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Lead-Time Bias and Interhospital Transfer after Injury: Trauma Center Admission Vital Signs Underpredict Mortality in Transferred Trauma Patients

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Abstract

Background—Admission physiology predicts mortality after injury but may be improved by resuscitation prior to transfer. This phenomenon, which has been termed lead-time bias, may lead to underprediction of mortality in transferred patients and inaccurate benchmarking in centers receiving large numbers of transfer patients. We sought determine the impact of using vital signs on arrival at the referring center vs. on arrival at the trauma center in mortality prediction models for transferred trauma patients.

Study Design—We performed a retrospective cohort study using a state-wide trauma registry including all patients age≥16 with Abbreviated Injury Scale scores ≥ 3 admitted to level I and II trauma centers in Pennsylvania from 2011–2014. The primary outcome measure was the risk-adjusted association between mortality and interhospital transfer (IHT) when adjusting for physiology (as measured by Revised Trauma Score, RTS) using the referring hospital arrival vital signs (model 1) compared to trauma center arrival vital signs (model 2).

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Results—After adjusting for patient and injury factors, IHT was associated with reduced mortality (OR 0.85, 95% CI 0.77–0.93) using the RTS from trauma center admission but with increased mortality (OR 1.15, 95% CI 1.05–1.27) using RTS from the referring hospital. The greater the number of transfer patients seen by a center, the greater the difference in center-level mortality predicted by the two models (b −0.044, 95% CI −0.044 - −0.0043, p= <0.001).

Conclusions—Trauma center vital signs underestimate mortality in transfer patients and may lead to incorrect estimates of expected mortality. Where possible, benchmarking efforts should use referring hospital vital signs to risk-adjust IHT patients.

INTRODUCTION

The validity of efforts to benchmark trauma center mortality is dependent upon the validity of the underlying risk-adjustment models, which in turn are a function of the variables used to construct them. Mortality prediction models such as the Trauma Injury Severity Score (TRISS)[1] and A Severity Characterization of Trauma (ASCOT)[2] include factors to control for presenting physiology, patient reserve (as measured by age), and injury severity. Unlike injury severity and age, which are fixed at the time of presentation to a trauma center, vital signs are dynamic and subject to modification by interventions prior to trauma center admission. Since vital signs themselves are a proxy of cellular shock (i.e. patients are not dying because they are hypotensive, but rather hypotensive because they are dying), correction of vital signs may be accomplished without resolving the underlying cause of derangement. Measurements of patient physiology may therefore be influenced by the time from injury at which they are taken as well as the interventions undertaken to correct them. All other factors held equal, patients who have been resuscitated may present with less deranged vital signs than those who have not, leading to lower predicted mortality using these ‘corrected’ vitals relative to patients presenting with less resuscitation.

This phenomenon, known as “lead-time bias” has been previously demonstrated in transferred critical care patients[3,4] but the degree to which it impacts injured patients undergoing transfer from non-trauma centers to trauma centers is not well described. Although non-trauma centers may not have the capacity to definitively manage injured patients, they may resuscitate and stabilize patients in the hours prior to transfer. This may in turn result in arrival vital signs at the trauma center that belie the initial physiologic derangement of the patient. Measures of presenting physiology have long been known to be associated with mortality in injured patients[1,5,6], but risk of mortality may be under-predicted in patients who have been resuscitated at a referring hospital prior to transfer.

The influence of lead-time bias on estimated center level mortality would be expected to be small at centers that receive few transfer patients and larger in centers that receive greater proportions of transfer patients. Pennsylvania is a largely rural state with 95–99.3% of the land area meeting a census definition of rurality[7] and is home to 30 level I and II trauma centers. The percentage of admissions derived from interhospital transfer at these centers ranges from 0–63%[8], making this a promising environment to investigate the effects of lead-time bias. We hypothesized that in transfer patients, risk-adjustment using presenting vital signs from the referring hospital would result in higher predicted probability of mortality

than would using vital signs from the receiving trauma center and that differences in center-level expected mortality would be a function of the number of transfers. As a secondary goal, we sought to characterize the impact of changing physiology over the course of transfer on mortality in transfer patients.

