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The Association of Chronic Conditions with Clinical Outcomes Following Traumatic Injury in Older Adults

A dissertation submitted in partial satisfaction of the requirements for the degree

Doctor of Philosophy

in

Public Health (Epidemiology)

by

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The Dissertation of Richard Yee Calvo is approved, and is acceptable in quality and form for publication on microfilm and electronically:

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2015

DEDICATION

To my parents, Richard and Anne Calvo, my sister, Randyn Calvo, and my beautiful wife, Vi Nguyen, who have provided me with unrelenting support through my life. Thank you for your patience, support, and encouragement.

EPIGRAPH

The good life is a process, not a state of being. It is a direction not a destination.

Carl Ransom Rogers

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LIST OF ABBREVIATIONS

AIDS – Acquired Immunodeficiency Syndrome

AIS – Abbreviated Injury Scale

CAD – Coronary Artery Disease

CHF – Cardiac Heart Failure

CI – Confidence Interval

COPD – Chronic Obstructive Pulmonary Disease

CVA – Cerebrovascular Accident

GCS – Glasgow Coma Scale

EDW – Enterprise Data Warehouse

EMS – Emergency Medical Services

HIV – Human Immunodeficiency Virus

HLOS – Hospital Length of Stay

HR – Hazard Ratio

ICD-9-CM – International Classification of Diseases, Version 9, Clinical Modification

ICU – Intensive Care Unit

ISS – Injury Severity Score

RR – Respiratory Rate

RTS – Revised Trauma Score

SBP – Systolic Blood Pressure

sHR – Subhazard Ratio

SNF – Skilled Nursing Facility

TMPM – Trauma Mortality Prediction Model

TRISS – Trauma and Injury Severity Score

TQIP – Trauma Quality Improvement Program

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PREFACE

This dissertation is original, unpublished, and independent work by the author, Richard Yee Calvo.

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ABSTRACT OF THE DISSERTATION

The Association of Chronic Conditions with Clinical Outcomes Following Traumatic Injury in Older Adults

by

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Doctor of Philosophy in Public Health (Epidemiology)

University of California, San Diego, 2015

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BACKGROUND. The San Diego trauma population is aging over time and older trauma patients represent a vulnerable population at risk for mortality and severe morbidity. Reductions in validity of the prognostic metrics may be improved by evaluating chronic diseases, but there is

minimal evidence to support this. Few studies have evaluated mortality after trauma center discharge, and none have evaluated mortality in the context of discharge as a competing risk.

METHODS. Three studies were performed to evaluate chronic conditions on trauma-related outcomes as part of historical cohort study on blunt-injured patients age ≥55 years admitted between 01/2006-12/2012. The first evaluated chronic conditions on in-hospital mortality (with a competing event) and hospital length of stay (HLOS). The second evaluated chronic conditions and mortality after trauma center discharge. In the third study, a chronic disease-based prognostic model for trauma-related mortality was constructed and compared to other leading metrics.

RESULTS. There were 4653 unique patients who met all criteria for inclusion. Of 40 conditions, 23 were associated with in-hospital mortality. HLOS was associated with 32 of 40 conditions. Of 4442 survivors, 938 died within two years of discharge. Patients discharged to care facilities showed worse survival within the first 30 days (early-term mortality). Injury-related variables were associated only with early-term mortality, while chronic conditions were associated with two-year mortality after discharge. The model development procedure identified twelve conditions for inclusion. Model tests showed moderate performance for mortality and ours was superior versus other chronic disease metrics. Validation showed moderate performance of our model that did not significantly differ from other chronic disease metrics. Injury metrics, overall, were poor at predicting mortality.

CONCLUSION. Chronic conditions vary in their relationship with mortality by time. In older trauma populations, chronic conditions show stronger associations with mortality than injury-related measures. Discharges to care facilities are valid competing events to in-hospital mortality and should be accounted for when assessing the quality of trauma care. Our developed model performed well with twelve variables compared to others with far more. Results can be used to inform patients and care providers of the risks outside the realm of injury.

CHAPTER 1.

Background and Significance/Research Objectives

Introduction

Physical trauma, including unintentional and violence-related injuries, is the leading cause of death in the United States among people aged 1-44 years.[1] Trauma mechanisms are classified as blunt (e.g. motor vehicle crash), penetrating (e.g. gunshot), or other, with blunt mechanisms being predominant. Over 70% of all causes of trauma in San Diego are unintentional.[2] While trauma remains the fifth leading cause of death nationally, evidence has shown that a significant proportion of patients survive the initial injury with varying levels of disability.[3,4] Previous research within an urban trauma center in San Diego county between 2000 and 2011 identified a significant increase in the proportion of deaths due to comorbidities and eventual withdrawal of life sustaining care.[5,6]

Among aging populations, life expectancy and technological advancements in treatment have increased substantially compared to previous estimates.[7,8] Aging populations have grown over the years in number and activity level. In a report by the US Consumer Product Safety Commission, the baby boomer generation (those born between 1946 and 1964)[9] experiences more injury than younger generations, with recovery occurring much more slowly by comparison.[10] However, the growth of aging populations and the epidemic of chronic diseases is a pressing problem that commands attention. The interaction between trauma and chronic conditions may disproportionately affect aging demographics, putting strain on both the public health and medical systems. Moreover, aging populations have been shown to respond differentially to injury compared to younger populations.[11,12] Stress due to trauma may result in an inadequate pumping capacity of the myocardium, resulting in myocardial ischemia.[13] Age-related decline in cellular function leading to organ failure may be accelerated due to trauma. Consequently, age itself has been implicated to be directly related to physiologic reserve and the capacity to recover from injury.[14]

The San Diego Trauma System

San Diego County utilizes a unique regionalized trauma care system implemented in 1984.[15] Regionalization of the trauma system has been shown to have positively improved survival after trauma compared to California counties without regionalized systems.[16–18] With a population of 3,140,069 as of 2011, San Diego County has six total trauma centers (two level 1 adult trauma centers, three level 2 adult trauma centers, and one level 1 pediatric trauma center), each with its own specific patient catchment area. Catchment areas were developed by the San Diego County Emergency Medical Service (EMS) Agency and based on the roadway systems, geography, and regional population densities. Transportation to a trauma center via pre-hospital EMS is determined by the geographic location of injury unless otherwise specified by the patient. Over the last decade, the number of annual traumatic events requiring hospitalization has increased steadily, reaching 10,417 based on the most current estimates.[19]

Under the direction of the San Diego County EMS, a county-wide trauma registry service was implemented to evaluate trauma quality and performance improvement opportunities.[20] Currently, EMS and all trauma centers in San Diego County utilize a relational database-based software by Digital Innovations, Inc.[21] All trauma centers are required to maintain their own registry. Each month, EMS receives patient data from trauma centers to review patient information and study the best practices in trauma care. Trauma registries contain markers of quality such as cost and complications, patient demographic information, clinical information, treatments, procedures, laboratory results, comorbid disease, injury characteristics, courses of care, and in-hospital outcomes. These registries have been integral in providing a foundation for local and national improvements to trauma care.[20,22,23]

Among the five adult trauma centers in San Diego, the Scripps Mercy Hospital catchment area encompasses the second-most urban region of San Diego and receives the largest share of EMS transport volume in all of the county.[20] The catchment area reaches to the US-Mexico

border and covers a surface area of approximately 611.1 square kilometers.[24] The hospital houses an American College of Surgeons verified level 1 trauma center consisting of five trauma surgeons and a naval residency program for vascular, trauma, and acute care surgery. Mercy Trauma accommodates over 2400 trauma activations per year, servicing approximately a quarter of the entire county.[6]

The San Diego County Trauma System Medical Audit Committee is the system's quality assurance entity. Comprised of representatives from the county EMS, County Medical Examiner's office, and trauma medical directors and nurse managers from each of the six trauma centers, the medical audit committee meets monthly to assess and improve the quality of care delivered by trauma centers.[2] Variations in practice are discussed, and opportunities for improvement in care delivery are highlighted.[25] Under the peer review process, deaths are categorized as preventable, potentially preventable, or non-preventable. Morbidity is characterized by absence or presence of systematic flaws in the delivery of care. The San Diego medical audit committee has been considered a model quality improvement program for the nation's trauma systems.[16,17,26] The medical audit committee process provides a minimization of biases related to physician decisions, misclassification of mortality causes, and misclassification of iatrogenic morbidity. Details on the medical audit committee process are described elsewhere.[2,26]

The San Diego County Trauma System Triage Criteria

The San Diego trauma triage protocol was designed to establish criteria for the identification of trauma center candidates to be transported to a designated trauma centers. Based on age, physiologic, anatomic injury, and mechanism, the trauma triage criteria, in conjunction with a regionalized trauma system, has been in use for over two decades.[16,17] Although successful, changes in the population demographic may strain trauma centers due in part to the way elderly and diseased patients are classified as trauma. Inversely, other researchers studying Washington,

Maryland, and Pennsylvania trauma populations have concluded that under-triage is a predominant issue resulting in poorer health outcomes among the elderly.[27–29] However, San Diego County contains one of the highest geriatric populations in the United States and a regionalized trauma system, and results from other centers may not be generalizable to the San Diego County trauma population.

The existing criteria states that, independent of mechanism and severity of injury, all injured patients age ≥ 55 years old, patients on antithrombotic medications for chronic conditions, patients on dialysis with renal disease, patients with cardiac or respiratory disease, patients with bleeding disorders, or patients with evidence of any level of loss of consciousness are classified as trauma and transported to trauma centers.[30] Decision to transport to a trauma center is ultimately left to the EMS providers. A final 'catch all' which may be regularly used for trauma and diseased patients is the "when in doubt, transport to trauma center" criterion due to the lack of specialized medical training among EMS providers for working with these traumatically injured subpopulations. Demitrades, *et al* speculated that elderly trauma patients may appear clinically normal despite exposure to severe injury. However, reduced physiologic reserve in conjunction with chronic disease may adversely affect survival.[31] Although a small proportion is downgraded to the emergency department, substantially more who are initially admitted as "walk-in" patients are upgraded as trauma consults.

The Changing Trauma Demographic

In the physical trauma setting, patients of advanced age have been shown to experience higher rates of withdrawal of life sustaining treatments compared to younger patients.[5,6] However, the effects of specific chronic conditions have rarely been assessed as risk factors in the relationship between advanced age and hospital mortality (including withdrawal of life sustaining treatment), and hospital length of stay which are the traditional measures of quality in trauma care.[5,32] Moreover, the relationship between chronic conditions and long-term survival have been

superficially assessed in traumatically injured populations.[14,32–36] Among patients surviving to discharge, many are sent to advanced care facilities and expire shortly after their exposure to injury.[37–40] The proportion of elderly patients composing the trauma population is steadily growing, and efforts must be made to prepare public health and medical systems for this change.

While there is much speculation as to why the distribution of adult trauma-related in-hospital mortality has changed, significant research efforts have focused on a changing trauma demographic as a primary factor.[3,6,41–43] A study by Calland, *et al* found that risk factors for mortality in trauma patients vary by age and injury mechanism, and also remarked upon the limitations of the existing metrics which do not adequately account for aging-related factors.[12] Another recent study of 11 years of trauma patients by Kahl, *et al* found that the proportion of elderly patients more than doubled, from 12.1% in 2000 to 24.6% in 2011.[6] Analyses among the causes of death following trauma identified linear reductions in the injury-related causes and increases in chronic disease-related causes. A study of Pennsylvania state trauma data over 10 years similarly found increasing trends in median age and blunt injury over time.[38] Chu, *et al* reviewed the literature and concluded that the rise in geriatric and diseased patients will require better management of services by trauma centers or risk becoming overwhelmed.[44]

Growing Chronic Disease Burden and Measurement Methods

Worldwide, results from the Global Burden of Disease 2010 study (GBD 2010) identified chronic diseases such as chronic obstructive pulmonary disease, heart disease, stroke, and diabetes, as being dominant contributors to increased disability adjusted life-years, and have displaced many acute issues since 1990.[45] Risk factors as measured by blood pressure, poor diet, increased alcohol consumption, substance abuse, and high BMI have substantially increased in prevalence, globally.[45] Within the United States, a recent study using the GBP 2010 data found that years of life lost due to premature mortality has increased among peoples affected by a multitude of chronic conditions which include Alzheimer's disease, drug use, chronic kidney

disease, cancers, and traumatic falls.[46] Recent studies in trauma have utilized the presence of chronic conditions as a measure of patient frailty after trauma, directly attributable to increased mortality risk.[11,12]

General concern for the impact of chronic conditions on clinical outcomes has existed since the early 1970s.[47] However, the effect of chronic diseases on clinical outcomes within a traumatically injured population has only been a topic in the trauma literature since the mid-2000s. While previous researchers have attempted to address the effect of chronic diseases on trauma-related outcomes, many have relied on pre-developed metrics, which have not been validated for a traumatically injured population. Two of the most commonly used metrics are the Charlson Comorbidity Index [48] and the Elixhauser Comorbidity Scale [49] which utilize the International Classification of Diseases, Version 9, Clinical Modification (ICD-9-CM) codes and diagnosis related groups to calculate the probable burden of disease on mortality. However, these and other metrics had been developed within specific subpopulations, demonstrate high variation in the diseases utilized, address different outcomes, and reveal derived relative weights based on varying statistical methodology. Evaluation of chronic disease prevalences, scoring, and validating conditions that are specific to trauma populations has not yet been performed.

The Charlson Comorbidity Index encompasses 19 medical conditions weighted 1-6 with total scores ranging from 0-37 on the basis of strength in the relationship with 1-year survival.[48] Charlson and colleagues utilized a training population of 607 hospitalized patients admitted to a New York hospital during one month in 1984 and followed them for one year. Cox proportional hazards modeling was used to generate predicted survival. A validation set of 685 breast cancer inpatients was used for final model testing. Variable selection was based on methods used by Hutchinson, *et al* [50] in which biologically plausible and statistically significant variables in bivariate analyses were retained for adjusted analyses. In the development of the index, the relative risk for each condition was calculated for mortality. A weight was subsequently assigned

based on the magnitude of the association. For example, adjusted relative risks between 1.0 and 1.2 are assigned a weight of zero; relative risks ≥ 1.2 and < 1.5 receive weights of 1; relative risks ≥ 1.5 and < 2.5 receive weights of 2; relative risks ≥ 2.5 and < 3.5 receive weights of 3; having two conditions with relative risks ≥ 2.5 and < 3.5 receives a weight of 6. Weighted index scores are combined into a 4-category variable to group patients based on the number of conditions: 1) patients with no comorbidities, 2) patients with 1 or 2 comorbidities, 3) patients with 3 or 4 comorbidities, and 4) patients with 5 or more comorbidities. Additional scores have been created based on the interaction between age and comorbidity. However, these are not regularly used and were initially designed for 10-year survival following cancer diagnosis.

The Elixhauser Comorbidity Scale provides a different account of measuring chronic conditions by including ICD-9-CM procedure codes, diagnosis codes, and diagnosis related groups in its calculation. This scale contains 30 subcategories of major comorbid illnesses and is used by the Agency for Healthcare Research and Quality (AHRQ) to assess hospital resource utilization. The scale was developed from a population of 1779167 Californian inpatients across 438 hospitals in 1992 using the Statewide Inpatient Database from the Healthcare Cost and Utilization Project (HCUP).[49,51] Initial outcomes of analysis were log-transformed hospital length of stay, total charges, and in-hospital mortality. The Elixhauser scale explicitly attempts to calculate the effect of iatrogenic comorbidities resulting from surgical procedures. In its purest form, the Elixhauser scale does not derive weights or points for its comorbidities. However, other researchers have augmented the scale to fit their respective populations.[52-54]

Recent studies have utilized aggregate scoring metrics to control for chronic disease burden where the overall objectives were to characterize trauma-related treatments or outcomes, ignoring the individual risks of specific conditions. Some researchers have attempted to revise or create metrics to make the more attributable to a traumatically injured population.[36,54–59] In 2008, Moore, *et al* evaluated specific chronic conditions in a Canadian trauma population and revised

weights attributable to conditions in the Charlson, *et al* [48] metric in an effort to improve accuracy of statistical models for predicting in-hospital mortality.[55] Although models did improve, the magnitude of improvement was mild (approximately 2.5%). Moreover, conditions thought to be harmful for survival were found to actually be protective. Similarly, Thompson, *et al* found that despite increases in prevalent chronic conditions, addition of conditions to existing injury-based metrics yielded minor improvements in prediction of mortality.[36] Thompson, *et al* utilized logistic regression to model mortality rather than survival analysis which may inaccurately estimate the risk for death for each condition. Both studies utilized regional databases which lacked the detail and sensitivity of local registries. In addition, selection criteria in the previously mentioned studies included all trauma cases irrespective of patient age and mechanisms of injury. Among younger and more severely injured study populations, chronic disease burden is not expected to significantly affect survival as in-hospital mortality will likely be predicted by the number, severity, and type of injuries sustained.

Although scarce, some trauma-based literature has focused on specific diseases and their effect on clinical outcomes following injury. Cardiovascular diseases, the metabolic syndrome, substance abuse disorders, and psychiatric conditions have been shown to directly affect outcomes and care following trauma.[42,59–65] Lonjon, *et al* found that prevalent diabetes mellitus is related to post-operative infection following trauma.[66] Moreover, a prospective study of 461 spinal cord injured patients found that diabetics and heart disease patients were at a 2- and 3-fold higher risk for death compared to spinal cord injured patients without these conditions, respectively.[67] Obesity has been associated with substantial complications following ankle fracture.[68] In addition, Neville, *et al* found that obesity was significantly associated with increased mortality and organ failure among a blunt injured population.[69] Contrary to other research on the topic, Bukur, *et al* found that cirrhotic patients were more likely to survive after trauma with aggressive treatment and resources.[70] Indices used to define frailty in trauma populations have

keyed in on the chronic conditions of diabetes, congestive heart failure, hypertension, stroke, myocardial infarction, chronic obstructive pulmonary disease, and impaired sensorium as being predictors of poor outcomes and dependency on care service.[11]

Chronic Disease Data Collection Methods

At Scripps Mercy Hospital, chronic diseases are collected using two methods: using administrative records containing ICD-9-CM diagnosis codes, and with the comorbidity coding system included in the Digital Innovations trauma registry. The primary use of ICD-9-CM diagnosis codes is to provide the finance department with standardized codes for billing purposes. Diagnosis related groups were developed by the Heath Care Financing Administration to classify patients by the expected costs they will incur during their hospital stay for Medicare reimbursement.[71] Classification is based on demographic, diagnostic, and therapeutic attributes of care to determine theoretical resource utilization. The theoretical amount of resources utilized by a patient allows for the production of a hierarchical classification to differentiate patients by resource demands and associated costs. Patients are initially assigned based on weighted the ICD-9-CM codes.[71–73] These diagnosis related group codes have been previously utilized to also classify disease severity.[39,49,74] Major Diagnostic Categories are the highest level of the hierarchy which classify diagnosis related group codes by organ systems. Selection of comorbidities for collection by the trauma registry originated from prevalence studies of chronic conditions co-existing among trauma patients in 1989-1993.[33–35]

The use of electronic medical records for research is longstanding. Although not its primary purpose, there is significant value in accessing information from electronic medical records to answer research questions.[75] Despite varying degrees of data incompleteness,[76] significant efforts are made to accurately measure and input information into records systems. Traditionally, data incompleteness has been the result of fragmented healthcare systems and limited capacity for communication between providers and departments.[75] However, the adoption

of trauma registries has improved the quality of data and provides for a standardized and interoperable format for information exchange. A list of the chronic conditions from the trauma registry and the codes used for their identification are shown in Appendix 1.

Chronic Disease Burden in Trauma Patients

Previous analyses have shown that, among the Scripps Mercy Hospital trauma population, chronic conditions have increased steadily over 2006-2011.[6] Cardiac diseases (222.9 per 1000), psychiatric disorders (74.4 per 1000), hematologic disorders (71.1 per 1000), neurological disorders (85.0 per 1000), substance abuse disorders (341.1 per 1000), and pulmonary diseases (50.9 per 1000) are among the most prevalent based on unpublished data of patients from May 2006- December 2011. Diseases may be prevalent long before the trauma, though Scripps Mercy Hospital services a high proportion of San Diego's underserved areas resulting in many conditions being newly diagnosed at the time of their trauma admission.

History of cardiac surgery is regularly ascertained among patients, as they directly affect the course of care by trauma physicians. These conditions are among the most prevalent in the elderly population, and declining function of cardiac myocytes may not be identified through simple evaluation of blood pressure.[77] A study by Ferraris, *et al* which looked 13198 trauma patients admitted in 2002-2006, found that 4% of patients with cardiac disease history died following trauma. History of heart failure and beta-blocker usage was statistically significantly related to in-hospital mortality after adjustment for injury severity score, Glasgow coma score, respiratory diseases, cancers, and cardiac medication use.[78] However, this study combined several other cardiovascular risk factors such as diabetes and warfarin use in the category of cardiac diseases which may not be appropriate for condition-specific analyses. Congestive heart failure has been associated with in-hospital mortality in an elderly trauma cohort after adjustment for relevant covariates.[32] Another study identified ischemic heart disease as being significantly related to extended hospital length of stay (HLOS) in patients aged 55 and older only.[33]

Psychiatric disorders have been associated with trauma before and after the injury has occurred.[79,80] These conditions are particular debilitating due to substantial qualify of life reductions and decreased physical capacity of self-care and recovery.[80] Survivors of traumatic injury have been shown to have increased prevalence of stress disorders and depression with time in a longitudinal study of injured Australians.[81] Another study of traumatically brain injured (TBI) Australians found that poorer mental health status and psychiatric symptoms, including suicidality, were related to frequency and recentness of the injury.[82] In addition, a Danish study of hospitalized patients found that those who experienced TBI were significantly more likely to attempt suicide, indicating an alarming need for proper psychological evaluation and care methods in this population.[83] Another study performed among a northern Californian population identified psychiatric conditions as a significant predictor of extended length of stay following trauma.[33]

Existing conditions affecting the respiratory system have associated with reduced survival after trauma. Pulmonary diseases, which are readily collected by trauma systems, are asthma, chronic obstructive pulmonary disease (COPD), and other chronic pulmonary conditions (pulmonary hypertension, inflammatory pulmonary disease, chronic bronchitis, emphysema). Garshick, *et al* found that, although respiratory diseases were underlying causes of death in 5.4% of their spinal cord injured population, it was a contributing cause in 24.3%.[67] Asthma has been implicated as a factor related to the systemic inflammation of organ systems following trauma.[84] COPD has been independently associated with mortality and increased length of stay in the elderly.[32,33]

Not surprisingly, substance abuse and dependencies are the most prevalent class of chronic conditions affecting the traumatically injured. Drug and alcohol usage is a correlate of traumatic brain injury due to falls, motor vehicle accidents, violence, and eventual mortality.[85–87] While the literature seems to be focused on traumatic brain injury and substance abuse, alcohol

and drug dependencies have been associated with increased risk for trauma and mortality among non-TBI patients as well.[88] However, past research did not find a relationship with drug or alcohol use and in-hospital mortality in a statewide trauma registry.[32]

Hematologic disorders include acquired coagulopathy, conditions requiring warfarin therapy, hemophilia, and pre-existing anemia. These conditions are directly assessed as part of the trauma triage criteria, since reduced clotting factors are directly related to traumatic hypotension and hemorrhage. People aged 55 and older on antithrombotic medications are immediately activated as trauma patients regardless of injury severity due to these risks.[30,31,89] In a study of elderly trauma patients with a fall primary mechanism, hematologic diseases as a class have been associated with increased mortality.[32]

Neurological chronic conditions include a multitude of issues: spinal cord injury, multiple sclerosis, Alzheimer's disease, history of seizures and epilepsy, chronic demyelinating disease, dementia, organic brain syndrome, Parkinson's disease, and cerebrovascular diseases including stroke. Specifically for an aging population, these conditions place the population at an increased risk for trauma which eventually requires placement in a long-term care facility. Neurological conditions have been implicated as a huge risk factor for falls as a mechanism of injury.[90] Many of these patients eventually require withdrawal of life sustaining treatments due to the severity of their disease, injury, and significant reductions in quality of life.[5,91]

Trauma Outcomes Research

Past research on trauma outcomes has primarily focused on the in-hospital endpoints of length of hospital stay, surgical complications rates, resource utilization, cost, readmission, and mortality.[37,38,40,92–98] Although these measures are objective, changes in technology, treatments, and the patient demographic have posed numerous limitations to use of these measures.[40] Moreover, recent research has identified that patients who have experienced trauma and are subsequently discharged are still at significant risk for death.[37,38,40,99] Functional discharge status

and location of discharge has often been the default outcome used to address survivorship.[4,100–103] However, it has been suggested that trauma patients discharged to intermediate or palliative care facilities are not included in trauma center estimates and therefore may differentially affect research pertaining to mortality.[5,39,104–106]

The concept of the "trimodal distribution of trauma deaths" originated in 1982 to describe the temporal distribution of adult in-hospital mortality following trauma. The three modes are defined traditionally as early death due to hemorrhage within the first hour after admission, early death as a result of cardiovascular or neurologic injury between one and four hours, and late death due primarily to multi-organ failure after approximately a week in the hospital. Although it is still a part of the standard trauma teaching curriculum, recent evidence has indicated a reduced applicability of this concept to current trauma populations.[6,107,108]

Historically, quality of trauma care has been assessed using in-hospital indicators based on perceived errors in practice, complication rates, and delays in diagnosis and treatment.[38,40,92–94,109] Three of the largest databases in trauma, the American College of Surgeons Committee on Trauma Major Trauma Outcomes Study, the National Trauma Databank, and the Trauma Quality Improvement Program (TQIP) have provided the foundation for nearly all of the predominant benchmarks of quality of care.[18,40,93,110,111] Although objective, changes in technology, treatments, and the patient demographic have posed numerous limitations to use of these measures.[40,109]

Some researchers have suggested redefining trauma quality metrics to reflect changes in clinical outcomes rather than evaluate the efficiency of medical processes.[112–114] Exemplifying this push is the work being performed using the TQIP data.[110] The TQIP database was established to create and implement a standard of care reflective of current technological advances, medical training, and trauma population. The TQIP database focuses on in-hospital outcomes to assess quality; specifically, in-hospital death and in-hospital complications. Results from such studies have provided the foundation for proposed changes to the benchmarking processes for trauma

centers. However, none of the leading studies have addressed the combination of trauma and chronic diseases on in hospital mortality, hospital length of stay or post-hospital long-term survival. Moreover, existing measures do not account for discharge to care facilities or mortality following discharge as competing events to in-hospital deaths.

The topic of post-discharge mortality is a relatively new frontier in trauma research. Existing literature on the topic has primarily occurred outside the United States where chronic disease prevalence, treatment methods, and access to care are significantly different.[98,99,115,116] Information on patients' post hospital discharge are rarely collected as they necessitate significant consent requirements be met. Unlike traditional prospective studies, inclusion in trauma registries is not voluntary, and contacting patients for purposes other than treatment, payment, or healthcare operations can be considered violations of the Health Insurance Portability and Accountability Act of 1996. Data from The Office of Statewide Health Planning and Development and state vital records databases have been used to evaluate post-discharge survival, readmission rates, other outcomes.[37,39,117] Results from such studies have provided the foundation for proposed changes to the benchmarking processes for trauma centers. However, none of the leading studies have addressed the combination of trauma and chronic diseases on long-term development of clinical outcomes.

