Is There A Golden Hour in Combat Casualty Evacuation?

Joint Theater Trauma Registry 2003 through 2011

Scott H. Robinson

A thesis submitted in partial fulfillment of the requirements for the degree of

Master of Public Health

University of Washington

2014

Committee:

Joel D. Kaufman

Michele A. Soltis

Charles N. Mock

Program Authorized to Offer Degree:

School of Public Health

Department of Environmental and Occupational Health Sciences

University of Washington

Abstract

Is There A Golden Hour in Combat Casualty Evacuation?

Joint Theater Trauma Registry 2003 to 2011

Scott H. Robinson

Chair of the Supervisory Committee:

Professor Joel D Kaufman

Department of Environmental and Occupational Health Sciences

Background

In the late 1960s and early 1970s it was asserted that the most critical aspect of trauma care was early arrival to surgical care, especially within the first sixty minutes after injury. This presumed relationship between time and mortality became popularly known as "The Golden Hour", and has driven Emergency Medical System (EMS) organization since.

In robust civilian Emergency Medical Services trauma transport and treatment systems, large studies are now showing that there is no relationship between relative increases in total pre-hospital time and mortality. These new surprising and robust results contradict the conceptual framework that drove the development of rapid response EMS systems in our nation and across the globe.

Purpose

The purpose of this study is to test the hypothesis that there is a relationship between total out of hospital time and mortality in the US military combat casualty care system, especially whether there is a "Golden Hour". We did this using data from the main data collection on

casualty care and outcome within the military, the Joint Theater Trauma Registry, with the secondary aim of informing improvements to this data collection system.

Methods

The Joint Theater Trauma Registry collects data primarily at the point of surgical care on patients evacuated to and treated at a theater surgical hospital. A data set of all patients with a known value for total pre-hospital time was requested and provided to the researchers. Data was available on evacuations occurring between 2003 to early 2012. Using logistic regression, adjusted odds ratios were calculated for the association of total out of hospital time and mortality. We also report adjusted odds ratios and p values for multiple other descriptors of interest.

Results

We found lower in-hospital mortality among casualties with longer pre-hospital time. Using a time variable grouped by 20 minute intervals, we determined an odds ratio of 0.890 (95% CI of 0.823 to 0.963) for mortality trend associated with increasing pre-hospital time. Testing for interaction between Injury Severity and increasing prehospital time revealed a magnification of this protective effect. Casualties arriving with an Injury Severity Score (ISS) score of between 16-50 had a 1.3 times greater survival with prehospital times greater than sixty minutes as compared to those with less than sixty minutes, and the same comparison for patients with ISS scores of 51 or greater yielded a four fold higher survival.

Conclusion

In-hospital mortality is significantly lower for patients with longer pre-hospital times, and this effect is magnified for patients with greater injury severity. This observation may be

explained by selection out of the group available for analysis, or due to more rapid evacuation of the most seriously injured but survivable injuries. Overall, rather than testing the golden hour hypothesis, our findings likely represents a winnowing effect, in which longer pre-hospital times and greater injury severity result in death during the pre-hospital period.

TABLE OF CONTENTS

List of Tables

List of Figures

CHAPTER I: Background and Significance

Time and Mortality from Trauma

Since the 1970s the provision of pre-hospital care and the organization of trauma services have been dominated by the dogma of the golden hour concept, that there is a short window of time within which to get trauma patients to surgical care[17, 18, 19]. That concept has never been rigorously demonstrated to be true, and has recently come under increasingly robust scrutiny.

Newgard et. al. 2010[1], in analysis of a multi-site cohort of 3656 patients with hemodynamic instability at the time of arrival of Emergency Medical Services (EMS), found no significant association between prehospital time (the time between 911 call and arrival at a trauma center) and subsequent in-hospital mortality. This challenge to the dogma of the golden hour has resulted in a new focus on pre-hospital care research, and even suggested that the "routine lights-and-sirens" approach to trauma transport may not be necessary.

Cudnik et. al, 2012[11] analyzed predictors of mortality among 557 patients transported by air to a level I trauma center, and found no association between the distance from the trauma center and mortality. However, 97% of these patients had a blunt mechanism of injury limiting the generalizability of this data to combat casualties.

McCoy et al 2013[5] examined 19,167 trauma patients transported over a 14 year period, with an overall mortality of 4.5%. With respect to generalizability, the study authors separately analyzed the blunt and penetrating trauma; 15% of patients had penetrating trauma, making this one of the more useful data sets for comparing to combat casualty data. They stratified the patients by Injury Severity Score (ISS) using bins of 0-15, and 16-75. They performed logistic regression and found an odds ratio of 2.90 (1.09 – 7.74) of mortality for scene time greater than 20 minutes, compared to less than 9 minutes for penetrating trauma, and no association between increased transport time and mortality. The same analysis for blunt trauma revealed no association between mortality and scene time, transport time, or total transport time. They interpreted their results as supporting the golden hour concept for penetrating trauma while validating the growing data set questioning the golden hour concept for most civilian trauma patients.

It is possible that McCoy et al's ISS categorization leads to confounding in their analysis. Among their patients with blunt trauma, the percent mortality among patients with an ISS score greater than 15 was 22.6%, while for penetrating trauma the percent mortality among those with an ISS score greater than 15 was 40.9%. The mean Revised Trauma Score (RTS) for penetrating trauma compared to blunt was 7.1 vs 7.5, and was more variable with a standard deviation of 1.9 vs 1.13. When taking into account the extreme mortality seen in, for example, the data published by Morrison et al[4] for ISS >50 it seems plausible that including the 51-75 ISS group with the 16-50 group in one bin was insufficient to control for confounding by ISS in this study. Finally, the mean evacuation times for both blunt and penetrating trauma in this study was 26 minutes, and no patient had a total pre-hospital time greater than 60 minutes. From the sparse data published to date on combat casualties, total pre-hospital times greater than 60 minutes are common.

M.M. Dinh et.al, [7], looked specifically at subdural hemorrhage and found that there was no statistically significant benefit in survival to arrival at the hospital within 60 minutes of injury compared to the greater than 60 minutes group; finer subdivision of patients into 30 minute blocks found a survival benefit for the groups arriving in less than 90 minute and less than 120 minute. However, the difference in mortality was not apparent until 24 days post injury. Others have also looked at subdural hemorrhage and obtained similar results[6].

Hence, there is an increasing evidence base that mortality from trauma is not closely linked to a golden 60 minute time window, and this has meaningful implications for the organization of military trauma care systems.

Another consideration for studies of this type is control for confounding by injury severity and other factors[2-4, 8-11]. ISS scoring appears to have substantial validity for scoring penetrating and polytrauma as compared to the blunt trauma more common in civilian trauma systems[9]. It is also not clear what is the most appropriate method of categorizing ISS scores to best control for confounding while preserving statistical power.

Kahl et. al. 2013[14] looked at 27,276 patients admitted for trauma to Scripps Hospital in San Diego between 2000 and 2011, and found that the annual mean of ISS varied from 8.0 to 10.1 across the study period, with mean ISS among those who died varying from 35.2 to 28.3. After ISS, they found age >65 to be the most significant predictor of mortality after trauma. The implications of this analysis is primarily that ISS categorization for the primary analysis should include higher values than 25 or it will it result in excluding most

persons at risk for mortality from the primary analysis with the potential consequence of very low power.

Morrison 2013[4] analyzed the difference in 30 day mortality for North Atlantic Treaty Organiation (NATO) troops evacuated to a single Role III hospital in Afghanistan conditioned on the level of provider (physician or aviation medic) that was present on the airframe used for evacuation. This study was unique among the current published data from Afghanistan/Operation Enduring Freedom (OEF) and Iraq/Operation Iraqi Freedom (OIF) in providing a detailed description of pre-hospital time for both cohorts. In this study the median (interquartile range) pre-hospital times were 78 (58) and 75 (93) minutes respectively. These total times describe the time from 9 line MEDEVAC request to patient arrival at the ED. For the purpose of this analysis, the most valuable part of the study is the detailed description of mortality by ISS in the 1721 patients for whom they had complete enough data, which I reproduce in part below in the my discussion of power and sample size, but will summarize as showing extremely high mortality in the ISS greater than 50 group. The more generically important result from this study was a finding of statistically and clinically relevant improvement in mortality for physician-provided en route care in patients with an ISS between 16 and 50. Our take home message from this is that patients with an ISS between 16 and 50 are the relevant patients to study for an effect of prolonged evacuation times, as they are the mostly likely to benefit from earlier intervention or be harmed by late intervention in the absence of physician provided en route care. Further implications are that assets available to the different theaters will vary significantly, as MERT-E and other medical evacuation configurations of the Chinook (CH-47) helicopter were not used in the Iraq theater, and were to the best of our knowledge utilized exclusively

in Afghanistan where the greater elevations made alternatives to the UH-60 Blackhawk platforms necessary.

The overall pattern that emerges from this data is that prehospital time is only weakly correlated with mortality for trauma patients, and that few studies have been able to address this taking into account injury severity. One additional gap is the lack of comprehensive studies of military trauma. Morrison et. al. recently described differences between patients in mortality based on both ISS cutoffs and the level of the provider providing en route care during evacuation from the point of injury to definitive surgical care, but this study did not examine the effect of the total transport or out of hospital time itself. A study of military casualties asking specifically what the effect of the total time out of hospital has on mortality is critical, especially since military casualties in general appear to have much greater total pre-hospital times than the great majority of civilian trauma victims. Studying a military specific population is important, because of the differences in mechanism of injury and systems of evacuation even for patients with the same level of injury severity raises the question in military circles of whether conclusions from data on civilian casualties are generalizable to military care systems.

Any study of military populations at war must take into account or at least acknowledge differences across time and between conflicts in tactics, terrain, and technology. The most obvious difference between Iraq and Afghanistan is the terrain. The average elevations in Iraq are several thousand feet lower than in Afghanistan. Overcoming the challenges presented by high altitude for helicopter evacuation has required the use of helicopter types (specifically the Chinook CH-47) that are larger and incidentally faster in Afghanistan, that were rarely used in Iraq for casualty evacuation. Other differences include the general impossibility of ground evacuation in Afghanistan, the much larger distances to be crossed, and the much greater predominance in Iraq of combat in urban environments. The

technologies employed also differ between theaters. In Iraq, highly lethal devices known as EFPs were employed against coalition forces that have been almost absent from the Afghanistan theater. Protective technology such as mine resistant vehicles were not available at earlier timepoints, and were only gradually introduced, starting in 2006 and not becoming the standard vehicle for years.

If the golden hour hour dogma mandating rapid transport to surgical care is not based on physiology, the important feature of a care system may be early provision of non-surgical skilled care and not provision as early as possible of definitive surgical care (as implied by both Morrison 2013 and Apodaca 2013). The military has a ready resource that is currently available but largely sits unused in the current battlefield environment, the Physicians and Physician Assistants assigned to every Battalion of combat soldiers while on deployment. Findings about the golden hour have the potential to prompt changes in not just MEDEVAC policy and allow for a more efficient and safer employment of helicopter evacuation, but also changes in tactical employment efficiency of battalion level medical assets, and to the training of unit medics.

CHAPTER II: Materials and Methods

Data

The data was obtained by request from the Joint Theater Trauma Registry, maintained by the Army Institute for Surgical Research (AISR) at Brooke Army Medical Center of Fort Sam Houston.

The Joint Theater Trauma Registry(JTTR) collects information on every patient treated for trauma in both deployed and garrison military treatment facilities (MTF). It collects more complete information on battle injuries than on non-battle injuries, and has grown over time, so more recent injuries have more detailed information and are more likely to have complete information[17].

Data on all patients with battle injuries sustained in the Iraq and Afghanistan theaters who were evacuated to a surgical hospital between 2001 and 2012 was requested from the JTTR. The following data points were provided as a result of this request: Theater of Operation (Iraq or Afghanistan), Medical Treatment Facility (MTF), Injury Year, Calculated Minutes from Date/Time of Injury to Arrival at Initial Role 3 MTF, Patient Category (Army Navy, etc.), Age, Battle/Non-Battle Injury, Mechanism of Injury (Blast, Gunshot, etc.), Injury Type (Penetrating, Blunt, etc.), Mode of Arrival (Helicopter, Ground etc), Glasgow Coma Scale, 2005 ISS, Initial Emergency Departament (ED) International Normalized Ratio (INR), and Outcome (lived/died prior to transfer out of Theater). All data was provided de-identified.