METHODS

We performed a retrospective cohort study using the Pennsylvania Trauma Outcomes Study (PTOS) registry of injured adult patients admitted to level I and II trauma centers in Pennsylvania from 2011–2014. Patients presenting to level III or IV centers in PA were excluded because the number of centers was small (n=4) and varied over the study period. To ensure the quality of data collection at the center-level, specially trained registrars at each trauma center prospectively abstract detailed data from the medical chart of each patient meeting inclusion criteria into the PTOS registry. These data are collected according to standardized definitions[9] put forth by the PTSF and a subset of charts is re-reviewed to ensure inter-rater reliability by registrars. Additionally, subsets of submitted data are re-abstracted by the PTSF during site accreditation visits to verify accuracy. As data quality is linked to accreditation, centers are strongly incentivized to accurately report data and rates of missing data are low. Data for this work were provided by the Pennsylvania Trauma Systems Foundation (Mechanicsburg, PA), which specifically disclaims responsibility for any analyses, interpretations, or conclusions presented herein. This study was conducted after approval of our institutional IRB.

Patients with moderate or severe injuries (minimum abbreviated injury scale (AIS) ≥ 3) of age≥16 years were considered for inclusion. Patients who were transferred between trauma centers or who had a primary mechanism of injury of burn were excluded. Because a prerequisite of transfer is survival to the point of transfer, to allow for fair comparison between transfer and non-transfer patients, deaths in the emergency department (in both transferred and non-transferred patients) were excluded from analyses. The primary outcome measure was in hospital mortality and the primary exposure of interest was interhospital transfer status. To build multivariable logistic regression models on mortality, we first examined patient factors including age, injury severity score (ISS), mechanism of injury (blunt vs. penetrating), sex, and presenting physiology known or suspected to be associated with mortality.

Missing physiologic data is a known source of bias in injury research[10,11]. To reduce bias secondary to complete case analysis, missing data was imputed using chained multiple imputation[12]. As a proxy of overall physiology, we used the revised trauma score (RTS)[13] and presenting temperature. For transfer patients, RTS was calculated twice; once using vital signs on presentation to the non-trauma center, and once using vital signs on arrival to the trauma center. Variables considered for inclusion in multivariable logistic regression models on mortality included age, sex, race, ethnicity, ISS, maximum AIS, admission vital signs (heart rate, systolic blood pressure, Glasgow Coma Score (GCS), motor subscore of the GCS verbal subscore of the GCS, eye subscore of the GCS, RTS, and transfer status. Those variables associated with mortality with p≤0.1 in univariate logistic regression were included in multivariable models. Due to the clustered nature of data at the level of the trauma center,

robust variance estimators were used in all logistic regression models. In keeping with the principle of parsimony, we selected final models based on minimization of Akaike's Information Criteria (AIC) and Bayesian Information Criteria (BIC). Estimates from multivariable logistic regression models on mortality were generated using the 'mi estimate' package in STATA v14.0 (College Station, TX), which adjusts coefficients and standard errors for the variability between imputations according to the combination rules by Rubin[14]. Hosmer-Lemeshow goodness of fit tests were used to examine model calibration and receiver operator characteristic (ROC) curves were used to examine model discrimination.

Two multivariable logistic regression models on mortality were constructed. In the first model, RTS was calculated using the first set of vitals recorded at the trauma center for both transfer and non-transfer patients. In the second, temperature and RTS were derived from the first set of vitals recorded at the non-trauma center for transfer patients and from the first set of vitals recorded at the trauma center for patients presenting directly to the trauma center. Interhospital transfer status was included in the model as an indicator variable to determine the overall effect size of the association between transfer and mortality after controlling for confounding factors. Transfer status as an indicator variable was then removed from the models and each model was used to predict mortality for each patient. The intraclass correlation (ICC) was used to examine the correlation between the predicted mortality for the two models. We then calculated center-level expected mortality by summing the predicted probability of mortality for all patients presenting to a given center for each of the two models. The difference in the expected number of deaths as predicted by the two models was then regressed against overall transfer volume to examine the relationship between the impact of lead-time bias on expected center level morality and volume of transfer patients.

