Mortality Benefit of Transfer to Level I versus Level II Trauma Centers for Head-Injured Patients

K. John McConnell, Craig D. Newgard, Richard J. Mullins, Melanie Arthur, and Jerris R. Hedges

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Objective. To determine whether head-injured patients transferred to level I trauma centers have reduced mortality relative to transfers to level II trauma centers.

Data Source/Study Setting. Retrospective cohort study of 542 patients with head injury who initially presented to 1 of 31 rural trauma centers in Oregon and Washington, and were transferred from the emergency department to 1 of 15 level I or level II trauma centers, between 1991 and 1994.

Study Design. A bivariate probit, instrumental variables model was used to estimate the effect of transfer to level I versus level II trauma centers on 30-day postdischarge mortality. Independent variables included age, gender, Injury Severity Scale (ISS), other indicators of injury severity, and a dichotomous variable indicating transfer to a level I trauma center. The differential distance between the nearest level I and level II trauma centers was used as an instrument.

Principal Findings. Patients transferred to level I trauma centers differ in unmeasured ways from patients transferred to level II trauma centers, biasing estimates based on standard statistical methods. Transfer to a level I trauma center reduced absolute mortality risk by 10.1% (95% confidence interval 0.3%, 22.2%) compared with transfer to level II trauma centers.

Conclusions. Patients with severe head injuries transferred from rural trauma centers to level I centers are likely to have improved survival relative to transfer to level II centers.

Key Words. Trauma centers, quality of care, injury severity scale, instrumental variables

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Although regional and statewide trauma systems have become more common in the last decade (MacKenzie et al. 2003) several level I trauma centers have recently closed, and approximately 19 have been threatened throughout the country (Trauma Information Exchange Program 2003). While there is general agreement that statewide trauma systems save lives (Mullins et al. 1994; MacKenzie 1999; Mullins and Mann 1999; Jurkovich and Mock 1999; Nathens et al. 2000), there continues to be debate about whether an equivalent quality of care is delivered at level I and level II trauma centers. Level I and II trauma centers are often assumed to provide the same level of care (Clancy et al. 2001; MacKenzie et al. 2003); yet, the two levels differ in important ways. Level I centers generally have higher patient volume, provide a wider range of specialized personnel and technological resources (Clancy et al. 2001; MacKenzie et al. 2003), but operate with higher costs of care (Goldfarb, Bazzoli, and Coffey 1996). Without evidence of enhanced patient outcomes at level I trauma centers, increasing economic pressures can be expected to challenge the merit of increased trauma system personnel and technological resource commitments by level I trauma centers.

Previous studies aimed at identifying benefits of level I trauma center care have failed to show a benefit compared with patients treated in level II centers (Clancy et al. 2001), or in characteristics associated with level I centers, such as higher patient volume (Waddell and Kalman 1991; Thompson et al. 1992; Barone et al. 1993; Norwood and Myers 1994; Helling et al. 1997; Allen, Hicks, and Bota 1998; Richardson et al. 1998; Demarest et al. 1999; Cooper et al. 2000; Margulies et al. 2001). The failure to detect a benefit may have arisen because previous studies did not properly account for differences in mortality risk that cannot be detected in the observed data. The purpose of this study is to account for this shortcoming, and to determine whether head-injured patients transferred to level I centers experience improved mortality benefits compared with those transferred to level II centers in a rural trauma system.

Observational studies of trauma cases can provide reliable and detailed data on patient transfers and outcomes. However, an analysis of the effect of transfer to a higher-level trauma center must account for the nonrandom transfer of patients to selected centers. In general, more severely injured patients are more likely to be transferred to level I centers. To a certain extent, measures of injury severity, such as the Injury Severity Scale (ISS) score, can help to adjust for this type of referral bias. However, the diverse and heterogeneous nature of injury-related mortality may make it difficult to completely adjust for all factors that affect prognosis and that determine whether a patient will be transferred to a level I or level II center. It is likely that unobserved factors (e.g., effect of patient co-morbid factors upon current health status and

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physiological response to initial therapy) not recorded in routine health services data may have a bearing on the patient's outcome. As a consequence, estimates of the benefits of care at a level I center can be biased toward zero, because observed characteristics may not fully account for the fact that more severely injured patients are more likely to be transferred to a level I center.

Most studies assessing the effect of trauma center status on outcome have ignored the problem of unobservable confounders or have mentioned it as a potential limitation. Yet this approach is unsatisfactory, because it does not allow for appropriate policy inference. In this study, we use the method of instrumental variables, which can generate unbiased, consistent estimates when unobservable factors are present and correlated with the treatment and outcome variables (McClellan, McNeil, and Newhouse 1994; Ettner 1996; Foster 2000; Frances et al. 2000; Howard 2000; Malkin, Broder, and Keeler 2000; Cawley 2000; Goldman et al. 2001). In our analysis, we use differential distance between the transferring center and the nearest level I and level II centers as an instrument.