Data Analysis

The database ultimately provided for analysis from the JTTR by AISR was comprised of 10433 patient evacuations. 507 patients were excluded for having a recorded time of zero for pre-hospital time. Further exclusions were 18 patients whose age was less than 18, 21 patients without ISS scores, and 9 persons without data for outcome. This left 9878 individual evacuations for analysis. During the years studied, there were 51,475 battle injuries officially recorded by the Department of Defense Trauma Registry, and 4693 battle

deaths (including both died of wounds (DOW) and those killed in action (KIA))[25].
The patient population was described by the following variables: gender, patient description, military operation (OIF/OEF/OND), mechanism of injury, dominant injury type (blunt, penetrating, burn, other, unknown), date of evacuation (month/year), transport time in minutes, transport method (helicopter, etc.), level of facility transported to, outcome, ISS score, and age. For some patients, the area specific area score(s) used to calculate the combined Injury Severity Score (ISS) value were also available.

The main source of data entered into the JTTR is whatever information is available about the patient's circumstances of injury at the time of arrival to the hospital. Automated data extraction from the electronic medical record also assists in population of the database. Information sources include the patient, those accompanying the patient, the medical record, and DD1380 (if present).

DD1380, Field Medical Card

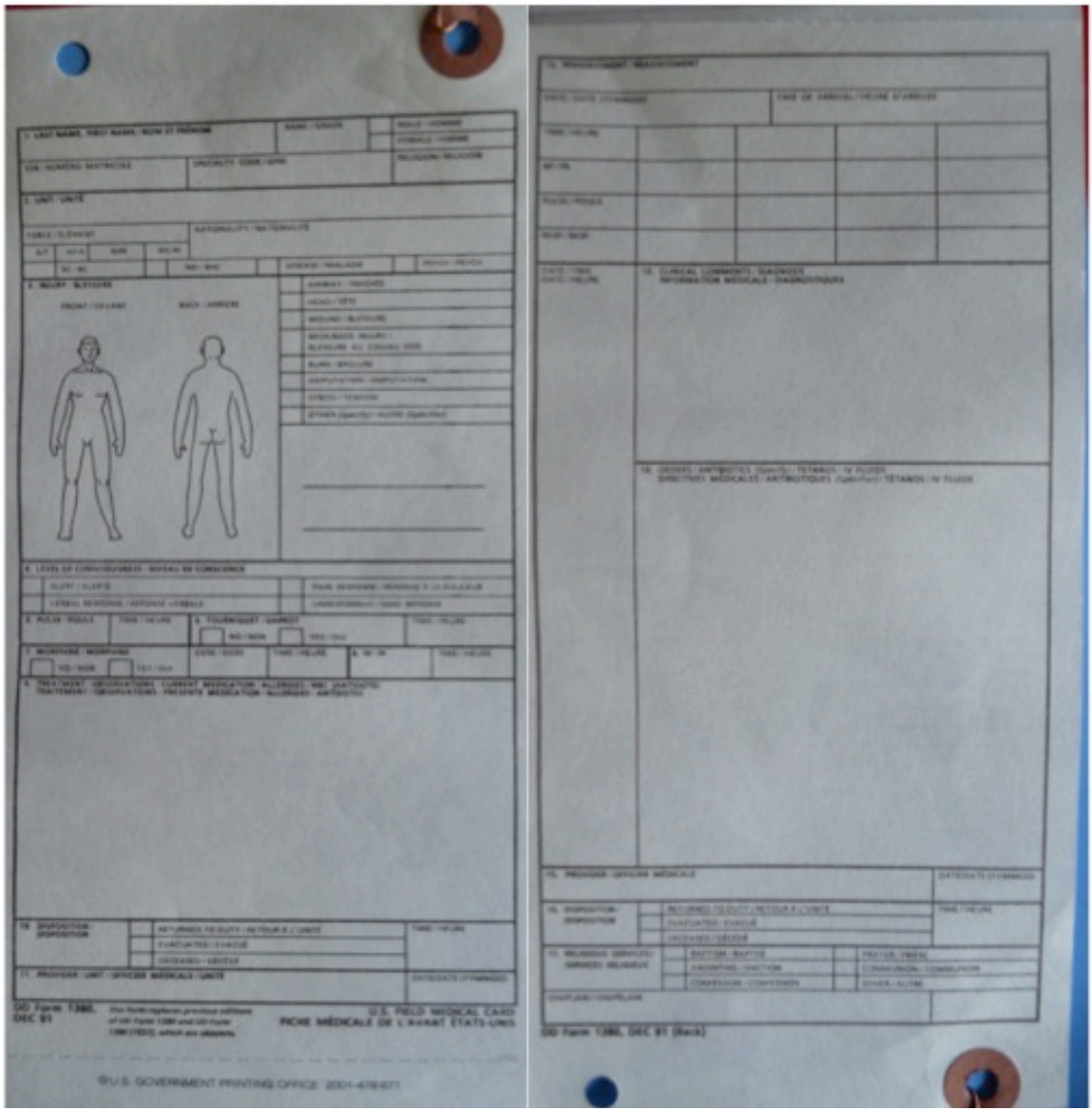


Figure 1, Field Medical Card

The DD1380 is filled out by the medic present at the scene of injury and attached to the patient, if time to do so, the 1380, and a medic to fill it out are available before the patient is transported to the hospital.

The dataset provided included only those patients who arrived alive to a medical treatment facility, as shown in figure 2 below. Thus, this database is comprised only of those soldiers

who are considered to have Died of Wounds (DOW) or to have survived wounding (WIA), with all those Killed In Action (KIA) excluded.

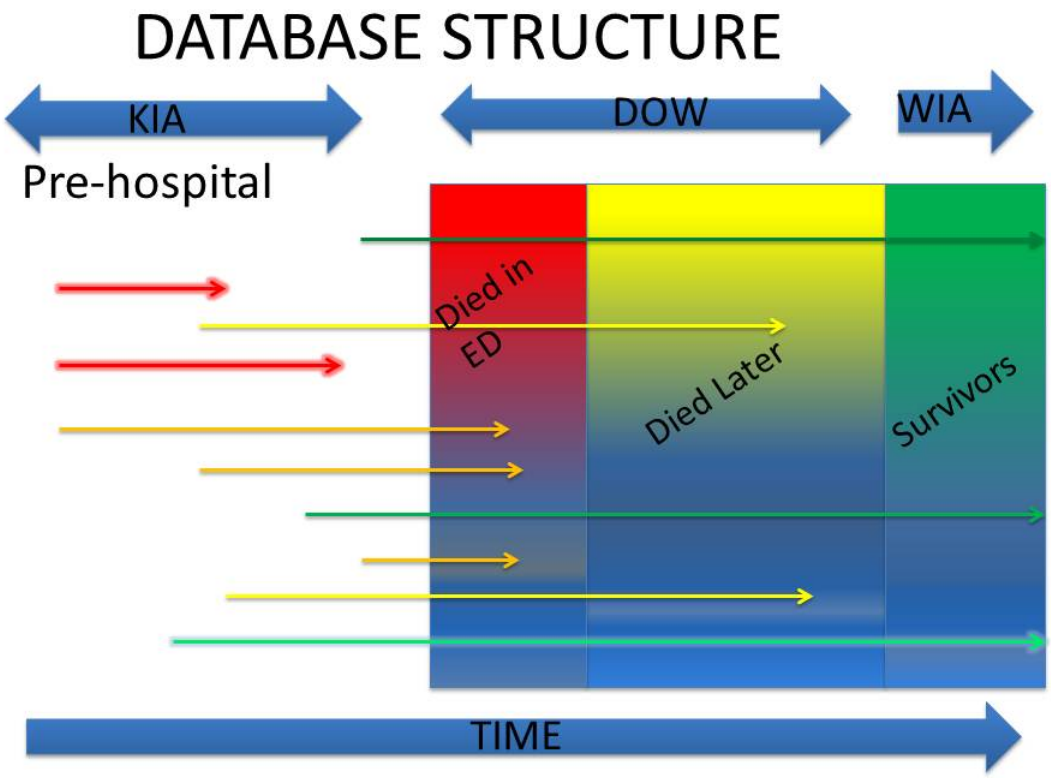


Figure 2, Visual Depiction of Database Contents. KIA are not included in the database.

Role

Those not taken from point of injury to a CSH were eventually taken to a CSH but the pre-hospital time was only counted to the first point of contact with a fixed facility. A Surgical Role II, or in US Army parlance a Forward Surgical Team, performs damage control surgery only, and does not have the ICU capacity for prolonged post-surgical care. Thus, patients are evacuated after surgical assessment and care to a Role 3 (CSH) if they are treated at a Role I.

Some patients were first treated at battalion aid station (Role 2b/Role 1), which is a medical treatment facility staffed with either a Physician or a Physician's Assistant (one or more), and does not perform surgery other than emergency procedures such as chest tube placement. The wounded patient would then be evacuated to a Role III for surgical assessment and care.

Time

The variable describing total out of hospital time was calculated by subtracting the time of injury as recorded on the 1380, estimated from the time of request for medical evacuation, or gathered from the patient or patient's attendants, from the time of arrival to the hospital.

Injury Severity Score

The Injury Severity Score (ISS) is provided to the JTTR by the treating surgeon. The surgeon assesses each of six body areas (Skin, Extremity, Head/Face/C-Spine, Face, Chest/T-Spine, Abdomen/L-spine), and assigns a score of 0-6. An area specific score of 6 is defined as un-survivable, and results in a automatic combined ISS of 75. Scoring is by surgeons specifically trained in assigning ISS scores, with generally good inter-rater reliability[9]. Area scores are characterized from minor, moderate, serious, severe, critical and unsurvivable. The highest three area scores are squared and added together to arrive at the combined Injury Severity Score.

For the purpose of this analysis, the raw ISS scores were lumped into three groups. ISS Category 1, or scores of 0 to 15, ISS Category 2, with scores between 16 and 50, and ISS Category 3, including the remaining scores from 51 to 75. This was done to match the system used by Morrison et. al. as detailed below.

From the data available for area specific scores, a variable titled "headinjury" was created that identified those persons with an area specific score for Head/Face/C-spine of 4 or greater (severe, critical, or un-survivable).

Outcome

The data about outcome was provided both as dead/alive at discharge from the emergency department, and as a final status at time of discharge from hospital. The time frame between the time of injury and death or discharge is undefined, and was not provided by AISR in order to preserve the de-identified character of the dataset.

Date

The date of injury was provided in the form of month and year.

Mechanism of Injury

Mechanism of injury was provided, differentiating among such diverse mechanisms as explosive device, fall, and electrocution, 19 categories in all.

Dominant Injury Type

Dominant injury type is distinct from mechanism of injury, and was coded as Blunt, Penetrating, Burn, Other, and Unknown. This represents the surgeon's judgement as to the primary injury that the patient received from whatever injury cause the patient encountered. For instance, a blast might cause blunt, burn or penetrating injury, and the most grievous injury sustained would be the one coded for the JTTR record. This way of categorizing injury most closely matches that of the civilian trauma literature, and is the method of categorizing injury that was used primarily in this analysis.

Military Operation/Theater

The code for the operation during which the patient was evacuated was coded as OEF (Afghanistan), OIF (Iraq), or OND (Operation New Dawn, the last few months of the Iraq war, after 'combat operations' had officially ceased). For the purpose of analysis, we created a new variable titled Theater which identified the theater as Iraq or Afghanistan, as differentiating from OEF and OIF the few persons evacuated during OND resulted in unstable estimates.

Statistical Methods

The primary analysis for association of mortality with increases in out of hospital time was by accomplished by performing regression analysis.

Prior to performing logistic regression analysis, each variable was regressed for prediction of mortality without adjustment to determine the crude odds ratios (OR) for association, which are reported in table 1 in the results section. This test is equivalent to the Mantel-Haenszel test. We then used logistic regression with the aim of determining what association there is between total pre-hospital time and mortality when controlling simultaneously for multiple variables. Both general, and stratified analyses were performed, stratifying by each category of ISS for the final model arrived at in the general analysis. Last, several sensitivity analyses were performed to examine for confounding.

Terms Included in the Regression Model

To examine the relationship between time and mortality, dichotomous variables dividing pre-hospital time at 60 minutes and 90 minutes were used in a fully adjusted regression model, and compared to terms describing time in smaller intervals.

A model using time divided into 20 minute intervals up to 100 minutes was assessed in order to assess for trend and as categories for the potential presence of a more complicated structure to the first 100 minutes of pre-hospital time. Finally, time divided into 30 minute intervals across the entire range of pre-hospital times was tested for both trend and as categories.

Calendar year was included in the regression model in order to assess for trend across years, and also tested categorically.

A term for theater was included, in order to differentiate country specific factors which could be related to differences in mortality.

Mechanism of injury was tested for confounding with a term differentiating blast injuries from non-blast injuries, but not included in the fully adjusted model.

