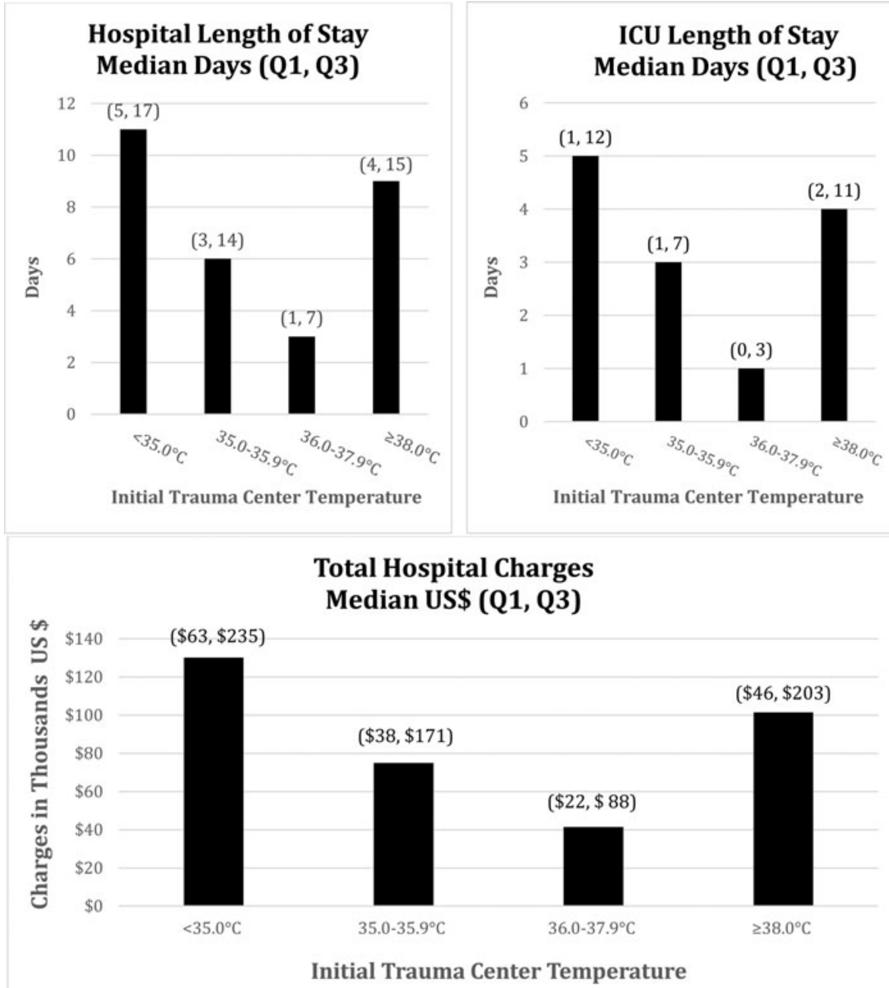


Figure 2. Unadjusted non-mortality outcomes by initial trauma center temperature. Values reported represent the raw or unadjusted median Hospital, ICU LOS, or hospital charges with (Q1 = 25th Percentile and Q3 = 75th percentile).

length of stay, ICU length of stay and hospital charges in patients with either high or low temperatures. We have been unable to find any previous studies that reported an association between alterations in body temperature and healthcare resource utilization.

The causes of the abnormal temperatures observed in this study remain unclear. In ICU settings, thermodysregulation or infection are common causes of temperature abnormalities in TBI patients.[31–33,36] In this study interfacility transfers were excluded and the vast majority of cases in the EPIC population arrive at the hospital less than 30 minutes after the injury. Thus, given the brief amount of time that transpires between the injury event and arrival at the trauma center, in the prehospital setting, variations in body temperature are much more likely to be caused by exposure to environmental temperature extremes rather than underlying pathophysiological processes.