The Measurement of Trauma

Measurement of risk factors and outcomes related to trauma and injury has evolved since the early 1970s when Susan Baker, a trauma epidemiologist, wrote an editorial to the Journal of Trauma on how to best evaluate trauma care and compare patient populations across different regions.[118] The Abbreviated Injury Scale (AIS) was developed by the Association for the Advancement of Automotive Medicine to assess injuries in 1971. Later in 1974, Baker, *et al* sought to validate the AIS using mortality in a traumatically injured Baltimore, Maryland population. The AIS, at the time, ranked injuries on a scale of 1 (minor) to 6 (unsurvivable) for

each of six potential regions (Head/Neck, Face, Chest, Abdomen, Extremity, and External). Their analyses validated the use of individual AIS scores for predicting death rates, but also found that simple summation of these scores across body regions in instances of polytrauma was insufficient.[119] In what would be named the Injury Severity Score (ISS), these researchers identified that the sum of the squares of the scores of the three most severely injured regions strongly correlated with mortality ($ISS = A^2 + B^2 + C^2$ where A, B, C are the AIS scores of the three most severely injured ISS body regions). The range of ISS is from 1 to 75. If any single region is assigned an AIS of 6, a patent is automatically scored an ISS of 75 regardless of other criteria. Despite the advent of improved injury scoring systems, ISS, in its unmodified form, has remained the *de facto* measurement of injury severity.[93,119–122] Despite having impossible values in the calculation of scores (patients cannot have an ISS of 7, 15, 23, 28, 31, 37, 39, 40, 44, 46, 47, 49, 52, 53, 55, 56, 58, 60-65, 67-74), and its derivation from an ordinal variable, it is traditionally treated as continuous or processed into additional ordinal categories.[93,115,119-122]

The AIS was later restructured to include the regions of: Head (1), Face (2), Neck (3), Thorax (4), Abdomen (5), Spine (6), Upper Extremity (7), Lower Extremity (8), and External/Other (9).[123,124] However, ISS scores were not revised to reflect this new categorization scheme. This AIS version allows for the detailed coding of blunt and penetrating trauma, including non-traditional trauma such as burns, asphyxiation, and electrocution. All injuries are coded using a six digit pre-dot and single digit post-dot code (e.g. 123456.7) to denote types and specific types of anatomic structures injured, and severity of all injuries. These pre-dot values are structured accordingly: the first digit indicates the general region, digit 2 indicates the type of anatomic structure, digits 3 and 4 indicate the specific anatomic structures (e.g. part of spinal column, tissues, concussion for brain), and digits 5 and 6 define specific types of injury (e.g. fracture, laceration, ruptures). The post-dot value (7) is the marker of severity and is identical to the older AIS version.

Other Trauma-related Markers of Injury Severity

Various clinical markers of patient responsiveness, and physical and cognitive functionality have been recognized as potential predictors of outcomes following trauma.[125,126] Upon trauma patient admission, demographic and injury factors are acquired to prepare medical staff and hospital resources. These markers have shown to be resourceful in the design and implementation of metrics for trauma surgeons.[111,127–129]

Blood pressure values and pulse have been utilized as a baseline estimate of presentation with hemodynamic instability (hypovolemic, cardiogenic, septic, obstructive shock)[130] in the trauma bay, and is regularly analyzed for of the triage and survival among trauma patients.[32,108,111,112,131] Admission systolic blood pressure (SBP) and diastolic blood pressure are associated with mortality and cardiac arrest in the injured, and are utilized in existing predictive metrics for these and other clinical outcomes.[111,121,129,132,133] Cut points for SBP to define hypotensive shock have varied by study but have typically been in the range of SBP < 90 to 110 mmHg.[129,133,134]

Similarly, patient initial respiratory rate (RR, measured in unassisted breaths per minute) has been used to evaluate the probability of trauma-related outcomes and triage resources.[111,135] Abnormal respiratory rates (tachypnea for increased RR and bradypnea for decreased RR) are correlated with altered tidal volume, respiratory distress, lung injury, irregular blood gas concentrations, and a requirement for mechanical ventilation.[134,136,137] Respiratory acidosis due to hypoventilation is strongly linked to head trauma, illicit drug use, and chronic conditions such as bronchitis, asthma, and cancer.[136,138–141] Respiratory alkalosis is a condition defined by lowered arterial carbon dioxide levels from hyperventilation and typically represents the evidence of pulmonary edema, presence of a pulmonary embolism, or overly aggressive mechanical ventilation in trauma patients.[136,141–143] Although RR has been used in the development of statistical models to predict outcomes, advances in resuscitative treatments (e.g. permissive

hypotension, damage control resuscitation) have reduced its validity for modeling injury-related mortality.[6,144–146]

The Glasgow Coma Scale (GCS) score, developed in 1974, is a composite score based on functional status of three systems: eye reactivity, verbal response, and motor skills.[147] The GCS was originally developed as a method for evaluating severity and duration of impaired consciousness and cognitive function, but has become a standard in the assessment of functional status at admission.[126,128,148] The GCS has been incorporated into several intensive care unit scoring systems such as the Acute Physiology and Chronic Health Evaluation, Simplified Acute Physiology Score, and the Sepsis-related Organ Failure Assessment Score for inpatient morbidity and mortality.[149–151] Scores for the GCS range from 3 to 15, with 15 indicating full awareness and 3 characterizing coma or death. The GCS is currently the standard for evaluating unconsciousness but its use is restricted to traumatically injured populations.[126,148] Moreover, GCS is not measureable in patients who are intubated, intoxicated, or otherwise sedated.[152]

Two of the most widely used trauma metrics are the Trauma & Injury Severity Score (TRISS) and the Revised Trauma Score (RTS) for physiologic derangement. Both of these are used by clinicians to predict the probability of trauma mortality (or survival) and are calculated using combinations of demographic variables, clinical measures, and multiple logistic regression.[93,110,111,121,153] Although they were developed in the 1970s and early 1980s, both have become the current standard in the prediction of trauma outcomes.[111,121,144]

Originally termed the "Trauma Score", the RTS was modified to provide pre-hospital healthcare workers with an immediate numerical triage tool for trauma center transport and evaluate survival following trauma. Scores for the RTS are produced through summing coded values from three other variables obtained at admission: the total GCS score, the SBP, and the RR. In 1989, Champion, *et al* published a revised set of value ranges and points system for each of the three component variables to create the Triage RTS. The Triage RTS calculation is a

simple sum of the coded values which range from 0 to 12.[111] Variable weights for survival probability (historically denoted as "P_s") were derived from the Major Trauma Outcome Study using the logit model:

$$P_s = 1 / (1 + e \text{ ^ } -(\beta_0 + \beta_1(GCS) + \beta_2(SBP) + \beta_3(RR)))$$

Where: $\beta_0 = -3.5718$, $\beta_1 = 0.9368$, $\beta_2 = 0.7326$, and $\beta_3 = 0.2908$, and the values input for GCS, SBP, and RR are the corresponding coded values. The actual RTS is calculated using a modified equation:

$$RTS = 0.9368\ (GCS) + 0.7326\ (SBP) + 0.2908\ (RR)$$

Values calculated in this fashion range from 0 to approximately 8, with an RTS of 0 correlating to a P_s of 0.027; 1 to a P_s of 0.071; 2 to P_s a of 0.172; 3 to a P_s of 0.361; 4 to a P_s of 0.605; 5 to a P_s of 0.807; 6 to a P_s of 0.919; 7 to a P_s of 0.969, and 8 to a P_s of 0.988.

The TRISS score was developed in 1983 by the same research group as the RTS to identify patients at high risk for mortality and to benchmark trauma services.[154] However, unlike the RTS which only utilizes physiologic parameters, TRISS utilizes the RTS as a variable (representing patient physiologic derangement) and includes additional measures of ISS (anatomic injury severity), patient age ≥ 55 or < 55 (coded 1 and 0, respectively), and the underlying mechanism of injury to predict survival after trauma. Two sets of coefficients for each variable were derived from multiple logistic regression analysis of patient included in the Major Trauma Outcomes Study: one for blunt mechanisms of injury and another for penetrating mechanisms of injury. After its modification in 1987, the logit equation appeared as such:

$$P_s = 1 / (1 + e \text{ ^ } -(\beta_0 + \beta_1(RTS) + \beta_2(ISS) + \beta_3(Age)))$$

Where: $\beta_0 = -0.4499$, $\beta_1 = 0.8085$, $\beta_2 = -0.0835$, and $\beta_3 = -1.7430$ for blunt mechanisms of injury, and $\beta_0 = -2.5355$, $\beta_1 = 0.9934$, $\beta_2 = -0.0651$, and $\beta_3 = -1.1360$ for penetrating mechanisms of injury.[74] Resulting P_s values are subsequently assigned to patients shortly after admission once values for all variables are recorded. In addition, TRISS scores are used as a quality improvement

measure to calculate expected trauma-related mortality and evaluate it against observed deaths.[146,155] Unexpected mortality and survivorship is subsequently used for internal and external assessment of patient care by trauma audit committees.

These metrics that are currently used to probabilistically predict trauma outcomes based on clinical and demographic patient profiles are losing validity over time. A recent study identified that despite changes to the TRISS algorithm, it is gradually losing calibration over time.[144] Many researchers have attempted to revise the TRISS to recover lost validity.[121] The revisions that incorporated chronic disease metrics have all resulted in modest improvements in prediction.[55,56,59,127] Unfortunately, these modifications only further perpetuate the use of metrics that have not been designed for the traumatically injured. Recommendations have been made to generate entirely new predictive models for the adult injured population.[112,144,156,157]

Predictive Modeling in Trauma

Researchers who have compared predictive metrics have revealed discrepancies in the measurement and validity of each for use in varying clinical populations.[52,158-161] However, these metrics have been shown to be valuable in providing rule-based clinical decision support.[162–166] Predictive metrics provide a means for objective estimation of risk and offer healthcare providers with tools to rapidly identify these patients.[165] Since the early 1980s, the use of computer-based decision support has grown,[162,165] and many existing electronic medical records have incorporated decision support algorithms into the general practice.[167,168]

Prognostic and diagnostic metrics exist for use in a variety of medical situations. The Marshall score and Rotterdam score are used to classify severity brain injuries based on computed tomography scans and provide clinicians with probability values for early and late mortality, respectively.[169,170] As previously mentioned, other scoring systems are used to predict morbidity and mortality among intensive care unit patents to properly allocate resources.[35,149,150,161,165] The Vanderbilt University Pharmacogenomic Resource for Enhanced Decisions in Care & Treatment

project utilizes genetic data to model the probability of adverse reactions dependent on dosing and frequency of medications. In a step towards personalizing medicine, results from this project seek to revise treatment strategies at the point of care.[171] Similarly, Kuperman, *et al* identified provider order entry of medications as an opportunity for clinical decision support to minimize duplication of treatments, errors in dosing, and issues with pharmacologic interactions.[166]

Currently, the established trauma treatment criteria do not focus on the potential effects of chronic conditions in injured patients; only a handful of conditions are actively considered during admission to the trauma bay. In the trauma setting, stabilization of the patient and treatment is the priority followed by rehabilitation and recovery. However, as older patients constitute a greater proportion of the injured over time, the likelihood of recovery and survival may be dependent on the existence and severity of chronic conditions more so than the injury itself.

Existing measures used in the trauma setting have often focused on prediction of mortality and trauma-related morbidity to assist in clinical decision-making and prepare hospital resources. Recent research has identified that patients who have experienced trauma and are subsequently discharged are still at significant risk for death.[37,38,40,99] Moreover, it has been suggested that trauma patients discharged to intermediate or palliative care facilities are not included in trauma center estimates and therefore may differentially affect research pertaining to mortality.[5,39,104–106] A study by Claridge, *et al* using National Death Index data for six years linked to a Level I trauma center dataset identified a mortality rate of 3.6% within 30 days of discharge, 4.1% within 3 months of discharge, and 5.2% within 1 year of discharge, contrasted to an in-hospital mortality rate of 3.3%.[40] A study of Washington trauma patients performed by Davidson, *et al* identified a mortality rate of 10% within the first year of discharge.[37] Although some research efforts focused on addressing long-term survival, minimal attention has been placed on redefining trauma quality to reflect changes in health status following discharge.

Dissertation Objectives

Three separate studies were performed as part of a large over-arching study on the interplay between chronic conditions and clinical outcomes in traumatically injured older adults. The first evaluated the association between prevalent chronic conditions on the traditional quality metrics of in-hospital mortality and hospital length of stay. The second study evaluated trauma-related factors and chronic conditions as predictors of mortality following discharge from a trauma center. For the third study, a chronic disease-based competing risk prognostic model for in-hospital mortality was developed. The performance of our developed model was compared to the previously described Charlson and Elixhauser metrics as well as a selection of trauma-specific metrics.

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CHAPTER 2.

Association of chronic conditions on hospital length of stay and in-hospital mortality among older adults admitted to a trauma center

ABSTRACT

BACKGROUND. The proportion of older patients admitted to trauma centers is increasing. The prevalence of chronic conditions among injured populations has also shown a marked increase with time. Older patients have been shown to suffer poorer outcomes despite lower injury severity, which are representative of reduced physiologic reserve, complications due to disease, and stress from their injury. While prevalent chronic conditions are considered a risk factor among older trauma populations, minimal research has been performed on this topic. The purpose of this study was to evaluate an array of prevalent chronic conditions on two clinical outcomes: hospital length of stay (HLOS), and in-hospital mortality.

METHODS. Blunt-injured trauma patients at a single trauma center who were age 55 or older were included in the study. Demographic and injury variables were evaluated across three outcome categories of discharge to home, discharge to a care facility (skilled nursing facility, long-term acute care, hospice, or rehab), or in-hospital death. Probability of survival due to injury was measured with the Trauma Mortality Prediction Model (TMPM). Twenty-nine prevalent chronic conditions in the domains of cardiac, psychiatric, hematologic, neurological, substance abuse, pulmonary, diabetes mellitus, and a selection of 19 conditions from the Elixhauser comorbidity measure, were analyzed for their association with in-hospital mortality. A violation of the proportional hazards assumption was identified for TMPM probability of death, and models were stratified by a 50% mortality probability cut point. Adjusted competing risk proportional hazards models were used to assess the effect of each condition on in-hospital mortality with discharge to a care facility as a competing event. Linear mixed models were used to evaluate chronic conditions on HLOS.

RESULTS. The primary analysis included 4653 patients admitted between January 1, 2006 and December 31, 2012. Patients who died in-hospital were similar to those who were discharged to a care facility regarding admission year, number of total trauma admissions, age,

ethnicity, admission systolic blood pressure, and HLOS. Patients who died were more likely to be male, have a fall-type injury, have higher injury severity scores, and longer cumulative ICU times. The most prevalent chronic conditions were hypertension (614.9 per 1000 trauma patients) cardiac arrhythmia (277.2 per 1000), coronary artery disease (259.6 per 1000), Type 2 diabetes (257.2 per 1000), and drug abuse (208.1 per 1000). In patients with a high probability of survival, competing risks models identified history of cardiac surgery, coronary artery disease, congestive heart failure, myocardial infarction, hemophilia, coagulopathy, fluid/electrolyte disorders, liver disease, and peripheral vascular disorders to be significantly associated with in-hospital mortality. Only four Elixhauser comorbidities were related to mortality in this analysis. Linear models found that 32 of 40 conditions were associated with HLOS.

CONCLUSION. For older trauma populations, more attention must be placed on the management of chronic conditions. Trauma patients may benefit from having a geriatric medicine consultation before discharge. To better estimate mortality risk, discharge to a care facility appears as a valid competing event to in-hospital mortality. Pre-packaged comorbidity metrics that were not developed for trauma populations may have reduced validity when applied to injured older patients. The trauma triage criteria should be updated to include criteria reflecting the conditions that are associated with the highest amount of risk for death.

INTRODUCTION

Within the last decade, the trauma patient demographic has significantly changed to reflect an older and more diseased population.[1–3] Recent estimates show that there has been a dramatic increase in the proportion of older trauma patients, from 12.1% in 2000 to 24.6% in 2011.[1] Consequently, the causes of death among the injured have shifted from those related to injury (i.e. hemorrhage) to others being functions of advanced age.[1] These changes have added complexity to the delivery of care among trauma patients.[2–6] Older trauma patients have been shown to experience worse clinical outcomes likely due to reduced physiologic reserve.[7,8] Specifically, patients of advanced age and those with chronic conditions receive disproportionately more care with higher resource utilization and cost compared to non-chronically ill and younger populations.[6,9–11]

The effect of specific chronic conditions on clinical outcomes following trauma is not well understood, but presence of these conditions may impact decision-making. Understanding the role of chronic conditions in trauma is complicated by the severity of injury taking precedence. Traditionally, trauma care has focused on the stabilization of the patient, treatment of the injury, and options for rehabilitation. However, little work has been performed on the effects of comorbidity among injured patients towards long term recovery and high quality survival. The trauma literature tends to account for the burden of chronic conditions by using existing metrics such as the Elixhauser comorbidity measure and the Charlson Comorbidity Index, which weighs select chronic conditions based on perceived risk of death.[12,13] However, these and other metrics were originally developed using data from specific medical subpopulations and have high variability in the diseases measured, address different outcomes, and utilize derived relative weights based on varying statistical methodology. In addition, these metrics were not designed, nor validated, for a traumatically injured population.[14–16]

Traditional markers of quality in trauma research include hospital length of stay and in-hospital mortality. However, little research has been performed to assess the relationship between specific chronic conditions and these outcomes in older trauma populations.[2,17,18] Hospital length of stay is associated with increased complications, higher resource utilization, and overall more complex cases.[19,20] Regarding mortality, previous research has shown a reduction in mortality due to acute hemorrhage and a proportionate increase in death pertaining to complications of chronic conditions.[1] Conversely, patients who survive to discharge are seldom evaluated again by the same trauma service. Studies have identified that patients discharged from trauma centers are still at a high risk for death.[21–24] A recent study identified discharge to hospice as an event masking the observation of an in-hospital death which current mortality reporting does not take into account.[25] Such an event may be considered a competing risk, defined as an event that prevents the observation of the event of interest or modifies the chance that the event occurs.[26] Moreover, the measures of hospital performance derived from in-hospital mortality may be inaccurate as patients discharged prior to death are not counted in the trauma mortality census.

The objective of this study was to identify chronic condition predictors of in-hospital mortality using survival analysis with discharge to a care facility as a competing event among older trauma patients. In addition, chronic disease predictors were evaluated for their association to longer hospital lengths of stay (HLOS) after accounting for relevant factors.

METHODS

Data Sources

Retrospective cohort study design methodology was used and draws data from two primary sources. The Scripps Mercy Hospital trauma registry was used to identify all unique blunt-injured trauma patients admitted between January 1st, 2006 and December 31st, 2012. All patients were age 55 years or older at the date and time of admission. Specific exclusion of patients was performed among those who were discharged or died within 6 hours after admission. The index admission was the most recent trauma visit, for which basic demographics, injury characteristics, clinical and laboratory values, treatments, procedures, discharge status and location, transfers, in-hospital mortality, intensive care unit (ICU) length of stay, HLOS, complications, and diagnoses were extracted from the trauma registry. Among patients who died, the electronic medical records and county medical audit logs were reviewed to identify the presence of withdrawal of care, defined as withholding cardiopulmonary resuscitation protocols, withdrawal of medications, ceasing medical procedures such as laboratory or other testing, mechanical ventilation, and all other measures not related to patient comfort. Withdrawal of care determination, including the processing of do-not-resuscitate orders, limitations to care, organ harvest, and palliative care services is documented elsewhere.[2] For all trauma patients, the corporate Enterprise Data Warehouse (EDW; via IBM Cognos Connection v. 10.2) was queried for the following data used for billing: The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure and diagnosis codes, diagnosis-related group, major diagnostic category, health insurance, and readmission.

Chronic Condition Extraction and Definitions

Prevalent chronic conditions were identified using extracted alphanumeric comorbidity codes from the trauma registry (Digital Innovations, Inc. “Trauma Collector” software) and ICD-9-CM codes from the EDW. In the trauma registry, patients were coded as having a chronic

condition based on trauma physician diagnosis, notification by the primary care physician, or medication use indicating illness. Metabolic panels were performed on all patients and used to identify liver, kidney, heart, or muscle conditions. Blood tests were used to test coagulation time, blood sugar levels, and anemia. Respective ICD-9-CM codes for each chronic condition under study were scanned and coded as being present or absent. Registry data were entered by a trained and certified trauma nurse registrar, after abstraction from patient medical charts. Patients were characterized as having a chronic condition if they held a respective code from either source.

Twenty-one (21) chronic conditions obtained from the trauma registry included: Cardiac conditions (history of cardiac surgery, coronary artery disease, congestive heart failure, hypertension, and myocardial infarction), history of a psychiatric disorder, hematologic disorders (conditions requiring warfarin therapy, hemophilia, and pre-existing anemia), neurological conditions (spinal cord injury, Alzheimer's disease, history of seizures and epilepsy, chronic dementia, Parkinson's disease, and cerebrovascular accidents), substance abuse disorders (chronic ongoing drug abuse and chronic alcohol abuse), pulmonary disorders (asthma and chronic obstructive pulmonary disease), and diabetes mellitus (type 1 and type 2). Also assessed were 19 conditions found in the Elixhauser comorbidity measure: cardiac arrhythmia, valvular disease, pulmonary circulation disorder, peripheral vascular disorders, paralysis, neurodegenerative disorders, chronic pulmonary diseases, hyperthyroidism, renal failure, liver disease, lymphoma, metastatic cancer, solid tumor without metastasis, coagulopathy, obesity, weight loss, fluid and electrolyte disorders, deficiency anemia, and depression. The following conditions were excluded due to low prevalence: pulmonary heart disease, attention deficit disorder, intellectual disability, multiple sclerosis, chronic demyelinating disease, organic brain syndrome, prior history of pulmonary disease, peptic ulcer disease, and HIV/AIDS. Among patients with multiple trauma admissions, only characteristics from the most recent visit were used. However, prevalent chronic conditions captured during previous visits were carried forward to the most recent admission.

The primary outcomes were in-hospital mortality and HLOS in hours. Discharge location was categorized as either discharges to home (with or without assistance) or to any care facility (skilled nursing facility [SNF], hospice, long-term acute care facility, behavioral health unit, or rehabilitation facility). Patients who left against medical advice were classified as being discharged to home. The Trauma Mortality Prediction Model (TMPM) probability of death value by Osler, *et al* [27] was used to evaluate and account for injury severity. Probability of survival is calculated as the arithmetic difference between 100% and the TMPM probability of death. This model has been repeatedly validated for use in other trauma centers and has been shown to be superior to other methods of measuring injury burden.[28,29]

Statistical Analysis

Basic distributional differences in injury-related factors and chronic condition prevalence by the three outcome categories were identified using the chi-square test for categorical variables, ANOVA for means of continuous variables, and Kruskal-Wallis test for medians of continuous variables. Pairwise distributional differences between discharge to a care facility and in-hospital death were performed with the chi-square test, t-test for means, and rank-sum test for medians. Age- and gender-adjusted prevalence of chronic conditions was performed using logistic regression. Age and gender were used for adjustment due to distributional differences in prevalence by these two variables.

To evaluate chronic disease predictors of in-hospital mortality, Cox proportional hazards models were constructed. All models were adjusted for patient age at admission and TMPM probability of survival. Gender was removed from modeling steps due to its lack of statistical significance with the outcome and did not affect the associations between chronic conditions and mortality. Competing risks proportional hazards regression was used to evaluate the effect of specific chronic diseases with in-hospital mortality using the Fine and Gray extension of the Cox proportional hazards model.[30] Competing risks regression considers the sub-hazard distribution

(also known as a cause-specific hazard) for the competing event to produce a sub-hazard ratio (sHR), which is the ratio of the hazard of failing from the primary outcome of interest instead of the competing event. Specifically, the sub-hazard ratio is the ratio of the hazards comparing the cumulative incidence functions for presence versus the absence of a chronic condition. For these models, the competing event was discharge to a care facility. Due to a violation of the proportional hazards assumption by the TMPM probability of death variable, models were stratified by probability of death at a 50% cutoff. The 50% mortality probability cutoff was selected to explore the relationship between chronic conditions in two distinct groups of patients: those with a high expected mortality and those with a low expected mortality. Statistically significant chronic conditions were based on a p-value < 0.050. Differences in Fine and Gray model estimates for each chronic condition that differ by ± 10% from the standard Cox were considered significant, meaning that the magnitude of risk was significantly changed after accounting for discharge to a care facility as a competing event to mortality.

Hospital length of stay was log transformed due to evidence of skew and kurtosis. To evaluate chronic disease predictors of longer HLOS, mixed-effects linear regression modeling was employed with fixed effects being patient age, log-transformed TMPM value, admission verbal Glasgow Coma Scale (GCS) score, and admission systolic blood pressure. These variables were selected based on having a statistically significant bivariate relationship with HLOS. Admission year was included as a random effect due to significant variations among covariates and hospital length of stay by calendar year. Statistically significant chronic conditions were based on a p-value < 0.050. All data were managed and analyzed using Stata/SE v. 12.0 (StataCorp LLC, College Station, TX).

RESULTS

In total, 17589 admissions were recorded during the study period. Of these, 5444 (30.9%) were among patients aged 55 years and older at admission. Nearly all (98.0%) admissions were classified as a blunt mechanism of injury. After removing duplicate patients, there were 4964 unique patients. Among unique patients, 311 were excluded due to having a hospital length of stay less than six hours. Analyses focus on the remaining 4653 unique patients.

The Kaplan-Meier curves for patients stratified by their TMPM probability of death at a 50% cutoff are shown in Figure 2.1. Rapid divergence of the curves occurred immediately after the 6-hour minimum HLOS required for inclusion. At any point in time, patients with low expected mortality due to their injury (TMPM Probability of Death < 50%) experienced greater survival compared to those in the high expected mortality stratum (TMPM Probability of Death ≥ 50%). Among patients with a high probability of death, in-hospital mortality plateaued after approximately 360 hours (15 days) after which 75% of the patients had expired. Patients in the low probability of death stratum experienced high rates of mortality up to approximately 720 hours (30 days), at which approximately 28% had expired by at time.

The characteristics of the study population are shown in Table 2.1. Between 2006 and 2012, there was a steady increase in the number of elderly trauma patients each year. During the study period, 276 (5.9%) patients had more than one trauma admission and 4358 (93.7%) had at least one chronic condition. Over 50% of patients were discharged within 72 hours from admission. The population as a whole was predominantly white (76.8%), insured (94.5%), and had over 50% probability of survival due to trauma by the TMPM score (98.0%). Regarding outcomes, 176 (3.8%) died in-hospital, 3009 (64.7%) were discharged home, 1418 (30.5%) were sent to a care facility, and 50 (1.1%) left the hospital against medical advice. Among those who died, 92.6% received a form of withdrawal of care.

Table 2.2 is a display of patient characteristics and hospital variables by outcome category. The median time in hours to each outcome were 38.5 (IQR: 20.7-73.3) for patients discharged home, 88.8 (IQR: 50.3-153.3) for those sent to a care facility, and 81.1 (IQR: 30.1-189.2) for in-hospital deaths. Pairwise analysis comparing those discharged to a care facility versus in-hospital deaths identified higher proportions of male gender, uninsured status, severe injury severity, higher TMPM probability of death, and longer total ICU length of stay among patients who died. Between the primary and competing outcomes, patients were largely similar with regard to age at admission, ethnicity, admission systolic blood pressure, and hospital length of stay.

Age- and gender-adjusted disease prevalence by outcome category are shown in Table 2.3. The most prevalent chronic condition was hypertension (614.9 per 1000 trauma patients) followed by cardiac arrhythmia (278.5 per 1000), coronary artery disease (260.3 per 1000), Type 2 diabetes (257.3 per 1000), and drug abuse (206.5 per 1000). Regarding cardiac conditions, patients who died in-hospital were more likely to have a history of cardiac surgery, coronary artery disease, congestive heart failure, and myocardial infarction compared to the other two groups. Among neurological conditions, in-hospital deaths were more likely to have had spinal cord injury, Alzheimer's disease, and history of cerebrovascular accidents. Other conditions exhibiting higher prevalence among those who died in-hospital include hemophilia and type 1 diabetes. Patients who died in-hospital had the lowest prevalence for both chronic drug and chronic alcohol abuse. For Elixhauser comorbidities, deaths were more likely to have had cardiac arrhythmias, pulmonary circulation disorders, paralysis, neurodegenerative disorders, chronic pulmonary conditions, renal failure, liver disease, metastatic cancer, coagulopathy, obesity, excessive weight loss, and fluid & electrolyte disorders.