Dominant Injury Type was grouped into Penetrating, Blunt, Burn, Unknown&Other, as differentiating Unknown and Other resulted in estimate instability due to the low numbers and because Other is not further defined within the data collection as provided, making it effectively unknown.

Patient category was grouped into US military, NATO military, Host National military, and US Contractors. Also tested was a variable for patient category that subdivided the US Services and Host Nationals by country.

A term was included to assess the effect of evacuation to Forward Surgical Team or Level II Battalion Aid Station, as compared to evacuation directly to a Combat Support Hospital.

Controlling for Injury Severity

The most important confounder considered a priori for association between pre-hospital time and mortality is Injury Severity Score (ISS) and using the data reported on patients in Afghanistan from three papers[2,3,4], we report mortality and fraction of all evacuations by ISS.

Extrapolating from these three papers, and using as one estimate of mean pre-hospital time (and SD) the numbers reported by Morrison, and comparing that to other reports of the mean evacuation times for Afghanistan in 2010 (NYTimes.com), the possible range for exposure to pre-hospital times greater than 60 minutes is 15% to greater than 60%. There is

no published data on the mean evacuation or pre-hospital time for patients in the Iraq theater of operations.

A comparison of the mortality figures for Apodaca vs. Morrison shows first of all how few casualty-related deaths occur among patients with an ISS score of less than 19. Further scrutiny show how few total patients are in the ISS >50 group, and how the extreme mortality among that ISS group might distort any analysis that didn't control for that.

Methods Table 1, Mortality by ISS score in prior work

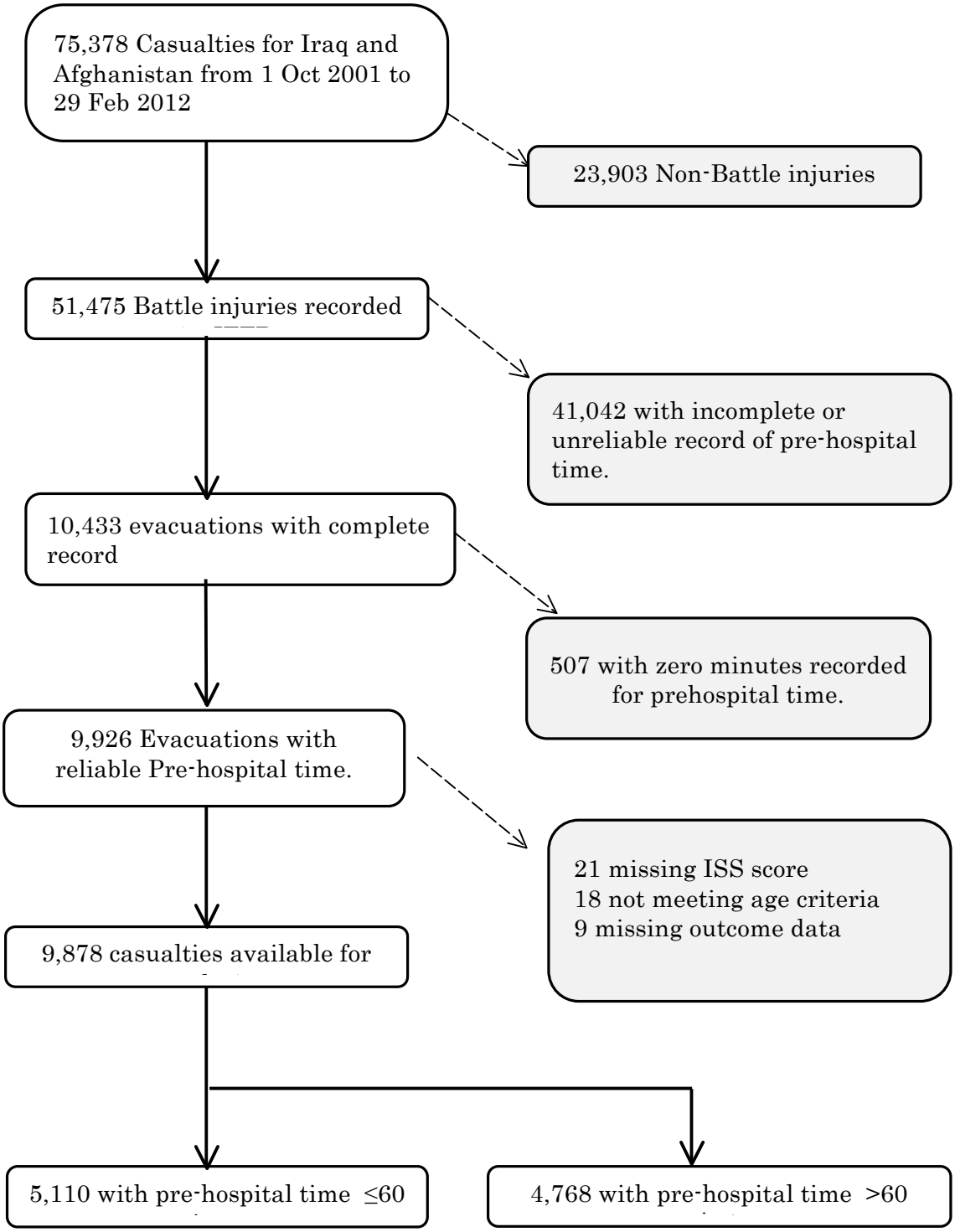
		Apodaca Pedro vs MERT by ISS study			Overall Mortality
ISS	<10	10 to 19	20-29	30-75	
Percent of total evacs	0.45	0.29	0.19	0.08	
Mortality by ISS	0.02	0.03	0.07	0.19	0.04
		Morrison Study			
ISS		1 to 15	16-50	51-75	
Percent of total		0.61	0.34	0.05	
Mortality by ISS		0.02	0.14	0.61	0.09
		Apodaca MERT vs PEDRO			
ISS		ISS <10	ISS 10 to 25	ISS 26+	
Percent of total		0.50	0.38	0.12	
Mortality by ISS		0.01	0.04	0.13	0.04

The percent of total evacs within in each ISS category is roughly similar in the two datasets (Apodaca et. al. examined the same cohort in two papers). We intend to categorize patients by ISS score in the same or similar way as Morrison.

All statistical analysis was performed using STATA ver. 12.

CHAPTER III: RESULTS:

Primary analysis casualty inclusion flow diagram.



Results Figure 1, Cohort Inclusion Flow Diagram

Section 1, Distribution of primary exposure and primary outcome by main patient descriptors.

Results Table 1, Summary of Distribution of Primary Exposure and Outcome

Variable Value	% of Sample	Mean Prehospital Time	MedianPrehospital Time	n	% in > 60 min group	% of >60 minute group	% Mortality	% Mortality for >60 minutes
ALL	100	91.1	60	9878	48.27	n/a	3	2.3
Female	1.2	98.7	62.5	120	49.6	1.2	5.9	0.9
Male	98.8	91.1	60	9788	48.3	98.76	2.98	2.3
Patient Category:								
US Army	38.4	83.2	57	3798	42.8	34	2.5	1.2
USMC	14.29	92.3	60	1414	48.7	14.4	2.2	1
USN	1.01	100.5	55	101	44	0.9	0	0
USAF	0.78	72	44	78	27.27	0.4	2.6	0
USCG	0.01	56	56	1	0	0	0	0
US Contractors	6.24	82.7	57	623	43.51	5.6	3.3	2.6
NATO	12.47	90.6	60	1232	49.27	12.73	1.7	1.5
Iraq Military	14.41	94.2	65	1433	51.65	15.42	4.7	3.1
Afghan Military	12.41	116	80	1228	64	16.5	5.1	5.4
Mechanism of Injury:								
Blunt Object	0.15	195.2	120	15	73.3	0.23	0	0
Bullet	24.21	91.3	60	2398	25.1	24.2	0	2.8
Burn	0.13	124.6	115	13	0.19	0.13	4.1	0
Chemical	0.02	115.5	115.5	2	50	0.02	0	0
Crush	0.04	53.8	64	4	50	0.04	0	0
Electrical	0.01	30	30	1	0	0	0	0
Explosive Device	69.07	89.7	60	6845	47.3	67.7	2.7	2.1

Fall	0.6	108.7	71	59	55.93	0.7	3.4	3
Helo Crash	0.39	76.9	60	39	48.72	0.4	2.6	5.3
Inhalation Injury	0.04	201.3	155	4	75	0.06	0	0
Knife/Sharp object	0.17	138	90	17	64.71	0.23	5.9	9.1
MVC	1.74	108.9	65	172	52.91	1.91	2.3	2.2
Machinery	0.13	117.8	85	13	69.2	0.19	0	0
Other (specify)	1.21	106.1	60	120	46.7	1.2	2.5	0
Pedestrian	0.02	145	145	2	100	0.04	0	0
Plane crash	0.01	37	37	1	100	0.04	0	0
Unknown	2.03	94.1	60	202	49.25	2.1	3.5	1
Dominant Injury Type:								
Blunt	28.49	104.3	65	2822	53.13	31.35	0.8	0.7
Burn	2.11	93.3	60	208	49	2.1	7.2	2.9
Other	0.08	136	135	8	75	0.1	0	0
Penetrating	68.6	85.6	60	6797	46.1	65.5	3.8	3
Unknown	0.73	91.2	70	73	56.9	0.9	4.2	2.4
Mode of Transport:								
MedAir	61.59	91.3	61	6092	50.26	64.14	2.8	2.2
MedGround	5.47	88.8	57	540	43.7	5	4.6	2.1
Non_Medical Transport	7.5	77.4	46.5	744	36.8	5.7	3	2.6
Unknown	25.44	95.3	60	2532	47.8	25.2	3.2	2.3
Facility Level:								
CSH (ROLE III)	75.61	92.5	60	7498	49.18	77	3.1	2.3
SURG (ROLE II)	22.85	87.7	60	2258	46.17	21.9	2.9	2.1
BAS (ROLE II/I)	1.54	76.6	44	151	34.87	1.11	2	3.8
YEAR:								
2002	0.03	180	60	3	33.3	0	0	0
2003	0.15	144.7	120	15	80	0.3	6.7	8.3

2004	2.57	98.5	65.5	262	55.91	2.98	4.7	2.1
2005	6.48	93.9	65	642	50.9	6.8	3.3	2.5
2006	13.39	84.9	60	1331	45.7	12.7	3.3	2.7
2007	18.04	86.3	60	1786	43.6	16.3	3.7	1.3
2008	8.4	98.6	65	832	52.2	9.1	4.2	3.7
2009	15.08	96.1	65	1494	53.4	16.7	3.1	2.3
2010	20.76	96.2	60	2051	49.05	13.13	2	2
2011	13.72	84.7	60	1357	46.2	13.13	2.3	2.6
2012	1.37	68.7	47	135	34.07	0.96	1.5	0
Survived	96.98	91.8	60	9588	48.64	97.73	--	--
Died	3.02	69.1	48	311	36.24	2.27	--	--
ISS_0-15	80.54	95.4	63	7965	50.9	84.9	0.73	0.6
ISS_16-50	18.87	74.1	54.5	1864	38	14.9	11.5	11
ISS_51+	0.59	64.4	40	79	22.41	0.27	44.8	30.8
OEF (Afghan.)	53.63	96.8	63	5306	51.55	57.28	2.6	2.5
OIF (Iraq)	46.37	84.6	60	4602	44.48	42.72	3.5	1.9
AGE 18-34	86.5	90.8	60	8567	47.8	85.6	2.9	2.2
AGE 35+	13.5	93.3	63	1341	51.4	14.4	3.8	2.9
Head Injured	4.65	76.9	55	459	39.2	3.8	29.6	26.7

Section 2. Logistic Regression results.

Section 2a.

Increasing total-pre-hospital-time is demonstrated by logistic regression analysis of the entire dataset to be negatively associated with mortality. This finding is robust, as it is found for each method of categorizing the time value explored. All models testing the full dataset resulted in values for increasing time that were protective, meaning that at the time of arrival to the ED larger values of pre-hospital time predict lower in-hospital mortality relative to a characteristic matched patient with a shorter pre-hospital time.

This table compares the Odds Ratio for mortality for each variable with no other adjustors than the values of the variable itself, with the odds ratio determined when the variable is included or substituted into the fully adjusted logistic regression model.