We then used coarsened exact matching[15] (CEM) as a second method of causal inference to confirm point estimates of the effects of transfer derived from our second logistic regression model (using referring center vital signs to compute RTS for transfer patients). In brief, CEM is a nonparametric method of pre-processing data similar to propensity score matching that can be used to control for some or all of the potentially confounding influence of pre-treatment variables between the treated and control groups. Once matching has occurred, standard statistical testing can be performed to estimate the true difference in outcome attributable to the exposure. Beneficial properties of CEM include ease of use, ease of interpretation, and the ability to be employed with imputed data. Transfer and non-transfer patients were matched based on age, ISS, mechanism of injury, RTS and temperature. For transfer patients, presenting temperature and vital signs from the referring center were used whereas for non-transfer patients we used vital signs from presentation to the receiving center. After matching, logistic regression on mortality using transfer as the exposure variable using CEM generated weights and robust variance estimates to account for correlation within CEM derived strata.

To examine the relationship between change in physiology during transfer and mortality, transfer time was calculated as the difference between arrival to the non-trauma center and trauma center for transfer patients. The marginal structure of the relationship between change in RTS and mortality was then examined using logistic regression modelling to

control for presenting physiology, age, sex, injury mechanism, and change in temperature between centers.

RESULTS

In total, 51,002 patients were considered for analysis (see Figure 1 for flow diagram of included and excluded patients) of which 49,468 met inclusion criteria with no exclusion criteria. Overall, the cohort had a median age of 58 years (IQR 36–78), was 85% Caucasian and 62% male. The mechanism of injury was blunt in 92%, and the median ISS was 14 (IQR 10–18). Transfer patients accounted for 15,576/49,468 (31%) of the cohort. Compared to non-transfer patients (Table 1), transfer patients were older, more likely to be Caucasian, more likely to have sustained blunt injury, and had lower median ISS scores. Temperature and RTS were statistically significantly different between the two groups, although the magnitude of these differences was small enough to be of questionable clinical significance. The median time from referral center arrival to trauma center arrival was 3.9 hours (IQR 2.8–5.2).

Prior to imputation, the percentage of missing data for the variables considered in univariate analyses ranged from a high of 8.2% (respiratory rate on arrival to the trauma center) to a low of 0.004% (age). In univariate regression, transfer was associated with decreased odds of mortality (OR 0.78, 95% CI 0.72–0.85); i.e., transfer patients had a 22% decrease in the odds of mortality relative to non-transfer patients. Univariate analyses of mortality using other potential predictors of interest revealed that age, sex, mechanism of injury, RTS and temperature were each associated with mortality. Including these factors in a multivariable logistic regression slightly increased the point estimate for the association between transfer and mortality but transfer still remained significantly associated with decreased mortality (OR 0.85, 95% CI 0.77–0.93). The area under the curve (AUC) for this model was 0.90 (95% CI 0.89–0.90), indicating excellent discrimination, while the Hosmer Lemeshow chi squared statistic was 57.18. The AIC and BIC of model 1 were 21,131 and 21,207, respectively, and the results of 10-fold cross-validation revealed no statistically significant difference in AUC when using the full vs. the cross-validation datasets (AUC 0.90 vs. 0.90, $p = 0.77$).

We then constructed a second multivariable regression model (Model 2) using the same variables as the first model but with RTS and temperature values derived from vital signs on admission to the non-trauma center for the transfer patients. For patients presenting directly to the trauma center, the first set of vitals on presentation to the trauma center were used. The results of the two models can be seen in Table 2. While the point estimates for sex, ISS, age, injury mechanism, RTS and temperature remained essentially unchanged in model 2, the point estimate for the association between transfer and mortality was reversed, indicating that under this model transfer patients had a 16% increase in the odds of mortality relative to non-transfer patients (OR 1.16, 95% CI 1.05–1.27). In ROC curve analysis, the AUC for model 2 was 0.89 (95% CI 0.89–0.90) and was statistically significantly different from model 1 ($p<0.001$). Calibration of model 2 was slightly better than model 1, with a Hosmer Lemeshow chi square statistic of 56.37, while the AIC and BIC of model 2 were 20,528 and 20,658, respectively, and as with model 1 the results of 10-fold cross-validation revealed no

statistically significant difference in AUC when using the full vs. the cross-validation datasets (AUC 0.89 vs. 0.89, p = 0.06).