In-hospital Mortality

Results for the adjusted and stratified Cox proportional hazards models and Fine & Gray models are shown in Table 2.4. The prevalence of deficiency anemia was insufficient for analysis in the high probability of survival group. Among patients with greater than 50% probability of survival, cardiac conditions (history of cardiac surgery, coronary artery disease, congestive heart failure, and myocardial infarction) were found to be statistically significantly related to mortality in both the Cox and Fine & Gray regression models. Hemophilia, coagulopathy, fluid & electrolyte disorders, liver disease, and peripheral vascular disorders were also significantly related. In this subgroup, COPD was the only condition that was not significantly related in Cox models, but became related in the analysis of competing events. Of all related conditions, risk estimates for congestive heart failure, MI, hemophilia, coagulopathy, fluid & electrolyte disorders, and peripheral vascular disorders were all significantly changed between Cox and Fine & Gray models. Conditions with the highest risk for death were liver disease, coagulopathy, hemophilia, and congestive heart failure with sub-hazard ratios exceeding 2.5. A full listing of results of this analysis are shown in Appendix 3.

Among patients with less than 50% probability of survival, only hypertension, Parkinson's disease, and depression were statistically significantly related to mortality in the standard Cox regression (Table 2.4). However, in the Fine & Gray competing risks regression, coronary artery disease, hypertension, Parkinson's disease, hemophilia, depression, asthma, deficiency anemia, lymphoma, pulmonary circulation disorders, solid tumor without metastasis, and weight loss were all statistically significantly related to mortality. Of these conditions, all were positive risk factors with the exception of hemophilia and pulmonary circulation disorders, which were significantly protective in the competing risks models. The risk for death was the highest for Parkinson's disease, weight loss, and depression. Among patients who died in this group, all but one received withdrawal of life sustaining treatments (data not shown). A full listing of results from this analysis are shown in Appendix 4.

Hospital Length of Stay

Hospital length of stay was significantly associated with 32 of the 40 chronic conditions tested before stratification by outcome (Table 2.5). Among patients discharged home, 26 conditions studied were significantly related to longer lengths of stay. Specifically, many of the chronic conditions were metabolic, cardiac, or pulmonary conditions. Among psychiatric conditions, only history of psychiatric disorders, depression, and neurodegenerative disorders were related to longer HLOS. Paradoxically, warfarin therapy, chronic drug abuse, and chronic alcohol abuse were associated with shorter HLOS. Among those discharged to a care facility, longer lengths of stay were related to CHF, hemophilia, pre-existing anemia, chronic alcohol abuse, coagulopathy, fluid & electrolyte disorders, paralysis, pulmonary circulation disorders, valvular disease, and weight loss. Lower HLOS was related to Alzheimer's disease, seizures, chronic dementia, history of psychiatric disorders, and hyperthyroidism. Patients who died in-hospital were more likely to have longer HLOS if they had a history of psychiatric disorders, COPD, coagulopathy, hemophilia, or liver disease. Lower HLOS (or consequently, more rapid deaths) were highly related to peripheral vascular disorders only. The only conditions consistently associated with the longer HLOS before and after stratification were the clotting disorders of hemophilia and coagulopathy. Evidence of effect modification of length of stay by discharge location was identified in patients with a history of psychiatric disorders. Among survivors to home and in-hospital deaths, history of psychiatric disorders lengthened the HLOS of trauma patients by a factor of 0.175 and 0.474, respectively. Among those discharged to a care facility, patients with a history of psychiatric disorders were discharged more quickly by a factor of 0.109 than those without the condition. A full listing of the results from this analysis are shown in Appendix 5 for the full sample and Appendix 6 for the outcome-stratified analysis.

DISCUSSION

In this cohort of older traumatically injured patients, multiple comorbidities were significantly related to both clinical outcomes of in-hospital mortality and HLOS. Although injury severity remains the dominant predictor of in-hospital mortality, several chronic conditions were related to mortality even after stratification by injury-related survival probability. The overwhelming majority of traumatically injured elderly patients had a predicted probability of survival due to their injury greater than 50%. Thus, it is conceivable that in-hospital mortality in this subpopulation may be related to factors outside the classifiable realm of injury or injury severity. Among these patients, cardiac conditions and history of cardiac surgery, hemophilia, coagulopathy, renal dysfunction, peripheral vascular disorders, and liver disease were statistically significantly related to in-hospital mortality in both Cox proportional hazards model and competing risks models. Conversely, other chronic conditions such as Alzheimer's disease, dementia, Parkinson's disease, asthma, depression, anemia, psychiatric disorders, stroke, and substance abuse disorders that are traditionally considered detrimental were not significantly associated with mortality. In addition, the present study demonstrates that the chronic conditions that affect survival differ by the severity of injury. These results support the increasing concern regarding the growth of aging trauma population as well as warrant additional study on the management of chronic conditions following trauma service discharge. To our knowledge, the present study is the first to address the relationship between 40 chronic conditions and in-hospital mortality in a cohort of older American trauma patients. Additionally, this study is also the first to utilize competing risks regression to classify in-patient mortality risk following trauma.

From a prognostic standpoint, it may be obvious that chronic diseases are related to in-hospital mortality.[31] However, the underlying mechanism in the interplay between injury, aging, and specific chronic conditions as they ultimately contribute to mortality requires further study. The present study demonstrates that some conditions may be more detrimental than others, and

are worthy of more attention from a healthcare practitioner's perspective. Moreover, trauma researchers who use pre-packaged comorbidity metrics such as the Elixhauser comorbidity scale and the Charlson Comorbidity Index should interpret their results with caution as these metrics were developed for use in non-trauma populations and may not be completely valid for injured populations. This claim is evidenced by the results of the present study which found that 15 of the 19 comorbidities of the Elixhauser scale were not significantly associated with in-hospital mortality in the subgroup with over 50% probability of survival, and 14 of the 19 conditions were not related in the subgroup with under 50% probability of survival. Additional support comes from a National Study on Costs and Outcomes of Trauma (NSCOT) analysis which identified only liver disease, myocardial infarction, strokes, cardiac arrhythmia, dementia, and depression as being associated with in-hospital mortality, and their subsequent inclusion into multivariable models showed no difference in discrimination compared to the entire Charlson Comorbidity Index.[16] Future efforts should seek to reevaluate the diseases and relative weights applicable towards trauma patients.

Of the 40 conditions assessed, only ten were significantly related to in-hospital mortality among patients with a probability of survival of 50% or greater. These conditions reflect the gradual deterioration of organ function and advanced age complicated by the stress of injury and hospitalization.[32] In patients with less than 50% probability of survival, eight of ten conditions that were related to mortality differed from those found in the high survival subgroup analysis. Deficiency anemia, Parkinson's disease, asthma, depression, lymphoma, solid tumors without metastasis, and weight loss all had sub-hazard ratios exceeding 2.5, reflecting an extremely frail subpopulation, the futility of care, and a potential for withdrawal of life sustaining treatments. In this subgroup, pulmonary circulation disorders and hemophilia were found to be associated with lower mortality. However, these associations are likely an artifact of the data as only two patients

had pulmonary circulation disorders and only one had hemophilia in this subgroup. Crude analyses of these conditions did not yield statistically significant associations.

Cardiac conditions, hemophilia, coagulopathy, and fluid & electrolyte disorders were consistent predictors of both in-hospital mortality and longer hospital lengths of stay. Results from the present study are in accord with a study by Ferraris, *et al* who identified congestive heart failure and beta blocker usage as primary risk factors for in-hospital mortality in a cohort of traumatically injured patients aged 20 years and older.[33] Similarly, Hong, *et al* identified patients with coagulopathy and fluid & electrolyte disorders as two of the highest related conditions to mortality in a Korean trauma population.[34] On HLOS, the present study and that of Hong, *et al* similarly identified paralysis and depression as being related to longer lengths of stay.

In contrast to the present study, Hong, *et al* also identified metastatic cancer and pulmonary circulation disorder as being heavily related to mortality, which the present study did not find. It should be noted that pulmonary circulation disorder was highly related to longer hospital lengths of stay in both the discharged to care and survivors to home outcome groups. Alzheimer's disease was not related to longer lengths of stay in the present study, but were among the highest contributors in the Korean study. These discrepancies may be attributed to the latter study's sample population, which included patients aged 18 to 55 who are less likely to have a prevalent chronic condition. Previous studies have also identified obesity as a risk factor for both mortality and morbidity following trauma,[35,36] which was not found in the present study. However, this difference may be due to differences in measurement as the present study utilized ICD-9-CM codes based on BMI at a cutpoint of 30 for obesity, Glance, *et al* used weight percentiles, and Ditillo, *et al* used BMI at a cutpoint of 40.

The San Diego trauma triage protocol was designed to identify patients in need of advanced trauma care. The existing criteria states that, independent of mechanism and severity of injury, injured patients aged ≥ 55 years old, on antithrombotic agents, on dialysis with renal

disease, with prevalent cardiac or respiratory disease, with bleeding disorders, or having evidence of any level of loss of consciousness are to be classified as trauma and transported to trauma centers.[37] A final general criterion is the "when in doubt, transport to trauma center" due to the lack of specialized trauma training among EMS providers. Although not statistically significant, the conditions of hypertension, dementia, Parkinson's disease, depression, lymphoma, and weight loss had protective hazards ratios in the group with high probability of survival. As a result, there may be over-triage among patients due to these conditions. Moreover, patients who were discharged home experienced lower HLOS compared to those who died or who were discharged elsewhere. These results reflect the growing majority of older, minimally injured trauma populations sent to a trauma service, require minimal care for their injuries, and are subsequently discharged. This difference in HLOS by discharge type also supports our use of survival analysis over other statistical methodologies that do not account for differences in surveillance time.

Regarding hospital length of stay, nearly every chronic condition studied was statistically significantly related in at least one strata. Long HLOS has been associated with increased incidence of complications, higher costs, and overall more complex cases, and therefore, chronic conditions are expected to be related to longer HLOS values. However, eight conditions actually resulted in shorter HLOS values in varying degrees. Among survivors to home, warfarin therapy, drug abuse, and alcohol abuse were negatively associated with HLOS. This represents the triage criteria and local admission practices of intoxicated patients to the trauma center which are consistent with minimally injured populations. These patients, once stabilized, are likely to be discharged without consequence. This trend is similar for patients with Alzheimer's disease, history of seizures, and chronic dementia, except they are discharged to a care facility relatively quickly for observation there. Particularly alarming is the -0.721 beta coefficient for peripheral vascular disorder among in-hospital deaths. Peripheral vascular disorders appear to result in rapid death following admission which also significantly presented itself in mortality analyses in

patients with a high probability of survival. Moreover, severe peripheral vascular disorder may be linked to palliative care and futility in older trauma populations.

The present study utilized the TMPM probability of death metric to classify severity of injury, which has been demonstrated as superior to other methods for classifying severity of injury.[28,29] While the TMPM metric has been validated in pediatric and general trauma populations,[28,38] the present study found that 64.2% of all deaths had a TMPM probability of death greater than 50%, surpassing the prediction, whereas only 2.5% of those with less than a 50% probability of death actually died. In our older trauma patient cohort, the discordance in the survivorship among those with over 50% probability of death, and mortality among those with less than a 50% probability of death may be evidence of reduced validity of the TMPM metric for older populations. While survival of severely injured trauma patients may be attributable to exceptional trauma care, deaths among those with low injury severity may potentially be explained by risk due to chronic conditions. The present study looks to provide a foundation for the development of future mortality risk prediction within a traumatically injured older population.

Results from the present study are particularly useful for healthcare practitioners at SNF, hospice, acute care, or rehabilitation centers, who regularly work with morbid patient populations following traumatic injury. In this population of patients with a high probability of survival due to traumatic injury, cardiac conditions were the predominant predictors of in-hospital mortality. In addition, patients discharged to a care facility with a chronic condition may require additional attention in the management of their chronic condition to improve recovery following injury. These results may also be used to help revise the trauma triage criteria to include specific chronic conditions as a basis for trauma center admission.

The present study contains several limitations that must be acknowledged. It has been noted that ICD-9-CM codes for identifying chronic conditions may underrepresent the actual

disease burden.[39] In addition, the present study was only able to analyze patients admitted to a single regional trauma center which may affect the generalizability of the results, and it is unknown if some patients were previously or subsequently admitted to other trauma centers for another traumatic events. Due to the nature of trauma, it is unknown if the incident traumatic event is a direct result of complications of the chronic condition. Patients with more severe injuries may not be capable of conveying their chronic condition status. We attempted to circumvent this issue by excluding all patients who expired or were discharged within the first 6 hours of admission. More importantly, the present study does not take into account the severity of the comorbidity, which may affect the risk for death in this population. Finally, there is a significant concern for type II statistical error due to an overall low in-hospital mortality rate. Conversely, in analyses among patients with less than 50% probability of survival subgroup, the reference group of "discharge to home" was the lowest in sample size. Substantially more chronic conditions were related to hospital length of stay compared to mortality analysis, possibly due to reduced statistical power. Future studies should seek cooperation from multiple trauma centers to insure a sufficiently large sample size for a more valued assessment on in-hospital mortality.

Despite the limitations mentioned, results from the present study help clarify several aspects in the interplay between comorbidity and trauma. First, among older populations, more attention must be placed on the management of chronic conditions following stabilization of the injury for better prognoses. Trauma physicians may benefit from having a geriatric medical consult to provide specialized care based on the comorbidities present. Secondly, patients who are discharged to a care facility with chronic conditions are still at risk for death. Kozar, *et al* found that a large proportion of patients discharged to hospice remain at a high risk for death with comorbidity frequency being a significant predictor, and that trauma quality metrics based on in-hospital mortality may over-estimate performance.[25] Third, the present study used discharge to any care facility as a competing event to in-hospital mortality. The use of competing risks

survival analysis is novel in trauma research and applicable given the risk of post-discharge mortality in older and fragile trauma populations. Fourth, previous research has suggested the development of guidelines for the withdrawal of life sustaining treatments.[2] The chronic conditions identified in this study may provide a foundation for the development of these guidelines. Moreover, certain conditions found to be associated with poor outcomes in the present study are not included in the current metrics to classify risk. These results may be used to contextualize trauma patients beyond just their injuries for both research and healthcare. Finally, many trauma services do not evaluate patients' health status at discharge. Measures of functional status at discharge has been shown to be useful at predicting post-discharge outcomes in other clinical populations.[40] Efforts should be made in trauma centers to develop and implement a measure of functional status at discharge for both quality measurement and to provide context for recovery.

In conclusion, the adverse consequences of chronic conditions coupled with traumatic injury pose a clinical challenge in the care of older patients. Follow-up studies to the present study will evaluate the effect of chronic conditions and trauma on post-discharge mortality, as well as combinations of chronic conditions as they relate to death. In addition, it is expected that a trauma-specific chronic disease metric will be developed to accurately classify risk for death based on injury severity and chronic disease prevalence in an older traumatically injured population. Given the growing older trauma populations and increases in chronic conditions over time, more attention must be placed on identification of the most significant risk factors for this population to better tailor treatment paths to improve probability of recovery.

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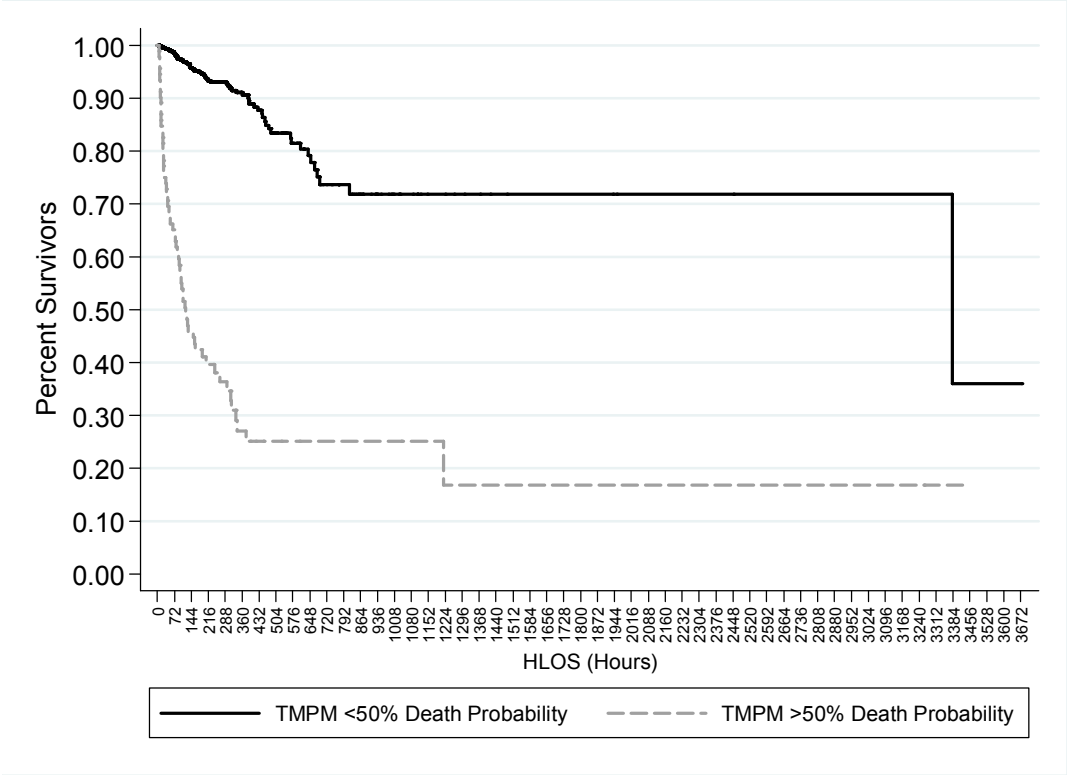

Figure 2.1. Kaplan-Meier Survival Curves for Older Trauma Patients by TMPM Probability of Death Categories

HLOS, Hospital Length of Stay; TMPM, Trauma Mortality Prediction Model

Table 2.1. Patient Characteristics: San Diego, CA 2006-2012

Variable	**n (%)**
Sample Size	4653
Trauma Admission Year	
2006	484 (10.4)
2007	543 (11.7)
2008	639 (13.7)
2009	669 (14.4)
2010	738 (15.9)
2011	732 (15.7)
2012	848 (18.2)
Trauma Admission Count	
1	4377 (94.1)
≥2	276 (5.9)
Age, years	
55-64	1405 (30.2)
65-74	1022 (22.0)
75-84	1214 (26.1)
≥85	1012 (21.8)
Gender	
Male	2196 (47.2)
Female	2456 (52.8)
Ethnicity	
White	3575 (76.8)
Black	324 (7.0)
Asian/Pacific Islander	256 (5.5)
Native American/Hawaiian	162 (3.5)
Other	336 (7.2)
Insurance Status	
Commercial	2063 (44.3)
Medicare	2038 (43.8)
Government	297 (6.4)
None	255 (5.5)
Comorbidity Prevalence	
None	295 (6.3)
One or More	4358 (93.7)
HLOS, hours	
6-23	1169 (25.1)
24-71	1723 (37.0)
72-168	1201 (25.8)
≥169	560 (12.0)
Discharge Location	
Home	3009 (64.7)
SNF/Hospice	992 (21.3)
Other Care Facility	426 (9.2)
Left Against Medical Advice	50 (1.1)
Death	176 (3.8)
Withdrawal of Life Sustaining Treatments among deaths	163 (92.6)
TMPM Probability of Death	
< 50%	4561 (98.0)
≥ 50%	92 (2.0)

HLOS, Hospital length of stay; TMPM, Trauma Mortality Prediction Model; SNF, Skilled Nursing Facility

Table 2.2. Patient Characteristics by Outcome Category: San Diego, CA 2006-2012

	Discharged Home	Discharged to Care Facility	Deaths	p-value*	Pairwise p†
Sample Size	3059	1418	176		
Trauma Admission Year, %					
2006	10.0	11.1	11.4	0.033	0.474
2007	10.9	12.8	16.5		
2008	13.2	14.5	17.1		
2009	14.2	14.9	14.2		
2010	16.1	15.6	14.2		
2011	16.4	14.3	15.3		
2012	19.3	16.9	11.4		
Trauma Admission Count, %					
1	94.6	92.6	96.6	0.057	0.143
2	4.6	6.4	2.8		
≥3	0.8	1.0	0.6		
Age in years, mean (sd)	71.5 (11.7)	78.2 (10.9)	77.8 (11.2)	< 0.001	0.608
Male Gender, %	55.5	45.9	61.4	< 0.001	< 0.001
Ethnicity, %					
White	75.5	79.9	75.6	0.028	0.217
Black	7.5	6.0	5.1		
Asian/Pacific Islander	5.9	4.5	7.4		
Native American/Hawaiian	3.9	2.5	4.6		
Other	7.3	7.1	7.4		
Insurance Status, %					
Commercial	44.6	45.1	34.1	< 0.001	< 0.001
Medicare	40.2	50.4	52.3		
Government	7.3	3.8	11.4		
None	7.9	0.7	2.3		
Systolic Blood Pressure, mean (sd)	147.7 (27.6)	147.5 (30.4)	147.2 (40.3)	0.938	0.939
Injury Type, %					
Fall	65.1	78.7	83.0	< 0.001	0.023
Motor Vehicle Accident	24.3	16.1	9.1		
Assault	4.6	2.1	1.7		
Cycling-related	1.7	0.6	1.1		
Pedestrian	0.4	0.4	0.0		
Other	4.1	2.1	5.1		
ISS Categories, %					
Minimal 1-8	66.2	41.6	17.1	< 0.001	< 0.001
Mild 9-14	18.9	26.3	10.8		
Moderate 16-24	11.4	21.2	13.1		
Severe 25-75	3.6	10.9	59.1		
TMPM Probability of Death, gmean (sd)	0.01 (6.23)	0.01 (6.13)	0.12 (8.85)	< 0.001	< 0.001
TMPM Probability of Death < 50%, %	99.8	98.3	64.2	< 0.001	< 0.001
ICU Stay in days, %					
0	81.0	59.7	21.6	< 0.001	< 0.001
1-2	15.8	24.2	36.9		
3-7	2.2	8.2	23.9		
≥7	1.1	7.9	17.6		
HLOS in hours, median	38.5	88.8	81.1	< 0.001	0.358

* denotes the resultant p-value for difference from the chi-square test for categorical variables, ANOVA for means of continuous variables, or Kruskal-Wallis test for medians of continuous variables across the outcome categories.

† denotes the p-value for difference resulting from the pairwise test of covariates by the two outcomes of discharge to care facility versus in-hospital deaths. Tests performed were: chi-square test for categorical variables, t-tests for means of continuous variables, or Rank-Sum tests for medians of continuous variables.

HLOS, Hospital length of stay; ICU, Intensive Care Unit; ISS, Injury Severity Score; SNF, Skilled Nursing Facility; TMPM, Trauma Mortality Prediction Model

Table 2.3. Age- and Gender-adjusted Chronic Disease Prevalence (per 1000) by Discharge Outcome: San Diego, CA 2006-2012

	Unadjusted Full Sample	To Home	To Care Facility	Deaths	p-value*
Sample Size	**4653**	**3059**	**1418**	**176**	
Cardiac Disorder					
Hypertension	615	616	635	639	0.479
Coronary Artery Disease	260	240	248	404	< 0.001
Congestive Heart Failure	133	91	159	248	< 0.001
Myocardial Infarction	82	73	88	162	< 0.001
History of Cardiac Surgery	74	66	60	128	0.003
Psychiatric Disorders					
Past History	197	158	269	168	< 0.001
Hematologic Disorders					
Warfarin Therapy	204	183	197	197	0.535
Pre-existing Anemia	96	72	138	124	< 0.001
Hemophilia	10	4	16	62	< 0.001
Neurological					
Cerebrovascular Accident	115	93	129	162	< 0.001
Chronic Dementia	98	45	90	49	< 0.001
Seizures	51	40	60	60	0.019
Alzheimer's Disease	45	23	39	44	< 0.001
Parkinson's Disease	19	13	21	12	0.089
Spinal Cord Injury	5	2	10	10	< 0.001
Chronic Substance Abuse					
Drug	207	174	125	92	< 0.001
Alcohol	137	99	69	61	0.001
Pulmonary Disease					
COPD	99	35	51	63	0.020
Asthma	39	41	30	41	0.164
Diabetes Mellitus					
Type 2	257	247	278	267	0.110
Type 1	39	32	50	60	0.007
Elixhauser Comorbidities					
Cardiac Arrythmia	279	236	287	293	0.001
Fluid and Electrolyte Disorders	149	109	209	331	< 0.001
Chronic Pulmonary Disease	113	104	128	139	0.043
Neurodegenerative disorders	104	69	160	271	< 0.001
Hyperthyroidism	101	82	95	60	0.111
Renal Failure	80	62	103	76	< 0.001
Depression	64	55	72	50	0.077
Valvular Disease	51	40	60	42	0.008
Peripheral Vascular Disorders	36	30	38	55	0.100
Liver Disease	33	18	33	78	< 0.001
Coagulopathy	28	17	41	115	< 0.001
Solid Tumor w/o Metastasis	23	19	23	35	0.253
Pulmonary Circulation Disorder	22	14	25	29	0.020
Obesity	18	13	23	6	0.027
Paralysis	17	6	36	51	< 0.001
Metastatic Cancer	13	9	20	31	0.002
Deficiency Anemia	10	8	12	5	0.407
Weight Loss	10	6	16	16	0.003
Lymphoma	6	5	8	10	0.431

* denotes the resultant p-value for any difference in disease prevalence across the outcome categories using the chi-square test.