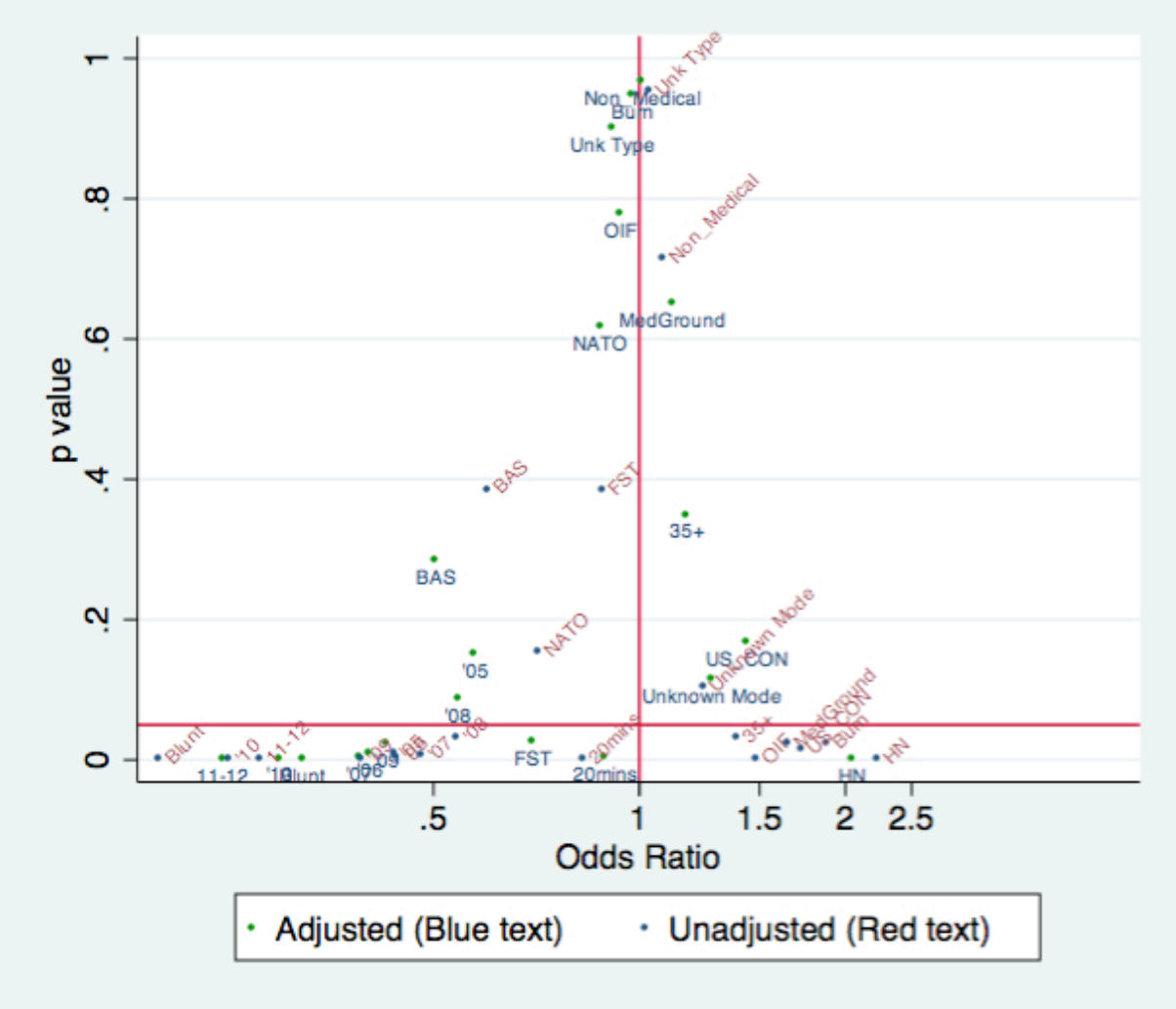
Results Table 2, Primary Result: Crude to Adjusted Odds Ratios

TABLE 2 Unadjusted Odds Ratios to Adjusted Odds Ratios				
Variable	Unadjusted OR	Unadjusted p value	Adjusted OR	Adjusted p value
1-20 min.	1.00		1.00	
21-40 minutes	0.75	0.12	1.01	0.98
41-60 minutes	0.59	*0.01	0.76	0.22
61-80 minutes	0.49	*0.00	0.71	0.19
81-100 minutes	0.43	*0.00	0.66	0.18
101+ minutes	0.37	*0.00	0.59	*0.03
60 min. dichotomous	0.58	*0.00	0.72	*0.02
90 min. dichotomous	0.57	*0.00	0.71	*0.03
20 minute increments	0.83	*0.00	0.90	*0.01
Time, continuous	0.99	*0.00	0.99	*0.01
Role | CSH Role 3	1.00			
FST Role 2a Surgical	0.88	0.38	0.68	*0.01
Role 2b/I non-surgical	0.60	0.39	0.49	0.26
Type: Penetrating	1.00			
Blunt	0.20	*0.00	0.31	*0.00
Burn	1.88	*0.02	0.97	0.93
Unknown	1.04	0.95	0.89	0.87
Other	N/a		N/a	
ISS 0-15	1.00			
ISS 16-50	17.66	*0.00	16.86	*0.00
ISS 51+	132.77	*0.00	121.79	*0.00

Theater (Iraq)	1.48	*0.00	0.78	0.21
Age 35+	1.39	*0.03	1.21	0.27
Mode of Transport Medical Air	1.00			
Medical Ground	1.65	*0.02	1.16	*0.55
Non Medical	1.09	0.72	1.04	0.89
Unknown Mode	1.24	0.10	1.28	0.11
US Army	1			
NATO	0.71	0.15	0.86	0.56
Host Nationals	2.23	*0.00	1.94	*0.00
US Contractors	1.72	0.02	1.37	0.22
2002-2004	1.00			
2005	0.44	*0.01	0.58	0.15
2006	0.44	*0.00	0.40	*0.01
2007	0.48	*0.01	0.39	*0.00
2008	0.54	*0.03	0.54	0.09
2009	0.39	*0.00	0.43	0.02
2010	0.25	*0.00	0.30	*0.00
2011-2012	0.28	*0.00	0.25	*0.00
All years	0.88	*0.00	0.85	*0.00
Patient Category:				
US Army	1.00			
USMC	0.87	0.52	1.26	0.34
USN/USCG	N/a		N/a	
USAF	1.02	0.97	0.81	0.78
US Contractors	1.63	*0.03	1.37	0.24
NATO	0.68	0.11	1.07	0.81
Iraq Military	2.12	*0.00	1.54	*0.03
Afghan Military	2.11	*0.00	3.15	*0.00
Female	1.95	0.09	2.09	0.12
Blast injury	0.69	*0.00	0.75	*0.04
Head Injury	22.29	*0.00	5.56	*0.00

Astericks * highlight those p values that are significant at the 0.05 level.

Increasing total-pre-hospital-time is demonstrated by logistic regression analysis of the entire dataset to be negatively associated with mortality. This finding is robust, as it is



Results Figure 2 Adjusted Odds Ratios Compared to Unadjusted Odds Ratios for Mortality

found for each method of categorizing the time value that I explored. All models including the full dataset resulted in values for increasing time that were protective.

Other changes of significance include that the p value of being transported by Medical

Ground ambulance goes from a significant p value of .02 to a highly non-significant p value of .56. Additionally, the term for Forward Surgical Team goes from insignificant at

.38 to a significant p value of .01. Burns and being greater than 35 years old also change to insignificant.

This is more easily visualized in this graph of odds ratios vs p values comparing the adjusted to the unadjusted values (Results Figure 2).

Comparison of the total number of battle deaths and wounded in action (WIA) for both conflicts reflected in the data from the Defense Casualty Analysis Service in Table 3 above, showing the percentage of WIA and battle deaths captured in this dataset by year and by theater. Examining the tables, there is no clear relationship between the percent of all deaths and WIA captured in the dataset and the odds ratio for mortality for each year in the dataset.

Results Table 3, Comparison of DCAS Data to this Dataset, OEF

OEF	DCAS data		**This Data Set**		Ratio this dataset/DCAS data		OR for mortality associated with pre-hospital time in Dataset	
	Deaths	WIA	**DOW**	**WIA**	deaths	WIA	OR	P value
OEF 2002	14	74		3	0.00	0.04	not enough data	
OEF 2003	9	99	1	7	0.11	0.07	not enough data	
OEF 2004	21	217	2	23	0.10	0.11	not enough data	
OEF 2005	50	268		7	0.00	0.03	not enough data	
OEF 2006	62	403		79	0.00	0.20	not enough data	
OEF 2007	78	748	9	197	0.12	0.26	0.61	0.07
OEF 2008	97	795	15	282	0.15	0.35	1.20	0.58
OEF 2009	195	2146	39	1226	0.20	0.57	0.87	0.26
OEF 2010	264	5250	39	1928	0.15	0.37	1.13	0.35
OEF 2011	246	5221	30	1276	0.12	0.24	1.31	0.06
OEF 2012	176	2964	2	133	0.01	0.04	1.29	0.88
Total OEF	1212	18185	137	5161	0.11	0.28	0.99	0.84

Results Table 4, Comparison of DCAS data to this Dataset, OIF

OIF	DCAS Data		**This Data Set**		Ratio this dataset/DCAS Data		OR for mortality associated with prehospital time in this Dataset	
	Deaths	WIA	**Deaths**	**WIA**	Deaths/ Deaths	WIA/ WIA	OR	p value
OIF 2003	315	2422		7	0.00	0.00	not enough data	
OIF 2004	713	8002	10	219	0.01	0.03	0.73	0.28
OIF 2005	673	5944	21	612	0.03	0.10	0.83	0.30
OIF 2006	704	6411	44	1200	0.06	0.19	0.90	0.36
OIF 2007	764	6119	56	1520	0.07	0.25	0.72	0.00
OIF 2008	221	2049	20	513	0.09	0.25	0.64	0.03
OIF 2009	74	679	7	218	0.09	0.32	0.73	0.44
OIF 2010	15	316	2	82	0.13	0.26	not enough data	
Total OIF	3481	31942	161	4419	0.05	0.14	0.79	0.00
Overall:	4693	50127	298	9580	0.06	0.19	0.79	0.00

The DCAS data to this dataset comparison shows a general increase in percent inclusion over time, but inclusiveness does not appear to be a confounder or explain the difference in OR for mortality with increasing pre-hospital time between theaters. **The mortality rate among injured in Afghanistan, across the conflict is 6.2%, as compared to same statistic for Iraq of 9.8%. This compares to the DOW rate, for this data set of patients who arrived alive to hospital, of 2.6% for Afghanistan and 3.5% in Iraq.**

The most dramatic change after adjustment with logistic regression is that Theater (OIF) becomes non-significant, and becomes associated with lower mortality rather than increased mortality. The next is that being taken to a Forward Surgical Team (FST) becomes statistically significant, and is

associated with lower mortality. Further, age greater than 34 becomes non-significant. The values for Burn also changes, but there are so few burns in the database that interpretation of that change is unclear.

We considered inclusion of an interaction term for interaction between ISS and prehospital time. For a model using the 60 minute cut point to categorize pre-hospital time, with interaction between prehospital time and each ISS category, the likelihood-ratio test statistic was chi2(2) of 0.76, with a probability greater than chi2 of 0.6836, or no statistical difference for prediction of mortality between the models.

The results of using an interaction term were, however, illuminating:

Results Table 5, Interaction between Pre-Hospital Time and Injury Severity

	Time and ISS	OR for Survival	P value	Lower CI	Upper CI	OR> 60/ OR < 60
All Data	Time > 60 minutes & ISS 0-15	1.362	0.248	0.807	2.300	
	Time < 60 minutes & ISS 16-50	0.112	0.000	0.073	0.171	
	Time < 60 minutes & ISS 51+	0.010	0.000	0.003	0.034	
	Time > 60 min & ISS 16-50	0.151	0.000	0.095	0.240	1.3
	Time > 60 min & ISS 51+	0.041	0.000	0.011	0.156	4.0
OIF	Time > 60 minutes & ISS 0-15	2.905	0.014	1.238	6.814	
	Time < 60 minutes & ISS 16-50	0.100	0.000	0.059	0.169	
	Time < 60 minutes & ISS 51+	0.021	0.000	0.007	0.059	
	Time > 60 min & ISS 16-50	0.212	0.000	0.114	0.393	2.1
	Time > 60 min & ISS 51+	0.095	0.086	0.006	1.398	4.5
OEF	Time > 60 minutes & ISS 0-15	0.690	0.366	0.309	1.542	

	Time < 60 minutes & ISS 16-50	0.110	0.000	0.051	0.235	
	Time < 60 minutes & ISS 51+	0.010	0.000	0.003	0.034	
	Time > 60 min & ISS 16-50	0.100	0.000	0.046	0.219	0.9
	Time > 60 min & ISS 51+	0.029	0.000	0.005	0.160	2.8

As tabulated in Results Table 5, there is a strong negative association between increasing Injury Severity Score and increasing prehospital time across the whole dataset, and for ISS 51+, the OR for survival is 4 times higher among patients with pre-hospital time greater than 60 minutes. Further, despite the overall OR for survival for ISS 16-50 in Afghanistan (OEF) being neutral across evacuation time, a similar relationship is found for ISS 51+ by time in OEF as in OIF.