After removal of the indicator term for transfer, the mortality predicted by two models was disparate. A scatterplot of the predicted mortalities of the two models can be seen in Figure 3. Overall, mortalities predicted from the two models were tightly correlated (ICC = 0.95, 95% CI 0.94–0.95) but this correlation was greater for predictions for the non-transfer patients (ICC = 0.99, 95% CI 0.99-0.99) and less for transfer patients (ICC = 0.76, 95% CI 0.75–0.76). In transfer patients, the median change in the predicted mortality was −11.5% (IQR −39.4% - −3.6%) when using trauma center admission vitals vs. referring hospital vitals. After summing the predicted mortality by center to generate expected center level mortality for each of the two models, we found a significant inverse relationship between the difference in center-level mortality predicted by the two models and overall number of transfer patients (b −0.044, 95% CI −0.044 - −0.0043, p= <0.001) indicating that on average, for every 229 patients received by a trauma center the estimate of expected center-level mortality decreased by 1 (Figure 3).

To validate our finding of increased mortality for transfer patients when risk-adjusting using referring center vital signs, we used coarse exact matching to estimate the association between transfer and mortality by matching transfer and non-transfer patients on age, sex, mechanism of injury ISS, and presenting RTS and temperature on presentation (at referring hospital for transfer patients; at trauma center for non-transfer patients). “In examining balance in variables used in our multivariable regression between transferred and non-transferred patients prior to CEM, the multivariate L1 distance (a comprehensive measure of global imbalance in which 0 indicates perfect global balance and 1 indicates complete separation) was 0.712, with univariate L1 values ranging from 0.037 to 0.118. After CEM, the multivariate L1 distance decreased to 0.644 with univariate L1 values ranging from 0 to 0.119, indicating improved balance after matching. In examining the differences in variable means between the transferred and non-transferred patients, the mean difference between groups was reduced to <0.05 for all variables in the model.. CEM resulted in 1329 matched strata and matched 28886/33892 (85%) of non-transfer patients and 14,976/15,576 (96%) of transfer patients. After applying CEM-derived weights, transfer was associated with a 20% increase in the odds of mortality referent to non-transfer patients (OR 1.20, 95% CI 1.17 to 1.24), concordant with the magnitude and direction of the point estimate of the association between transfer and mortality derived from model 2.

For patients transferred in less than 24 hours, higher RTS on arrival to the non-trauma center was associated with longer transit times, with each point of RTS was associated with an additional 13.8 minutes of transfer time (95% CI 10.0–17.9 minutes). When comparing physiology between the referring hospital and the trauma center in transfer patients, 13,000/15,576 (83%) exhibited no change in RTS, 949/15,567 (6%) had an improvement in RTS, and 1626/15,576 (10.4%) had a decline RTS over transfer time. There was strong evidence of interaction between change in RTS over transfer and RTS calculated on admission to the non-trauma center (Log-rank test for nested models p<0.001), and so an interaction term between these variables was included in the final multivariable logistic regression model. The marginal probabilities of mortality for patients presenting with stable

vs. unstable vital signs by change in RTS during transfer after controlling for age, ISS, sex, mechanism of injury, and change in temperature can be seen in Figure 4. For an initially unstable trauma patient with no change in RTS during transfer, the adjusted marginal predicted mortality was 18.5% (95% CI 16.8%–20.3%). With a 7 point decrease in RTS over the course of transfer, the predicted mortality approximated 60% for both stable and unstable patients.

DISCUSSION

In this study, we examined the impact of lead-time bias on predicted mortality of moderately or severely injured patients transferred to trauma centers. We found that on average, using trauma center admission vitals resulted in lower predicted probabilities of mortality than if presenting vital signs at the referring center were used. Lead-time bias may therefore be an important consideration in risk-adjustment for transfer patients. This phenomenon has been suggested as a possible explanation for the finding that interhospital transfer patients have been reported to be at increased risk of mortality in surgical[16] and medical[17,18] intensive care cohorts, even after case mix adjustment. A study examining the Pediatric Index of Mortality 2 (PIM2) approach for predicting mortality in transfer pediatric intensive care unit patients demonstrated that physiologic data such as systolic blood pressure and base excess improved from the time of presentation at the referring hospital to the receiving hospital, but the relative improvement in PMI2 scores when using physiology at the receiving center did not translate into appreciable changes in standardized mortality ratios. However, this study examined only a single center with a fixed number of transfer patients, and so the importance of these findings to efforts to benchmark across a group of centers remains unknown.