COPD, Chronic Obstructive Pulmonary Disease

Table 2.4. Stratified Age- and TMPM-adjusted Results from Cox and Fine & Gray Models for Mortality by Select Chronic Conditions: San Diego, CA 2006-2012

	TMPM Probability of Death < 50% (N = 4561)			**TMPM Probability of Death >= 50% (N = 92)**		
	Cox	**Fine & Gray**		**Cox**	**Fine & Gray**	
Chronic Condition	**HR**	**sHR**	**95% CI**	**HR**	**sHR**	**95% CI**
Alzheimer's Disease	1.81	1.44	0.76-2.73	0.80	0.90	0.30-2.71
Asthma	1.34	1.46	0.60-3.54	2.77	2.78	1.69-4.55
Cerebrovascular Accident	1.53	1.44	0.89-2.34	1.11	1.20	0.68-2.13
Chronic Dementia	0.78	0.67	0.37-1.20	0.88	0.81	0.31-2.11
Coagulopathy	2.53*	3.05	1.68-5.56	0.64	0.68	0.32-1.43
Congestive Heart Failure	2.37*	2.80	1.89-4.15	0.611	0.60	0.27-1.33
COPD	1.43	1.69	1.04-2.73	0.73	0.80	0.38-1.68
Coronary Artery Disease	1.87*	1.98	1.35-2.92	1.611	1.75	1.06-2.89
Deficiency Anemia	-	-	-	2.79	2.66	1.77-3.99
Depression	0.62	0.70	0.29-1.70	3.92*	4.02	1.57-10.27
Fluid/Electrolyte Disorders	1.71*	2.09	1.42-3.07	0.84	0.83	0.48-1.43
Hemophilia	3.33*	5.76	2.98-11.11	0.40	0.44	0.29-0.67
History of Cardiac Surgery	2.25*	2.10	1.22-3.61	0.88	0.90	0.45-1.78
Hypertension	0.82	0.79	0.53-1.16	1.84*	1.85	1.09-3.12
Liver Disease	4.38*	4.43	2.25-8.72	1.07	1.07	0.47-2.45
Lymphoma	1.03	1.24	0.18-8.31	3.62	3.87	2.39-6.29
Myocardial Infarction	1.84*	2.10	1.26-3.48	0.89	0.91	0.40-2.06
Parkinson's Disease	0.71	0.49	0.07-3.52	5.38*	6.22	2.71-14.30
Peripheral Vascular Disorders	2.76*	2.18	1.07-4.43	0.94	0.84	0.13-5.28
Pulmonary Circ. Disorders	1.19	1.30	0.53-3.19	0.32	0.33	0.14-0.77
Solid Tumor w/o Metastasis	1.54	1.54	0.65-3.68	3.84	3.67	2.31-5.84
Warfarin Therapy	1.41	1.37	0.88-2.12	0.89	0.84	0.46-1.52
Weight Loss	0.55	0.98	0.25-3.83	3.37	4.04	2.07-7.86
Variables						
Discharge Category, %						
Home	67.0			5.4		
Care Facility	30.6			26.1		
In-Hospital Death	2.5			68.5		
Withdrawal of Care in those who died, %	89.4			98.4		
HLOS, median (IQR)	49.8 (23.8 – 97.8)			108.2 (32.6 – 258.4)		

* denotes statistical significance at $p \leq 0.05$

CI, Confidence Interval; COPD, Chronic Obstructive Pulmonary Disease; HR, Hazard Ratio; IQR, Interquartile Range; sHR, Subhazard Ratio; TMPM, Trauma Mortality Prediction Model

Table 2.5. Adjusted Estimates of Association from Linear Mixed Models for Log-transformed Hospital Length of Stay by Chronic Condition: San Diego, CA 2006-2012

	Discharged to Care			Survivors to Home			In-hospital Deaths		
Variable	**β**	**SE**	**P**	**β**	**SE**	**P**	**β**	**SE**	**P**
Alzheimer's Disease	-0.204	0.093	0.029	0.022	0.096	0.821	0.210	0.343	0.541
Asthma	0.099	0.137	0.475	0.217	0.079	0.006	0.265	0.447	0.553
CAD	0.089	0.053	0.096	0.116	0.038	0.002	0.046	0.179	0.796
Cardiac Arrythmia	0.058	0.051	0.255	0.085	0.040	0.032	-0.147	0.196	0.454
CHF	0.137	0.061	0.023	0.257	0.056	<0.001	0.177	0.213	0.405
Chronic Dementia	-0.199	0.067	0.003	0.025	0.070	0.724	0.560	0.301	0.062
Chronic Alcohol Abuse	0.267	0.093	0.004	-0.213	0.045	<0.001	0.663	0.354	0.061
Chronic Drug Abuse	-0.054	0.075	0.471	-0.153	0.039	<0.001	0.306	0.296	0.302
Chronic Pulmonary Conditions	0.030	0.070	0.669	0.184	0.052	<0.001	0.311	0.258	0.227
Coagulopathy	0.283	0.125	0.024	0.820	0.119	<0.001	0.673	0.283	0.017
COPD	0.108	0.070	0.122	0.212	0.059	<0.001	0.517	0.249	0.038
CVA	0.067	0.067	0.316	-0.001	0.055	0.990	0.024	0.227	0.915
Deficiency Anemia	0.288	0.211	0.171	0.529	0.178	0.003	0.180	1.161	0.877
Depression	-0.030	0.094	0.749	0.155	0.066	0.018	0.163	0.418	0.696
Fluid & Electrolyte Disorders	0.398	0.057	<0.001	0.530	0.050	<0.001	0.203	0.194	0.297
Hemophilia	0.509	0.200	0.011	0.890	0.240	<0.001	0.823	0.378	0.029
History of cardiac surgery	-0.107	0.091	0.239	0.150	0.063	0.017	-0.246	0.239	0.303
History of Psych. disorders	-0.109	0.054	0.042	0.175	0.044	<0.001	0.474	0.232	0.041
Hypertension	-0.027	0.052	0.602	0.081	0.033	0.015	0.094	0.192	0.622
Hyper-thyroidism	-0.152	0.072	0.033	0.022	0.056	0.700	-0.562	0.342	0.100
Liver Disease	-0.056	0.135	0.678	0.237	0.094	0.012	0.701	0.356	0.049
Lymphoma	0.132	0.258	0.608	0.672	0.217	0.002	-0.167	0.830	0.841
Metastatic Cancer	0.106	0.173	0.539	0.134	0.165	0.414	0.114	0.494	0.818
Myocardial Infarction	0.139	0.082	0.092	0.228	0.061	<0.001	-0.242	0.237	0.305
Neuro-degenerative Disorders	0.115	0.068	0.090	0.250	0.062	<0.001	0.177	0.197	0.370
Obesity	0.296	0.159	0.063	0.182	0.125	0.145	0.365	1.166	0.754
Paralysis	0.416	0.135	0.002	0.698	0.200	<0.001	-0.226	0.411	0.582
Peripheral Vascular Disorder	-0.084	0.115	0.464	0.113	0.092	0.220	-0.721	0.359	0.044
Pre-existing Anemia	0.289	0.067	<0.001	0.562	0.062	<0.001	0.262	0.267	0.326

Table 2.5. - Continued

	Discharged to Care			Survivors to Home			In-hospital Deaths		
Variable	**β**	**SE**	**P**	**β**	**SE**	**P**	**β**	**SE**	**P**
Pulmonary Circulation Disorders	0.446	0.131	0.001	0.895	0.133	<0.001	0.325	0.450	0.470
Renal Failure	0.003	0.074	0.971	0.399	0.066	<0.001	-0.109	0.309	0.724
Seizures	-0.262	0.106	0.013	0.126	0.075	0.091	-0.103	0.377	0.786
Spinal Cord Injury	0.221	0.249	0.374	0.963	0.354	0.007	1.585	0.825	0.055
Type 1 Diabetes	0.130	0.113	0.251	0.193	0.088	0.028	-0.193	0.379	0.610
Type 2 Diabetes	-0.064	0.053	0.233	0.086	0.037	0.019	0.046	0.201	0.818
Valvular Disease	0.216	0.090	0.016	0.150	0.081	0.065	-0.292	0.401	0.467
Warfarin Therapy	-0.099	0.056	0.081	-0.196	0.042	<0.001	-0.201	0.209	0.335
Weight Loss	0.508	0.179	0.005	0.610	0.211	0.004	0.640	0.677	0.344

Models were adjusted for: fixed effects; patient age, log-transformed TMPM value, admission verbal Glasgow Coma Scale score, and admission systolic blood pressure, and random effect; admission year.

CVA, Cerebrovascular Accident; COPD, Chronic Obstructive Pulmonary Disease; CAD, Coronary Artery Disease; CHF, Congestive Heart Failure

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CHAPTER 3.

The association of chronic conditions and mortality after discharge from a trauma center in older patients

ABSTRACT

BACKGROUND. Previous research on trauma patients who survive to discharge found that mortality after discharge remains high. The aging trauma population is a unique and growing demographic that requires scrutiny. It is also less understood how trauma and chronic conditions each contribute to post-discharge mortality among minimally injured older populations. The present study evaluates 47 chronic conditions and their impact on mortality among older adult trauma patients surviving to discharge from a Level I trauma center.

METHODS. Blunt-injured trauma patients admitted to a Level I trauma center between January 1, 2006 and December 31, 2012 aged 55 years and older who survived their trauma stay were examined. Patients were discharged to: home, skilled nursing facility or hospice (SNF/Hospice), other acute care facility including rehab, or left against medical advice. Hospital-level variables assessed include: Trauma Mortality Prediction Model (TMPM) probability of death, ICU and hospital length of stay (HLOS), Injury Severity Score (ISS), and Glasgow Coma Scale (GCS) score. Of the chronic conditions evaluated, 25 originated from comorbidity codes in the hospital trauma registry and 22 were from the Elixhauser Comorbidity Index, captured using ICD-9-CM codes. All-cause mortality following discharge was identified by linking patient records to four primary sources: the national Social Security Death Master File, the hospital administrative data warehouse, the local county death certificate registry, and the state Death Statistical Master File. Cox proportional hazards models were used to evaluate the relationship between trauma-related factors and chronic conditions on mortality up to 2 years post-discharge.

RESULTS. A total of 4442 patients survived to discharge. Probability of death as measured by the TMPM was low with a median of 1.2% in 2006 to 1.0% in 2012. Linear reductions were also seen in both ICU and HLOS. Record linkage methods identified 1344 post-discharge deaths ranging from day of discharge to 8.1 years after. Analyses focused on 2 year mortality, for which there were 938 patients. Patients discharged to SNF/Hospice or other care

facility showed severely worse survival within the first 30 days. All trauma-related variables violated the proportional hazards assumption as well as 13 chronic conditions. Variables related to early-term mortality after discharge include: TMPM probability of death, ISS, GCS score, HLOS, paralysis, neurodegenerative diseases, metastatic cancer, solid tumors, and fluid & electrolyte disorders. Late-term death was highly associated with Parkinson's disease, and pulmonary heart disease. Three cardiac conditions (history of cardiac surgery, coronary artery disease, and myocardial infarction), history of psychiatric disorders, three hematologic disorders (warfarin therapy, hemophilia, and pre-existing anemia), four neurological disorders (Alzheimer's disease, seizures, chronic dementia, and stroke), chronic obstructive pulmonary disease, and types 1 and 2 diabetes were associated with a constant risk for death within two years of discharge.

CONCLUSION. Older adult trauma patients admitted across seven years and who survived to discharge were still at significant risk for death. Patients discharged to a SNF/Hospice or other care facility were at a much greater risk for death within the first 30 days of discharge compared to those who went home. Mortality risk due to injury occurred in early time intervals but associations diminished with time. Conversely, chronic diseases were the predominant predictors of death later after discharge. A focus on the management of chronic diseases is necessary to improve survival after discharge following trauma.

INTRODUCTION

Research on adult trauma patients after discharge suggests that the mortality is high, and that those discharged to a care facility are at a greater risk for death than those who return home.[1,2] A study of all adult Washington trauma patients identified a mortality rate of 10% within the first year of discharge.[1] Another study on a Level I trauma center patient population over six years identified that the post-discharge mortality rate within 3 months of discharge exceeded that of the in-hospital mortality rate.[3] In addition, researchers found that a large proportion of patients discharged to hospice were at a high risk for death, and that trauma quality metrics based on in-hospital mortality may be insufficient for evaluating trauma center performance.[4] While relevant for classifying trauma populations and defining quality of care, post-discharge mortality is a relatively new frontier in trauma research.

The trauma demographic is aging.[5–9] In older populations, the risk of hospitalization for a traumatic injury increases with age, with the majority of risk occurring after the age of 70 years for all racial and ethnic subgroups.[10] Although these patients experience lower injury severity, they fare worse after trauma compared to younger populations.[11–13] Regarding post-injury survival, older trauma patients carry a substantial risk for death after discharge, likely due to reduced physiologic reserve in conjunction with chronic disease burden.[14]

Chronic diseases are important determinants of health status in trauma patients.[15] A strong understanding of the effect of comorbid conditions on clinical outcomes in trauma may reveal opportunities to improve the delivery of care and more rapidly identify patients at high risk for adverse events.[16] Past research has shown increases over time in the prevalence of chronic conditions among older traumatically injured populations, as well as an increased proportion of in-hospital mortality due to complications from chronic conditions over and above the sequelae of injury.[9,17] However, the role of specific chronic conditions on mortality following trauma center discharge is relatively unknown.

It is plausible that older trauma patients who survive to discharge ultimately die from complications pertaining to their chronic disease status. Previous research among older head-injured trauma patients shows that a large proportion survive the initial insult only to require extensive long-term management of their pre-existing conditions.[18,19] Recent efforts have been made to revise methods in caring for head-injured elderly populations to reflect care requirements imposed by their comorbidities.[8,19,20] Specifically, Kozar, *et al* identified that comorbidities were significantly related to hospice care, underscoring the importance of comorbidities in the care of minimally injured elderly patients.[4]

The present study assessed the relationship between chronic conditions and mortality following discharge from a Level I trauma center among older trauma patients. Objectives of the present study were to: 1) characterize post-discharge survival among these patients, 2) determine the relationship between injury and post-discharge survival, and 3) Determine the relationship between chronic conditions and post-discharge survival.

METHODS

Study population

Patients were eligible for this study if they were admitted to Scripps Mercy Hospital Level I trauma center between January 1, 2006 and December 31, 2012 with a blunt primary mechanism of injury. All eligible patients had a hospital length of stay (HLOS) greater than 6 hours, were aged 55 years and older at admission, and survived their trauma stay to discharge. Patients were excluded if their records lacked sufficient information for full name, date of birth, city of residence, or social security number to be matched to a post-discharge death record.

Variables

The exposures of interest were chronic conditions captured during the trauma admission. The present study evaluated 47 chronic conditions: 25 conditions collected by the hospital trauma registry, and 22 conditions from the Elixhauser Comorbidity Index. The conditions from the trauma registry and their clinical domains included: cardiac conditions (history of cardiac surgery, coronary artery disease, congestive heart failure, pulmonary heart disease, myocardial infarction, hypertension, and congenital cardiac disease), psychiatric conditions (history of a psychiatric disorder and attention deficit disorder), hematologic disorders (conditions requiring warfarin therapy, hemophilia, and pre-existing anemia), neurological conditions (spinal cord injury, multiple sclerosis, Alzheimer's disease, history of seizures and epilepsy, chronic dementia, Parkinson's disease, and cerebrovascular accidents), substance abuse disorders (chronic ongoing drug abuse and chronic alcohol abuse), pulmonary disorders (asthma and chronic obstructive pulmonary disease[COPD]), and diabetes mellitus (Type 1 and Type 2). Elixhauser comorbidities selected for evaluation included: cardiac arrhythmia, valvular disease, pulmonary circulation disorder, peripheral vascular disorders, chronic pulmonary diseases, hyperthyroidism, renal failure, peptic ulcer disease, HIV/AIDS, lymphoma, rheumatoid arthritis, coagulopathy, obesity, weight loss, depression, paralysis, other neurodegenerative diseases, liver disease, metastatic

cancer, solid tumors, fluid & electrolyte disorders, and psychoses. Comorbidity codes were extracted from the trauma registry (Digital Innovations, Inc. “Trauma Collector” software) and International Classification of Diseases, version 9, Clinical Modification (ICD-9-CM) codes from the hospital Enterprise Data Warehouse (EDW; via IBM Cognos Connection v. 10.2). The ICD-9-CM codes were scanned and patients were coded as being present or absent with each respective condition. Patients were characterized as positive for a chronic condition if they held a respective code from either source. Among patients with multiple trauma admissions, only demographic and injury characteristics from the most recent visit were used. However, prevalent chronic conditions captured during previous visits were carried forward to the most recent admission.

The primary outcome was all-cause mortality after trauma center discharge. Post-discharge mortality was identified using four primary sources: the National Social Security Death Master File (SSDMF), the hospital EDW, the County Office of Vital Records and Statistics death certificate registry, and the state Death Statistical Master File. Obituaries in local newspapers were also reviewed as an auxiliary source. The Social Security Death Master File was valid for deaths up to March 31, 2014 and was linked to patient records. Linkage to the EDW deaths for non-trauma admissions was valid up to October 20, 2014. For the state and county data, matched death records were valid up to December 31, 2012. Obituary entries were valid up to November 30, 2014. Overall, patients were censored if they did not experience an event by March 31, 2014.

Hospital-level factors that were evaluated as confounders include: age (in years) at admission, total Glasgow Coma Scale (GCS) score, the Trauma Mortality Prediction Model (TMPM) Anatomic Injury Severity-based probability of death score, Injury Severity Score (ISS), HLOS, intensive care unit (ICU) length of stay, and location of discharge. Patients who were not admitted to the ICU were coded as having zero ICU days. The Glasgow Coma Scale (GCS) score, is a composite score measuring neurological deficit based on three systems: eye reactivity, verbal

response, and motor skills,[21] and is regularly assessed at admission.[22–24] The TMPM probability of death calculation is a measure of injury severity which has been demonstrated as superior to other measures of injury burden.[25–27] The ISS is currently the *de facto* method of measuring injury severity calculated by taking the sum of the squares of the scores (rated on an ordinal scale of 1-6) of the three most severely injured body regions. Despite threats to its validity to current trauma populations, ISS is used in nearly every trauma center in the nation. For the purposes of multivariable modeling, skewed variables were log-transformed. Discharge locations were categorized as discharge to home (with or without assistance), skilled nursing facility or hospice service (SNF/Hospice), other care facility (acute care facility, behavioral health unit, or rehabilitation facility), or left against medical advice (AMA).

Statistical Analysis

Cuzick's nonparametric tests and Cochran-Armitage tests for trend were used to identify linear trends by calendar year for medians of continuous variables and ordinal categorical variables, and proportions of discrete categorical variables, respectively. For each hospital factor and chronic condition, the proportional hazards assumption was tested in bivariate fashion by comparing a full model containing the variable of interest as a time dependent covariate (interacting with log-time) to a reduced model without the time dependency using the likelihood ratio test. Statistically significant interactions with time were identified using a p-value cutoff of 0.100. Cox proportional hazards models were constructed to assess survivorship using the following timeframes: within the first 30 days of discharge, between 30.1 and 90.0 days of discharge, and between 90.1 and 730.5 days of discharge (approximately 3 months to 2 years). For variables that satisfied the proportional hazards assumption, age-adjusted hazard ratios were calculated for 2-year cumulative post-discharge mortality. Post-discharge mortality was evaluated up to two years due to the potential for significant differences in long-term follow-up time among patients discharged in the later years.

For all Cox proportional hazards models, the magnitude, association, and statistical significance of the chronic disease status variables were assessed using hazard ratios and their respective 95% confidence intervals. Intervals that did not contain 1.0 were considered statistically significant. All data were managed and analyzed using Stata/SE v. 12.0 (StataCorp LLC, College Station, TX).

RESULTS

Among 4751 patients surviving to discharge, 45 (1.0%) were excluded due to insufficient information to perform a record linkage with post-discharge mortality data sources. Of the remainder, 264 (5.6%) patients were excluded for a hospital length of stay less than six hours. After all exclusions, 4442 patients were eligible for analysis. Record linkage methods, in total, identified 1344 post-discharge deaths ranging from the same day of discharge to 8.1 years after. The majority of matches (78.7%) were found via the SSDMF; 7.0% were matched via the EDW; 14.3% were matched from a combination of state and county data sources.

Table 3.1 displays the descriptive statistics for select demographic and injury-related characteristics of the eligible study population. The mean (SD) age of the population at admission was 73.7 (11.9) years and 52.4% were male. Most patients (94.9%) had health insurance and were unmarried (61.6%). Among these patients, the median (IQR) trauma length of stay was slightly over two days at 49.6 hours (23.9 – 97.6). Falls (69.5%) were the dominant mechanism of injury, and the median (IQR) TMPM probability of death was 1.0% (0.4% - 2.2%). The majority of patients were discharged home (67.1%), followed by SNF/Hospice (22.3%), and other care facility (9.6%).

Table 3.2 is a display of clinical endpoints by calendar year of hospital admission. The number of unique older trauma patients meeting eligibility criteria steadily increased from 461 (456 with only one visit) in 2006 to 821 (739 with only one visit) in 2012. Patient age at admission increased over the study period from a mean of 72.0 years in 2006 to 74.6 in 2012. Likewise, linear increases in discharge to home and reductions in discharge to another care facility were identified, while the rates of discharge to SNF/Hospice and AMA remained relatively similar year to year. Two-year post-discharge cumulative mortality fluctuated by admission year, with a high of 27.0% in 2009 and a low of 11.1% in 2012. Regarding hospital-level characteristics of injury and treatment, trend-based reductions in median HLOS (67.4 hours

in 2006 to 46.7 hours in 2012), TMPM probability of death (1.2% in 2006 to 1.0% in 2012), and total ICU days (67.9% with none in 2006 vs. 77.7% in 2012) were identified over the study period. For the entire sample, 938 (21.12%) died within 2 years of discharge.

Figure 3.1 shows the survival curves to 2-years following discharge. Immediate deviations were observed for patients discharged home compared to those discharged to SNF/Hospice and other care facilities. Curves for patients discharged to a SNF or hospice service and to other care facility were similar up to approximately 90 days following discharge. Among those discharged to a SNF or hospice, nearly 40% died by 2-years after discharge. Patients who left the trauma center AMA exhibited similar survival to those discharged home.

Table 3.3 shows the hazard ratios for the hospital-related variables by time intervals after discharge. Variables which violated the proportional hazards assumption include: total GCS score, log-transformed HLOS, log-transformed TMPM probability of death, ISS, total prior trauma visit count, and discharge location. Among these variables, total GCS score, log-transformed HLOS, log-transformed TMPM probability of death, ISS, ICU length of stay, and discharge locations exhibited the largest statistically significant magnitudes during the 30-day mortality strata. Regarding mortality over time from discharge, reductions in magnitude were observed for all but one hospital-related factor. Total trauma center admissions increased in magnitude with post-discharge time. Compared to patients with only one trauma center admission, those with three or more total trauma center admissions were 2.78 times the risk for death at 1-year post-discharge.

Age-adjusted hazard ratios for select chronic conditions by time interval and for 2-year cumulative mortality are shown in Table 3.4. Among all conditions in the trauma registry, six chronic conditions violated the proportional hazards assumption. After stratification by time, congestive heart failure was statistically significantly associated with mortality in all time strata, and gradually increased in magnitude as a risk factor over time (HR = 1.94 for 30d mortality to

HR = 2.77 for 2-year mortality). Pulmonary heart disease was only significantly associated with mortality among patients who died between 90 days and 2 years after discharge but patients with this condition were at 4.71 times the risk for death than those without the condition during this period. Parkinson's disease was significantly related to mortality only after 90 days of discharge, and was associated with 2.37 times the risk for death compared to those without Parkinson's disease. Patients with chronic alcohol abuse exhibited an increased risk for death of 1.60 only in the 90 days to 2 year interval.

Seven Elixhauser comorbidities violated the proportional hazards assumption. Liver disease, while not related to 30 day mortality, showed a 3.13 to 2.95 increased risk for death across the latter two time intervals. Likewise, psychoses showed a statistical and significant increased risk for death between 90 days and 2 years after discharge (HR 2.30, 95% CI 1.44-3.69), but not in earlier intervals. Five conditions exhibited elevated risk for death in earlier age strata which gradually decreased over time. These were paralysis, other neurodegenerative conditions, metastatic cancer, solid tumors, and fluid & electrolyte disorders. Paralysis was attributable to a 5.28 increased risk for death within the first 30 days of discharge, which dropped to 2.36 in the 90d to 2yr interval. Other neurodegenerative conditions performed similarly, with a statistically significant HR of 3.70 within 30 days of discharge, which gradually reduced to 1.58 for the 90 days to 2 years interval. Patients with metastatic cancer had 10.9 times the risk for death within 30 days of discharge which eventually decreased to 4.49 between 3 months and 2 years. Similarly, a solid tumor diagnosis was related to a 5.34 increased risk of death in the first 30 days, and a 6.27 increased risk for death between 30 and 90 days compared to those without solid tumors, but dropped to 2.48 in the final interval.

Among trauma registry conditions satisfying the proportional hazards assumption, history of cardiac surgery, coronary artery disease, congestive heart failure, history of psychiatric disorders, warfarin therapy, hemophilia, pre-existing anemia, Alzheimer's disease, seizures,

chronic dementia, cerebrovascular accidents, COPD, Type 1 diabetes, and Type 2 diabetes were all positively related to 2-year cumulative mortality. Regarding Elixhauser comorbidities, cardiac arrythmia, valvular disease, pulmonary circulation disorders, peripheral vascular disorders, chronic pulmonary diseases, renal failure, HIV & AIDS, lymphoma, coagulopathy, and severe weight loss conferred a statistically significant constant amount of risk for death within two years. Patients with HIV/AIDS, severe weight loss, and lymphoma showed a significantly elevated risk for death for 2-year cumulative mortality as well as by specific time intervals. A complete listing of the estimates for all chronic conditions can be found in Appendix 7.

DISCUSSION

To our knowledge, the present study is the first to assess the relation between chronic diseases and long-term mortality among older blunt injured trauma patients. We found that older adult trauma patients admitted across a recent seven-year period and who survived to discharge remain at significant risk for death. Over 10% of the study population died within six months of discharge, and over 21% died within two years. Compared to those discharged home, patients sent to a SNF/Hospice or other care facility had 2.79 and 3.89 times the risk for death within the first 30 days of discharge, respectively. Injury-related covariates were associated with only short-term mortality, and failed to consistently predict mortality beyond six months of discharge. Among the 47 chronic conditions analyzed, cardiac conditions, psychiatric disorders, hematologic conditions, and cancers were consistent predictors of post-discharge mortality within two years. These findings suggest that additional concern should be placed on patients discharged to destinations other than home, and for those with the specific chronic conditions of paralysis, HIV/AIDS, metastatic cancer, solid tumors, lymphoma, and severe weight loss, as they conferred a significant amount of risk for death during the study period. These results seek to inform trauma physicians and collaborating healthcare providers of the continued mortality risk to their patients which extend beyond injury care to insure a higher degree of survival after discharge.

In one of the most cited studies on trauma-related post-discharge mortality, Davidson, *et al* analyzed a database of adult patients admitted to Washington State trauma centers.[1] The authors identified a significant excess in trauma-related mortality following discharge as early as one year. Among all the covariates assessed, chronic conditions were identified as important predictors of long-term mortality. However, Davidson and colleagues used the Charlson Comorbidity Index to score the aggregate comorbidity burden of patients on a scale of 0 to 2, and failed to assess the role of specific conditions on mortality. The researchers nonetheless

acknowledged the potential that the excess mortality witnessed may be due to chronic conditions and not to injury.

Over the study period, the number of older trauma patients nearly doubled. Coinciding with this growth was an increasing trend in age at admission, reflecting a dual challenge for the trauma center in its ability to care for more patients with higher complexity due to age. There were also notable reductions in ICU length of stay, total hospital length of stay, and TMPM probability of death. These changes support the notion that, over time, the older trauma demographic experiences injuries of lower severity with relatively quick times to stabilization and discharge. However, results from the present study suggest that the mortality risk due to injury was offset by mortality risk due to chronic conditions.

With the exception of ICU length of stay, all trauma-related factors assessed in the present study violated the proportional hazards assumption. In the analyses by post-discharge time interval, much of the risk attributable to injury is captured in the early intervals. The relationship between injury after discharge and mortality appears to follow an autoregressive theme for the early periods, where risk due to injury gradually decreases over time after discharge from the trauma center. Injury severity, as measured by the TMPM probability of death, failed to predict mortality after 30 days, signifying a shift in the risk from injury. Three other hospital-level factors, ICU length of stay, total GCS score and HLOS, retained their statistical significance across all intervals. However, other research has shown that GCS score and HLOS may be affected by issues pertaining to chronic disease status rather than injury.[28–30] Given that the probability of death due to injury is low in this study population, it is highly plausible that the diminished neurological status reflected by GCS and the complexity of care reflected by HLOS and ICU LOS is due to chronic condition severity rather than injury.

Among the chronic conditions satisfying the proportional hazards assumption, three cardiac conditions (history of cardiac surgery, coronary artery disease, and myocardial

infarction), history of psychiatric disorders, three hematologic disorders (warfarin therapy, hemophilia, and pre-existing anemia), four neurological disorders (Alzheimer's disease, seizures, chronic dementia, and strokes), COPD, and both types of diabetes conferred a constant age-adjusted amount of risk for death within the first 2 years of discharge. This risk ranged from 20% for type 2 diabetes to 89% for patients with hemophilia. Ten comorbidities from the Elixhauser Comorbidity Index were also significantly associated with mortality after trauma and their risk estimates ranged from 1.46 for peripheral vascular disease to 3.90 for HIV/AIDS. These results provide a foundation for trauma physicians to prioritize chronic conditions based on their potential detriment to their patents. In addition, such work can be used to inform patients and families of the need to remain vigilant and adherent toward the management of these conditions after discharge.