We performed the reverse regression, to measure the association of ISS category and prehospital time directly. Using a fully adjusted model with the 60 minute dichotomous prehospital term as the dependent variable, the OR for association of ISS 16-50 with prehospital time greater than 60 minutes is 0.61 with a 95% confidence interval of 0.55 to 0.68. The same figures for ISS 51+ are an OR of 0.35, and a confidence interval of 0.18 to 0.66.

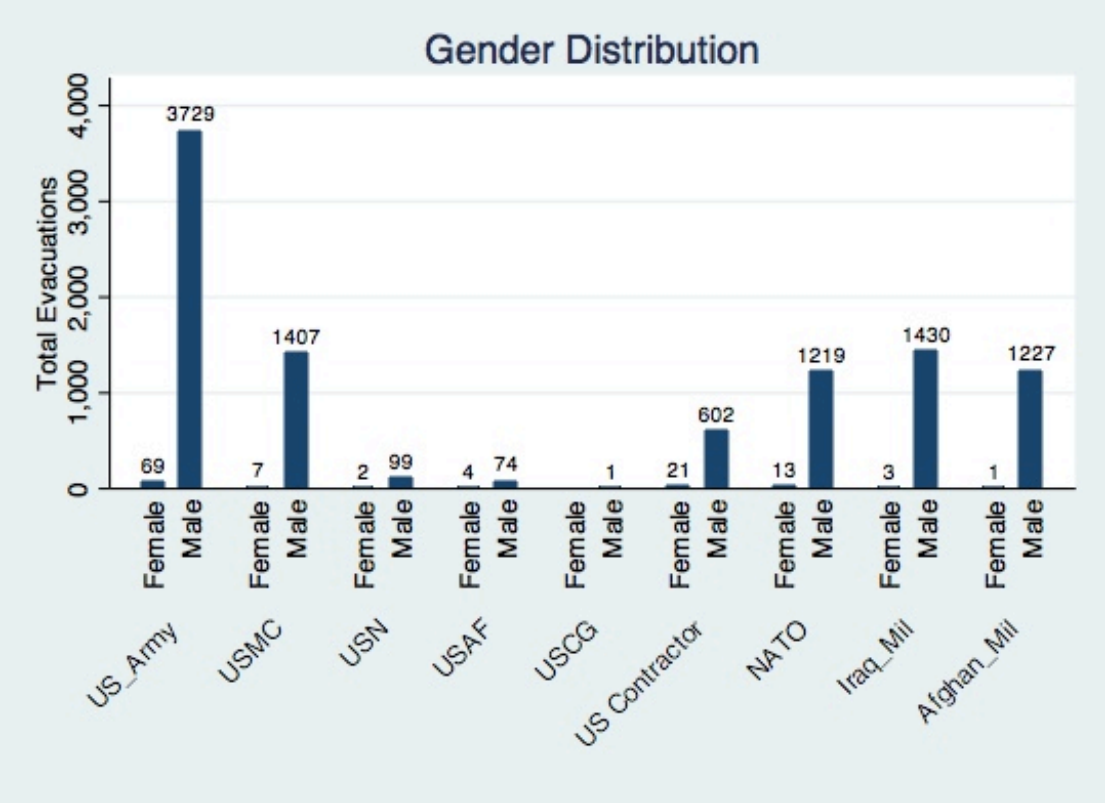
Last, we performed sensitivity analysis with calendar years grouped into 3 intervals, to measure the change over time in the OR for mortality of prehospital time greater than 60 minutes.

The trend with increasing years over all years was 0.89 (0.86, 0.92), for year group 2003 to 2005, OR 0.99 (95% CI of 0.59 to 1.10), 2006 to 2008 an OR of 0.99 (95% CI of 0.90 to 1.10), and for 2009 to 2012 an OR of 0.88 (95% CI of 0.81 to 0.95).

Section 2b. Terms included or excluded from primary regression model.

Gender

With respect to gender, 1.21% of evacuations captured in the dataset were of women, for a total of 120 evacuations of the 9878 analyzed.



Results Figure 3, Gender Distribution by Service

Testing the sensitivity of the results for the inclusion or exclusion of women, a sensitivity analysis excluding all females and comparing the differences between the odds ratios and p values of the remaining terms before and after exclusion of females showed little change. (see appendix for tree graphic showing this result graphically). The main effect of excluding

females is a general decrease in statistical confidence, but with no values becoming insignificant that were significant.

The same holds true for a comparison of inclusion of a term for Gender and a model without such a term.

A likelihood ratio test comparing the the main model to a model with a gender term finds no significant difference between the two. Likelihood-ratio test statistic chi2(1) = 2.16, Prob > chi2 = 0.1415. Gender was therefore not included in the adjusted model.

Year of Injury

The effect of categorizing the year versus testing for a trend across years was examined, and likelihood ratio test revealed no significant difference, with Likelihood-Ratio test chi square statistic (with six degrees of freedom) of 7.83 and probability greater than chi2 of 0.250. LR test for inclusion of versus exclusion of a term for year was highly significant, with a likelihood-ratio test statistic of chi2(1) = 10.58 and probability greater than chi2 of 0.0011.

Pre-hospital Time categorized compared to Pre-hospital time uncategorized.

A similar examination of the effects of time as 20 minute increments categorized compared to time as 20 minute increments for trend was performed.

The Likelihood-ratio (LR) test result for comparison of the full model reveals no significant difference between time in 20 minutes categorized, and time in 20 minute increments for trend, with a value of chi2(4) = 0.96 and a probablility greater than chi2 of 0.9154.

The term for time in 20 minute increments up to 100 (testing for trend), and the term for year were therefore incorporated as uncategorized terms that function as tests for trend and not further categorized in the final results as reported.

Patient Category

For the purposes of analysis, the patients were lumped into four representative categories: the United States military, NATO personnel, Host National military personnel, and United States contractors and other employees. This raises the question of whether more fine distinctions would make a difference to the overall analysis. A graphic is included in the appendix which shows the differences in the regression output for the four-way patient categorization vs. a nine-way patient categorization.

No substantive differences in Odds Ratios or p values were seen for most of the dependent variables. Host National split into separate terms for Afghan military forces and Iraqi military forces, both of which remained significant, and the ORs for both of which remained greater than one, consistent with the consolidated term of Host National (HN).
The lack of substantial difference between these two methods of categorizing the patients is reflected in the Likelihood-ratio test, with a test statistic of chi2(3) = 7.28 and probability greater than chi squared of 0.0635.

As the consolidated term results in improved stability of the regression results generally, we report the values for the consolidated term as our final result.

Patient Age

Inclusion of a term for patient age versus a model without a term for patient age resulted in a likelihood-ratio test statistic of chi2(1) = 0.85 and probability greater than Chi squared of 0.3558. Because older patients have been consistently shown in other studies to be at higher risk of mortality, this term was included as being a potential confounder a priori.

Injury Type

Inclusion of a categorized term for injury type was compared to no term for injury type, with the result being a LR test statistic of chi2(3) = 29.45 and Probability greater than chi squared of less than 0.0001.

Head Injury

A term identifying those patients with an Area Injury Scale score of 4 or more was created, and added to the model, and then a likelihood test performed. The LR test resulted in a test statistic of chi2(1) = 126.60 and probability greater than chi squared of less than 0.0001. The term for severe head injury was included in the model both because of it's high level of significance and because head injury is a topic of interest and was thought a priori to be a potential confounder.

Mode of Transport

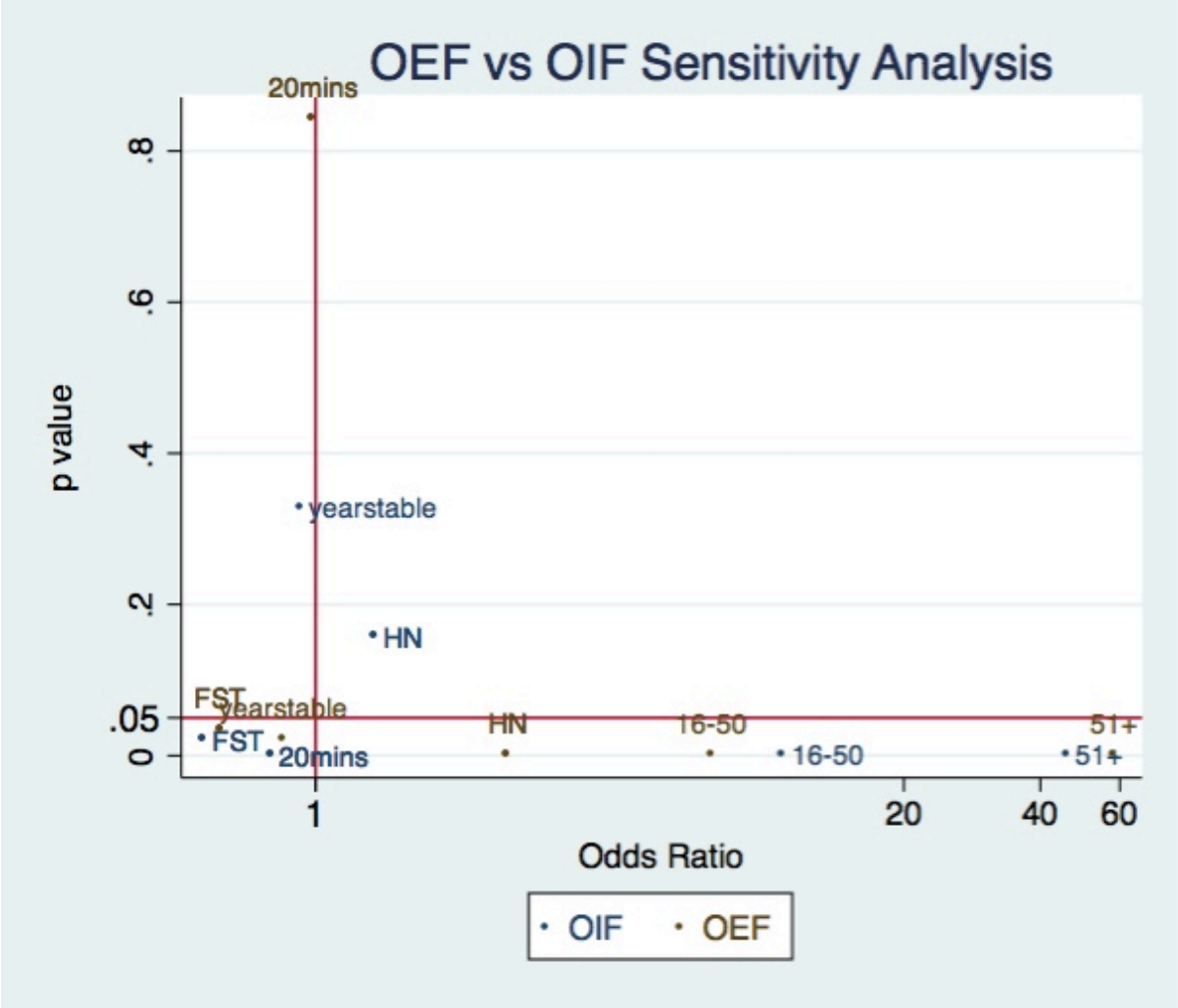
Likelihood ratio test for inclusion of a categorized term for mode of transport was included in the model per a priori reasoning. Surprisingly, inclusion of a term adjusting for mode was insignificant, with a likelihood ratio test statistic chi2(3) = 2.59 and probability greater than chi squared of 0.4590.

Facility Level

Testing for significance of inclusion of a term adjusting for type of facility treated at resulted in a likelihood-ratio test statistic of chi2(2)= 6.22 and a probability greater than chi squared of 0.0445.

Results Section 3. Inter-Theater Differences: Comparing Iraq to Afghanistan

A sensitivity analysis consisting of serial regressions applying the primary regression model but restricting the analysis to each theater of war separately was performed. The results of this analysis are shown in the comparative graphic below.



Results Figure 4, Regression results for Iraq and Afghanistan

OEF = Afghanistan, OIF= Iraq, FST= Forward Surgical Team, 20mins = Pre-hospital Time, HN= Host Nation Military. ISS Cat 2= 16-50, ISS Cat 3= 51+.