The mechanism through which lead-time bias operates in mortality risk-adjustment after trauma is somewhat different than the classic examples in epidemiology (e.g. a new screening test detects a disease earlier in its course, resulting in an apparent increase in survival time without actually impacting on disease) but is conceptually similar in that the time at which an exposure is measured has an impact on apparent outcomes. Physiology used for risk-adjusting transferred patients is measured later in the post-injury time course than for patients directly admitted to the trauma center. As this physiology may have been improved by resuscitation, such a patient will have a lower apparent risk of mortality relative to an identical patient presenting directly to the trauma center whose physiology was measured before much resuscitation could occur. This in turn would lead to lower estimates of expected center-level mortality and thus apparent increases in the observed-to-expected mortality ratio at centers receiving large numbers of transfers. Given the explosion of new trauma centers in the US and the increase in rates of interhospital transfer this may portend, accurate risk adjustment of transferred patients is critical to the validity of benchmarking efforts.

After accounting for the presence of lead-time bias, we also found that transfer is on average associated with increased risk-adjusted mortality relative to patients presenting directly to a level I or level II trauma center. While the existing body of literature on the association between transfer and mortality in trauma is inconsistent, this finding stands in contrast to

two recent meta-analyses on this topic which did not demonstrate an overall association between interhospital transfer and mortality [19,20]. However, as noted by the authors of these studies and at least one critic[21], the ability to perform valid meta-analysis is impeded by heterogeneity of the available literature. The decision for interhospital transfer is complex and may be influenced by a multitude of factors beyond the immediate medical needs of the patient including patient and patient family preference, provider preferences[22], insurance status[23], and institutional referral patterns. Additionally, trauma is a heterogonous disease state with varying degrees of time-sensitivity. Given the complexity surrounding interhospital transfer, it is perhaps unsurprising that the literature on this topic in the injured patient is mixed. We believe the most likely explanation for the discrepancy between our findings and these meta-analyses is that the relationship between transfer and mortality is likely a function of the setting in which it is studied.

Because of the time cost associated with transfer, patients who present to non-trauma centers with abnormal vital signs and those who deteriorate during transfer represent a cohort of patients at high risk for mortality. The association between changes in physiology during pre-hospital transfer to the trauma center have been previously reported in a single center retrospective cohort study by Lichtveld et al., who demonstrated that deteriorating physiology as measured by Triage Revised Trauma Score was associated with a 3.6-fold increase in the odds of mortality (OR 1.7–7.6) relative to patients who had unchanged physiology during transfer[24]. The impact of changing physiology during interhospital transfer on mortality for injured patients has not to our knowledge been reported, but we found adjusted mortality increased steeply as RTS declined. Although this relationship is not unexpected, future work in this area should critically examine possible opportunities for performance improvement. There is strong literature to support the concept that trauma systems improve outcomes for injured patients [25,262728], but it is possible that there are subsets of patients presenting to non-trauma centers who should undergo stabilizing interventions prior to transfer. Definitive care may not always be possible at referring centers and yet many of these centers may have resources that are underutilized while focus is placed on rapid transfer of unstable patients to trauma centers. In some cases, aggressive temporizing measures such as angioembolization or laparotomy to control hemorrhage could potentially be undertaken to stabilize patients prior to transport. However, whether such a paradigm of ‘damage control interhospital transfer’ will prove feasible or useful remains to be seen.