METHODS

Study Population

We analyzed data from the Rural Trauma Registry (RTR), a retrospective cohort of injured patients initially evaluated at a rural trauma center (level III, IV, or V centers) in Oregon and Washington from January 1991 to December 1994. The design for the RTR database and reliability of the data have been described in detail elsewhere (Mullins et al. 2002). In brief, data in the RTR database were collected for injured patients first evaluated in 32 hospitals located in rural communities in Oregon and Washington. These 32 centers were randomly selected among centers maintaining fewer than 100 acute care beds and located more than 20 miles from another acute care hospital. These rural hospitals were either concurrently, or shortly afterwards, categorized as level III, IV, or V trauma centers by state health division audited processes. To achieve adequate assessment of outcome, patient data were also collected from the level I and II trauma centers to which many of the patients were transferred. The criteria for assigning level I and level II status are very similar in Washington and Oregon.

The subjects of this study were patients with head injury, retrospectively identified from descriptions in their medical records as meeting the criteria for diagnosis of skull fracture, cerebral contusion, traumatic subarachnoid hemorrhage, subdural or epidural hematoma, other traumatic intracranial bleed, reported loss of consciousness, or closed head injury (ICD-9-CM codes: 800, 801, 803, 804, 851, 852, 853, or 854, as detailed in descriptions from their medical records). From the original study sample of 1,266 patients, we restricted our analysis to patients with head injuries who were transferred directly from the emergency department of these rural trauma centers to level I or II trauma centers. Patients in these analyses were transferred from 31 rural hospitals (level III, IV, or V trauma centers) to one of three categorized level I or 12 categorized level II trauma centers. We studied head-injured patients because they have high mortality and have been shown to benefit from trauma care (Mullins et al. 1998b; Mullins et al. 1996). Patients excluded from these analyses included any individuals not transferred to a level I or II center; patients transferred after admission to the initial hospital (i.e., all patients in our study were transferred from the emergency department); and patients who died at the initial hospital. Of the 551 patients fitting these criteria, 9 patients were excluded because of missing data, leaving 542 observations in the final analysis.

Dependent Variable

Our dependent variable was 30-day postdischarge mortality, defined as death during hospitalization or within 30 days after hospital discharge. Thirty-day postdischarge mortality has been shown to be a better outcome measure among hospitalized brain-injured patients than in-hospital mortality (Mullins et al. 1998a).

Treatment Variable

Our treatment variable was a dichotomous variable representing transfer to a level I trauma center, with transfer to a level II trauma center acting as the reference case. The decision about where to send the patient was made by the attending physician at the emergency department where the patient initially presented.

Level I trauma centers provide comprehensive trauma care and are required to have immediate availability of trauma surgeons, anesthesiologists, nurses, and all surgical subspecialties, including cardiac surgery, orthopedics, neurosurgery, cardiology, ophthalmology, plastic surgery, gynecologic surgery, and head and neck surgery. Level I centers are also required to have immediate availability of resuscitation equipment and neuroradiology and hemodialysis. American College of Surgeons' volume performance criteria stipulate that level I centers annually treat 1,200 admissions or 240 major trauma patients or an average of 35 major trauma patients per surgeon. Level I centers provide formal leadership in trauma education, research, and system planning. Most level I trauma centers in the U.S. are university-affiliated teaching hospitals (MacKenzie et al. 2003). Level II trauma centers are also expected to provide comprehensive trauma care but have less stringent volume performance standards relative to level I centers, and no required fulfillment of leadership in teaching or research (MacKenzie et al. 2003).

Independent Variables

Our independent variables consisted of a number of measures of injury severity, and information on patient demographics. The data were collected by trained medical record abstractors using a structured data collection instrument.

The ISS score is a measure of injury severity based on an anatomical scoring system that provides an overall score for patients with multiple injuries. RTR personnel, abstracting information from the medical records of both the rural and transfer hospitals, assigned each injury an Abbreviated Injury Scale (AIS) score, allocated to one of six body regions (head, face, chest, abdomen, extremities [including pelvis], external/soft tissue) (Baker et al. 1974). The scores of the three most severely injured body regions were squared and added together to produce the ISS score, which takes on values from 0 to 75, with higher numbers representing more severely injured patients. The log of the ISS score was used as a regressor, since its effect on mortality is larger in initial increments (0–30) than later increments (45–75). We also included a dichotomous variable for severe head injury that took a value of 1 when the head AIS score had a value of 5 (the most severe, but potentially survivable head injury) and 0 for an AIS less than 5.

RTR personnel abstracted data from the medical record to determine the AVPU score, which represented a measure of neurologic status on presentation to the initial hospital. We used the AVPU, rather than the Glasgow Coma Scale (GCS), because the GCS was missing in 234 observations (43%). This high rate of missing values for GCS is not uncommon in RTRs (Hedges et al. 1997). Because of the large number of persons missing values for GCS, we used another clinical measure of mentation that is more commonly recorded in rural centers, the AVPU score. In cases where the AVPU was not present but GCS was, we converted GCS to AVPU using methods described previously (Olson et al. 2001). The AVPU score has clinical acceptability and relevance, as it is commonly taught as part of Advanced Trauma Life Support courses (the main source of training and education for many rural practitioners in the care of the injured patient), which may have also increased the likelihood that it was recorded. The brain-injured patients in our study were classified as alert (A), responsive to vocal stimuli (V), responsive to painful stimuli (P), or unresponsive (U). Three dichotomous variables were created for AVPU score, with alert (A) patients acting as the reference group. Rural Trauma Registry personnel also used medical records to determine whether the patient was hypotensive (defined as any single systolic blood pressure <70 mmHg or two measurements <90 mmHg) during the stay in the initial emergency department (ED), which was coded as a dichotomous variable.