Increasing total pre-hospital time is associated with lower mortality with strong significance across the full dataset. This contrasts sharply with the results of the sensitivity analysis of OEF, while the same analysis of only the Iraq data is largely congruent.

These two tables show the raw mortality numbers that the sensitivity analysis results reflect, and demonstrate that a difference in mortality associated with increases in pre-hospital time is found across both ISS and across injury type, and is not subtle.

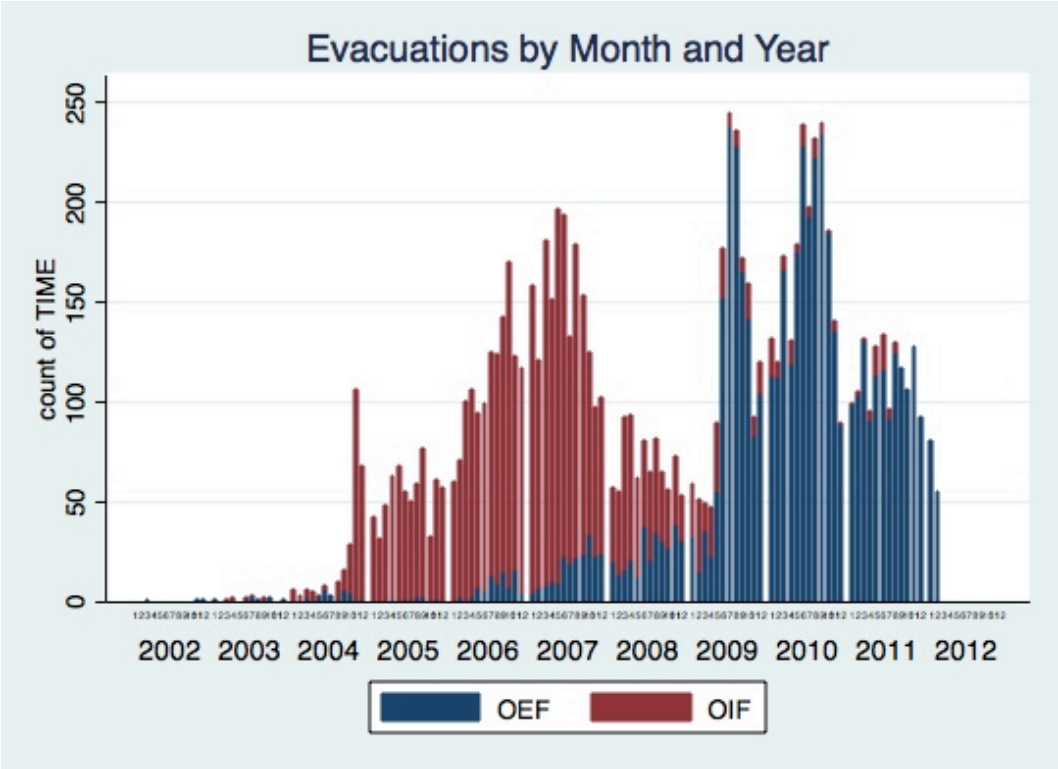
Results Table 6, In Hospital Mortality for Blast and Non-Blast Injury By Time and Theater

Theater and Pre-Hospital Time				
Blast casualties	OEF		OIF	
	≤60_minutes	>60_minutes	≤60_minutes	>60_minutes
Survivor	1,881	1,852	1,602	1,306
Nonsurvivors	45	44	68	25
% Mortality	.023	.023	.041	.019
	Theater and min60			
Non-Blast casualties	OEF		OIF	
	≤60_minutes	>60_minutes	≤60_minutes	>60_minutes
Survivors	607	789	734	615
Nonsurvivors	22	24	49	14
% Mortality	.035	.030	.063	.022

Results Table 7, In Hospital Mortality by ISS category, by Time and Theater

Mortality by ISS and Exposure to Pre-hospital Times > 60 Minutes						
Theater and Injury Severity Category	Survived		Died in Hospital		Died in Hospital	
	≤60 minutes	>60 minutes	≤60 minutes	% Mortality	>60 minutes	% Mortality
OEF						
ISS_0-15	1,900	2,307	9	0.5%	19	0.8%
ISS_16-50	589	349	49	7.7%	47	11.9%
ISS_51+	10	6	10	50%	3	33.3%
OIF |						
ISS 0-15	1,978	1,713	23	11.5%	7	0.4%
ISS 16-50	430	282	87	16.8%	31	9.9%
ISS_51+	13	3	12	48%	1	25%

The number of evacuations changed over time, with distribution by month and year shown here:

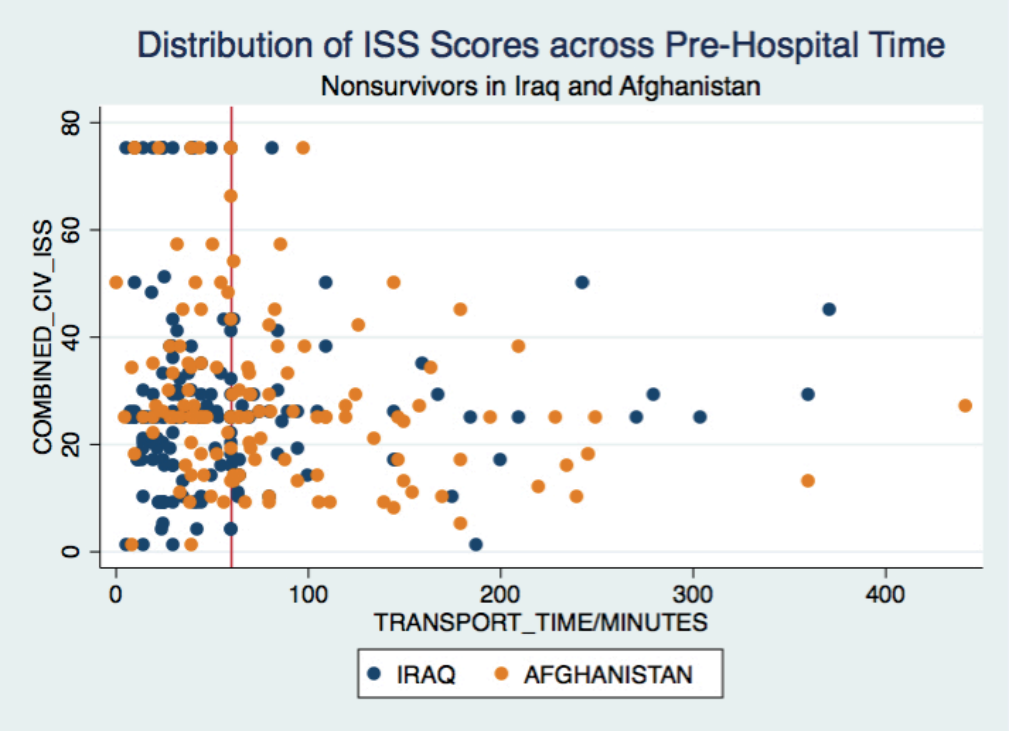


Results Figure 5, Patient Distribution between Theaters by Month and Year. OIF= Iraq, OEF= Afghanistan

One clear feature demonstrated by this graph (Fig. 5) is the increasing availability of patients for inclusion into this sample of the JTTR over the course of time.

The graph shows the changing composition of the database by theater over time, and by month seems visually to show some degree of seasonality, especially in Afghanistan (OEF). This is confirmed by Chi square test for distribution, with a probability of less than 0.001 that distribution by month is random in Afghanistan. A graphic of casualties by month is included in the appendix comparing theaters.

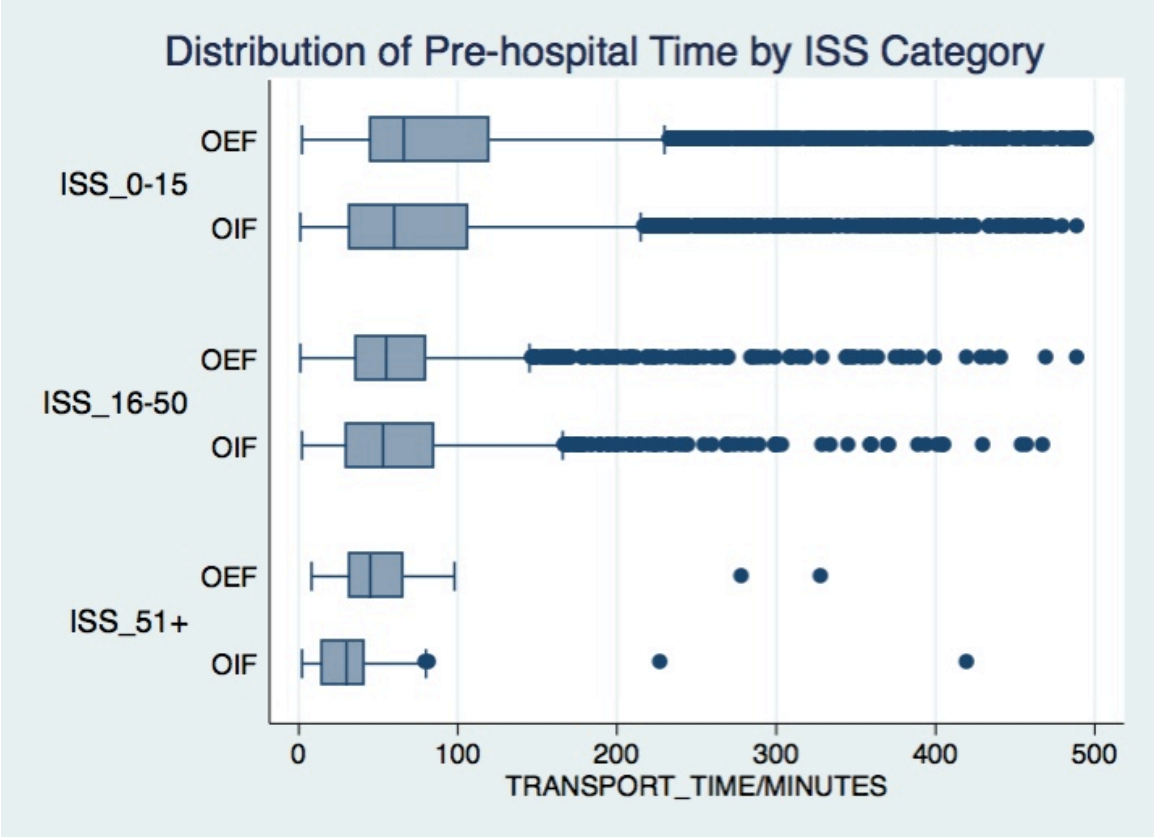
The important relationship is that a comparison across the full spread of years included in the dataset, and a comparison of theaters, are roughly the same comparison. Specifically, a comparison of the year 2005 to the year 2010 is a comparison across 5 years, but it is also almost entirely a comparison of Iraq to Afghanistan.



Results Figure 6, Scatterplot of ISS vs Time for Died of Wounds in Iraq and Afghanistan

Figure 6 and Figure 7 allow visual comparison of the distribution of injury severity in Iraq and Afghanistan across pre-hospital time, and contrast survivors and nonsurvivors. The vertical line is at 60 minutes.