The methodology of this study is consistent with current risk-adjustment strategies, and our results can be considered as level III evidence that use of admission physiology at trauma centers for transfer patients results in under-prediction of expected mortality. Strengths of this study include the large sample size, the use of multiple imputation to reduce bias secondary to missing data, and the confirmation of our findings using coarsened exact matching as an alternative method of causal inference for observational data. However, as with any study of this nature, there are limitations which must be acknowledged. First, although this study examines the concept of lead-time bias through the lens of interhospital transfer, we do not account for pre-hospital lead-time bias that could occur as a result of differential resuscitation in the prehospital setting. For instance, it is possible that patients transported by pre-hospital providers to non-trauma centers might be more or less likely to

undergo vigorous resuscitation in the field, and this could in turn bias our findings either towards or away from the null hypothesis. From a pragmatic standpoint, however, the intent of this work was not as much to understand the causes of lead-time bias as much to demonstrate that it exists in interhospital transfer for trauma patients. Future efforts may help define the specific pathways through which lead-time bias is introduced into risk adjustment efforts. Second, since the impact of lead-time bias on center level expected mortality is a function of the number of transfers a trauma center receives it may not be of great importance in determining outlier status in all benchmarking efforts. However, in a rural state such as Pennsylvania where some centers receive >50% of overall volume in transfer patients, the threat to validity of risk-adjustment efforts appears to be real. Third, because the PTOS registry only contains injured patients who presented to or were transferred to a trauma center, we cannot offer insight into the outcomes of injured patients who present to non-trauma centers but are not transferred trauma centers (because of death or other reason). We chose to exclude patients who died in the ED after presenting directly to the trauma center in an attempt to engender fair comparison between transferred and non-transferred patients, but as we have no information on the patients who may have died prior to transfer in the ED of non-trauma centers, we are unable to make direct comparisons between these two groups. If the two groups were systematically different, this could introduce the risk of bias into our findings. Finally, because the median time of transfer was 3.8 hours, it is possible that the majority of injured patients who would be expected to die may have done so prior to transfer. If resulted in elimination of the subset of patients with the most deranged physiology, it would tend to bias are findings towards the null hypothesis and thus makes our findings more striking.

In conclusion, this is the first work to demonstrate the presence of lead-time bias when using presenting physiology to risk-adjust center-level outcomes. The results of this study are applicable to trauma patients with moderate or severe injuries presenting directly to or arriving by transfer to trauma centers, but may not be generalizable to less severely injured patients (maximum AIS<3) or pediatric trauma patients. The use of presenting vital signs from the non-trauma center to calculate RTS for transfer patients is a straightforward endeavor which could easily be employed in any risk-adjustment effort in which referring hospital vital signs for transfer patients are available. Compared to the standard of using vital signs on arrival to the trauma center for both transfer and non-transfer patients, this approach should result in less biased estimates of expected mortality at centers receiving large numbers of transfer patients.

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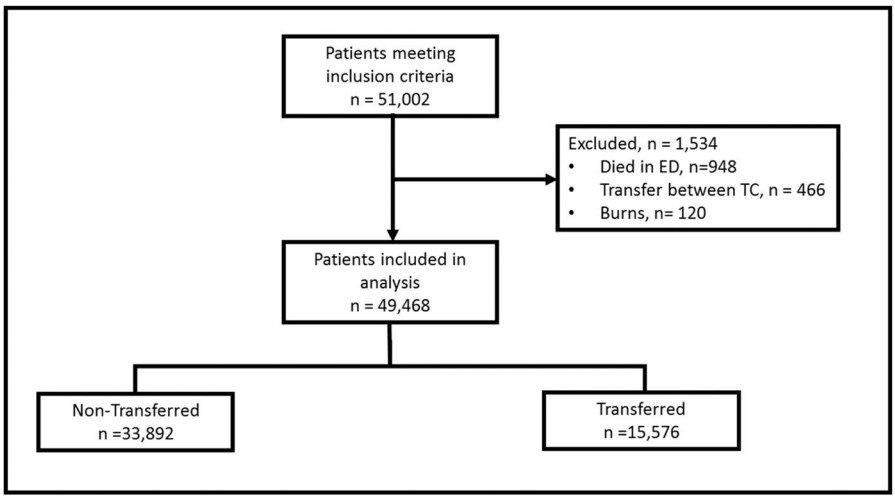

Figure 1.

Flow chart of patients who met inclusion/exclusion criteria for the study population. ED, emergency department; TC, trauma center.