A unilateral dilated pupil is a potentially predictive variable that may be indicative of head injuries requiring emergent intervention. This variable was collected for 476 observations (12% missing) and tested in the model described below, but was not significantly related to mortality ($p = .91$). We regard the finding of a unilateral dilated pupil as a very specific, but insensitive, indicator of serious head injury. There is also the potential for variability in the recognition and recording of this finding in rural centers, based on the background and training of different health care providers. For these reasons, we did not include this variable in our final model.

RTR personnel also determined patient characteristics that were unrelated to the injury, including, gender, age, and a history of previous comorbid conditions, including any of the following: chronic obstructive pulmonary disease (COPD), diabetes, coagulopathy, liver disease, coronary artery disease, pregnancy, or "other significant medical condition" as recorded in the data (Morris, MacKenzie, and Edelstein 1990). We created dichotomous variables for children <12 years old and adults >55 years old, with the reference group being individuals ≥ 12 and ≤ 55 years.

Instrumental Variable

We defined our instrument, differential distance, as the distance from the initial trauma center to the nearest level I center subtracted by the distance from the initial trauma center to the nearest level II center. For example, if the distance to the nearest level I center was 100 miles and the distance to the nearest level II center was 25 miles, the differential distance would be $100 - 25 = 75$. Differential distance, rather than direct distance, was used because it is likely to influence the choice of where to send the patient but presumably is not associated with other factors that could affect patient outcome.

The validity of instrumental variables models depends on two key assumptions. First, the instrument must be correlated with the treatment variable. In our model, this assumption translates into the requirement that differential distance is a significant predictor of transfer destination. This assumption is easily tested using a Wald test (Bound, Jaeger, and Baker 1995; Staiger and Stock 1997), which tests the significance of differential distance in predicting whether the patient was transferred to a level I or level II trauma center.

The second assumption is that the instrument is not correlated with the outcome, except indirectly through the treatment variable. In our model, we assume that differential distance is not correlated with mortality outcomes, except through transfer destination. Unlike the first assumption, this assumption cannot be directly verified. We examined three potential relationships between differential distance and outcomes that were not related to the treatment variable: (1) the relationship between differential distance and the actual distance traveled (and time required for travel); (2) the potential for differential distance to act as a proxy for remote areas and different types of care received at the initial hospitals that were further away from level I centers; and (3) the potential for injuries to be more severe in remote areas.

Statistical Analysis

Since we modeled a dichotomous outcome (mortality) and dichotomous variable of interest (level I versus level II), we used a bivariate probit model, jointly estimating two equations, each with a dichotomous outcome. We did not use the more familiar "two-stage" approach. A two-stage model that first used a probit to estimate the probability of transfer to a level I center, and then estimated the mortality benefit of transfer to a level I center that used those fitted values in a second probit equation, would not produce consistent estimators. It would be possible to adjust fitted values of the first equation so that they could be used in a two-stage approach, but the full information, maximum likelihood bivariate probit estimation is more efficient (Wooldridge 2002).

We present two analyses in order to illustrate the consequences of referral bias that arise because of unobservable factors. The first analysis used a standard, single-equation probit model. The main outcome variable was a dichotomous variable representing 30-day postdischarge mortality. Covariates included demographic characteristics, measures of injury severity, and a dichotomous variable coded as 0 for patients transferred to a level II center and 1 for patients transferred to a level I center.

The second analysis used an instrumental variables approach, using a bivariate probit to jointly estimate two equations. The first equation had the same outcome measures as those presented in the first, single-equation probit analysis. The second equation in the bivariate probit estimated the decision to transfer the patient to either a level I or level II center. The covariates in this equation included the measures of injury severity and patient demographics included in the first equation, as well as differential distance, which acted as the instrumental variable. Since the 542 patients were transferred from 31 rural hospitals level III, IV, or V trauma centers to 1 of 15 level I or level II trauma centers, we created a variable that identified the transferring center and receiving center pairs. In all regressions, the standard errors of the estimators are adjusted for clustering by transferring center-receiving center pairs.

We performed two standard tests to assess the appropriateness of our instrumental variables model. First, we used a Wald test to determine the strength of our instrument, differential distance (Bound et al. 1995; Staiger and Stock 1997). Second, we used a Hausman test to determine whether a standard, single equation could be used, or whether we must use instrumental variables to remove the bias associated with the unobservable factors (Knapp and Seakes 1998).