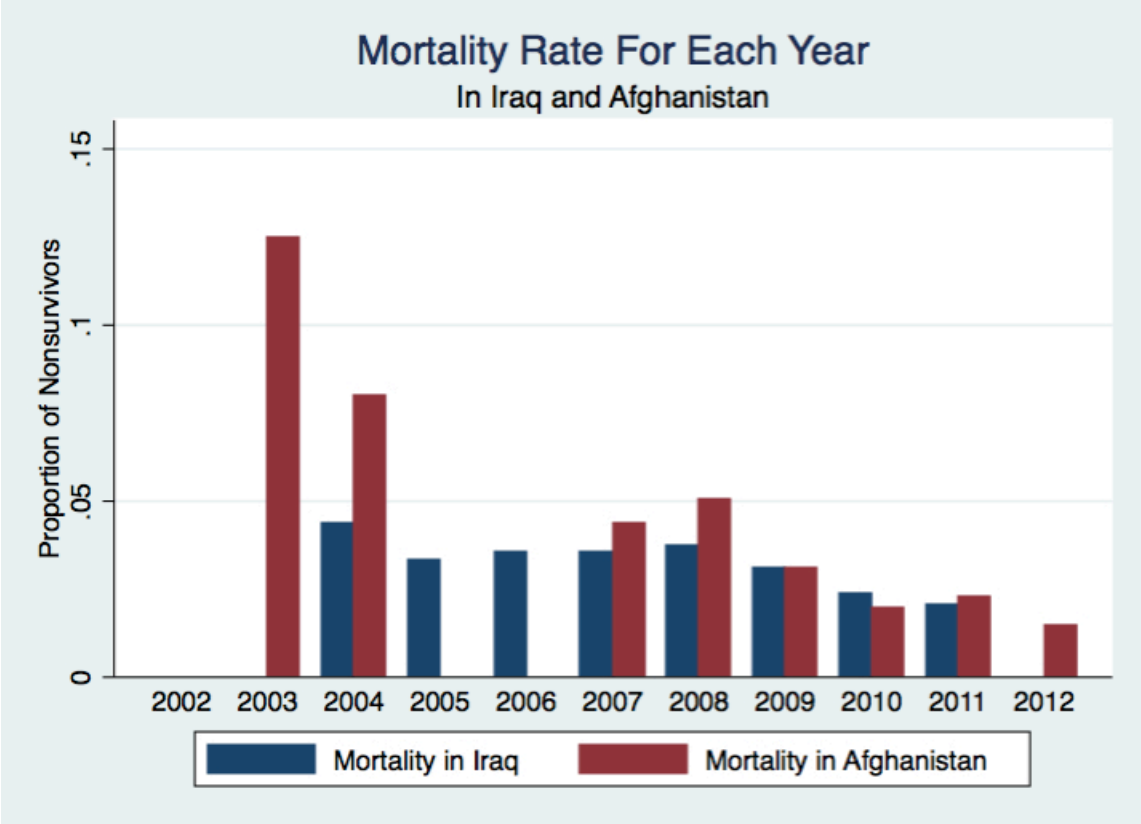
For nonsurvivors, there is an immediately apparent difference in the number of deaths occurring at longer pre-hospital times at most values on the ISS scale. Afghanistan has many more deaths included in the dataset at longer pre-hospital times.



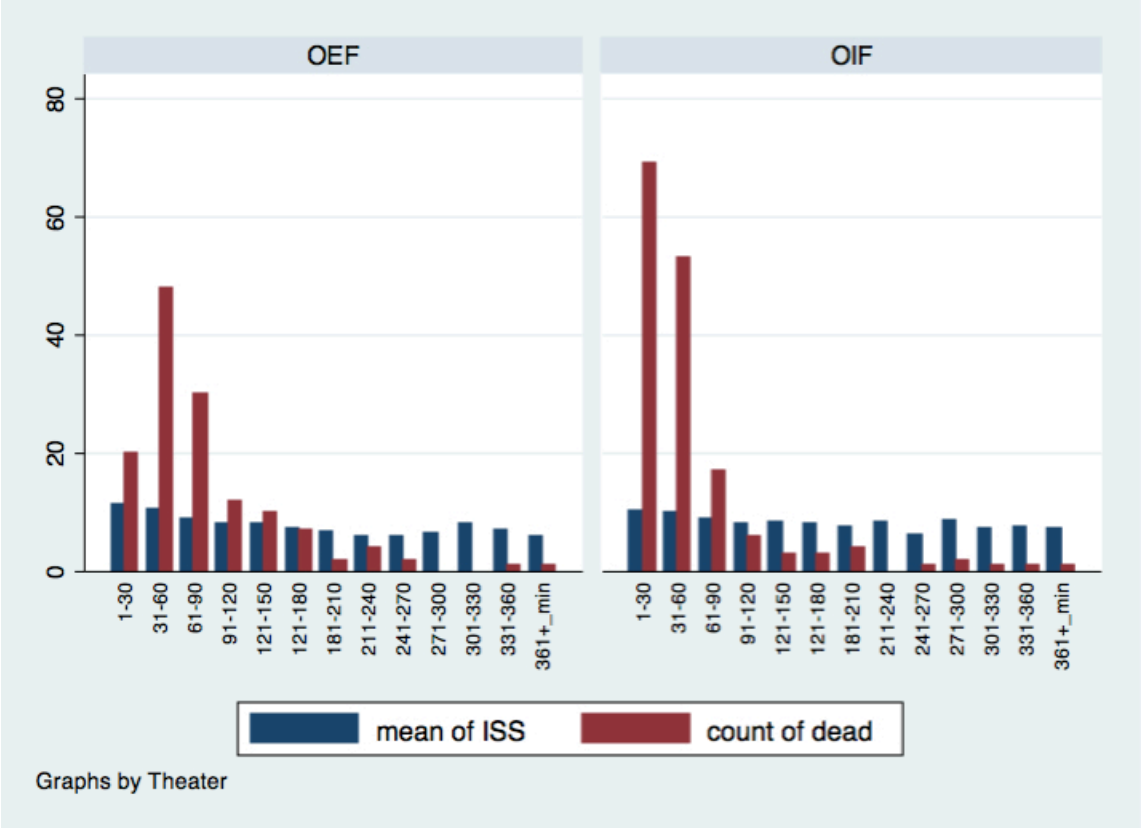
Results Figure 7 Distribution of pre-hospital time for each ISS Category by Theater.

Further, as seen in Results Figure 7, Iraq and Afghanistan show a similar relationship within each theater between ISS score and evacuation time, with greater severity of ISS being associated with shorter pre-hospital times, between theaters there is clear difference, with Afghanistan having in general longer evacuation times.

This inter-theater difference in mortality occurs within the context of a background rate of mortality that decreased over time, at least after 2008, within this dataset.



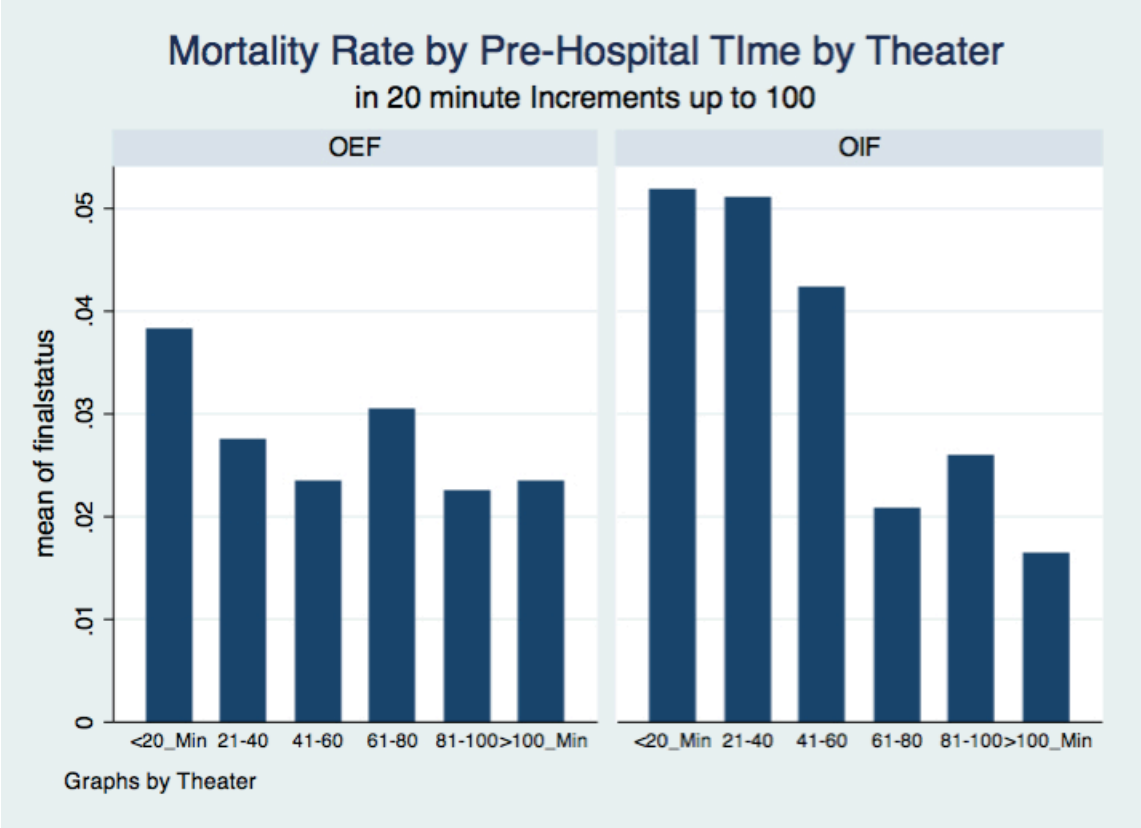
Results Figure 8, In-hospital Mortality Rate by Theater and Year.



Results Figure 9, Count of DOW and Mean ISS by Pre-hospital Time by Theater

Above is a comparison of the Iraq theater to the Afghan theater for each 30 minutes of pre-hospital time, by count of nonsurvivors, compared to the mean ISS for all patients. Especially note that the mortality count for Iraq (OIF) is skewed earlier than the mortality count for Afghanistan (OEF).

This transforms to mortality rates by theater across pre-hospital time, as shown here:



Results Figure 10, Mortality Rate by Pre-hospital Time by Theater

The following graphic depicts the mortality rate pre and post sixty minutes by ISS score. Looking primarily at the ISS scores in the range 16 to 50, it is clear that for pre-hospital times less than 60 minutes, Iraq has higher mortality, but for pre-hospital times greater than 60 minutes, Afghanistan has higher mortality rates in the two lower ISS groups. This is important because it is consistent across the range, and that range makes up the bulk of the data where there are casualties to count.

The distribution of ISS between Iraq and Afghanistan is similar for Survivors, but for non-survivors, the ISS 51+ group is much larger. In OIF, the ISS 51+ group represents 9.84% and 2.56% of nonsurvivors in the unexposed and exposed, while for OEF the ISS 51+ group

comprises 14.71% and 4.35% of the nonsurvivors, in the less than 60 minutes and greater than 60 minutes exposure groups respectively.

A sensitivity analysis restricting the time periods considered to only those with significant numbers available for comparison from both theaters was performed. For OEF, the time trend term, restricting analysis to 2006 to 2009, resulted in an Odds Ratio of 0.859 , p value of 0.106 , and 95% CI for the Odds Ratio of 0.714 to 1.033. For OIF, the time trend, restricting analysis to 2006 to 2009, resulted in an Odds Ratio of 0.787 with a p value of < 0.001 and a 95% CI for the Odds Ratio of 0.690 to 0.897. This restriction of the time period considered to only those with significant inter-theater overlap is the only sensitivity analysis to produce comparable ORs for the time trend term between the two theaters, and despite the greatly restricted number of evacuations analyzed for Afghanistan by this sensitivity analysis, the p value comes close to a 90% significance (90.6%).

Mortality rates by year and ISS bear out this complex relationship between theater, year, pre-hospital time, and Injury Severity Category. Across calendar years, OEF has consistently higher in-hospital mortality for patients with greater than 60 minutes pre-hospital time compared to OIF, while OIF has consistently higher in-hospital mortality than OEF for times less than 60 minutes.

Chapter IV: Discussion

We observed a strong and consistent relationship between longer pre-hospital time and in-hospital survival among evacuated personnel, as well as a strong positive association between ISS category and mortality. We believe it is most likely that improved survival with greater pre-hospital times represents a winnowing effect and is not reflective of a true benefit to the patient of longer evacuation time. That is, since our dataset did not include those who died prior to arrival at hospital, we cannot accurately assess survival in the cohort of all individuals with potentially survivable injuries. Limiting analysis to only those who survived to hospital has created biases in the results which limit interpretability of our findings. The difference between theaters reflects the greater overall in hospital mortality among all battle injured in OIF (~50% higher in OIF than OEF), and is magnified by the significantly shorter evacuation times of that theater which may have resulted in a higher proportion of unsalvageable patients arriving at all ISS categories. However all of these conclusions cannot be completely determined from the data available for analysis here.

The greater proportion of patients in the highest ISS category (ISS 51+) in OEF, nearly twice that of OIF despite the generally longer evacuation times, may suggest that some of the differences in association of pre-hospital time and mortality between theaters are due to improvements in point of injury and in-flight medical care provided to the patients in the pre-hospital period. Again, information to directly assess this is not present in the data available.

Section 1: Interpretation of the Regression Analysis

The difference in the association between mortality and time in Iraq as compared to Afghanistan may be related to time trends rather than Iraq-specific factors. The data set was constructed to study and guide improvements in in-hospital care, and as such gathers data primarily on those patients who arrive to the hospital alive. In the specific instance of

the data provided to us for analysis, any patients who were DOA are counted by the military as KIA, and were not provided for analysis, meaning that differences in the quality of pre-hospital care in part show up as missing events. The major feature of the data from Iraq is that the distribution of non-survivors is truncated at longer pre-hospital times, and for higher values of ISS. These two factors work together to result in relatively fewer mortality events being counted at longer pre-hospital time intervals. The strongly similar distribution and interaction of ISS and pre-hospital time across theaters reinforces this conclusion.