Among conditions that violated the proportional hazards assumption, a high risk for early-term mortality was identified for patients with the Elixhauser Comorbidity Index conditions of metastatic cancer, solid tumors, paralysis, neurodegenerative diseases, liver disease, and fluid & electrolyte disorders, and gradually diminished in later timeframes. Conversely, specific conditions originating from the trauma registry of congestive heart failure, pulmonary heart disease, Parkinson's disease, chronic drug abuse, and chronic alcohol abuse, exhibited the highest risk for death after one year of discharge. The discrepancy between these sets of conditions may be explained by the amount of burden imposed on patients in managing these conditions over a long duration. The self-management of cardiac conditions, Parkinson's disease, and substance abuse disorders may be performed using a combination of behavioral change and medication adherence, whereas the management of cancers, neurodegenerative conditions, those with paralysis, liver disease, and fluid & electrolyte disorders require additional effort from care providers.

Metastatic cancers and solid tumors pose a unique problem for trauma surgeons, presenting a vulnerable and frail subpopulation whose tolerance to life sustaining treatments may have depleted due to injury. This logic may be extended to lymphoma, which showed a high amount of constant age-adjusted risk within two years of discharge. Fluid & electrolyte disorders and neurodegenerative diseases reflect a systemic problem resulting from the loss of independence. Electrolyte disorders pertaining to sodium regulation are more prevalent among patients with neurological conditions and represent a significant mortality risk even among uninjured patients.[31] Similarly, paralysis and weight loss among older trauma patients each conferred a significant mortality risk, and represent a dependency of care or decline among injured older patients. Although only significant in the age-adjusted model, mortality risk associated with HIV/AIDS was the highest among all comorbidities satisfying the proportional hazards assumption. Like cancer, mortality after trauma among patients with HIV/AIDS may represent an increased susceptibility to infection or a propensity for modified cognitive function following a head injury.[32,33]

The discharge location categories of SNF/Hospice and care facility (versus discharge to home) yielded highly elevated hazard ratios for mortality within 30 days of discharge that gradually decreased over time. This finding demonstrates that, among trauma patients discharged to a higher level of care, the greatest amount of risk for death exists within the first 30 days. Surprisingly, patients discharged to a care facility had the highest 30 day risk for death (at nearly 4 times the risk of those discharged home), but markedly dropped by the next time interval. This may reflect patients sent to another acute care center for the injury for which they ultimately succumb to. Among patients discharged to SNF/Hospice, the risk is prolonged up to 2 years after discharge. This discrepancy is likely due to two main factors: patents discharged to a care facility receive services and assistance for their conditions and rehabilitation up to a certain point, and are thereafter required to care for themselves. Temporary long-term care facilities were included in

this classification and have previously been related to post-discharge mortality in an older traumatically brain injured population.[17] Patients discharged to SNF/Hospice may overall have a poorer functional capacity, but the vigilance and consistent care provided by care workers at these facilities may reduce the risk for death within 30 days of discharge. However, patients discharged to a SNF/Hospice and those discharged to another care facility exhibited similar rates of death up to the 90 day cut point, whereas the care facility group mortality rate began to slow.

Current trauma quality of care standards focus on in-hospital measurements to validate their performance. Trauma patients discharged to intermediate or palliative care facilities are not included in trauma center mortality estimates, which may result in inaccurate measurement of the quality of care.[8,34–37] As patients remain at risk for death after discharge, quality metrics on trauma mortality should be modified to at least evaluate 30-day post-discharge mortality. The work by Kozar, *et al* highlights the growing proportion of trauma patients who are discharged to hospice and subsequently die as a potential cause for incorrect estimates of center performance.[4] Other work by Claridge, *et al* found that approximately 50% of all post-discharge death in patients aged 65 years and older was not attributable to trauma, and reinforced the notion that the assessment of clinical outcomes after trauma should extend beyond hospital discharge.[3] Trauma may be a catalyst for decline in the elderly, even those that are minimally injured. Trauma centers should prioritize educating patients and care staff to properly manage their conditions in order to reduce their post-discharge mortality risk.

The present study has several limitations. First, this study is composed of only trauma patients admitted to a level 1 trauma center and is without a non-trauma population to serve as a control. Due to this, the attributable risk for each chronic condition as well as that of the injury itself cannot be calculated. Second, the severity of the chronic conditions affecting our trauma population was not assessed. Since conditions originated from either trauma registry comorbidity codes or ICD-9-CM diagnosis codes, only binary variables for their presence or absence were

evaluated. Upcoming changes to the ICD-10-CM and procedure coding systems can potentially provide additional information on disease severity for future analyses. Third, there were no measures for functional status at discharge to assist with the classification of high risk patients, nor were advance directives evaluated which may predispose patients for death in a care facility. Fourth, we were only able to capture chronic disease statuses during the patients' trauma admission. Changes to the chronic disease profile after discharge may have affected the risk for death which could not be evaluated. Fifth, subsequent trauma admissions to other centers were not captured. However, the local trauma system utilizes a trauma catchment area where all patients within a certain region are transported to preferentially one center for treatment. Among older patients, it is unlikely that patients were admitted to other trauma centers around the county. Sixth, the present study did not assess admission to the trauma service from a care facility. Such a variable may have provided additional context on the functional status prior to injury to better classify mortality risk. Finally, the linkage procedure for identifying post-discharge deaths resulted in less matches for the latter years. However, patients admitted during these later years were less injured, had lower HLOS, and were exposed to less time in the ICU compared to patients admitted earlier. In addition, our use of survival analysis (which does not assume equal follow-up time for all patients) as well as our restriction of post-discharge mortality within 2 years of discharge sought to minimize any bias due to difference in surveillance time.

Unlike other studies performed on post-discharge mortality, the present study restricted its sample population to patients aged 55 years or older at admission. Since this study focused on chronic conditions as the primary exposure on mortality, chronic disease prevalence may be confounded by age; where younger trauma patients may be less likely to have these diseases. Younger patients, in general, are healthier and more resilient than older patients, conferring an additional survival advantage. Among other studies that utilize chronic disease burden metrics to predict outcomes in a cohort of trauma patients of all ages, comorbidity measures will almost

certainly be associated with mortality due to probable inter-correlation with older age, reduced physiologic reserve, and more resource utilization. The present study restricted the patient population to one which is more likely to have prevalent chronic conditions, thus reducing the chances of artificial associations between the presence or absence of a condition that can be explained due to age. Although not analyzed in this study, future work should be performed to assess the combined effects of chronic conditions on mortality in this older traumatically injured population.

In conclusion, the growth of older trauma populations combined with increases in the prevalence of chronic conditions pose a major threat to trauma systems. Future work should focus on the proper classification and triage of older trauma patients at high risk for death and the inclusion of increased attention to comorbid conditions as part of discharge planning after trauma in these older adults. In addition, trauma quality metrics must be reevaluated to reflect changes in the aging American trauma population. These results seek to raise awareness of the current state of the aging trauma population and attempt to educate healthcare practitioners of the need to change perspectives to include chronic conditions to classify risk.

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Table 3.1. Demographics and Clinical Characteristics of Eligible Patients Surviving to Discharge: San Diego, CA 2006-2012

Variable	Value
Sample Size	4442
Gender, %	
Female	47.6
Male	52.4
Age in years, mean (SD)	73.7 (11.9)
Insurance Type, %	
Commercial	44.8
Medicare	43.8
Government	6.2
None	5.1
Marital Status, %	
Single	26.0
Married	38.4
Separated	0.9
Divorced	9.3
Widowed	21.6
Other	1.9
Unknown	2.0
No Reported Comorbidities, %	6.3
HLOS in hours, median (IQR)	49.6 (23.9 – 97.6)
ICU Days Categorized, %	
None	74.2
1-2	18.6
3-6	4.1
7+	3.2
Primary Mechanism, %	
Fall	69.5
MVC	21.6
Assault	3.8
Cycling	1.4
Pedestrian	0.4
Other	3.4
Total Trauma Visits Within Study Period, %	
1	93.9
2	5.3
3+	0.8
TMPM Probability of Death, median (IQR)	1.0% (0.4% - 2.2%)
Discharge Location, %	
Home	67.1
SNF/Hospice	22.3
Another Care Facility	9.6
AMA	1.0

AMA, Left Against Medical Advice; HLOS, Hospital Length of Stay; ICU, Intensive Care Unit; IQR, Interquartile Range; MVC, Motor Vehicle Collision; SD, Standard Deviation; SNF, Skilled Nursing Facility; TMPM, Trauma Mortality Prediction Model

Table 3.2. Clinical Endpoints by Admission Year: San Diego, CA 2006-2012

	2006	2007	2008	2009	2010	2011	2012	Trend p
Sample Size	461	512	602	636	709	701	821	
Total Trauma Visits, %								
1	98.9	97.8	96.7	93.2	92.4	92.2	90.0	< 0.001
2	1.1	2.0	2.8	6.1	6.8	6.6	8.3	
≥3	0.0	0.2	0.5	0.6	0.9	1.3	1.7	
Age at Admission, mean	72.0 (11.5)	72.8 (11.5)	73.6 (11.8)	74.2 (12.1)	74.2 (12.2)	73.5 (11.8)	74.6 (11.7)	< 0.001
Discharge Location, %								
Home	64.4	64.1	65.1	66.2	68.0	69.8	69.4	0.003
SNF/Hospice	20.4	23.1	24.3	23.3	22.6	22.0	20.8	0.560
Care Facility	13.9	12.5	9.8	9.8	8.6	6.9	8.3	< 0.001
AMA	1.3	0.4	0.8	0.8	0.9	1.4	1.5	0.152
2-year Mortality, %	21.3	24.6	22.9	27.0	26.2	18.1	11.1	< 0.001
HLOS, median (IQR)	67.4 (30.3-115.8)	57.4 (26.7-118.9)	48.8 (23.0-101.3)	49.0 (23.1-96.6)	48.3 (22.9-92.9)	46.2 (22.4-81.8)	46.7 (23.3-90.7)	< 0.001
TMPM Probability of Death, median (IQR)	1.2 (0.5-2.7)	1.1 (0.4-2.3)	1.0 (0.4-2.3)	0.9 (0.3-2.1)	1.0 (0.4-2.1)	1.0 (0.3-2.1)	1.0 (0.4-2.1)	0.022
ICU Days Categorized, %								
None	67.9	70.9	74.3	75.0	73.9	76.0	77.7	< 0.001
1-2	21.3	19.7	17.8	18.6	19.6	18.4	16.2	
3-6	6.7	4.1	5.3	3.5	4.4	2.7	3.1	
≥7	4.1	5.3	2.7	3.0	2.1	2.9	3.1	

AMA, Left Against Medical Advice; HLOS, Hospital Length of Stay; ICU, Intensive Care Unit; IQR, Interquartile Range; SNF, Skilled Nursing Facility

Table 3.3. Age-adjusted Hazard Ratios for Hospital-level Factors by Post-discharge Time Intervals: San Diego, CA 2006-2012

	30d mortality (N = 4438)		30-90d mortality (N = 4280)		90d-2yr mortality (N = 4124)	
Variable	**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Total GCS Score	0.78	0.74-0.82	0.84	0.79-0.90	0.91	0.87-0.95
Log HLOS	1.69	1.44-1.98	1.49	1.27-1.76	1.18	1.09-1.28
Log TMPM Death Probability	1.15	1.04-1.26	1.05	0.96-1.15	0.99	0.94-1.03
ICU Length of Stay	1.09	1.06-1.12	1.05	1.01-1.10	1.04	1.01-1.06
ISS	1.04	1.03-1.06	1.01	0.99-1.03	1.00	0.99-1.01
Trauma Visit Count						
1	1.00	-	1.00	-	1.00	-
2-3	1.91	1.14-3.20	0.93	0.46-1.90	1.77	1.34-2.34
4+	0.71	0.10-5.11	1.41	0.35-5.68	1.53	0.73-3.22
Discharge Location						
Home	1.00	-	1.00	-	1.00	-
SNF/Hospice	2.75	1.92-3.96	1.88	1.33-2.66	1.96	1.65-2.33
Care Facility	3.89	2.51-6.03	1.79	1.08-2.97	1.44	1.10-1.89
AMA	-	-	1.30	0.18-9.37	1.59	0.71-3.56

AMA, Left Against Medical Advice; CI, Confidence Interval; GCS, Glasgow Coma Scale; HLOS, hospital length of stay; HR, hazard ratio; ICU, intensive care unit; ISS, Injury Severity Score; SNF, Skilled Nursing Facility; TMPM, Trauma Mortality Prediction Model

Table 3.4. Age-adjusted Hazard Ratios for Select Chronic Conditions by Post-discharge Time Intervals: San Diego, CA 2006-2012

	30 day mortality		30-90 day mortality		90 day-2 year mortality		2 year Cum.
Variable	**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**	**HR**
Trauma Registry Conditions							
Alzheimer's Disease	1.48	0.88-2.49	1.73	1.04-2.89	1.81	1.38-2.39	1.77
Attention Deficit Disorder	-	-	-	-	3.10	0.43-22.08	1.54
Congestive Heart Failure	1.94	1.37-2.76	2.06	1.44-2.93	2.77	2.32-3.30	N/A
Coronary Artery Disease	1.45	1.05-2.01	1.54	1.12-2.13	1.54	1.31-1.82	1.45
Chronic Alcohol Abuse	1.01	0.53-1.91	0.86	0.44-1.67	1.60	1.25-2.07	N/A
Chronic Dementia	1.81	1.24-2.63	1.53	1.02-2.27	1.82	1.48-2.24	1.75
COPD	1.95	1.30-2.91	1.49	0.95-2.34	1.96	1.58-2.42	1.86
CVA	1.42	0.95-2.11	1.18	0.77-1.81	1.18	0.95-1.48	1.22
Hemophilia	1.88	0.88-4.01	4.00	2.27-7.06	1.77	1.14-2.73	1.89
History of Cardiac Surgery	1.30	0.79-2.16	1.45	0.89-2.38	1.34	1.03-1.75	1.30
History of Psych. Disorders	1.33	0.94-1.88	1.61	1.14-2.26	1.70	1.43-2.02	1.59
Myocardial Infarction	1.28	0.77-2.12	1.90	1.22-2.96	1.53	1.19-1.96	1.47
Parkinson's Disease	1.25	0.51-3.06	1.30	0.53-3.17	2.37	1.64-3.43	N/A
Pulmonary Heart Disease	2.85	0.40-20.4	-	-	4.71	2.11-10.52	N/A
Pre-existing Anemia	1.74	1.15-2.61	1.91	1.27-2.86	1.83	1.48-2.27	1.76
Seizures	1.39	0.68-2.83	1.03	0.46-2.34	1.19	0.82-1.72	1.30
Type 1 Diabetes	2.50	1.38-4.50	1.25	0.55-2.83	1.43	0.98-2.10	1.62
Type 2 Diabetes	1.14	0.80-1.61	1.15	0.81-1.64	1.24	1.04-1.48	1.20
Warfarin Therapy	1.25	0.89-1.75	1.43	1.02-2.00	1.43	1.20-1.71	1.33
Elixhauser Comorbidities							
Cardiac Arrythmia	1.34	0.97-1.85	1.58	1.14-2.18	1.69	1.43-1.99	1.48
Chronic Pulmonary Diseases	1.42	0.93-2.18	1.21	0.76-1.91	1.59	1.28-1.96	1.49
Coagulopathy	2.15	1.05-4.37	4.08	2.31-7.20	1.56	0.99-2.46	1.89
Fluid & Electrolyte Disorders	2.47	1.76-3.47	1.68	1.16-2.46	1.39	1.14-1.71	N/A
HIV/AIDS	7.57	1.04-54.99	8.35	1.15-60.47	1.92	0.27-13.66	3.90
Liver Disease	0.73	0.18-2.98	3.13	1.52-6.46	2.95	2.04-4.26	N/A
Lymphoma	1.94	0.48-7.84	6.85	3.03-15.50	2.78	1.39-5.59	3.16
Metastatic Cancer	10.91	6.50-18.32	9.85	5.18-18.73	4.49	2.59-7.78	N/A
Neurodegenerative Diseases	3.70	2.59-5.29	2.42	1.59-3.66	1.58	1.24-2.02	N/A
Paralysis	5.28	2.86-9.75	1.00	0.25-4.05	2.36	1.44-3.89	N/A
Peripheral Vascular Disease	1.85	1.03-3.33	0.94	0.41-2.12	1.64	1.18-2.29	1.46
Psychoses	0.52	0.07-3.70	1.02	0.25-4.14	2.30	1.44-3.69	N/A
Pulmonary Circulation Disorder	2.72	1.50-4.91	1.71	0.80-3.67	1.80	1.21-2.69	1.90
Renal Failure	1.83	1.21-2.78	2.26	1.51-3.38	2.11	1.70-2.63	2.03
Severe Weight Loss	4.31	2.02-9.21	6.13	3.01-12.50	2.63	1.36-5.09	3.17
Solid Tumors	5.34	3.23-8.83	6.27	3.79-10.37	2.48	1.64-3.77	N/A
Valvular Disease	1.27	0.72-2.24	1.34	0.76-2.37	1.45	1.09-1.93	1.48

CI, Confidence Interval; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident;HR, Hazard Ratio

N/A denotes variables that violated the proportional hazards assumption and therefore are not eligible for a 2-year cumulative HR estimate

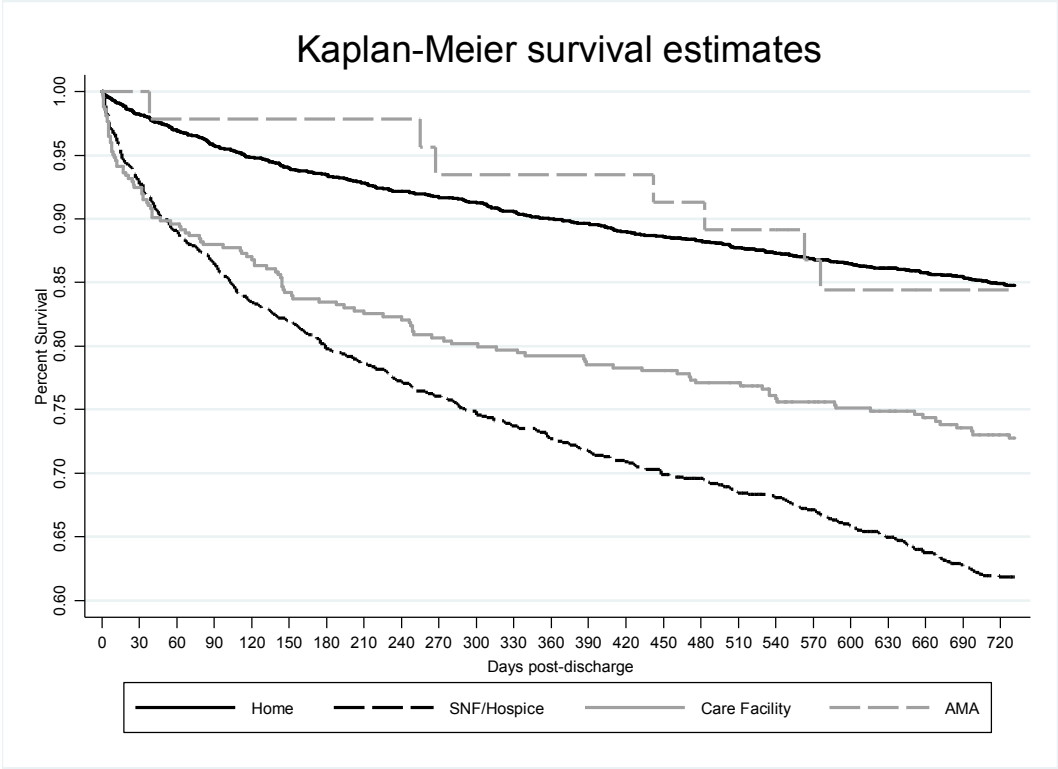

Figure 3.1. Kaplan-Meier Failure Curves by Discharge Location: San Diego, CA 2006-2012

AMA, Left Against Medical Advice; SNF, Skilled Nursing Facility

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CHAPTER 4.

Development, validation, and comparison of a chronic disease-based prognostic model for mortality after traumatic injury in older adults

ABSTRACT

BACKGROUND. Older trauma patients are a vulnerable and growing population, and have been shown to fare worse than their younger counterparts despite having lower severity of injury. Potential reasons include frailty, reduced physiologic reserve, and chronic disease. Previous research on this topic has encountered difficulty in classifying risk for this group, and existing metrics may not be valid. Discharge before death further complicates the issue of predicting mortality in this population. The objectives of this study were to develop a chronic disease-based prognostic model for trauma-related mortality and evaluate the validity of existing predictive metrics in a cohort of older trauma patients.

METHODS. The primary study population was comprised of 4561 blunt injured trauma patients aged 55 years and older at admission and with a Trauma Mortality Prediction Model (TMPM) probability of death less than 50%. Post-discharge mortality was ascertained by matching patient identifiers to national, state, county, and hospital death records. Post-discharge death was categorized as occurring either within 90 days of discharge or between 90-days and 1 year of discharge. Trauma-related mortality was defined as death occurring either during the inpatient stay or within 90 days of discharge. This population was split into a training set (80%) for model development and a test set (20%) for model testing. A second cohort of trauma patients admitted during the 2013 calendar year was used as an external validation set. Cox proportional hazards models were iteratively constructed using prevalent chronic conditions identified in the hospital trauma registry and the hospital administrative dataset. Beta estimates were retained for in-hospital mortality to construct a risk score. The Charlson Comorbidity Index and Elixhauser Comorbidity Score were used for comparison. Concordance statistics (c-statistic) and their respective 95% confidence intervals were used to measure discrimination between models.

RESULTS. The model development procedure identified twelve conditions for the final model: congestive heart failure, myocardial infarction, warfarin therapy, hemophilia, pre-existing

anemia, Alzheimer's disease, chronic dementia, cerebrovascular accident/stroke, chronic drug abuse, liver dysfunction, cancers, and renal dysfunction. Testing of the model showed moderate c-statistics for in-hospital mortality which improved with time from admission (c-statistic: 77.7, 95%CI: 69.6-85.8 within the first 7-days to c-statistic:79.7, 95%CI: 76.7-83.7 within 120 days) were superior to those derived from the Elixhauser Score and Charlson Index. The TMPM outperformed the TRISS and RTS metrics, but all were worse as compared to the chronic disease metrics. In validation, the developed model had moderate performance (c-statistic 66.7) which did not statistically significantly differ from that of the Charlson Index or Elixhauser system. The newly developed metric was superior to all chronic disease and injury metrics at predicting long term mortality after 90 days from discharge.

CONCLUSION. Our chronic condition-based prognostic metric for trauma-related mortality performed well compared to other chronic disease metrics despite only requiring data on twelve conditions. Evaluation of death after discharge is necessary to properly quantify trauma-related mortality risk using chronic conditions in a population of patients with low injury-based probability of death. Additional validation of our metric is warranted.

INTRODUCTION

Older patients represent a complex subset of the traumatically injured population that warrants additional concern. Older trauma patients have been demonstrated to fare worse than their younger counterparts despite experiencing less severe injuries.[1–3] Potential reasons for this phenomenon regard the interplay between aging, frailty, reduced physiologic reserve, and co-occurring disease.[4–8] Chronic disease prevalence has increased significantly over time and is thought to be a driving force behind poor outcomes in older patients.[9, 10] Previous research has shown significant associations between chronic conditions and mortality in older trauma patients regardless of varying severity of injury.[11, 12] As the proportion of older trauma patients increases, so does the corresponding burden on healthcare systems and providers to manage the resources to necessarily improve the probability of positive health outcomes.[2, 13]

Prognostic metrics used to calculate the probability of death in trauma patients are instrumental in assisting trauma surgeons in clinical decision making, managing hospital resources, and benchmarking the quality of care. For example, patients declared to be at a high risk for death but who ultimately survive provide an educational opportunity for which methods could be improved. Conversely, patients who die but had a high probability of survival are reviewed by a medical audit committee with a goal to prevent similar events in the future. Two of the most widely used trauma metrics for the prediction of trauma-related mortality are the Trauma & Injury Severity Score (TRISS) and the Revised Trauma Score (RTS).[14, 15] Developed over 40 years ago, both metrics remain in regular use across all trauma centers in the nation. However, researchers have indicated a diminished applicability of these metrics to current trauma populations.[16, 17] Moreover, none have accounted for early death after discharge where risk remains high.[18–20]

To improve the existing metrics, some researchers have attempted to address the effect of chronic diseases on trauma-related outcomes by using pre-developed metrics. Among the most

used are the Charlson Comorbidity Index [21] and the Elixhauser Comorbidity Scale [22] which process International Classification of Disease (ICD) codes to determine prevalent conditions and their effect on mortality. However, these metrics were developed in non-trauma subpopulations and vary significantly in the diseases captured, outcomes addressed, and statistical methodology for their development. Attempts to revise existing trauma mortality metrics to incorporate chronic diseases have varied in success.[23–28] Unfortunately, these modifications perpetuate the use of metrics that were not designed for use in traumatically injured study populations.

To properly classify trauma patients, methods in the measurement of risk must change to reflect the aging trauma demographic. Among the leading predictive models in trauma, none incorporate the role of chronic conditions on mortality. The concept that chronic diseases risks are overtaking those of traumatic injury has been underappreciated in practice. Among older patients, in-hospital mortality and early death after discharge may both reflect chronically ill patients that are divided by the nature of discharge, placement issues, family preference, or insurance status. To address this, we used a new statistical strategy which focuses on chronic disease profiles in older trauma patients as a primary predictor of trauma-related mortality defined as both in-hospital mortality and death occurring within 90 days of discharge.[11]

METHODS

Study Population

Unique blunt-injured trauma patients admitted between January 1, 2006 and December 31, 2012 were selected for this study from the hospital trauma registry and compose the main study population. All patients were aged 55 years or older at time of admission. Exclusions were made for patients who were discharged or died within 6 hours after admission and those who had a probability of survival less than 50% based on anatomic injury via the Trauma Mortality Prediction Model (TMPM).[29] A total of 4561 (98.0%) patients had a high probability of survival and met all inclusion criteria. A secondary dataset containing 2620 blunt-injured adult trauma patients admitted during the 2013 calendar year was retained for model validation. Primary data originated from the hospital trauma registry containing injury-related characteristics, vital signs, procedures, discharge status, discharge location, and length of stay information. The hospital administrative database was used as a secondary data source for discharge status, insurance, and other codes traditionally used for billing.

Variables and Outcomes

Chronic diseases were selected for the study based on their collection in the hospital trauma registry. Details on chronic disease identification have been previously published.[11, 12] In total, 45 chronic conditions captured by the trauma registry included: Cardiac conditions (history of cardiac surgery, coronary artery disease, pulmonary heart disease, congestive heart failure (CHF), hypertension, myocardial infarction), psychiatric disorders (history of psychiatric disorders, attention deficit disorders, mental retardation), hematologic disorders (coagulopathy, conditions requiring warfarin therapy, hemophilia, and pre-existing anemia), neurological conditions (spinal cord injury, multiple sclerosis, Alzheimer's disease, history of seizures and epilepsy, chronic demyelinating disease, chronic dementia, organic brain syndrome, Parkinson's disease, and cerebrovascular accidents [CVA/stroke]), substance abuse disorders (chronic

ongoing drug abuse and chronic alcohol abuse), pulmonary disorders (prior history with ongoing treatment, asthma, chronic obstructive pulmonary disease [COPD]), diabetes mellitus (type 1 and type 2), Immunosuppression (HIV/AIDS, routine steroid therapy, transplants, active chemotherapy), gastrointestinal conditions (peptic ulcer disease, gastric/esophageal varices, pancreatitis, inflammatory bowel disease), liver dysfunction (includes bilirubin > 2 mg%, cirrhosis), cancer (includes undergoing therapy, lymphoma, metastasis, or old malignancy), autoimmune conditions (rheumatoid arthritis, systemic lupus erythematosus), obesity, and renal dysfunction (serum creatinine > 2mg%, non-transplant related dialysis). Data were supplemented with International Classification of Diseases version 9 Clinical Modification (ICD-9-CM) codes from the hospital administrative database by scanning the diagnosis codes relevant for each condition. Disease definitions and codes can be found in Appendix 1. Only conditions with a prevalence or of 1% or greater were used in the prognostic model development effort.