A number of complementary models were estimated in order to test the robustness of our model. First, we estimated three additional, more parsimonious bivariate probit models, to examine the effect of removing some of the explanatory variables. In addition, we estimated the model with the full set of covariates using a two-stage linear probability model. In this model, we treated the dichotomous outcomes as continuous variables and ran the standard two-stage least squares instrumental variables model. While this model has drawbacks (for example, it can produce predicted probabilities outside the unit interval), it serves as a useful method for comparison against the bivariate probit model (Angrist 2001; Wooldridge 2002). We used *Stata* version 8.0 (Stata Corp., College Station, TX) for all analyses.

The coefficient estimates of our models are not directly interpretable in terms of policy relevance. Therefore, to aid in interpretation of these coefficients, we determined the mean difference in mortality attributable to transfer to a level I center. First, based on the model coefficients, we estimated the predicted mortality for each patient, assuming all patients were treated at a level I center, and then estimated the predicted mortality assuming all patients were treated at a level II center. We used the difference of the mean of these two values to determine the absolute mortality benefit of transfer to level I trauma centers. We used bootstrapping with 1,000 repetitions to derive 95% bias-corrected confidence intervals (CIs).

Finally, since our instrumental variables estimates depend on the assumption that differential distance is not correlated with mortality, except through transfer destination, we conducted a series of tests and examinations of the data aimed at identifying trends in times or distances of patient transport, care at the initial hospital, or patient injury severity. These examinations of the data can be useful in identifying any potential problems with our instrument.

RESULTS

Descriptive means for all model variables are given in Table 1. We present these means in three ways: for the entire population; by transfer destination (level I and level II); and for patients transferred from centers that were relatively close, or relatively far from the nearest level I center. Of the 542 patients in our analysis, 270 (49.8%) were transferred to 1 of 12 level II centers and 272 (50.2%) were transferred to 1 of 3 level I centers. Thirty-six (13.3%) patients transferred to level II centers and 42 patients transferred to level I centers (15.4%) died during hospitalization or within 30 days of hospital discharge. In general, more severely injured patients were transferred to level I centers.

The last two columns in Table 1 were created by dividing the patient populations into two groups of roughly equal size, based on the median differential distance of 39.4 miles. A comparison of these two groups, patients relatively close to level I centers compared with patients relatively close to level II centers, provides some insight into the instrumental variables mechanism. The groups appear to be approximately comparable in terms of demographics and measures of injury severity. They differ primarily in the distance from level I trauma centers and in the likelihood of transfer to level I trauma centers, with 80.4% of patients relatively close to level I centers transferred to level I centers, and only 21.3% of patients closer to level II centers transferred to level I centers. Despite the other similarities between the two groups, the patients closer to level I trauma centers have a lower mortality rate. If grouping by proximity to level I trauma centers is an effective randomiza-

Table 1: Patient Characteristics, by Total Sample; Transfer Destination; and Relative Proximity to Level I Trauma Center

Variable	*All Patients (n = 542)*	*Transferred to Level I Centers (n = 272)*	*Transferred to Level II Centers (n = 270)*	*Differential Distance < 39.4 Miles (n = 265)*	*Differential Distance ≥ 39.4 Miles (n = 277)*
Age	28.5 (20.3)	29.8 (19.8)	27.1 (20.8)	28.6 (20.4)	28.4 (20.2)
Female (%)	29.5	26.8	32.2	28.3	30.7
Transferred within Oregon (versus Washington) (%)	57.8	39.7	75.9	44.5	70.4
ISS	19.8 (11.4)	21.4 (11.7)	18.3 (10.7)	19.6 (11.1)	20.2 (11.5)
History of comorbid condition(s) (%)	12.9	13.6	12.2	14.7	11.2
AVPU score					
Patient alert (AVPU = A) (%)	49.4	48.1	50.8	48.3	50.5
Patient responds to vocal stimuli (AVPU = V) (%)	10.2	8.1	12.2	10.2	10.1
Patient responds to painful stimuli (AVPU = P) (%)	9.4	8.1	10.7	8.3	10.5
Patient unresponsive (AVPU = U) (%)	31.0	35.7	26.3	33.2	28.9
Patient hypotensive at initial ED presentation	6.1	6.3	5.9	5.7	6.5
Patient transferred to level I center (%)	50.2	—	—	80.4	21.3
Distance to nearest level I center	154.9 (79.5)	115.0 (41.8)	195.1 (87.8)	103.9 (28.3)	203.8 (82.0)
Differential distance between transferring center and nearest level I and level II centers	67.5 (84.0)	17.5 (56.9)	117.8 (76.7)	3.7 (38.8)	128.5 (69.1)
30-day mortality (%)	14.4	15.4	13.3	12.8	15.9

Note: Number in parentheses indicates standard deviation.

ED, emergency department; ISS, Injury Severity Scale.

tion, a simple measure provides some insight into the mortality benefits of transfer to level I centers. With a 59.1% increase in the percentage of patients taken to level I centers, there is an approximate 3.1% decline in mortality. The full instrumental variables model aims at developing a more detailed statistical estimation of the mortality benefits of level I centers.