The attempt to show a linkage between environmental conditions and body temperature in trauma patients has led to mixed results. One TBI study that evaluated environmental temperatures and patient outcomes demonstrated no association between them.[43] On the other hand, in both general trauma and TBI patients, some previous reports have demonstrated that the incidence of hypothermia is higher in the colder months of the year.[20,26] In addition, recent combat experience in Iraq and Afghanistan (predominantly warm climates) demonstrated that 7.4% of general trauma patients and as many as 47% of TBI patients had elevated temperatures on arrival at the forward aid stations.[41,44,45]

It is interesting that the prevalence of elevated temperatures in our study (177, 1.5%) was much lower than that of low temperatures (2256, 19.0%) or very low temperatures (473, 4.0%). Given the recent military literature described above and the relatively hot temperatures commonly encountered in Arizona (average summer high temperatures above 39°C), this finding was not anticipated. In part, this unexpected finding could be due to differences in injury location and prehospital care. For instance, civilian trauma patients may be more likely to be injured inside air-conditioned vehicles and transported in air-conditioned ambulances. These factors could mitigate an initial exposure to high environmental temperatures or increase the incidence of low temperatures.

Patients in the low and very low temperature groups had a significant increase in the adjusted odds of mortality when compared to those with a normal temperature. This is not a new finding in trauma patients. However, the incidence of hypothermia after sustaining a moderate or severe TBI was surprisingly high. In fact, 23% of patients had an initial temperature <36.0°C. Thus, since environmental exposure may be a key cause of temperature variations that occur during the initial care of trauma patients, it appears that hypothermia should be avoided if at all possible in the prehospital setting.

Similarly in patients with elevated temperatures, there was a clear increase in mortality and in poor non-mortality outcomes. This, in conjunction with multiple ICU studies where hyperthermia was associated with poor outcomes, makes a compelling argument that variations in body temperature in either direction from normal should be avoided in TBI.

While there may be some validity to the current recommendations aimed at treating low and high temperatures in trauma patients, the design of our study does not allow us to make conclusions about the potential effectiveness of such treatment. However, these findings do support future study of the effectiveness of such treatment. Our findings supply an important reminder that, even under the optimal conditions in a controlled ICU setting, inadvertent occurrence of hypothermia or hyperthermia is common and poses significant risks to TBI patients. While in-hospital treatment of hypothermia has been associated with improved outcomes following injury, this has not been demonstrated in patients with elevated temperatures.[46] Therefore, any consideration of taking measures to prevent or treat body temperature abnormalities in the prehospital setting must carefully take into account the absence of demonstrated benefits and the potential risks. However, these finding do support future study of the effectiveness of such treatment and could help direct the future development of evidence-based guidelines for the field triage of patients with severe trauma.

## Limitations

This study has several limitations. First, this is a retrospective, observational evaluation. Thus, it cannot be used to prove a causal effect of body temperature on outcome. Second, this study utilized CDC Barell Matrix among other criteria to identify patients with moderate or severe TBI. Use of diagnosis based inclusion criteria, may have introduced inclusion bias.[37,47] Additionally, by using this inclusion criteria, patients with other traumatic injuries were likely included in this study and the effect of temperature on TBI cannot be isolated. Third, we do not know whether there were attempts to treat body temperature either in the prehospital or trauma center environments. Thus, we are not able to identify associations with treatment. Finally, temperatures were recorded at 8 different trauma centers across the state and we are not able to determine the method, accuracy, or exact time of the measurements. Because this study assumes that ITCT was measured with the initial set of vital signs at the trauma center and patients without an ITCT were excluded, it is possible that other patient care activities took precedence over the measurement of body temperature and measurement of ITCT was delayed. Given that patients without a measured ITCT (excluded cases) had a higher ISS and were more likely to have penetrating trauma, this seems likely and may have introduced selection bias.

## Conclusion

In this statewide study of major TBI, both low and high initial trauma center body temperatures were associated with a significant increase in severity adjust mortality and poor non-mortality outcomes. Future work is needed to identify the cause of prehospital body temperature variation in patients with TBI and whether initiation of in-field measures to prevent temperature abnormalities is safe and effective.

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