The primary outcome was trauma-related mortality, defined as: in-hospital death during the index trauma admission, or death within the first 90-days of discharge among survivors of the index admission. Post-discharge mortality information was collected for deaths occurring within one year of discharge evaluated during two time intervals: within 90 days of discharge, and between 90 days and 1 year after discharge. Details on post-discharge mortality assessment are shown elsewhere.[11] In brief, patient identifiers were matched using four data sources: the national Social Security Death Master File, the hospital administrative database, the county medical examiner's database, and the state death index. For patients who died in-hospital, follow-up time was calculated as the hospital length of stay (HLOS). For the post-discharge deaths, follow-up time was calculated as the sum of the HLOS and survival days from discharge until death. Patients who survived their trauma admission to discharge and did not die within 90 days were right-censored at a time equal to their HLOS plus 90 days. Testing and validation of models were performed using the Fine and Gray competing risks regression with discharge to a care facility

(defined as skilled nursing facility, hospice care, acute care facility, rehabilitation center, and behavioral health unit) as a competing event when post-discharge information was not available. Patients discharged to care facilities were censored at the end of their HLOS.

Statistical Analysis

Chi-square tests were used to evaluate differences in chronic disease prevalence by data subset. Primary model development utilized the Cox proportional hazards modeling technique to evaluate the relationship between covariates and the primary outcome of trauma-related mortality. Hazard ratios, 95% confidence intervals, and p-values were calculated to demonstrate the magnitude of the relationship between chronic conditions and mortality. The proportional hazards assumption was assessed using the likelihood ratio test comparing a model containing a time-covariate interaction to that without the interaction assessed at a p-value cutoff of 0.100. Correlation between chronic conditions was evaluated using tetrachoric correlation coefficients (rho) for binary data.[30] Rho values greater than 0.5 or less than -0.5 were considered to be strongly correlated. All data were managed and analyzed using Stata/MP v.12.1 (StataCorp LLC, College Station, TX) and the R Statistical Software (R Foundation, Vienna, Austria).

Model Development

Data were randomly partitioned into two sets: 3620 patients in a training set for model development (80.0%), and 906 in a test set for model testing (20.0%). The training set was further partitioned into quarters for development of a chronic disease-based mortality model. To develop a chronic disease-based mortality model, the Cox proportional hazards models were used on the primary outcome of trauma-related mortality. Covariate selection was performed in three stages (shown in Appendix 8). Stage 1 iteratively used three of the four subsets of the training dataset to evaluate each chronic condition in univariate fashion. Conditions were modeled a total of four times, omitting one subset in each iteration with replacement. Chronic conditions were selected from this stage for the second stage of modeling if they achieved a p-value < 0.100 in at least two

of four iterations. The second stage introduced all of the eligible chronic conditions into a combined model which was again re-run four times in the same method as the previous stage. In each iteration of the second stage, one variable was removed at a time if it both failed to achieve a $p < 0.100$ (in any iteration) and had the highest average p-value across the 4 iterations. Variables were retained for the final stage if they achieved a p-value < 0.100 in at least one of four iterations of the combined models. For the third and final stage, the remaining candidate chronic conditions were combined and modeled in the entire training set. Variables were excluded based on a p-value > 0.100. Within the final variable subset, Akaike Information Criteron (AIC) values and likelihood ratio tests were used to evaluate changes in model fit after removal of variables with p-values > 0.05. If exclusion of a variable resulted in a worse-fit model, the variable was retained. A chronic disease risk score for trauma-related mortality was calculated using the resultant beta coefficients from the final model.

Assessing Model Validity

Quantitative assessment of the best-fit model performance on the various data sets was performed using time-dependent concordance statistics (c-statistic) displayed as percentages.[31, 32] The 95% confidence intervals for each c-statistic were generated via bootstrapping with 100 replicates. Time points for evaluation of the c-statistics was based off of conventional time frames following admission and discharge. The c-statistics calculated at the end of follow-up represent an overall assessment of models. In the test set, c-statistics among the prognostic models were calculated for trauma-related mortality and for in-hospital mortality with discharge to a care facility as a competing event. Validity of the risk score to long-term post-discharge mortality between 90 days and 1 year was also evaluated among all survivors beyond 90-days after discharge in the primary study population. For these analyses, patients who did not experience death by one year after discharge were censored at 365.25 days after discharge. External validity of the prognostic models was assessed in the validation dataset among all blunt-injured trauma

patients with a HLOS over six hours. In the validation set, c-statistics were calculated for only in-hospital mortality versus discharge to a care facility due to a lack of post-discharge information available for this cohort.

Calibration of the developed model was evaluated using the method developed by Gerds, *et al* which uses pseudo-values for right-censored data.[33] Predicted risk values from the model were grouped by decile and plotted against the proportion of observed mortality in each decile. Plots were generated for A) in-hospital death competing with discharge to care facility in the test set, B) long-term mortality (90-day to 1-year post-discharge mortality) among survivors in the primary set, C) in-hospital death competing with discharge to care facility in the validation set, and D) trauma-related death in the test set. Plots that followed the diagonal were defined as well-calibrated.

For comparison, c-statistics and their 95% confidence intervals were calculated for leading injury-related and chronic disease-predictive metrics. The TMPM probability of death, TRISS survival probability, and RTS are classified as injury metrics whereas the Charlson Comorbidity Index based on weighted comorbidities by Quan, *et al* [34, 35] and a point-based Elixhauser Comorbidity Score by van Walraven, *et al* were classified along with our model as chronic disease-based metrics. All models had c-statistics calculated.[36] Significant differences in predictive ability between model types was identified if a 95% confidence interval excluded the c-statistic of another model.

RESULTS

The prevalence of all chronic conditions and outcomes are shown in Table 4.1. Between the training and test sets, there were no significant differences in the primary outcome of in-hospital death or competing event of 90-day post-discharge death. All chronic conditions did not differ between data subsets. Among all the chronic conditions evaluated, all gastric disorders (peptic ulcer disease, gastric or esophageal varices, pancreatitis, inflammatory bowel disease) and all immunosuppression conditions (HIV/AIDS, routine steroid therapy, transplants, active chemotherapy) had prevalences less than 1% and were excluded from the model development procedure. Other conditions with low prevalence included: pulmonary heart disease, congenital cardiac disease, attention deficit disorder, mental retardation, spinal cord injury, multiple sclerosis, chronic demyelinating disease, organic brain syndrome, history of pulmonary condition with ongoing treatment, and lupus.

The model development procedure identified twelve chronic conditions that had a multivariable relationship with mortality. These conditions were: CHF, myocardial infarction, warfarin therapy, hemophilia, pre-existing anemia, Alzheimer's disease, chronic dementia, CVA/stroke, chronic drug abuse, liver dysfunction, cancers, and renal dysfunction (Table 4.2). Of these, cancers conferred the most amount of risk (HR = 4.37), while chronic drug abuse was deemed protective (HR = 0.54). Two variables held p-values over 0.05: warfarin therapy and liver dysfunction. Subsequent models that were created without these two variables produced AIC values and significant likelihood ratio test p-values indicating worse fit, and they were therefore retained. The competing mortality risk score from the training set was calculated as follows:

Risk = 0.6132615 (CHF) + 0.4452354 (Myocardial Infarction) + 0.2167003 (Warfarin Therapy) + 0.5648907 (Hemophilia) + 0.2932986 (Pre-existing Anemia) + 0.4769274 (Alzheimer's Disease) + 0.5770123 (Chronic Dementia) + 0.3480417 (CVA/Stroke) + -0.623796 (Chronic Drug Abuse)

+ 0.4672339 (Liver Dysfunction) + 1.474584 (Cancers) + 0.6964046 (Renal Dysfunction)

The range of calculated risk scores in the training set was -0.623796 to 3.577963 with a mean and standard deviation of 0.3541449 and 0.6889365, respectively. Figure 4.1 is a display of the cumulative hazard curves for trauma-related mortality by quartiles of the risk score. With increasing quartile, the cumulative hazard also increased with time. Patients in the third and fourth quartiles demonstrate slightly greater risk for death within the first seven days from admission after which the increase becomes relatively constant.

Significant correlation was identified between several chronic conditions (Table 4.3). Among conditions included in the final model, high positive correlation was identified between liver dysfunction and hemophilia (rho = 0.58), Alzheimer's disease and chronic dementia (rho = 0.89). High negative correlation was identified between cancer and hemophilia (rho = -1.00), chronic drug abuse and Alzheimer's disease (rho = -1.00), liver dysfunction and Alzheimer's disease (rho = -1.00), and liver dysfunction and chronic dementia (rho = -1.00). Among all conditions used for modeling, high positive correlations were found between history of cardiac surgery and coronary artery disease (rho = 0.75), coronary artery disease and congestive heart failure (rho = 0.55), coronary artery disease and myocardial infarction (rho = 0.58), history of psychiatric disorders and Alzheimer's disease (rho = 0.70), history of psychiatric disorders and chronic dementia (rho = 0.80), type 1 diabetes and type 2 diabetes (rho = 0.67), and renal dysfunction and non-transplant dialysis (rho = 1.00).

Markers of predictive performance for the newly developed model and other chronic disease and injury metrics applied to the test set are shown in Table 4.4. The newly developed model demonstrated the highest c-statistics and were statistically significantly superior to the Charlson Index across all time intervals from admission. Compared to the Elixhauser score, our developed metric performed similarly for predicting 7-day, 14-day, and 30-day mortality, but was

superior for 90-day and 120-day mortality. All chronic disease-based metrics maintained moderate to strong c-statistics across each time interval whereas the three injury-based metrics decreased in predictive performance with time. The TMPM, TRISS, and RTS metrics did not statistically differ from each other in predicting trauma-related mortality within the first 7- and 14-days from admission. However, the TRISS metric was statistically superior for predicting 30-day mortality compared to the other two injury metrics. For 120-day cumulative mortality, the TMPM probability of death metric was the only injury-based metric that maintained any viable predictive performance (having excluded 50.0% from the confidence interval). Greater ambiguity in prediction was seen when attempting to predict in-hospital mortality accounting for discharge to a care facility as a competing risk. The newly developed model consistently predicted mortality in all time intervals with the exception of within the first 24 hours. Both the Charlson index and Elixhauser score were able to predict cumulative two-week mortality, but were not statistically significant for predicting death by 4-weeks after admission. The RTS metric displayed moderate c-statistics for predicting early mortality within 24 hours, 72 hours, and 1 week from admission only. The TMPM and TRISS metrics failed to show any statistically significant viability at predicting in-hospital mortality in this series.

Discrimination of the models applied to the validation set are shown in Table 4.5. Analyses were performed on adult patients over the age of 18 years who had HLOS > 6 hours. Analyses using competing risks regression on in-hospital mortality with discharge to a care facility as a competing event showed similar c-statistics across all of the chronic disease metrics at each time interval. All chronic disease metrics failed to predict in-hospital death within the first 72 hours from admission. However, the Elixhauser score became viable for deaths within 1 week from admission. For the 2-week and 4-week time intervals, all three chronic disease-based metrics showed moderate discrimination that were not statistically significantly different from each other. In contrast, all three injury-based metrics performed well at predicting death within

the first three time intervals. However, c-statistics reduced to non-significance at predicting mortality within the 2-week interval for the TMPM metric and 4-week time interval for the TRISS metric. The RTS maintained statistically significant c-statistics across all time intervals. Regarding long-term mortality prediction, the three chronic disease metrics showed moderate c-statistics that were all statistically significantly superior to all of the injury-based metrics. Compared to the Charlson Index, our developed model was statistically significantly better at predicting long term death across all time intervals. Compared to the Elixhauser score, statistically significant superiority was demonstrated in only two of five time intervals. Prediction of long-term death using any injury metric and across nearly all time intervals was poor.

Figure 4.2 shows the calibration plots for the developed model applied in four different scenarios. Because the model contained 12 binary variables, the linear combination of coefficients based on this model alone did not allow for a meaningful distribution of mortality probabilities for calculation. As a result, the model containing both our risk score and age at admission was used to generate the plot. For all applications of the model, the plot of the points generally followed the diagonal which indicated that models were calibrated for use in these datasets.

DISCUSSION

We developed a prognostic model for trauma-related mortality that was based on prevalent chronic conditions in older traumatically injured patients. Testing and validation of our model demonstrated consistent and strong discrimination compared to the other leading measures of chronic disease burden. Our calibrated and validated model was superior at predicting all trauma-related mortality compared to all of the other metrics evaluated. Despite not always being statistically significantly superior to the Charlson and Elixhauser metrics in all time intervals, our developed model showed similar discrimination using only 12 conditions. This is in contrast to the van Walraven, *et al* point-based revision of the Elixhauser score which used 28 conditions and the Quan, *et al* version of the Charlson Index which used 17 conditions. In addition, our metric showed general superiority to that of the Elixhauser and Charlson indices when modeling long-term death after discharge.

Older trauma patients with low severity of injury are notoriously difficult to classify and treat, and their in-hospital stay often results in greater resource utilization and poorer outcomes compared to younger populations.[37–39] Our research is warranted as older populations represent a trauma population for which the existing prognostic metrics fall short. Although several researchers remark on chronic disease as a contributing factor for mortality after trauma, few studies directly evaluate this relationship. Results from the present study show that chronic diseases can predict mortality in this population independent of injury.

The overall low in-hospital mortality rates in this population appear to run counter to the literature indicating that older patients fare poorly after trauma. Although only 113 in-hospital deaths occurred in the study population, nearly three times as many patients died within 90 days of discharge. These patients would traditionally be censored in studies that do not evaluate mortality after discharge, which would minimize the role of their prevalent contributory risk factors on death. Previous researchers have addressed the need to account for post-discharge

deaths in the calculation of quality of care.[18, 40] Our use of post-discharge death within a valid window of time to complement in-hospital mortality sought to address the true burden of chronic conditions on patients and its relationship to trauma-related death.

The validation data lacked information on post-discharge mortality and so discharge to a care facility was therefore used as a competing event. Excluding incarceration, older adults admitted to the trauma service predisposes them to only one of several outcomes: in-hospital death, discharge to SNF/Hospice, discharge to another care facility (acute, long-term, or rehab), leaving against medical advice, or discharge to home (with or without services). Discharge to a care facility provides a valid proxy for poor discharge status and subsequent death which has been demonstrated in multiple studies including this cohort of older injured patients.[11, 12, 18, 41] However, additional research must be performed on this particularly vulnerable population to investigate the rationale for discharge to care facilities and its role as a competing event to in-hospital death.

In a summary of the major fallacies of trauma research, del Junco *et al* discussed the fault of assuming uniform effects over time.[42] Although primarily directed toward conducting and analyzing clinical trials, the present study addresses this fault in two ways. First, we reassessed the quantification of risk in older trauma populations by developing a new chronic disease-based metric, as older metrics have shown reduced validity. Second, we decided that deaths occurring outside the hospital within a reasonable time after discharge represent a patient population for which the death is still attributable, in-part, to trauma. If researchers assume homogeneity of the discharged patients simply because they are no longer in the hospital, estimates of risk may be biased in favor of the characteristics of patients with placement issues, delays in family consultation, and factors that are temporally proximal to the time of admission. This bias omits the relevance of the entire spectrum of patient health, focusing only on that of injury and other hospital-based measures.[43]

Although the chronic conditions used for our model were defined by the hospital trauma registry, many overlapped with conditions found in the other chronic disease metrics. Our modeling procedure selected two cardiac conditions, three neurological disorders, three hematologic conditions, chronic drug abuse, liver dysfunction, cancers, and renal dysfunction as being the best combination of predictors for death. In this model, the greatest amount of risk comes from cancer and renal dysfunction which tend to equate with severe morbidity requiring end of life care. The remaining conditions of liver dysfunction, myocardial infarction, CVA/stroke, congestive heart failure, warfarin therapy, pre-existing anemia, Alzheimer's disease, and chronic dementia all coincide with advanced age, significant cardiovascular disease, and an overall frail state. These conditions all conferred a moderate increase in mortality risk that is consistent with risk estimates from another study that attempted to predict mortality using the National Study on the Costs and Outcomes of Trauma dataset.[44] Chronic drug abuse showed a protective effect for mortality which is consistent with the study by van Walraven, *et al* who updated the Elixhauser comorbidities using a points system based on more current data. Hemophilia is a condition not found in other chronic disease metrics but posed a unique risk to trauma patients because of the risk of hemorrhage.

Among all the candidate conditions used for modeling, only those related at the $p < 0.100$ level were retained for multivariable modeling. Because of the relatively low event rate, caution was required when selecting variables for inclusion to prevent overfitting. However, conditions that experienced high correlation with that of a selected variable may indeed be risk factors omitted due to redundancy in the multivariable model construction process. Specifically, coronary artery disease showed high correlation with both congestive heart failure and myocardial infarction, but failed to be statistically significant to mortality during the second stage of model development. It should be noted that initial rounds of multivariable model development showed history of cardiac surgery, coronary artery disease, congestive heart failure, and

myocardial infarction as being significant during stage 1 through but lost significance in early iterations of stage 2. Only one covariate was removed at a time due to fear of multicollinearity preventing proper estimation of the covariates and it was not until the very last iteration of stage 2 that coronary artery disease was dropped from the list of candidate variables. In the third stage, chronic alcohol abuse was eventually removed, but generally was not significantly related to mortality through much of the stage 2 iterations. As correlation was high between chronic drug abuse and chronic alcohol abuse, the explanatory power associated with alcohol abuse is likely to be captured by the drug abuse variable. The same is likely true for non-transplant dialysis which showed a perfect correlation with that of renal dysfunction. Non-transplant dialysis was significant in three of four stage 1 iterations and was retained long into stage 2.

While not a direct a validation step, our model performed well at predicting long-term mortality after 90 days compared to the other chronic disease metrics. All three of the chronic disease measures significantly predicted mortality in all time intervals. In contrast, all injury metrics showed poor discrimination over nearly all time intervals. Taken together, these results demonstrate that long-term mortality after discharge is likely due to adverse effects or poor management of chronic conditions versus injury, and the prevalent chronic conditions collected during the trauma admission provide a revealing amount of information for the prediction of long-term death. It is therefore recommended that trauma centers prioritize the collection of data on chronic disease status among its older trauma population as well as take steps to secure post-discharge mortality information to improve clinical decision-making.

This study is not without limitations. As previously discussed, the validation set did not have post-discharge mortality information and discharge to a care facility was used in its place. Although true validation steps would have been performed using the same outcome, our validation procedure demonstrates the applicability of competing risks regression and our chronic disease risk metric in centers with discharge location and no post-discharge death information. In

addition, validation would have been better performed in large-scale datasets such as the Trauma Quality Improvement Program (TQIP) or the National Trauma Data Bank to show large-scale applicability of our metric. However, these data sources aggregate prevalent chronic conditions into broad groupings. Previous attempts to apply our model to TQIP data using ICD-9-CM codes alone to define chronic conditions yielded significantly lower condition prevalence compared to that of our primary study population (data not shown). Secondly, the present study had a very low in-hospital mortality rate. Although part of the original study design was to focus on mortality in a poorly-classified trauma subpopulation and included post-discharge death as an added feature, our variable selection methodology which split the training set into quarters may have over stratified the already low events we had. Future variable selection methods may incorporate cross-validation measures as a substitute. Third, our model was developed in a subpopulation of trauma patients with high survival probability, a minimum HLOS of 6 hours, blunt injury, and age over 55 years. Our model may therefore not be generalizable to higher risk populations or at centers where condition prevalence is not well recorded.

Our study makes use of an adapted version of the Harrell's concordance index for competing risk at specific time intervals.[31] Concordance itself is the quantification of a model's ability to properly rank events by time and discriminate between primary and competing events. For our analyses that used competing risks regression, the c-statistics were not as high as originally expected. This can be explained in several ways. First, for competing risks regression, discrimination of an event of interest from a competing event may be hampered if the independent variables are positively related to both outcomes. High discrimination for the primary outcome occurs if the independent variables are minimally or inversely related to the secondary outcome. Second, we only sought to evaluate the raw predictive ability of each metric independent of other covariates. For this population a combination of injury- and chronic disease-based metrics should yield markedly higher c-statistics than individual metrics alone. Third, there

are several characteristics that are currently unmeasured in trauma. With reference to the calibration plot, reduced discrimination is shown by the void of data points over the entirety of the curve. The truncation of each set of points towards the middle of each plot demonstrates that even after inclusion of age, the distribution the risk score does not extend across the entire spectrum of risk which may also be compounded by our low event rate. Future work should be aimed at the development of composite models through the inclusion of a measure of frailty or ability to self-care for stronger mortality prediction.

In conclusion, our model tends to outperform the Elixhauser system and the Charlson Comorbidity Index, but necessitates data on only twelve conditions. Future research should be performed to develop a risk score for death shortly after discharge to better allow for greater applicability of our chronic disease model in trauma centers lacking post-discharge information. Such a model could provide a scored probability of death to classify patients at high risk for death after discharge and could be incorporated in competing risks models. Results from the present study may be used to guide the development of new triage criteria for older populations. The prediction of death using chronic conditions can provide trauma surgeons and other healthcare practitioners with more information to better define the required course of care, inform patients and their families of potential risks, and allocate healthcare resources.

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Chapter 4, in part, is currently being prepared for submission for publication. The dissertation author was the primary investigator and author of this material. Professors Suzanne Lindsay, Steven Edland, Caroline Macera, Lucila Ohno-Machado, and Deborah Wingard are included as co-authors of this work.

Table 4.1. Mortality Incidence and Condition Prevalence (per 100) by Data Set of the Primary Cohort

	Training	**Test**	**p-value**
	3620	**906**	
In-hospital Death, n (%)	88 (2.4)	25 (2.8)	0.571
Post-Discharge 90d Death, n (%)	254 (7.0)	57 (6.3)	0.440
90d – 365d Post-Discharge Death, n (%)	347 (8.5)		
Hypertension	61.6	61.5	0.970
Coronary Artery Disease	25.9	26.3	0.839
Type 2 Diabetes	25.7	25.6	0.945
Chronic Drug Abuse	21.3	18.4	0.055
Warfarin Therapy	20.6	19.7	0.521
History of Psychiatric Disorders	20.2	19.0	0.426
Chronic Alcohol Abuse	13.7	13.0	0.609
Congestive Heart Failure	13.5	12.8	0.563
Renal Dysfunction	13.1	12.7	0.732
Cerebrovascular Accident/Stroke	11.4	11.7	0.806
Chronic Obstructive Pulmonary Disease	10.1	9.3	0.465
Pre-existing Anemia	10.0	8.8	0.300
Chronic Dementia	9.8	10.0	0.830
Myocardial Infarction	8.1	8.7	0.521
History of Cardiac Surgery	7.2	7.8	0.499
Seizures	5.1	4.8	0.654
Alzheimer's Disease	4.5	4.9	0.622
Coagulopathy	4.1	4.8	0.378
Asthma	4.0	3.5	0.511
Type 1 Diabetes	3.9	3.8	0.843
History of Cancer (including Lymphoma)	3.6	3.2	0.595
Liver Dysfunction (including Cirrhosis)	3.4	2.9	0.403
Hemophilia	2.8	2.2	0.310
Obesity	2.7	3.0	0.654
Rheumatoid Arthritis	2.1	2.7	0.341
Parkinson's Disease	1.9	2.0	0.788
Dialysis (excluding Transplant Patients)	1.6	1.1	0.320
HIV/AIDS	0.6	0.6	0.998
Pancreatitis	0.6	0.6	0.998
History of Pulmonary Conditions	0.5	0.9	0.133
Routine Steroid Therapy	0.5	0.7	0.541
Spinal Cord Injury	0.4	0.6	0.492
Transplants	0.4	0.3	0.899
Pulmonary Heart Disease	0.2	0.2	0.869
Congenital Cardiac Disease	0.2	0.2	0.869
Mental Retardation	0.2	0.2	0.378
Multiple Sclerosis	0.2	0.0	0.185
Active Chemotherapy	0.2	0.2	0.724
Peptic Ulcer Disease	0.2	0.3	0.430
Gastric or Esophageal Varices	0.2	0.1	0.704
Inflammatory Bowel Disease	0.2	0.3	0.430
Systemic Lupus Erythematosis	0.2	0.4	0.114
Attention Deficit Disorder	0.1	0.1	0.803
Chronic Demyelinating Disease	0.1	0.0	0.617
Organic Brain Syndrome	0.1	0.0	0.386

AIDS, Acquired Immune deficiency Syndrome; HIV, Human Immunodeficiency Virus

Table 4.2. Estimates of Association for Trauma-related Mortality of the Final Model in Training Set

Variable	Beta	HR	95% CI	p-value
Congestive Heart Failure	0.6132615	1.85	1.44 - 2.37	< 0.001
Myocardial Infarction	0.4452354	1.56	1.14 - 2.13	0.005
Warfarin Therapy	0.2167003	1.24	0.97 - 1.58	0.081
Hemophilia	0.5648907	1.76	1.17 - 2.65	0.007
Pre-existing Anemia	0.2932986	1.34	1.01 - 1.78	0.043
Alzheimer's Disease	0.4769274	1.61	1.03 - 2.53	0.038
Chronic Dementia	0.5770123	1.78	1.27 - 2.50	0.001
CVA/Stroke	0.3480417	1.42	1.07 - 1.87	0.015
Chronic Drug Abuse	-0.623796	0.54	0.34 - 0.78	0.001
Liver Dysfunction	0.4672339	1.60	0.98 - 2.59	0.058
Cancer	1.474584	4.37	3.19 - 5.99	< 0.001
Renal Dysfunction	0.6964046	2.01	1.56 - 2.58	< 0.001

CVA, Cerebrovascular Accident

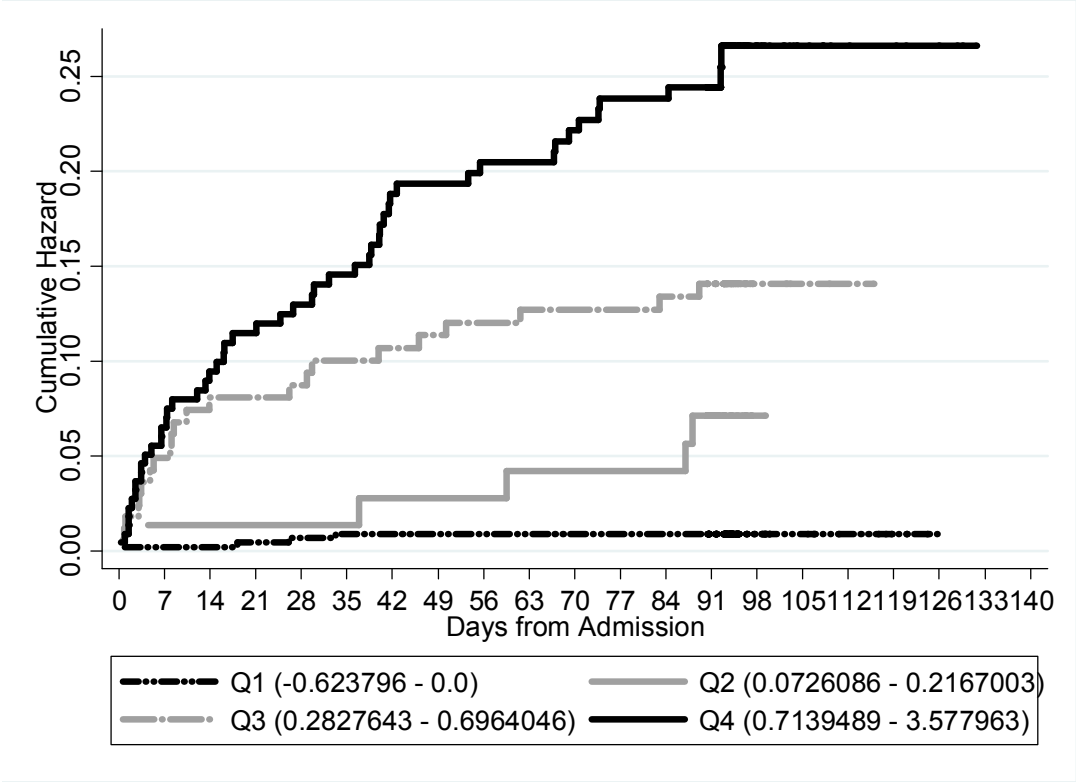

Figure 4.1. Cumulative Hazard Curves by Quartiles of Risk Score

Q# denotes the quartile number. Values in parentheses are the numeric range of the quartiles.