In order to compare the results of the instrumental variables model to a standard, single-equation model, we show the coefficients of the two contrasting models in Table 2. The results of the standard, single-equation probit model are shown in columns 2 and 3 of Table 2. Variables that are significantly associated with increased mortality (i.e., positive coefficients) include: age >55 years, log (ISS), head AIS of 5 (the most severe head injury), hypotension in the emergency department, and initial neurologic status other than alert (AVPU score of V, P, or U). The AVPU is clearly related to mortality in our sample, showing increasing significance and generally increasing magnitude with the progression from A (alert) to U (unresponsive). In this model, the coefficient for transfer to level I centers is negative (beneficial) but not statistically significant. However, these estimates may be biased if, after adjusting for observed characteristics, more severely injured patients are more likely to be transferred to a level I center. To develop an unbiased estimate of the effect of care at level I centers, we use the instrumental variables approach.

Using differential distance as an instrumental variable, the bivariate probit model results are displayed in the last two columns of Table 2. In essence, we jointly estimate the decision about where to send the patient and the outcome based on that transfer decision. The coefficient estimates of the first equation, with 30-day mortality as the outcome, are shown here. In contrast to the standard probit model, the instrumental variables estimation finds a mortality benefit of transfer to a level I center relative to a level II center ($p = .017$). Coefficients on the other variables are qualitatively similar for the single-equation probit model and the instrumental variables, bivariate probit model.

To aid in interpretation of these coefficients, we calculated the predicted mortality for all patients in our sample both as treated at a level I and at a level II center, and then computed the relative impact of level I treatment on mean mortality. Using estimates from the bivariate probit model, we estimated the mean absolute mortality benefit of transfer to a level I trauma center to be 10.1% (95% CI: 0.3%, 22.1%).

An important assumption of our model is that differential distance is a significant predictor of transfer destination. A Wald test confirmed that differential distance is a very strong predictor of transfer destination (Wald test = 26.6, $p < .001$). We also conducted a Hausman test to determine whether

Table 2: Multivariable Model Results for 30-Day Mortality, Adjusted for Clustering by Transferring–Receiving Center Pairs

	Standard Single Equation Probit Model		*Instrumental Variable Bivariate Probit Model*	
*Variable**	*Coefficient (95% Confidence Interval)*	*p-Value*	*Coefficient (95% Confidence Interval)*	*p-Value*
Patient transferred to level I center	−0.132 (−0.461, 0.195)	0.427	−0.684 (−1.248, −0.120)	0.017
Age				
$<$12 years	−0.048 (−0.555, 0.459)	0.854	−0.043 (−0.753, 0.189)	0.864
$>$55 years	1.011 (0.560, 1.462)	$<$0.001	1.008 (0.538, 1.478)	$<$0.001
Female	−0.112 (−0.443, 0.219)	0.507	−0.094 (−0.411, 0.223)	0.561
Comorbid condition(s)	0.318 (−0.107, 0.743)	0.142	0.354 (−0.072, 0.781)	0.104
Transferred within Oregon (versus Washington)	−0.187 (−0.538, 0.164)	0.296	−0.363 (−0.735, 0.008)	0.055
Log (ISS)	0.650 (0.215, 1.085)	$<$0.001	0.701 (0.273, 1.129)	0.001
Head AIS = 5	0.670 (−0.273, 1.067)	0.001	0.638 (0.237, 1.040)	0.002
AVPU score				
Patient responds to vocal stimuli (AVPU = V)	0.716 (0.028, 1.403)	0.042	0.645 (−0.109, 1.399)	0.093
Patient responds to painful stimuli (AVPU = P)	0.724 (0.171, 1.278)	0.010	0.698 (−0.109, 1.399)	0.010
Patient unresponsive (AVPU = U)	1.336 (0.801, 1.872)	$<$0.001	1.342 (0.842, 1.841)	$<$0.001
Patient hypotensive at initial ED presentation	0.451 (−0.051, 0.953)	0.079	0.432 (−0.072, 0.937)	0.093

*The reference groups are patients transferred to level II centers, age ≥ 12 and ≤ 55 years, male, transferred from emergency department (ED) in the state of Washington, no history of comorbid conditions, head AIS <5, AVPU score of A (patient alert), patient not hypotensive at initial ED presentation.

the instrumental variables model was appropriate; that is, if there were unobserved factors that influenced mortality and the decision to transfer to a level I or level II trauma center. Despite the use of detailed data and validated measures of injury severity, a Hausman test rejects at the 5% level our single-equation model (Knapp and Seakes 1998). This suggests that, even after adjusting for observed patient characteristics, transfer destination is still confounded by mortality risk and that an approach using instrumental variables may provide a less biased estimate.