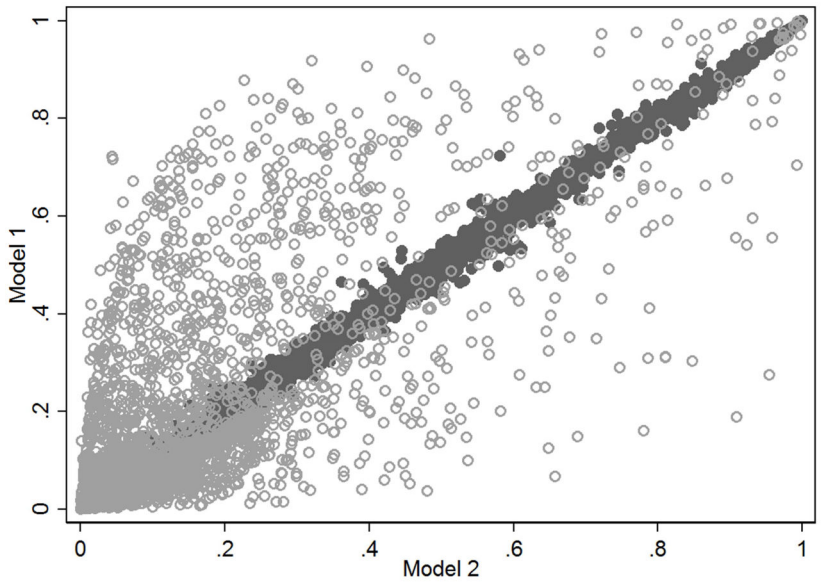

Figure 2.

Predicted mortality for model 1 (receiving hospital vital signs used to risk-adjust transfer patients) and model 2 (referring hospital vital signs used to risk-adjust transfer patients. Open circles, transfer patients; closed circles, non-transfer patients.

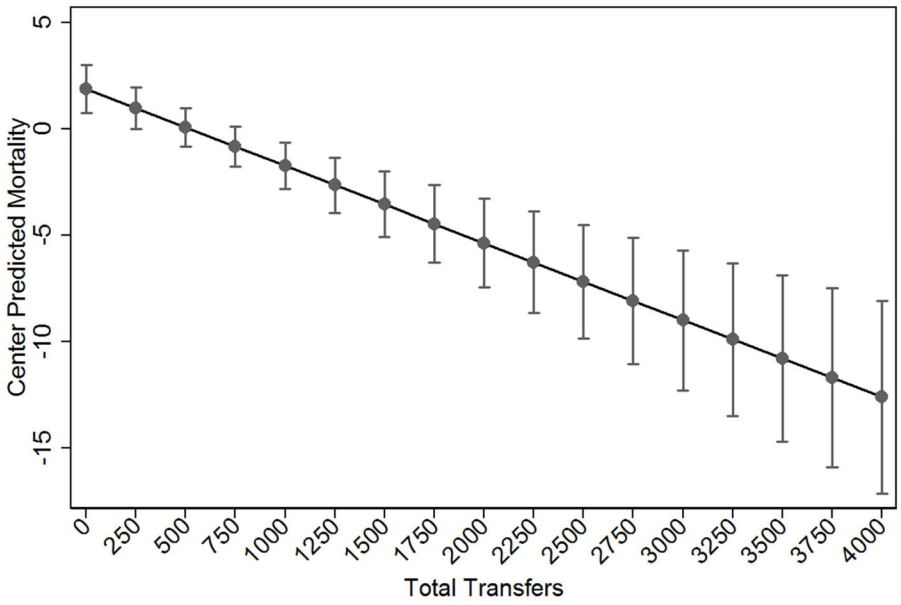

Figure 3.

Association between changes in center level predicted mortality secondary to lead-time bias and trauma center volume transfer volume. Adjusted predictions with 95% confidence intervals.