Table 4.3. Tetrachoric Correlation Coefficients for Chronic Conditions in the Training Set

#	Chronic Condition	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1	History of Cardiac Surgery	1.00													
2	CAD	**0.75**	1.00												
3	CHF	0.26	**0.55**	1.00											
4	Myocardial Infarction	0.37	**0.58**	0.41	1.00										
5	Hypertension	0.30	0.29	0.26	0.12	1.00									
6	Psychatric Disorders	0.07	-0.06	-0.04	-0.02	0.04	1.00								
7	Coagulopathy	0.00	0.04	0.07	-0.12	0.08	-0.00	1.00							
8	Warfarin Therapy	0.25	0.20	0.29	0.10	0.27	-0.02	0.19	1.00						
9	Hemophilia	0.27	0.18	0.27	0.24	0.16	0.09	0.16	-0.07	1.00					
10	Pre-existing Anemia	0.03	0.15	0.29	0.13	0.02	0.10	0.31	-0.13	0.26	1.00				
11	Alzheimer's Disease	0.14	0.11	0.11	0.17	0.12	**0.70**	-0.09	-0.14	0.16	0.01	1.00			
12	Seizures	-0.01	0.12	-0.08	0.02	0.05	0.14	-0.02	0.04	0.19	-0.35	-0.02	1.00		
13	Dementia	0.19	0.11	-0.00	0.05	0.17	**0.80**	0.09	0.03	-0.04	0.19	**0.89**	-0.00	1.00	
14	Parkinson's Disease	-1.00	0.17	**-1.00**	-0.01	0.14	0.18	0.14	0.23	-1.00	0.24	0.31	**-1.00**	0.43	1.00
15	CVA/Stroke	0.28	0.22	0.13	0.12	0.31	0.01	0.04	0.25	0.10	-0.06	0.15	0.09	0.17	0.09
16	Chronic Drug Abuse	-0.18	-0.23	-0.28	-0.22	-0.28	-0.10	-0.21	-0.33	-0.01	-0.17	**-1.00**	0.17	0.39	-0.07
17	Chronic Alcohol Abuse	-0.14	-0.21	-0.21	-0.06	-0.19	0.02	-0.01	-0.26	0.34	-0.08	-0.35	0.28	-0.25	**-1.00**
18	Asthma	-0.09	-0.08	-0.03	-0.12	0.12	0.08	0.15	0.04	-0.00	-0.16	-0.09	-0.02	-0.14	0.14
19	COPD	-0.02	0.08	0.33	0.06	0.08	0.05	0.07	0.14	0.13	0.11	-0.07	0.16	-0.04	0.23
20	Type 1 Diabetes	0.43	0.27	0.21	0.08	0.06	0.09	-0.07	0.28	0.30	-0.12	0.19	0.19	0.13	0.17
21	Type 2 Diabetes	0.25	0.22	0.24	0.07	0.27	-0.03	0.12	0.08	0.05	0.13	0.15	0.05	0.11	-0.12
22	Liver Dysfunction	0.04	-0.11	0.02	0.09	-0.10	-0.05	0.35	-0.22	**0.58**	0.41	**-1.00**	0.20	**-1.00**	**-1.00**
23	Cancers	0.30	0.18	0.22	0.01	0.08	0.05	0.09	-0.04	**-1.00**	0.23	0.09	-0.12	0.13	**-1.00**
24	Rheumatoid Arthritis	-0.11	0.22	0.25	0.11	0.13	-0.18	0.02	0.09	**-1.00**	0.16	**-1.00**	-0.05	-0.16	**-1.00**
25	Obesity	0.16	0.05	0.16	**-1.00**	0.22	0.02	0.20	0.18	**-1.00**	0.32	**-1.00**	0.24	**-1.00**	**-1.00**
26	Renal Dysfunction	0.28	0.29	0.39	0.24	0.09	-0.12	-0.06	0.09	0.20	0.47	-0.13	-0.08	0.18	0.06
27	Non-Transplant Dialysis	0.26	0.32	0.10	0.12	-0.05	-0.07	**-1.00**	-0.10	**-1.00**	0.19	**-1.00**	0.21	0.21	**-1.00**

CAD, Coronary Artery Disease; CHF, Congestive Heart Failure; COPD, Chronic obstructive pulmonary disease; CVA, cerebrovascular accident.

Table 4.3 - Continued

#	Chronic Condition	15	16	17	18	19	20	21	22	23	24	25	26	27
1	History of Cardiac Surgery													
2	CAD													
3	CHF													
4	Myocardial Infarction													
5	Hypertension													
6	Psychatric Disorders													
7	Coagulopathy													
8	Warfarin Therapy													
9	Hemophilia													
10	Pre-existing Anemia													
11	Alzheimer's Disease													
12	Seizures													
13	Dementia													
14	Parkinson's Disease													
15	CVA/Stroke	1.00												
16	Chronic Drug Abuse	-0.07	1.00											
17	Chronic Alcohol Abuse	-0.12	**0.76**	1.00										
18	Asthma	0.04	-0.10	-0.23	1.00									
19	COPD	0.04	0.15	0.13	0.27	1.00								
20	Type 1 Diabetes	0.08	-0.11	-0.11	-0.07	0.04	1.00							
21	Type 2 Diabetes	0.03	-0.19	-0.22	0.08	0.09	**0.67**	1.00						
22	Liver Dysfunction	-0.27	0.25	0.46	-0.06	-0.25	-0.03	0.08	1.00					
23	Cancers	-0.14	-0.23	-0.19	-0.06	0.12	-0.03	-0.10	0.13	1.00				
24	Rheumatoid Arthritis	-0.20	-0.13	-0.10	0.18	0.15	0.32	0.08	0.05	0.05	1.00			
25	Obesity	-0.18	0.04	-0.08	0.47	0.38	0.06	0.33	**-1.00**	**-1.00**	0.31	1.00		
26	Renal Dysfunction	-0.07	-0.44	-0.29	-0.13	0.08	0.33	0.34	0.11	0.30	-0.09	-0.06	1.00	
27	Non-Transplant Dialysis	-0.10	-0.26	**-1.00**	**-1.00**	-0.08	0.31	0.33	0.14	0.14	**-1.00**	**-1.00**	**1.00**	1.00

CAD, Coronary Artery Disease; CHF, Congestive Heart Failure; COPD, Chronic obstructive pulmonary disease; CVA, cerebrovascular

Table 4.4. Concordance Statistics and 95% Confidence Intervals by Time Interval from Admission and Modeling Type in the Test Set

Trauma-related Mortality					
	7 days	**14 days**	**30 days**	**90 days**	**120 days**
Ours	77.7 (69.6-85.8)	79.4 (73.4-85.3)	79.3 (73.8-84.7)	81.1 (76.9-85.3)	79.7 (76.7-83.7)
Charlson	68.7 (58.9-78.5)	68.0 (59.6-76.4)	66.6 (59.3-74.0)	72.1 (66.3-77.9)	71.3 (65.7-76.8)
Elixhauser	74.1 (64.9-83.4)	74.8 (67.2-82.3)	73.9 (67.2-80.5)	75.9 (70.5-81.3)	75.0 (69.8-80.1)
TMPM	65.0 (52.6-77.4)	62.6 (52.1-73.1)	63.7 (54.4-73.0)	61.8 (54.9-68.8)	61.8 (55.1-68.5)
TRISS	73.8 (62.0-85.5)	72.0 (62.0-82.0)	73.6 (65.6-81.5)	66.3 (59.4-73.2)	34.5 (18.9-50.0)
RTS	74.3 (64.2-84.3)	69.6 (61.3-77.9)	66.7 (59.9-73.5)	60.6 (55.5-65.7)	50.3 (38.4-62.2)
In-hospital Death vs. Discharge to Care Facility					
	24 hours	**72 hours**	**1 week**	**2 week**	**4 weeks**
Ours	58.0 (30.5-85.5)	74.4 (60.5-88.3)	69.5 (59.1-80.0)	71.6 (59.7-83.4)	75.4 (58.7-92.1)
Charlson	69.9 (48.7-91.1)	63.2 (49.3-77.0)	58.5 (44.1-72.9)	66.1 (52.3-79.9)	59.4 (41.5-77.4)
Elixhauser	68.5 (52.3-84.7)	58.9 (44.9-73.0)	59.3 (43.0-75.6)	66.4 (51.0-81.7)	65.2 (47.1-83.2)
TMPM	48.2 (21.7-74.7)	59.7 (40.4-79.0)	50.4 (33.3-67.4)	40.7 (24.0-57.5)	44.4 (26.8-62.0)
TRISS	63.0 (36.2-89.8)	65.4 (46.5-84.4)	58.2 (44.0-72.4)	43.8 (27.5-60.0)	42.7 (23.4-62.1)
RTS	77.9 (56.0-99.8)	72.2 (57.3-87.2)	68.1 (55.3-80.8)	62.1 (49.4-74.7)	52.4 (37.9-66.9)

TMPM, Trauma Mortality Prediction Model; TRISS, Trauma and Injury Severity Score; RTS, Revised Trauma Score.

Table 4.5. Concordance Statistics and 95% Confidence Intervals Time Interval and Modeling Type in the Validation Set

In-hospital Death vs. Discharge to Care Facility					
	24 hours	**72 hours**	**1 week**	**2 week**	**4 weeks**
Ours	53.2 (33.7-72.6)	59.3 (48.7-70.0)	55.3 (40.8-69.9)	67.1 (53.9-80.4)	66.7 (52.2-81.3)
Charlson	54.2 (27.3-81.2)	55.7 (41.8-69.7)	55.2 (43.4-67.0)	72.8 (62.2-83.5)	69.3 (56.8-81.8)
Elixhauser	57.8 (36.9-78.7)	62.0 (48.1-76.0)	67.1 (60.6-82.3)	71.4 (60.6-82.3)	68.9 (55.4-82.3)
TMPM	95.2 (89.0-101.3)	88.9 (81.3-96.4)	80.1 (69.5-90.8)	57.1 (40.6-73.6)	51.7 (34.3-69.1)
TRISS	96.6 (91.5-101.6)	91.1 (85.1-97.0)	86.2 (77.6-94.7)	66.5 (53.7-79.3)	63.1 (47.3-78.8)
RTS	98.0 (96.1-99.9)	81.4 (67.0-95.8)	80.4 (68.6-92.3)	66.4 (53.6-79.2)	65.0 (50.7-79.3)
Long-term Mortality 90- to 365-days					
	120 days	**150 days**	**180 days**	**270 days**	**365 days**
Ours	75.6 (69.1-82.1)	76.3 (71.6-80.9)	74.4 (70.3-78.5)	72.1 (68.7-75.5)	72.5 (69.7-75.4)
Charlson	65.7 (58.6-72.9)	65.9 (60.6-71.2)	67.4 (63.0-71.8)	65.6 (62.1-69.0)	64.4 (61.5-67.4)
Elixhauser	70.6 (63.5-77.8)	70.5 (65.3-75.6)	71.0 (66.6-75.4)	69.8 (66.3-73.2)	69.4 (66.5-72.3)
TMPM	57.9 (50.7-65.1)	50.5 (45.1-55.8)	51.2 (46.3-53.7)	50.0 (46.3-53.7)	49.5 (46.4-52.6)
TRISS	57.0 (49.5-64.4)	49.1 (44.2-55.7)	52.2 (47.2-57.1)	51.0 (47.2-54.8)	50.7 (47.4-53.9)
RTS	52.9 (48.6-57.1)	52.7 (49.6-55.7)	53.0 (50.1-55.9)	53.7 (51.5-55.8)	53.3 (51.5-55.1)

In Validation Set among ALL 2013 Trauma Patients with HLOS >= 6 hours

In-hospital death vs. discharge to Care Facility time frames are measured from admission.

Long-term Mortality 90- to 365-days time frames are measured from discharge and were performed among all survivors beyond 90 days of the primary dataset.

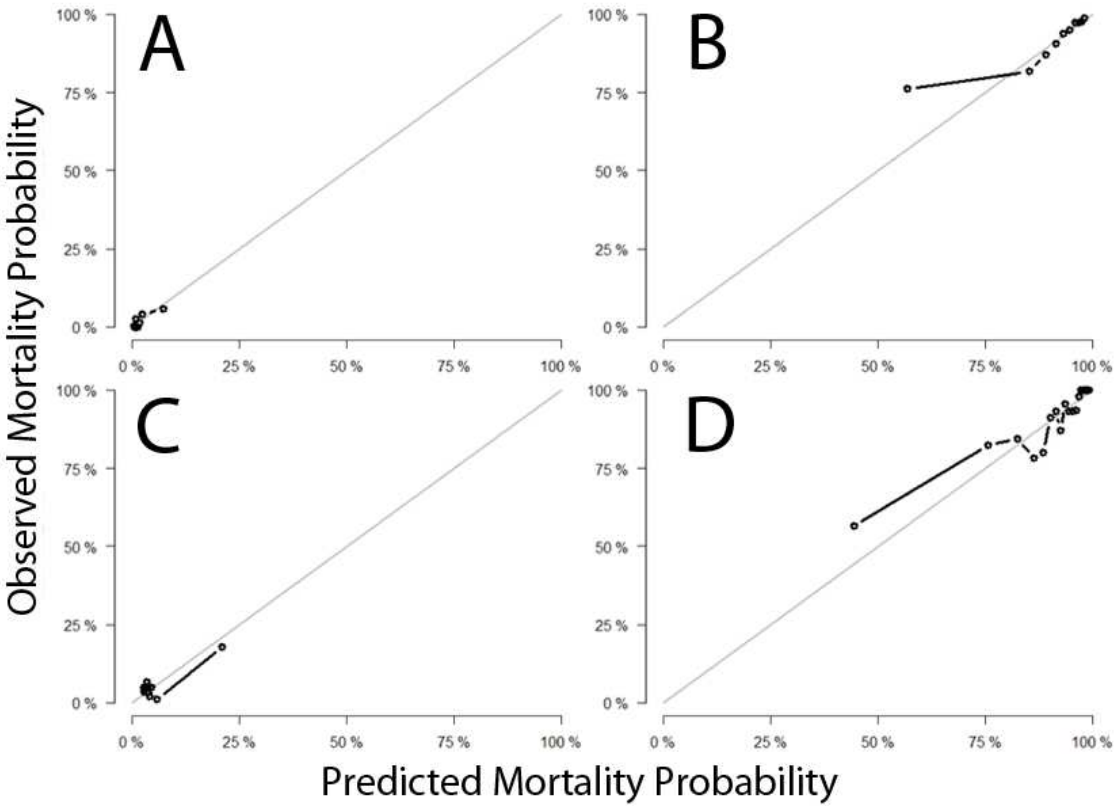

Figure 4.2. Calibration Plots of Our Model by Outcome and Set

A. In-hospital death versus discharge to care facility in the test set

B. For 90-day to 1-year post-discharge mortality among survivors in the primary set

C. For in-hospital death versus discharge to care facility in the validation set

D. For all trauma-related death in the test set

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CHAPTER 5.

Overall Conclusions and Discussion

Delivery of efficient and effective care to the growing proportion of minimally injured older patients, combined with increases in prevalence of chronic conditions, is a unique problem for trauma systems. The present dissertation revealed increasing trends in the admission of older traumatically injured patients admitted to a single trauma center. In addition, the temporal relationship between injury and chronic disease risk factors for mortality was further elucidated by through the examination of mortality occurring during the hospital stay and after discharge. While injury severity was a factor associated with death during the early in one's hospital stay, the magnitude of risk gradually reduced with time. In contrast, the associations between mortality and cardiac conditions, neurological disorders, hemophilia, liver dysfunction, cancers, and renal dysfunction increased in strength in later time intervals of the hospital stay and persisted after discharge. Results from this research help clarify the role of chronic conditions on indicators of quality in traumatically injured older patients.

The first developed recommendations for elderly trauma care originated with the paper entitled, "Management of shock and convalescence in the elderly and infirm" presented at the American Academy for Surgery in Trauma national conference 1951.[1] This paper focused on the treatment of shock and normalization of blood volume through improved use of transfusions as the best method of care for the elderly which alludes to mechanisms resulting in acute hemorrhage being the most prevalent in this group. Organ failure, reductions in physiologic reserve, and the development of adverse complications such as venous thromboembolic events were relevant risks in this era, and rectifying the blood volume loss in this patient population was thought to remedy the entire spectrum of patient health.

Revision of care guidelines for the management of older trauma patients has occurred sparsely over the last six decades. It was not until the 1988 national conference where Scalea, *et al* presented results from a study on blunt-injured elderly trauma patients and the excess of mortality in this subpopulation.[2] In this older group, decreased cardiac output and low oxygen

saturation were identified as features related to mortality. New recommendations were made in favor of rapid monitoring and diagnostic testing of older trauma patients to maximize survival. Although not directly addressed at the time, reduced cardiac output is associated with the chronic conditions of myocardial infarction, hypertension, valvular heart disease, congenital heart disease, cardiomyopathy, pulmonary disease, arrhythmias, drug effects, and electrolyte imbalance – all of which were evaluated in the present dissertation and were found to be associated with in-hospital and post-discharge mortality.

In 2001 and 2003 the Eastern Association for Surgery in Trauma developed two iterations of their guidelines for the triage, evaluation, and management of elderly trauma patients. In these publications, triage criteria for older trauma victims has been highlighted as a concern. To improve the criteria, it was suggested that information on chronic conditions be included in the triage protocol for the traumatically injured.[3] Although promising at the time, limitations in the existing body of literature on the topic of chronic conditions and in-hospital outcomes restricted the development of actual modifications to the recommended triage criteria. Furthermore, the authors expressed concern regarding the prognostic value of chronic conditions on clinical outcomes versus that of age alone. In this report, the most-cited paper associating chronic disease to mortality utilized aggregate Charlson Comorbidity Index scores rather than individual conditions, and utilized only administrative data which lacked the sensitivity of trauma registries.[4,5] A 2012 update to the Eastern Association for Surgery in Trauma triage guidelines eventually included a clause for pre-existing diseases but failed to identify specific conditions.[6] A more recent study by Ichwan, *et al* sought to examine the sensitivity of the Ohio state triage criteria for identifying geriatric trauma patients.[7] These researchers found that the standard criteria is insufficient for older adults over the age of 70 years, and offered new geriatric-specific criteria. However, this new criteria incorporated only measures of anatomic and physiologic injury, and apparently ignored chronic conditions entirely.

The overall low in-hospital mortality rate in this population was initially presumed to be offset by discharge prior to death. With reference to Chapter 2 and Chapter 4, analyses on mortality utilized the Fine and Gray proportional hazards model which accounted for competing-risk events that could not be censored in standard fashion.[8] These competing events are defined as events that impede or modify the occurrence of the primary outcome. Chapter 2 evaluated in-hospital mortality risk with discharge to a care facility (defined as discharge to a skilled nursing facility, hospice service, acute care facility, rehabilitation center, or behavioral health unit) as a competing event, which was selected due to previous studies which identified an increased risk for death among patients discharged to these locations.[9–11] It was not until the analyses in Chapter 3 were competed that the assumed association between discharge to care centers and mortality was substantiated with our own results. For Chapter 4, development of our chronic disease-based predictive model incorporated death occurring within 90-days of discharge to complement in-hospital mortality. Application of this model fared well in testing and validation phases which also used competing risks regression. Results from this dissertation demonstrate the utility of competing risks regression that is relevant for traumatically injured older patients.

The aging of the trauma population, increasing prevalence of diseases, and discovery of technologies employed to for trauma care have drastically changed over the last 60 years. Although life expectancy and overall risk for trauma-related mortality has improved among older patients, the identification of risk and management of care has not been thoroughly revised. The present dissertation showed that several chronic conditions may be used to better classify older patients by risk for death or extended length of stay.

This dissertation has several limitations that must be acknowledged. First, this research used a hospital-based as the basis of the historical cohort study design which is not suitable for rare conditions. Although prevalent chronic disease information from the registry was supplemented by administrative data, some conditions that were of low prevalence among

traumatically injured populations may not have been sufficiently evaluated. In addition, the study of chronic diseases on survival after trauma is subject to survival bias as people who do not survive long enough and expire due to their injuries will likely not have their chronic conditions recorded. Similarly, patients that leave against medical advice before diagnostics are performed, although few, may not have their chronic diseases recorded. Sensitivity analyses performed during assessment of data quality showed a potential for the underreporting of conditions among those with a HLOS less than six hours compared to the inverse. To address this, all three studies excluded patients with a HLOS less than six hours. Third, surveillance bias may sparsely exist throughout the registry as patients who are older will likely be screened for chronic diseases due to the trauma triage criteria, whereas patients who are younger or more injured will have their injuries focused upon. The present dissertation restricted its study population to those aged 55 and older with specific reference to the existing trauma triage criteria. Furthermore, as 98% of the blunt-injured study population had high probability of survival, differential surveillance of chronic conditions due to age is not likely. Fourth, the results from this dissertation may only be generalizable the San Diego trauma population, and still may be restricted to those residing in the Scripps Mercy Hospital catchment area. Future studies must be performed to further validate these results.

Specific efforts must be made to properly classify the risk for death in older trauma patients. Although our developed chronic disease-based prognostic model performed comparably to other existing chronic disease metrics at predicting in-hospital mortality, the low mortality rate at this single trauma center may affect reproducibility of the findings in other centers. Future efforts will be devoted towards the development of a metric to predict 90-day post-discharge mortality only to be applied to trauma populations at centers where post-discharge mortality data is not readily available. Such a metric could be used by care providers to inform next-of-kin or healthcare providers at centers of discharge of the potential mortality risk for the recovering

patient. Moreover, inclusion of a measure for disease severity may improve the prediction of our metric. Inversely, future research on this population may be performed on discharge to a care facility as the primary event of interest, with a competing event of in-hospital death. Such an analysis would identify a different set of risk factors related to being discharged at a lower functional capacity versus discharge to home under the framework that patients who died in-hospital could have been sent to a care facility if they had survived longer. There has only been one paper published on this topic and was performed in a non-trauma patient population.[12] Finally, a prospective cohort study addressing the prospective association on chronic conditions and injury itself may better elucidate the spectrum of risk attributable to chronic conditions in a traumatically injured population. While other counties throughout the nation may experience difficulty implementing such a study, San Diego's regionalized trauma system with specific catchment areas provides a unique potential for a community-based prospective study on the interplay between chronic disease, aging, and traumatic injury.

In conclusion, care for the traumatically injured older population must incorporate the spectrum of a patient's health beyond the injury itself. Existing methods for the measurement of trauma care quality must be reevaluated to reflect changes in the American trauma population and the growing propensity for early death after discharge. The present dissertation has estimated the associated risk from chronic conditions for death at multiple time intervals following traumatic injury which may be used to change care guidelines to improve outcomes. These studies seek to raise awareness of the current state of the older trauma population and attempt to educate healthcare practitioners of the need to change perspectives towards the delivery of high quality trauma care.

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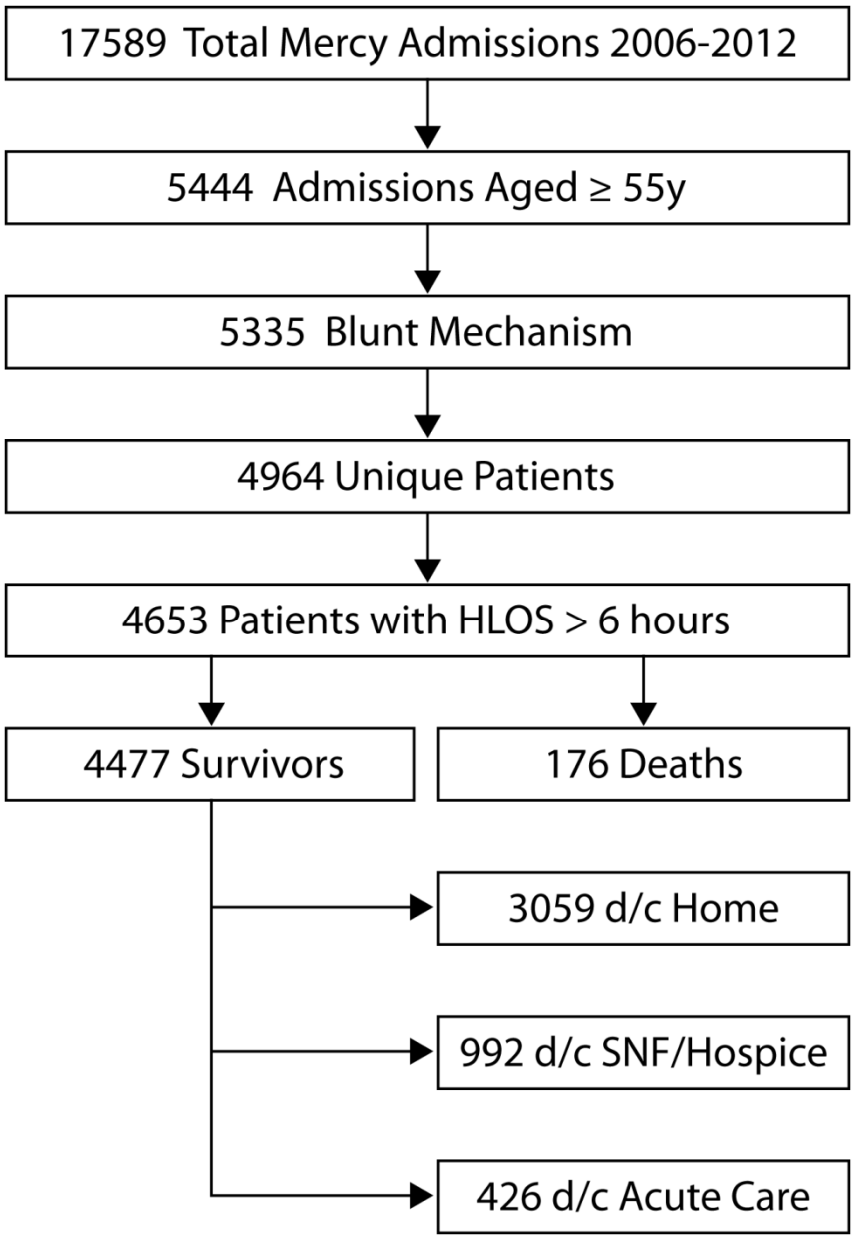
APPENDICES

Appendix 1. Trauma Registry Conditions and Coding Definitions (Chapters 2, 3, and 4)