We applied several different models to check the robustness of our results. In addition to the single-equation probit and bivariate probit models described above, we also estimated three additional bivariate probit models with a reduced set of covariates. In the first, we eliminated most measures of injury severity, using as covariates log (ISS), gender, dichotomous variables for children <12 years old and adults >55 years old, history of comorbid condition(s), whether the patient was transferred within Oregon (versus Washington), whether the patient was transferred to a level I or level II trauma center, and differential distance as an instrument. In the second, we eliminated most demographics, using as covariates three dichotomous variables for AVPU score, with alert (A) patients acting as the reference group, log (ISS), hypotension, head AIS of 5, whether the patient was transferred to a level I or level II trauma center, and differential distance as an instrument. In each of these reduced models, the elimination of additional variables was such that a likelihood ratio test rejected the hypothesis that the more parsimonious models were equivalent to the full model. Therefore, we also estimated a third model that retained the most significant variables: log (ISS), a dichotomous variable for AVPU score of U (unresponsive), head AIS of 5, age >55, whether the patient was transferred within Oregon, whether the patient was transferred to a level I or level II trauma center, and differential distance as an instrument. Using a likelihood ratio test, we could not reject the hypothesis that this model was equivalent to the full model. (Technically, the likelihood ratio test is not valid when used with clustering; however, since we were primarily interested in investigating the sensitivity of our finding to different models, we used this test as an indicator of substantial structural difference between models.) Estimates for the absolute reduction in mortality and 95% CIs for each of these models are displayed in Table 3. In addition, we used a two-stage, linear probability model using the original set of covariates. The results of this model are also shown in Table 3.

Point estimates of the mortality benefit of level I trauma centers range between approximately 7% and 13% for our instrumental variables models.

Table 3. Mortality Benefits of Transfer to Level I Trauma Center, Comparing Different Model Specifications

Model	*Estimated Mortality Benefit from Transfer to Level I Trauma Center (%)*	*95% CI (Bootstrapped with 1,000 Replications, Bias-Corrected)*
Single-equation probit*	1.9	(−3.2%, 6.5%)
Instrumental variables, bivariate probit†	10.1	(0.3%, 22.2%)
Bivariate probit, reduced covariates model 1‡	9.9	(−2.1%, 20.6%)
Bivariate probit, reduced covariates model 2§	7.3	(0.1%, 20.3%)
Bivariate probit, reduced covariates model 3¶	12.6	(1.9%, 26.1%)
Two-stage, linear probability model†	7.0	(0.04%, 13.8%)

*Covariates include: whether the patient was transferred to a level I or level II trauma center; dichotomous variables for children <12 years old and adults >55 years old; gender; a history of comorbid condition(s); whether the patient was transferred within Oregon; log (ISS); Head Abbreviated Injury Scale (AIS) of 5; AVPU score = V; AVPU score = P; AVPU score = U; hypotension in the emergency department (ED).

†Covariates include: whether the patient was transferred to a level I or level II trauma center; dichotomous variables for children <12 years old and adults >55 years old; gender; a history of comorbid condition(s); whether the patient was transferred within Oregon; log (ISS); Head AIS of 5; AVPU score = V; AVPU score = P; AVPU score = U; hypotension in the ED. Differential distance is used as the instrumental variable.

‡Covariates include primarily demographic variables: whether the patient was transferred to a level I or level II trauma center; whether the patient was transferred within Oregon; dichotomous variables for children <12 years old and adults >55 years old; gender; history of comorbid condition(s); log (ISS). Differential distance is used as the instrumental variable.

§Covariates include mostly measures of injury severity: whether the patient was transferred to a level I or level II trauma center; log (ISS); AVPU score = V; AVPU score = P; AVPU score = U; hypotension, and head AIS = 5; hypotension in the ED. Differential distance is used as the instrumental variable.

¶Covariates include: whether the patient was transferred to a level I or level II trauma center; dichotomous variables for adults >55 years old; whether the patient was transferred within Oregon; log (ISS); head AIS of 5; AVPU score = U. Differential distance is used as the instrumental variable.

The estimates show some sensitivity to model specification. In particular, if measures of injury severity are removed, the 95% CI is wide enough to include zero. The two-stage, linear probability model offers results qualitatively similar to the bivariate probit model, with the mortality benefit of level I care estimated to be 7.0%, and a tighter CI around this estimate that is close to zero.

As noted above, the instrumental variables models rely on two important assumptions: (1) differential distance must be a significant predictor of whether the patient is transferred to a level I or level II trauma center; and (2) differential distance must not be correlated with mortality, except through transfer to level I or level II trauma center. The first assumption has been verified using the Wald test. The second assumption cannot be statistically validated. However, we considered three ways in which this assumption could be violated. First, greater differential distance might imply more distance traveled and thus more time required to transfer the patient. Second, hospitals with larger differential distance measures are more remote from the large metropolitan areas where most level I trauma centers are located, and care may differ at these hospitals. Finally, patients initially presenting at more remote hospitals might be more severely injured than patients initially arriving at hospitals closer to level I trauma centers. We describe the examinations of each of these possibilities below.