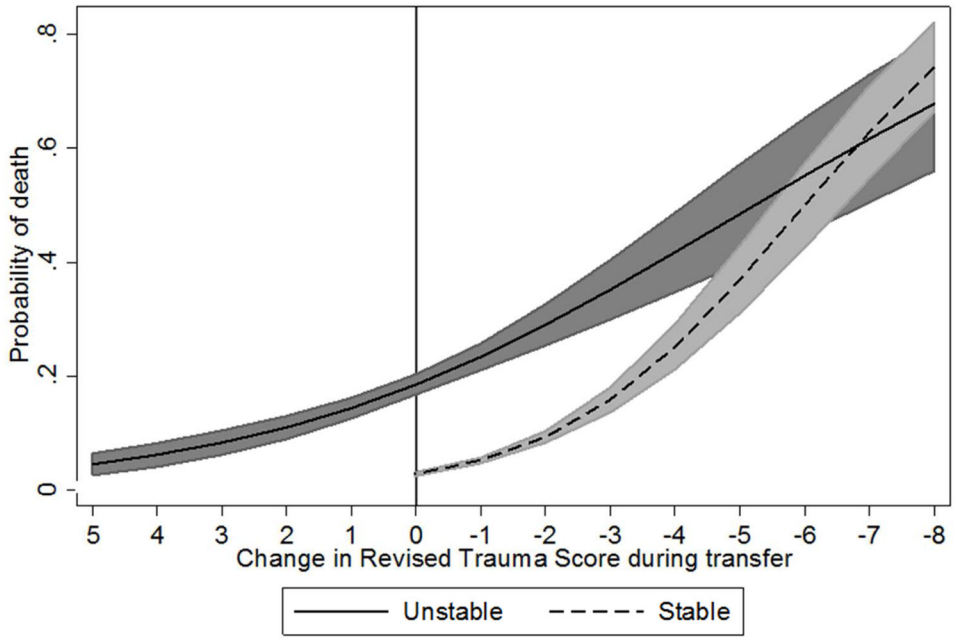

Figure 4.

Marginal probabilities of death in transferred patients by initial stability to non-trauma center, adjusted for adjusting for age, sex, ISS, injury mechanism, and change in temperature. Unstable defined as Revised Trauma Score <7.84 on admission to referring center. Adjusted predictions with 95% confidence intervals.

Table 1

Demographics, Mechanism, Injury Severity, and Presenting Vital Signs at Trauma Center Presentation for Non-Transferred and Transferred Patients

	Non-transferred, n=33,892	Transferred, n=15,576	p Value*
Age, y, median (IQR)	56 (33–76)	64 (43–81)	<0.001
Male sex, n (%)	21,447 (63%)	9,275 (59.6%)	<0.001
Race, n (%)			
Caucasian	26,857 (81.7%)	12,741 (90.8%)	<0.001
African American	5,007 (15.2%)	1,131 (7.5%)	
Other	998 (3.0%)	259 (1.7%)	
Blunt mechanism, n (%)	30,751 (90.7%)	14,992 (96.3%)	<0.001
Injury Severity Score, median (IQR)	14 (10–19)	10 (11–17)	<0.001
Revised Trauma Score, median (IQR)	7.84 (7.84–7.84)	7.84 (7.84–7.84)	<0.001
Temperature, °C, mean (SD)	36.5 (0.7)	36.6 (0.7)	<0.001

* p Values are for Mann-Whitney test for nonparametric continuous variables, t-test for parametric continuous variables, and chi square test for categorical variables.

Table 2

Multivariable Logistic Regression Models on Mortality

Variable	OR	95% CI	p Value
Model 1 *			
IHT	0.83	0.74 to 0.92	0.001
Female sex	0.75	0.67 to 0.84	<0.001
ISS, per point	1.08	1.08 to 1.09	<0.001
Age, per year	1.05	1.05 to 1.06	<0.001
Penetrating Mechanism	3.65	2.99 to 4.46	<0.001
RTS, per point	0.46	0.45 to 0.48	<0.001
Temperature, (°C)	0.84	0.80 to 0.89	<0.001
Model 2 †			
IHT	1.16	1.05 to 1.28	0.003
Female sex	0.72	0.66 to 0.80	<0.001
ISS, per point	1.08	1.08 to 1.09	<0.001
Age, per year	1.05	1.05 to 1.05	<0.001
Penetrating Mechanism	3.79	3.19 to 4.50	<0.001
RTS, per point	0.47	0.45 to 0.48	<0.001
Temperature, (°C)	0.89	0.84 to 0.94	<0.001

* Revised Trauma Score and temperature are derived from vital signs on admission to the trauma center for all patients.

† Revised Trauma Score and temperature are derived from initial vital signs at the referring center for transferred patients and initial vital signs at the trauma center for non-transferred patients.

OR, Odds Ratio; CI, Confidence Interval; IHT, interhospital transfer; ISS, Injury Severity Score; RTS, Revised Trauma Score.