	Registry Code	**ICD-9-CM Code**
Cardiac Diseases	Prefix = "A"	
History of Cardiac Surgery	Suffix = "01"	429.4, 997.1, 668.1, 996.61
Coronary Artery Disease	Suffix = "02"	414.xx, 747.3, 414.8
Congestive Heart Failure	Suffix = "03"	428
Pulmonary Heart Disease	Suffix = "04"	415.0, 416.9
Myocardial Infarction	Suffix = "05"	412, 411.81, 429.7, 410.x, 414.2
Hypertension	Suffix = "06"	401, 402, 404, 997.91, 459.30, 459.3
Congenital Cardiac Disease	Suffix = "07"	427.9, 746.85-746.89
Diabetes Mellitus	Prefix = "B"	
Insulin Dependent (Type 1)	Suffix = "01"	250.01, 250.03, 250.11, 250.13, 250.21, 250.23, 250.31, 250.33, 250.41, 250.43, 250.51, 250.53, 250.61, 250.63, 250.71, 250.73, 250.81, 250.83, 250.91, 250.93
Non-Insulin Dependent (Type 2)	Suffix = "02"	249.x, 250.00, 250.02, 250.10, 250.12, 250.20, 250.22, 250.30, 250.32. 250.40, 250.42, 250.50, 250.52, 250.60, 250.62, 250.70, 250.72, 250.80, 250.82, 250.90, 250.92, 648.0
Gastric Issues	Prefix = "C"	
Peptic Ulcer Disease	Suffix = "01"	531.7, 531.9, 532.7, 532.9, 533.7, 533.9, 534.7, 534.9
Gastric/Esophageal Varices	Suffix = "02"	456.0, 456.1, 437.89
Pancreatitis	Suffix = "03"	577.0, 577.1
Irritable Bowel Disease	Suffix = "04"	564.1
Hematologic Disorders	Prefix = "D"	
Acquired Coagulopathy	Suffix = "01"	288-289, 283.x, 286.7
Warfarin Therapy (i.e. Coumadin)	Suffix = "02"	V58.61, V58.83, 453.40
Hemophilia	Suffix = "03"	286.0-286.6
Pre-existing Anemia	Suffix = "04"	280.x-285, 678.x
Psychiatric Disorders	Prefix = "E"	
History of Psychiatric Disorders	Suffix = "00"	293.84, 294.x, 295, 296
Attention Deficit Disorders	Suffix = "01"	314.x
Mental Retardation	Suffix = "02"	315.x, 317-319
Immunosuppression	Prefix = "F"	
HIV/AIDS	Suffix = "01"	042
Routine Steroid Therapy	Suffix = "02"	V58.65
Transplants	Suffix = "03"	996.81, 279.3, 279.8, V87.46
Active Chemotherapy	Suffix = "04"	V58.1x, 285.3
Liver Diseases, including Cirrhosis	Prefix = "G"	070, 456.0, 456.1, 456.2, 570, 571, 572.2, 572.3, 572.4, 572.8, 573.3, 573.4, 573.8, 573.9, V42.7, 200-203.0, 238.6
Cancers	Prefix = "H"	200-203.0, 238.6, 196-199, 140-195
Autoimmune Disorders	Prefix = "I"	
Rheumatoid Arthritis	Suffix = "01"	714.0
Systemic Lupus Erythematosus	Suffix = "02"	373.34, 695.4, 710.0
Neurologic	Prefix = "J"	
Spinal Cord Injury	Suffix = "01"	952.xx
Multiple Sclerosis	Suffix = "02"	340

Appendix 1 – Continued

	Registry Code	ICD-9-CM Code
Alzheimer's Disease	Suffix = "03"	331.0
Seizures	Suffix = "04"	345.x
Chronic Demyelinating Disease	Suffix = "05"	341.x
Chronic Dementia	Suffix = "06"	290.x, 294.1x-294.2x
Organic Brain Syndrome	Suffix = "07"	294.0
Parkinson's Disease	Suffix = "08"	332.x
Cerebrovascular Accident (Stroke)	Suffix = "09"	433.x, 434.x, 436.x, V12.54
Obesity	Prefix = "K"	278.0
Pulmonary Disease	Prefix = "L"	
Prior History with Active Treatment	Suffix = "01"	V58.65
Asthma	Suffix = "02"	493.x
Chronic Obstructive Pulmonary Disease	Suffix = "03"	490-492.x, 466.0, 496
Renal Disorders	Prefix = "M"	
Chronic and Acute Kidney Disorders	Suffix = "01"	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 585, 586, 588.0, V42.0, V45.1, V56, 584.5-9, 593.9, 583.6
Non-transplant Dialysis	Suffix = "02"	V45.11, V56, 996.73, 996.56, E879.1, E870.2, E871.2, E872.2, E874.2, 792.5
Substance Abuse	Prefix = "N"	
Chronic Ongoing Drug Abuse	Suffix = "01"	292.x, 304.x, 305.x
Chronic Ongoing Alcohol Abuse	Suffix = "02"	291.x, 303.x



Appendix 2. Patient Flow Diagram (Chapter 2)

D/C, Discharge

Appendix 3. Full Cox and Fine & Gray results for mortality by chronic condition among patients with a TMPM probability of death less than 50% (Chapter 2)

	Cox		Fine & Gray			
Chronic Condition	**HR**	**P**	**sHR**	**LCI**	**UCI**	**P**
Trauma Registry Conditions						
History of Cardiac Surgery	2.25	0.001	2.10	1.22	3.61	0.007
CAD	1.87	0.001	1.98	1.35	2.92	0.001
CHF	2.37	<0.001	2.80	1.89	4.15	<0.001
Myocardial Infarction	1.84	0.010	2.10	1.26	3.48	0.004
Hypertension	0.82	0.312	0.79	0.53	1.16	0.230
Type 1 Diabetes	1.60	0.203	1.79	0.87	3.66	0.114
Type 2 Diabetes	1.00	0.995	0.82	0.52	1.30	0.405
Warfarin Therapy	1.41	0.117	1.37	0.88	2.12	0.163
Hemophilia	3.33	<0.001	5.76	2.98	11.12	<0.001
Pre-existing Anemia	1.19	0.489	1.23	0.75	2.01	0.411
Spinal Cord Injury	0.65	0.671	0.73	0.10	5.37	0.753
Alzheimer's Disease	1.81	0.067	1.44	0.76	2.73	0.265
Seizures	1.30	0.566	1.11	0.444	2.82	0.826
Chronic Dementia	0.78	0.418	0.67	0.37	1.20	0.176
Parkinson's Disease	0.71	0.736	0.49	0.07	3.52	0.481
CVA/Stroke	1.53	0.072	1.44	0.89	2.34	0.139
History of Psychiatric disorders	0.86	0.515	0.80	0.50	1.29	0.362
Asthma	1.34	0.520	1.46	0.60	3.54	0.408
COPD	1.43	0.145	1.69	1.04	2.73	0.033
Chronic Ongoing Drug Abuse	0.96	0.911	0.85	0.42	1.73	0.663
Chronic Ongoing Alcohol Abuse	0.71	0.431	0.81	0.34	1.92	0.631
Elixhauser Comorbidities						
Cardiac Arrythmia	1.15	0.477	1.22	0.82	1.81	0.322
Coagulopathy	2.53	0.001	3.05	1.68	5.56	<0.001
Chronic Pulmonary Disease	1.43	0.169	1.47	0.88	2.45	0.143
Depression	0.62	0.305	0.70	0.29	1.70	0.435
Fluid and Electrolyte Disorders	1.71	0.006	2.09	1.42	3.07	<0.001
Hyperthyroidism	0.77	0.489	0.58	0.28	1.22	0.153
Liver Disease	4.38	<0.001	4.43	2.25	8.72	<0.001
Lymphoma	1.03	0.973	1.24	0.18	8.31	0.826
Metastatic Cancer	1.96	0.143	2.06	0.75	5.69	0.163
Obesity	-	-	-	-	-	-
Neurodegenerative Disorders	1.51	0.067	1.49	0.92	2.41	0.104
Paralysis	0.92	0.828	0.90	0.35	2.27	0.816
Pulmonary Circulation Disorders	1.19	0.679	1.30	0.53	3.19	0.571
Peripheral Vascular Disorders	2.76	0.002	2.18	1.07	4.43	0.031
Renal Failure	0.92	0.782	0.94	0.49	1.79	0.851
Solid Tumor without Metastasis	1.54	0.273	1.54	0.65	3.68	0.327
Valvular Disease	0.75	0.494	0.74	0.32	1.73	0.488
Weight Loss	0.55	0.403	0.98	0.25	3.83	0.975
Deficiency Anemia	-	-	-	-	-	-

CAD, Coronary Artery Disease; CHF, Congestive Heart Failure; CVA, Cerebrovascular Accident; COPD, Chronic Obstructive Pulmonary Disease; LCI, Lower Confidence Interval Bound; HR, Hazard Ratio; sHR, Sub-hazard Ratio; UCI, Upper Confidence Interval Bound

Appendix 4. Full Cox and Fine & Gray results for mortality by chronic condition among patients with a TMPM probability of death greater than 50% (Chapter 2)

	Cox		Fine & Gray			
Chronic Condition	**HR**	**P**	**sHR**	**LCI**	**UCI**	**P**
Trauma Registry Conditions						
History of Cardiac Surgery	0.88	0.73	0.896	0.451	1.778	0.753
CAD	1.61	0.07	1.750	1.061	2.885	0.028
CHF	0.61	0.23	0.604	0.274	1.332	0.211
Myocardial Infarction	0.89	0.78	0.907	0.399	2.062	0.816
Hypertension	1.84	0.03	1.846	1.092	3.120	0.022
Type 1 Diabetes	0.77	0.65	0.643	0.252	1.641	0.356
Type 2 Diabetes	1.18	0.56	1.083	0.648	1.810	0.762
Warfarin Therapy	0.89	0.73	0.836	0.459	1.523	0.558
Hemophilia	0.40	0.37	0.44	0.29	0.67	<0.001
Pre-existing Anemia	1.36	0.56	1.158	0.467	2.873	0.751
Spinal Cord Injury	0.61	0.64	0.649	0.211	2.001	0.452
Alzheimer's Disease	0.80	0.72	0.896	0.296	2.711	0.847
Seizures	1.49	0.40	1.277	0.492	3.315	0.616
Chronic Dementia	0.88	0.80	0.808	0.309	2.111	0.663
Parkinson's Disease	5.38	0.03	6.220	2.706	14.297	<0.001
CVA/Stroke	1.11	0.76	1.204	0.681	2.129	0.524
History of Psychiatric disorders	1.14	0.72	1.049	0.463	2.377	0.909
Asthma	2.77	0.16	2.78	1.69	4.55	<0.001
COPD	0.73	0.47	0.80	0.38	1.68	0.566
Chronic Ongoing Drug Abuse	1.20	0.63	1.233	0.584	2.601	0.583
Chronic Ongoing Alcohol Abuse	0.73	0.48	0.861	0.418	1.773	0.684
Elixhauser Comorbidities						
Cardiac Arrythmia	0.67	0.16	0.711	0.419	1.207	0.206
Coagulopathy	0.64	0.43	0.676	0.321	1.425	0.304
Chronic Pulmonary Disease	0.80	0.58	0.866	0.443	1.693	0.674
Depression	3.92	0.03	4.021	1.574	10.270	0.004
Fluid and Electrolyte Disorders	0.84	0.56	0.832	0.483	1.434	0.508
Hyperthyroidism	1.50	0.42	1.229	0.502	3.005	0.652
Liver Disease	1.07	0.91	1.073	0.469	2.454	0.868
Lymphoma	3.62	0.21	3.872	2.385	6.286	<0.001
Metastatic Cancer	1.17	0.88	1.242	0.868	1.777	0.236
Obesity	0.72	0.75	0.713	0.227	2.240	0.563
Neurodegenerative Disorders	0.88	0.64	0.900	0.553	1.465	0.671
Paralysis	1.00	1.00	1.065	0.386	2.935	0.903
Pulmonary Circulation Disorders	0.32	0.270	0.333	0.144	0.766	0.010
Peripheral Vascular Disorders	0.94	0.934	0.842	0.134	5.281	0.855
Renal Failure	0.52	0.206	0.589	0.219	1.588	0.296
Solid Tumor without Metastasis	3.84	0.192	3.672	2.308	5.843	0.001
Valvular Disease	0.62	0.445	0.585	0.236	1.452	0.248
Weight Loss	3.37	0.251	4.038	2.074	7.860	0.001
Deficiency Anemia	2.79	0.315	2.659	1.774	3.985	0.001

CAD, Coronary Artery Disease; CHF, Congestive Heart Failure; CVA, Cerebrovascular Accident; COPD, Chronic Obstructive Pulmonary Disease; LCI, Lower Confidence Interval Bound; HR, Hazard Ratio; sHR, Sub-hazard Ratio; UCI, Upper Confidence Interval Bound

Appendix 5. Full Linear Mixed Modeling Results for log-transformed hospital length of stay in the full sample (Chapter 2)

	Full Sample		
Definition	**β**	**SE**	**p**
Trauma Registry Conditions			
history of cardiac surgery	0.023	0.105	0.666
CAD	0.106	0.033	0.001
CHF	0.315	0.042	<0.001
Myocardial Infarction	0.211	0.051	<0.001
Hypertension	0.072	0.030	0.016
Type 1 Diabetes	0.252	0.073	0.001
Type 2 Diabetes	0.068	0.032	0.035
Warfarin Therapy	-0.133	0.036	<0.001
Hemophilia	0.949	0.146	<0.001
Pre-existing Anemia	0.552	0.048	<0.001
Spinal Cord Injury	0.799	0.209	<0.001
Alzheimer's Disease	-0.018	0.071	0.796
Seizures	0.092	0.065	0.155
Chronic Dementia	0.031	0.051	0.536
Parkinson's Disease	0.043	0.104	0.678
CVA/Stroke	0.093	0.045	0.037
History of Psychiatric disorders	0.182	0.036	<0.001
Asthma	0.175	0.074	0.017
COPD	0.283	0.047	<0.001
Chronic Drug Abuse	-0.172	0.037	<0.001
Chronic Alcohol Abuse	-0.125	0.044	0.004
Elixhauser Comorbidities			
Cardiac Arrhythmia	0.121	0.033	<0.001
Coagulopathy	0.731	0.086	<0.001
Chronic Pulmonary Disease	0.191	0.045	<0.001
Deficiency Anemia	0.491	0.146	0.001
Depression	0.136	0.058	0.018
Fluid and Electrolyte Disorders	0.580	0.039	<0.001
Hyperthyroidism	-0.025	0.047	0.596
Liver Disease	0.280	0.080	<0.001
Lymphoma	0.526	0.175	0.003
Metastatic Cancer	0.272	0.123	0.027
Obesity	0.316	0.106	0.003
Neurodegenerative Disorders	0.340	0.047	<0.001
Paralysis	0.714	0.112	<0.001
Pulmonary Circulation Disorders	0.757	0.097	<0.001
Peripheral Vascular Disorders	0.039	0.076	0.606
Renal Failure	0.313	0.052	<0.001
Solid Tumor without Metastasis	0.149	0.094	0.115
Valvular Disease	0.235	0.064	<0.001
Weight Loss	0.699	0.143	<0.001

CAD, Coronary Artery Disease; CHF, Congestive Heart Failure; CVA, Cerebrovascular Accident; COPD, Chronic Obstructive Pulmonary Disease; SE, Standard Error

Appendix 6. Full Linear Mixed Modeling Results for log-transformed hospital length of stay by chronic condition stratified by outcome category (Chapter 2)

	Discharged to Care			Survivors to Home			In-Hospital Death		
Definition	**β**	**SE**	**p**	**β**	**SE**	**p**	**β**	**SE**	**p**
Trauma Registry Conditions									
History of Cardiac Surgery	-0.107	0.091	0.239	0.150	0.063	0.017	-0.246	0.239	0.303
CAD	0.089	0.053	0.096	0.116	0.038	0.002	0.046	0.179	0.796
CHF	0.137	0.061	0.023	0.257	0.056	<0.001	0.177	0.213	0.405
Myocardial Infarction	0.139	0.082	0.092	0.228	0.061	<0.001	-0.242	0.237	0.305
Hypertension	-0.027	0.052	0.602	0.081	0.033	0.015	0.094	0.192	0.622
Type 1 Diabetes	0.130	0.113	0.251	0.193	0.088	0.028	-0.193	0.379	0.610
Type 2 Diabetes	-0.064	0.053	0.233	0.086	0.037	0.019	0.046	0.201	0.818
Warfarin Therapy	-0.099	0.056	0.081	-0.196	0.042	<0.001	-0.201	0.209	0.335
Hemophilia	0.509	0.200	0.011	0.890	0.240	<0.001	0.823	0.378	0.029
Pre-existing Anemia	0.289	0.067	<0.001	0.562	0.062	<0.001	0.262	0.267	0.326
Spinal Cord Injury	0.221	0.249	0.374	0.963	0.354	0.007	1.585	0.825	0.055
Alzheimer's Disease	-0.204	0.093	0.029	0.022	0.096	0.821	0.210	0.343	0.541
Seizures	-0.262	0.106	0.013	0.126	0.075	0.091	-0.103	0.377	0.786
Chronic Dementia	-0.199	0.067	0.003	0.025	0.070	0.724	0.560	0.301	0.062
Parkinson's Disease	-0.094	0.140	0.503	0.076	0.135	0.575	-0.931	0.832	0.263
CVA/Stroke	0.067	0.067	0.316	-0.001	0.055	0.990	0.024	0.227	0.915
History of Psychiatric Disorders	-0.109	0.054	0.042	0.175	0.044	<0.001	0.474	0.232	0.041
Asthma	0.099	0.137	0.475	0.217	0.079	0.006	0.265	0.447	0.553
COPD	0.108	0.070	0.122	0.212	0.059	<0.001	0.517	0.249	0.038
Chronic Drug Abuse	-0.054	0.075	0.471	-0.153	0.039	<0.001	0.306	0.296	0.302
Chronic Alcohol Abuse	0.267	0.093	0.004	-0.213	0.045	<0.001	0.663	0.354	0.061
Elixhauser Comorbidities									
Cardiac Arrhythmia	0.058	0.051	0.255	0.085	0.040	0.032	-0.147	0.196	0.454
Coagulopathy	0.283	0.125	0.024	0.820	0.119	<0.001	0.673	0.283	0.017
Chronic Pulmonary Disease	0.030	0.070	0.669	0.184	0.052	<0.001	0.311	0.258	0.227
Deficiency Anemia	0.288	0.211	0.171	0.529	0.178	0.003	0.180	1.161	0.877
Depression	-0.030	0.094	0.749	0.155	0.066	0.018	0.163	0.418	0.696
Fluid and Electrolyte Disorders	0.398	0.057	<0.001	0.530	0.050	<0.001	0.203	0.194	0.297
Hyperthyroidism	-0.152	0.072	0.033	0.022	0.056	0.700	-0.562	0.342	0.100
Liver Disease	-0.056	0.135	0.678	0.237	0.094	0.012	0.701	0.356	0.049
Lymphoma	0.132	0.258	0.608	0.672	0.217	0.002	-0.167	0.830	0.841
Metastatic Cancer	0.106	0.173	0.539	0.134	0.165	0.414	0.114	0.494	0.818
Obesity	0.296	0.159	0.063	0.182	0.125	0.145	0.365	1.166	0.754
Neurodegenerative Disorders	0.115	0.068	0.090	0.250	0.062	<0.001	0.177	0.197	0.370
Paralysis	0.416	0.135	0.002	0.698	0.200	<0.001	-0.226	0.411	0.582
Pulmonary Circulation Disorders	0.446	0.131	0.001	0.895	0.133	<0.001	0.325	0.450	0.470
Peripheral Vascular Disorders	-0.084	0.115	0.464	0.113	0.092	0.220	-0.721	0.359	0.044
Renal Failure	0.003	0.074	0.971	0.399	0.066	<0.001	-0.109	0.309	0.724
Solid Tumor without Metastasis	0.012	0.148	0.934	0.204	0.113	0.071	-0.206	0.420	0.623
Valvular Disease	0.216	0.090	0.016	0.150	0.081	0.065	-0.292	0.401	0.467
Weight Loss	0.508	0.179	0.005	0.610	0.211	0.004	0.640	0.677	0.344

CAD, Coronary Artery Disease; CHF, Congestive Heart Failure; CVA, Cerebrovascular Accident; COPD, Chronic Obstructive Pulmonary Disease; SE, Standard Error

Appendix 7. Full listing of the Age-adjusted Hazard Ratios for Chronic Conditions by Post-discharge Time Intervals (Chapter 3)

	30 day mortality		30-90 day mortality		90 day-2 year mortality		2 year Cumulative
Variable	**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**	**HR**
Trauma Registry Conditions							
History of Cardiac Surgery	1.30	0.79-2.16	1.45	0.89-2.38	1.34	1.03-1.75	1.30
CAD	1.45	1.05-2.01	1.54	1.12-2.13	1.54	1.31-1.82	1.45
CHF	1.94	1.37-2.76	2.06	1.44-2.93	2.77	2.32-3.30	N/A
Pulmonary Heart Disease	2.85	0.40-20.4	-	-	4.71	2.11-10.52	N/A
Myocardial Infarction	1.28	0.77-2.12	1.90	1.22-2.96	1.53	1.19-1.96	1.47
Hypertension	0.84	0.60-1.16	0.98	0.70-1.37	0.95	0.81-1.13	NS
Congenital Cardiac Disease	-	-	1.56	0.22-11.21	0.41	0.06-2.88	NS
Warfarin Therapy	1.25	0.89-1.75	1.43	1.02-2.00	1.43	1.20-1.71	1.33
Hemophilia	1.88	0.88-4.01	4.00	2.27-7.06	1.77	1.14-2.73	1.89
Pre-existing Anemia	1.74	1.15-2.61	1.91	1.27-2.86	1.83	1.48-2.27	1.76
History of Psychiatric Disorders	1.33	0.94-1.88	1.61	1.14-2.26	1.70	1.43-2.02	1.59
Attention Deficit Disorder	-	-	-	-	3.10	0.43-22.08	1.54
Spinal Cord Injury	-	-	-	-	1.29	0.41-4.00	N/A
Multiple Sclerosis	-	-	-	-	1.27	0.18-9.05	NS
Alzheimer's Disease	1.48	0.88-2.49	1.73	1.04-2.89	1.81	1.38-2.39	1.77
Seizures	1.39	0.68-2.83	1.03	0.46-2.34	1.19	0.82-1.72	1.30
Chronic Dementia	1.81	1.24-2.63	1.53	1.02-2.27	1.82	1.48-2.24	1.75
Parkinson's Disease	1.25	0.51-3.06	1.30	0.53-3.17	2.37	1.64-3.43	N/A
CVA/Stroke	1.42	0.95-2.11	1.18	0.77-1.81	1.18	0.95-1.48	1.22
Asthma	0.69	0.26-1.87	0.33	0.08-1.35	1.02	0.68-1.52	NS
COPD	1.95	1.30-2.91	1.49	0.95-2.34	1.96	1.58-2.42	1.86
Chronic Drug Abuse	0.93	0.55-1.58	0.70	0.39-1.24	1.19	0.94-1.49	N/A
Chronic Alcohol Abuse	1.01	0.53-1.91	0.86	0.44-1.67	1.60	1.25-2.07	N/A
Type 1 Diabetes	2.50	1.38-4.50	1.25	0.55-2.83	1.43	0.98-2.10	1.62
Type 2 Diabetes	1.14	0.80-1.61	1.15	0.81-1.64	1.24	1.04-1.48	1.20
Elixhauser Comorbidities							
Cardiac Arrythmia	1.34	0.97-1.85	1.58	1.14-2.18	1.69	1.43-1.99	1.48
Chronic Pulmonary Diseases	1.42	0.93-2.18	1.21	0.76-1.91	1.59	1.28-1.96	1.49
Coagulopathy	2.15	1.05-4.37	4.08	2.31-7.20	1.56	0.99-2.46	1.89
Depression	0.69	0.30-1.56	0.80	0.37-1.70	1.13	0.82-1.56	NS
Fluid & Electrolyte Disorders	2.47	1.76-3.47	1.68	1.16-2.46	1.39	1.14-1.71	N/A
HIV/AIDS	7.57	1.04-55.0	8.35	1.15-60.5	1.92	0.27-13.7	3.90
Hyperthyroidism	0.83	0.51-1.36	0.53	0.30-0.96	1.10	0.88-1.39	NS
Liver Disease	0.73	0.18-2.98	3.13	1.52-6.46	2.95	2.04-4.26	N/A
Lymphoma	1.94	0.48-7.84	6.85	3.03-15.5	2.78	1.39-5.59	3.16
Metastatic Cancer	10.91	6.50-18.3	9.85	5.18-18.7	4.49	2.59-7.78	N/A
Neurodegenerative Diseases	3.70	2.59-5.29	2.42	1.59-3.66	1.58	1.24-2.02	N/A
Obesity	0.50	0.07-3.56	0.96	0.24-3.91	0.72	0.34-1.52	NS
Paralysis	5.28	2.86-9.75	1.00	0.25-4.05	2.36	1.44-3.89	N/A
Peptic Ulcer Disease	-	-	-	-	2.64	0.85-8.22	NS
Peripheral Vascular Disease	1.85	1.03-3.33	0.94	0.41-2.12	1.64	1.18-2.29	1.46
Psychoses	0.52	0.07-3.70	1.02	0.25-4.14	2.30	1.44-3.69	N/A

Appendix 7 – Continued

	30d mortality		30-90d mortality		90d-2yr mortality		2yr Cumulative
Variable	**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**	**HR**
Pulmonary Circulation Disorder	2.72	1.50-4.91	1.71	0.80-3.67	1.80	1.21-2.69	1.90
Renal Failure	1.83	1.21-2.78	2.26	1.51-3.38	2.11	1.70-2.63	2.03
Rheumatoid Arthritis	0.65	0.16-2.61	0.32	0.04-2.26	1.15	0.68-1.95	NS
Severe Weight Loss	4.31	2.02-9.21	6.13	3.01-12.5	2.63	1.36-5.09	3.17
Solid Tumors	5.34	3.23-8.83	6.27	3.79-10.4	2.48	1.64-3.77	N/A
Valvular Disease	1.27	0.72-2.24	1.34	0.76-2.37	1.45	1.09-1.93	1.48

CAD, Coronary Artery Disease; CHF, Congestive Heart Failure; CI, Confidence Interval; CVA, Cerebrovascular Accident; COPD, Chronic Obstructive Pulmonary Disease; HR, Hazard Ratio; NS, Not Significant

N/A denotes variables that violated the proportional hazards assumption and therefore are not eligible for a 2-year cumulative HR estimate

Appendix 8. Iteration Significance Counts of Chronic Conditions by Model Development Stage (Chapter 4)

Name	Stage 1.0	Stage 2.0	Stage 2.1	Stage 2.2	Stage 2.3	Stage 2.4	Stage 2.5	Stage 2.6	Stage 3.1 p	Stage 3.2 p	Stage 3.3 p	Stage 3.4 p
History of Cardiac Surgery	4	0	-									
CAD	4	0	0	0	0	0	0	-				
CHF	4	4	4	4	4	4	4	4				
Myocardial Infarction	4	4	4	4	4	4	4	4				
Hypertension	0	-										
History of Psychatric Disorders	4	0	0	0	-							
Coagulopathy	3	0	0	0	0	-						
Warfarin Therapy	4	1	1	1	1	1	1	1		0.082	0.077	0.081
Hemophilia	4	3	3	3	3	3	4	3				
Pre-existing Anemia	4	2	2	3	2	2	2	2				
Alzheimer's Disease	4	2	2	2	2	2	2	2				
Seizures	0	-										
Dementia	4	4	4	4	4	4	4	4				
Parkinson's Disease	3	0	0	0	1	1	1	1	0.296	-		
CVA/Stroke	4	3	3	3	3	3	3	2				
Chronic Drug Abuse	4	4	4	4	4	4	4	4				
Chronic Alcohol Abuse	4	0	0	0	0	0	0	1	0.162	0.152	-	
Asthma	1	-										
COPD	4	1	1	1	1	1	1	1	0.115	0.116	0.124	-
Type 1 Diabetes	4	0	0	-								
Type 2 Diabetes	0	-										
Liver Dysfunction	2	3	3	3	3	3	2	1				0.058
Cancers	4	4	4	4	4	4	4	4				
Rheumatoid Arthritis	0	-										
Obesity	0	-										
Renal Dysfunction	4	4	4	4	4	4	4	4				
Non-Transplant Dialysis	3	0	0	0	0	0	-					

CAD, Coronary Artery Disease; CHF, Congestive Heart Failure; CVA, Cerebrovascular Accident; COPD, Chronic Obstructive Pulmonary Disease

Stage 1: Iterative Univariate relationships evaluated at $p < 0.100$

Stage 2: Iterative Multivariable relationships evaluated at $p < 0.100$

Stage 3: Complete Training Set Multivariable relationships evaluated at $p < 0.100$