Differential distance is defined as: distance to the nearest level I center − distance to the nearest level II center. Thus, if differential distance is 100 miles we only know that the patient must be transported at least 100 miles to get to the level I center, but we have no information about the distance to the nearest level II center. The correlation coefficient between differential distance and actual distance traveled is 0.014, indicating a low level of correlation between the two. Furthermore, there is little evidence that distance traveled is correlated with mortality. The mean distance traveled for those patients who lived is 95.2 miles, and is 102.3 for those patients who died. This difference is not significant (Mann–Whitney test, $p = .41$). The correlation coefficient between differential distance and actual distance traveled for those patients who died is −0.029.

There is also the potential that time elapsed during transfer could confound our model. If so, we would expect that the transfer time interval would be longer for level II trauma centers, or perhaps that it would be longer among patients who died. The data gathered on patients contained some information on the time elapsed during transfer, although these data are less reliable than data on distance. We examined this data after excluding missing values ($n = 32$), negative values ($n = 2$), and outliers (i.e., transfer time intervals recorded as lasting more than 3 hours or less than 10 minutes, $n = 12$), leaving 495 observations. The mean recorded time elapsed during transfer was 64.3 minutes, with no significant difference between times for patients who lived and patients who died (Mann–Whitney test, $p = .94$), and no significant difference between times of transfer for level I and level II trauma centers (Mann–Whitney test, $p = .12$). Among patients who died, transfer time intervals to level I trauma centers were recorded to be 5 minutes longer on average, although this was not a significant difference (Mann–Whitney test, $p = .16$). Thus, it seems unlikely that time is a substantial confounder in our analysis, and the data do not appear to invalidate our instrument. The fact that different modes of transportation (i.e., ground, helicopter, fixed-wing aircraft) were used for transporting patients from rural hospitals may partly explain these findings. We did not include time elapsed during transfer as an independent variable in our models because RTR personnel could not resolve several of the inconsistencies in the data. We were also concerned that, since more severely injured patients would be likely to have expedited transfers, including transfer time interval would introduce the same biases that were our intent to remove.

As shown in Table 1, hospitals with greater differential distance are further away from the nearest level I center, which were major university centers. If care differed at more remote hospitals in a way that resulted in increased mortality, then our instrument would not be valid. One possibility might be that more remote hospitals were less likely to be level III trauma centers and more likely to be level IV or V trauma centers. We found that, in general, more remote hospitals are slightly more likely to be level IV or V hospitals, but this correlation was not statistically significant (Kendall's τ-b $= 0.23$; $p = .13$) We also checked for the potential for more remote hospitals to be less likely to have a physician present when the patient arrived at the ED. We found a similar result, with more remote hospitals slightly less likely to have a physician present when the patient arrived, although this too was not statistically significant (Cochran–Armitage test; $p = .14$).

The geographical distance from the nearest level I center was strongly associated with transfer patterns. Some hospitals in our sample always transferred patients to level I centers (six hospitals transferring 79 patients), and others always transferred to level II centers (11 hospitals transferring 142 patients). There were two hospitals that were closer to level I centers than level II centers that occasionally made transfers to level II centers, for a total of five observations (all five patients survived). We do not know the motivating factors for these decisions; the lack of bed availability or similar factors may have affected the final destination of these patients. In addition, there were five hospitals that were relatively closer to level II centers but always transferred to level I (for a total of 60 observations). Because differences in outcomes might be due to preexisting transfer patterns at certain hospitals (i.e., always transferring to a certain trauma center), we estimated our model on the 14 hospitals (transferring 321 patients) that did not exclusively transfer patients to either a level I or level II center (i.e., each of these hospitals sent patients to both level I and level II centers). When we estimated our model on this subset of 321 patients (59% of the original sample), we found that the mortality benefit of transfer to level I centers was not significant (estimated benefit: 3.3%, 95% CI: -6.6%, 22.1%). However, the coefficients on many other variables also lost significance. We estimated a more parsimonious model that included whether the patient was transferred to a level I center; a dichotomous variable for unresponsive patient (AVPU = U); log (ISS); a dichotomous variable for patient age > 55; and differential distance as the instrument. A likelihood ratio test did not reject the hypothesis that this more parsimonious model was significantly different from the full model ($p = .11$). In this restricted model, estimated mortality benefit of transfer to level I centers was significant at the 10% level (estimated benefit: 9.4%, 90% CI: 0.7%, 26.4%). The lack of strong significance may reflect differences in care that exist at the originating hospital, or may be because of the relatively small sample size, as the estimates based on this restricted sample otherwise qualitatively support our model.

Previous studies have shown that more rural areas have progressively higher mortality rates from motor vehicle trauma (Baker, Whitfield, and O'Neill 1987). If more severely injured patients present to more remote hospitals, then our instrument would be invalid. To test for the potential for more severe injuries in more remote areas, we looked for trends in our variables included in the model and in a number of additional variables, including AIS score for head, face, chest, abdomen, extremities, and external (soft-tissue) injuries, the presence of a penetrating (versus blunt) injury, and the presence of unequal dilated pupils. We looked for trends by dividing hospitals into 10 groups based on increasing levels of differential distance, and by separating patients based on differential distance and the originating hospital (31 groups). Most variables showed no significant trend that suggested increasing injury severity with more remote hospitals, with two exceptions. Thirty-three patients were recorded as hypotensive, and this was more frequent at more remote hospitals (Cochran–Armitage test, $p = .004$). In addition, there was a slight increase in the prevalence of patients with chest injuries (Cochran–Armitage test, $p = .08$), although these injuries were not progressively more severe at more remote locations. Thus, although most variables suggested that patients did not vary in substantially different ways across hospitals, we did find limited evidence that patients presenting to more remote hospitals are injured in ways related to geographical location.