There is suggestive evidence for multiple possible explanations for our results.
Afghanistan represents more than 50% of the patients in the data provided, however other available data[25] indicate that between 2004 to 2010 the aggregate number of patient evacuations in Iraq was more than twice those that occurred in Afghanistan. This indicates that our datset was likely incomplete and that data capture and completeness of inclusion of eligible patients into the dataset have clearly improved significantly as the years of conflict have passed[24].
It is also possible that the differences in results by theater may be explained by a greater lethality of means in Iraq as compared to Afghanistan. The mortality rate among injured in Afghanistan across the conflict is 6.2%, as compared to same statistic for Iraq of 9.8%. This is reflected in the DOW rate, for this data set of patients who arrived alive to hospital, of 2.6% for Afghanistan and 3.5% in Iraq. The two sets of data are consistent in finding mortality rates for Iraq that are consistently higher.
Missing data does not explain directly all of the higher mortality rates found at shorter evacuation times in Iraq as compared to Afghanistan, nor the significantly greater (roughly 50%) proportion of patients arriving alive to hospital in Afghanistan relative to Iraq that are in the highest ISS category (those with ISS scores greater than 50). Our results suggest that

it is possible that improvements in pre-hospital care, either at the point of injury or in enroute care, or both, have occurred as time has passed. The decrease in mortality rates that is seen in 2008 and after, and the fact that mortality rates in Afghanistan are very similar across pre-hospital time, lend support to this explanation.

Section 2: Limitations

The primary limitation of this dataset is the fact that the cohort is ascertained at the time of arrival alive to hospital, and not at the time of injury. Individuals who died prior to arrival at hospital are not included in the dataset, whether or not they had potentially survivable injuries, and whether or not an attempt at evacuation was initiated.

The JTTR, and the military generally, code patients who are picked up by medical evacuation but expire enroute to the hospital as KIA, not DOA (dead on arrival) as is the civilian practice. This has the consequence of making it difficult to differentiate after the fact those patients who survived long enough for medical evacuation assets to arrive but then died enroute (KIA) from those who died immediately of their injuries (also KIA, hence the problem). This is an important differentiation when studying military trauma care, as the majority of those who are going to die do so very quickly, and the important question is what can be done to save those lives that can be saved. Those patients with potentially survivable injuries should, generally, be a larger percentage of the DOA group when compared to the group of patients who do not survive until the arrival of medical evacuation assets.

The distinction is not important from the perspective of measuring in-hospital mortality. It is important for interpreting the results and attempting to arrive at an explanation that would drive change or confirm usefulness of changes already made in pre-hospital practice.

Without a good description of the injury severity and other characteristics of the population that died enroute to care, it is very difficult to determine which of several explanations for the results is the most likely. Eastridge et al.[21] have reported on the distribution of injuries in those patients who died in the prehospital period using the autopsy data collected by Armed Forces Medical Examiner System (AFMES), for the period 2001 to 2011. They document that 87.3% of all patients who died did so prior to arrival at a Medical Treatment Facility (MTF). Using a liberal definition of potentially survivable injury, they characterize 24.3% of these died prior to arrival patients as having non-survivable wounds. Unfortunately, they did not report on what percentage of those arriving alive at an MTF had non-survivable injury.

Differentiation of polytrauma versus single trauma is mostly impossible within the dataset. This is unfortunate as polytrauma is a topic of significant interest.

Because the years that passed between the bulk of the data analyzed for Iraq and the bulk of the analysis for Afghanistan, a clear conclusion about why there is such a difference between theaters is elusive using only data available in this dataset.

A second potential major limitation was the possibility of more rapid evacuation of the most seriously injured personnel who were determined in the field to have survivable injuries. If present, this phenomenon would result in confounding in our analysis in the direction observed. We did not find direct evidence of this phenomenon but cannot exclude the possibility that it occurred.

Potential for Bias at the point of data entry.

The Joint Theater Trauma Registry (JTTR) started collecting data in earnest in the latter half of 2004, although it had existed prior to that time. Data entry was initially an additional duty accomplished by the clerks also responsible for other patient data entry duties, with limited in theater representation by dedicated personnel. As time has continued to pass, the resources available, command emphasis, and manpower dedicated to ensuring that the JTTR captures as accurate and complete a data set as possible have all increased. There are dedicated senior active duty officers assigned in a coordinating and supervisory role at the higher command levels in theater, and data entry is required and accomplished at all surgical hospitals in the CENTCOM theater.

In a busy Combat Support Hospital, even something as seemingly obvious as the means by which the patient was transported to the hospital is not obvious to the treating physicians who are not likely to have directly witnessed the patient's arrival. Additionally, patients are often held at the CSH for only a few hours before being before being evacuated out of theater, with the result that even a conscious patient might not be available as a source of information.

Any medical registry has a selection bias towards inclusion of the more seriously ill, and the persons who died, out of an understandable impulse on the part of clinicians to ensure that these cases be included in the registry and aren't missed.

Also, sicker patients and patients who die are often simply more available for inclusion, whereas less severely injured patients may be ambulatory, or otherwise more mobile, such as not requiring as special arrangements be made for their evacuation. The most severely combat injured may require a period of time for stabilization in the ICU or on the ward prior to evacuation making them especially available for inclusion in the registry by the deployed

personnel responsible for data entry. During the initial establishment of the registry in Iraq, clerks with a primary responsibility of tracking evacuations were also responsible for JTTR data entry. Over time, policy changes mandating data collection, procedure changes, and increasing dedication of resources to the JTTR effort improved the fraction of all wounded in action included.

Comparison of the fraction included in this sample by year (provided above, results tables 4 and 5) and theater shows that inclusion increased systematically each year within each theater, with overall inclusion in Afghanistan being higher. This introduces a source of systematic bias into this study. The presumed effect of inclusion bias in a registry for which inclusivity increases over time would be initially higher severity and acuity that becomes less pronounced over time with greater inclusivity and as more systematic procedures for preventing bias are implemented more effectively. In the context of this study, this sort of inclusion bias should result in higher overall in-hospital mortality and severity in the earlier time periods with regression to the lower true mean over time. This pattern is in part consistent with the change in mortality across calendar year observed after 2008, and must therefore be considered seriously.

Section 3: Ideal Study

An ideal cohort study would initiate identification of cohort members at the time of injury, and include all patients with potentially survivable but life-threatening injuries; the analysis would exclude all those not at risk for death or with clearly unsurvivable injuries. Further, categorization of injury severity would ideally be conducted at the earliest opportunity, rather than after survival or death has been determined.

In order to accomplish this in a military context, obtaining complete data directly from combatant units[22] as well as from the Joint Theater Trauma Registry would be necessary. A

key data source for a study of this type is the autopsy reports by the Dover AFB Armed Forces Institute of Pathology on every battle injury death. The other key data source is necessarily the unit records (primarily "patrol reports") in which any wounding or killing event would be detailed. Finally the aviation unit records, or other means of medical evacuation if relevant, would need to be collected in order to get accurate times.

Section 3: Directions for future research.

It may be useful to continue examination of differences in pre-hospital care practices before and after 2008, as that is when the overall mortality curve for both theaters began to trend downwards. Our research has at least demonstrated that there are significant differences between pre-hospital time associated outcomes before and after that date that remain to be explained fully.

CHAPTER V: Disclosures and Acknowledgements

The opinions or assertions contained herein are the private views of the author(s) and are not to be construed as official or as reflecting the views of the Department of Defense.

We would like to acknowledge the invaluable assistance provided by the Army Institute of Surgical Research, all those involved in the collection of the data that has become the Joint Theater Trauma Registry, especially those who took the time to do this in the combat theater, and Dr. Rodd Marcum, all persons without whom this research would not have been possible.

References

1. Newgard CD, Schmicker RH, Hedges JR, Trickett JP, Davis DP, Bulger EM, et al. Emergency medical services intervals and survival in trauma: assessment of the "golden hour" in a North American prospective cohort. Annals of emergency medicine. 2010;55(3):235-46 e4.
2. Apodaca AN, Morrison JJ, Spott MA, Lira JJ, Bailey J, Eastridge BJ, and Mabry RL. Improvements in the hemodynamic stability of combat casualties during en route care. Shock, 2013;40(1):5-10.
3. Apodaca A, Olson CM, Bailey J, Butler F, Eastridge BJ, Kuncir E.Performance improvement evaluation of forward aeromedical evacuation platforms in Operation Enduring Freedom. J Trauma Acute Care Surg 2013;75(2) Supplement 2:S157-S163.
4. Morrison JJ, Oh J, DuBose JJ, O'Reilly DJ, Russell RJ, Blackbourne LH, Midwinter MJ, Rasmussen TE. En-route care capability from point of injury impacts mortality after severe wartime injury. Annals of Surgery. 2013;257(2):330-334.
5. McCoy EC, Menchine M, Sampson S, Anderson C, Kahn C. Emergency medical services out-of-hospital scene and transport times and their association with mortality in trauma patients presenting to an urban level I trauma center. Annals of Emerg Med 2013;61(2):167-174.
6. Arifin MZ, Gunawan W. Analysis of presurgery time as a prognostic factor in traumatic acute subdural hematoma. J Neurosurg Sci 2013;57:277-80.
7. Dinh MM, Bein K, Roncal S, Byrne CM, Petchell J, Brennan J. Redefining the golden hour for severe head injury in an urban setting: the effect of prehospital arrival times on patient outcomes. Injury, Int J. Care Injured 2013;44:606-610.
8. Stuke LE, Duchesne JC, Greiffenstein P, Mooney JL, Marr AB, Meade PC, McSwain NE, Hunt JP. Not all mechanisms are created equal: a single center experience with the national guidelines for field triage of injured patients. Trauma Acute Care Surg 2013;75(1):140-145.
9. Tohira et. al. Systematic review of predictive performance of injury severity scoring tools. Scan J Trauma Resuscitation Emerg Med 2012;20:63.
10. Cohen MJ, et. al. Clinical and mechanistic drivers of acute traumatic coagulopathy. J Trauma Acute Care Surg 2013;75(1)Supplement 1:S40-S47.
11. Cudnik MT, Werman HA, White LJ, Opalek JM. Prehospital factors associated with mortality in injured air medical patients. Prehospital Emerg Care 2012;16:121-127
12. Fatovich DM, Jacobs IG, Langford SA, Phillips M. The effect of age, severity, and mechanism of injury on risk of death from major trauma in Western Australia. J Trauma Acute Care Surg 2013;74(2):647-651.
13. Hashmi ZG, Dimick JB, Efron DT, Haut ER, Schneider EB, Zafar SN, Schwartz D, Cornwell EE, Haider AH. Reliability Adjustment: a necessity for trauma center ranking and benchmarking. J Trauma Acute Care Surg 2013;75:166-172.
14. Kahl JE, Calvo RY, Sise MJ, Sise CB, Thorndike JF, Shackford SR. The changing nature of death on the trauma service. J Trauma Acute Care Surg 2013;75(2):195-201.

15. Mica L, Rufibach K, Keel M, Trentz O. The risk of early mortality of polytrauma patients associated to ISS, NISS, APACHE II values and prothrombin time. J Trauma Management & Outcomes 2013;7:6.
16. Demidenko E,. Sample size determination for logistic regression revisited. Stat Med. 2007 Aug 15;26(18):3385-97.
17. http://www.usaisr.amedd.army.mil/joint_trauma_system.html
18. American College of Surgeons, Committee on Trauma, PHTLS Manual, 4th edition
19. American College of Surgeons, Committee on Trauma, ATLS Student Course Manual, 7th edition.
20. HRSA Document: Model Trauma System Planning and Development, 2006
21. Eastridge BJ, Mabry RL, Blackbourne LH, Death on the battlefield (2001Y2011): Implications for the future of combat casualty care. J Trauma Acute Care Surg 2012; 73(6), Suppl 5: S431-437.
22. Gofrit ON, Leibovici D, Michaelson M. The trimodal death distribution of trauma victims: military experience from the Lebanon War. J Trauma. 2000;49:515–529.
23. Mabry RLHolcomb JBBaker AJHagmann JH. United States Army Rangers in Somalia: an analysis of combat casualties on an urban battlefield. J Trauma 2000;49(3):515-28.
24. Therien SP[1], Nesbitt ME, Duran-Stanton AM, Gerhardt RT. Prehospital medical documentation in the Joint Theater Trauma Registry: a retrospective study.J Trauma. 2011 Jul;71(1 Suppl):S103-8.
25. https://www.dmdc.osd.mil/dcas/pages/main.xhtml accessed 11 June 2014.