DISCUSSION

Do the additional patient volume, physician experience, and trauma center resources required for level I certification have a positive effect on patient outcomes? Until now, most studies have suggested that care is comparable between level I and II trauma centers. An analysis by Clancy et al. (2001) on mortality outcomes for patients in North Carolina found no statistically significant difference between level I and II trauma centers. A number of other investigators have failed to find significant benefits in patient outcomes associated with the characteristics required for designation as a level I trauma center (Waddell and Kalman 1991; Thompson et al. 1992; Barone et al. 1993; Norwood and Myers 1994; Helling et al. 1997; Allen et al. 1998; Richardson et al. 1998; Demarest et al. 1999; Cooper et al. 2000; Margulies et al. 2001). However, these analyses typically rely on imperfect measures of injury severity and do not account for the possibility that available patient data do not adequately capture the patient's true mortality risk (Demetriades et al. 2001). As a result, patients transferred to or treated at level I centers may be different in substantial ways, even after adjusting for measures of injury severity. In this case, analyses of level I centers will result in biased estimates. The data in our analysis may serve as an indication of this phenomenon. Previous studies relying on recorded injury data may have resulted in biased estimates of the effect of transfer on mortality.

The results from the full instrumental variables model suggest that a 10% increase in the percentage of head-injured patients transferred to level I centers results in a 1.0% decline in absolute mortality among the population of patients with head injuries initially presenting to rural EDs. This favorable finding assumes that enhanced survival would occur through an increase in accessibility of service equivalent to that currently found at level I centers. We cannot exclude the possibility that greater transfers to level I centers, if accompanied by longer transports, may delay critical interventions. More aggressive use of aeromedical transport for head-injured patients may mitigate that potential (Mann et al. 2002).

Previous authors have noted that instrumental variables estimates are indicative of the treatment effect on the "marginal patient"; that is, the subgroup of patients whose treatment status depends upon the value of the instrumental variable (Harris and Remler 1998). In most studies using instrumental variables, there are many factors that are likely to decide whether a patient receives a specific treatment, with the instrument playing a small but significant role. In these cases, the estimated treatment effect may apply to a subpopulation of "marginal patients" that makes up a relatively small percentage of all patients considered. However, our instrumental variable is likely to play a very large and important role in the decision about where to transfer head-injured patients. In fact, differential distance was associated with rates of transfer to level I trauma centers ranging from 100% (for those hospitals closest to level I trauma centers) to 0% (for those hospitals furthest from level I trauma centers). Thus, we believe most of the patients in our sample qualify as "marginal patients," and assume that our estimates of mortality benefits would apply to the majority of head-injured patients transferred in such a rural trauma system. Nonetheless, these estimates may not apply to all injured patients, particularly not to those patients for whom proximity to the nearest trauma center is not a factor in determining where they should be treated.

This observational study has limitations and the results warrant validation in trauma centers outside of Oregon and Washington. The sample was limited to patients with head injuries and was based on transfers to level I and II centers, and may not be representative of all trauma patients treated in these centers. Our study was limited to available chart review data from 1991 to 1994, and may not reflect the state of care in current trauma centers. Different models and the selection of variables to include in these models produced some variation in estimates of mortality benefits for patients transferred to level I trauma centers, although the direction of effect was consistent (i.e., beneficial) and generally significant at the $p = .05$ level.

A crucial assumption of our analysis is that differential distance is not correlated with mortality, except through the transfer variable. Differential distance does not appear to be significantly correlated with the time or distance used to transfer patients, nor was it associated with measures of remoteness or the initial level of care. We found some evidence that patients at more remote hospitals might be more severely injured, since these patients were more likely to be hypotensive and have chest injuries, although this trend was not present among other measures of injury severity. We were also unable to show a statistically significant result (at the $p = .05$ level) when we examined the subset of hospitals that transferred patients to both level I and level II hospitals, although this finding may be because of a lack of power in the reduced sample.

On the basis of our analysis, the interhospital transfer of head-injured patients to level I trauma centers results in a significant mortality benefit when compared with those transferred to level II centers. This analysis has important implications for health service researchers, policy makers, and practitioners. Researchers must consider new methods of addressing referral bias when comparing hospital- or provider-level outcome differences. Health policy makers and funders must address the importance of referral bias when comparing crude outcome rates and when developing inter-facility transfer guidelines. Efforts to clarify the interventions and resources associated with improved outcome at current Oregon and Washington level I centers are warranted. Such knowledge would enhance practitioners' management of head-injured patients at select level II centers and guide transfer decisions elsewhere.

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