A POPULATION-BASED EVALUATION OF LONG-TERM OUTCOMES FOLLOWING MAJOR BURN INJURY

by

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ABSTRACT

Introduction: Advances in critical care and the regionalization of burn care have resulted in a significant decrease in mortality after burn injury such that most burn-injured patients are expected to survive. This thesis aimed to evaluate and characterize long-term outcomes following major burn injury.

Methods: Using linked health administrative data, we identified adults who sustained major burn injury during 2003-2014. First, we evaluated temporal changes in the incidence and in-hospital mortality of burn injury. We then estimated five-year risk-adjusted rates and principal causes of emergency department visits and readmissions. A self-matched longitudinal cohort study was performed to compare rates of mental illness-related healthcare utilization in the 3 years before and after burn. Finally, a matched cohort study was performed to estimate 5-year mortality after burn.

Results: The incidence of burn injury remained stable over time, and significant reductions in the overall in-hospital mortality rate occurred; the odds of death in 2010-2013 were significantly lower than 2003-2006 (odds ratio (OR) 0.39, 95% CI 0.25-0.61).

In the five years after discharge from the index burn admission, 70% of patients had ≥1 emergency department (ED) visit, and 30% had an unplanned readmission. The principal cause of healthcare utilization was unintentional injury, followed by mental illness and respiratory disease. Patients who received burn center care had significantly lower rates of ED visits (rate ratio 0.64, 95% CI 0.56-0.73) and readmissions (hazard ratio 0.77, 95% CI 0.65-0.92). Burn injury was not associated with a higher rate of mental health visits compared to the pre-injury period (RR 0.97, 95% CI 0.78-1.20), but was associated with a two-fold increase in self-harm (RR 1.95 (95% CI 1.15-3.33). Five-year mortality after burn injury was 11%, compared to 4% among matched controls. The hazard ratio was greatest during the first year after discharge (HR 4.15, 95% CI 3.17-5.42).

Conclusions: Burn injury confers a physical and psychological impact up to five years after discharge, associated with high rates of healthcare utilization and increased late mortality compared to matched controls. Further development of consolidated and focused burn care, and improved mental healthcare, offer an opportunity to improve outcomes after burn injury.

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LIST OF ABBREVIATIONS

ABA – American Burn Association

ASD – Acute Stress Disorder

CCSO – Critical Care Services Ontario

CI – Confidence interval

CIHI – Canadian Institute for Health Information

DAD – Discharge Abstract Database

DSM-IV – Diagnostic and Statistical Manual of Mental Disorders, 4th edition

ED – Emergency department

HR – Hazard ratio

ICD-10CA – International Statistical Classification of Diseases and Related Health Problems, 10th Canadian revision

ICES – Institute for Clinical and Evaluative Sciences

MRR – Mortality rate ratio

NACRS – National Ambulatory Care Reporting System

NBR – National burn repository (American Burn Association)

NIDRR – National Institute on Disability and Rehabilitation Research

OMHRS – Ontario Mental Health Reporting System

ONMARG – Ontario Marginalization Index

OR – Odds ratio

ORGD – Ontario Register General, Death

QALY – Quality-adjusted life year

QOL – Quality of life

PTSD – Post-traumatic stress disorder

RIO – Rurality Index of Ontario

ROC – Receiver operating curve

RPDB – Registered Persons Database

RR – Rate ratio

RUB – Resource Utilization Band of the Johns Hopkins case-mix system

TBSA – Total burned surface area

US – United States

USD – United States dollar

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CHAPTER 1: LITERATURE REVIEW

1.1 History

Modern burn care owes much of its evolution to tragedy. On November 28, 1942, the second-worst building fire in American history erupted at the Cocoanut Grove nightclub in Boston, Massachusetts. Over one thousand people were present in the building; four hundred and ninety-eight died in the fire.

One hundred and seventy patients were brought to two local hospitals. The hospitals, having completed disaster management training the week prior, quickly mobilized their staff and resources to care for the burn victims. Many patients were dead on arrival to the hospital; as emergency room beds filled with dead patients, the physicians quickly recognized the importance of determining on arrival whether or not patients were alive, and if their injuries were potentially survivable.

In caring for those who survived to receive hospital care, the two teams of surgeons at each hospital made observations that furthered our understanding of the pathophysiology of burn injury, and set the stage for many of the first experimental studies of wound dressings, antibiotics, and other aspects of burn care.

For the United States, World War II had begun the year prior, and the military anticipated that the number of burn victims would increase substantially compared to World War I. As a result, dedicated funding for burn research had been bestowed upon a number of surgeons in the United States, including one of the surgeons who led the care of the

Cocoanut Grove fire victims. He had been conducting animal experiments related to burn dressings for 5 months prior to the nightclub fire, and applied the insights gained from these to further experiments on the Cocoanut Grove victims. Ultimately, the knowledge generated from the care of the Cocoanut Grove victims formed the basis for the tenets of modern burn care. Such was the breadth of knowledge gained that Annals of Surgery devoted an entire issue to the reporting of the experiences of the burn teams at the Boston hospitals [1]. The surgeons made several observations which either furthered or stimulated our understanding of burn physiology, resuscitation, wound healing, and the metabolic response to injury.

Among their many achievements, these surgeons identified that fluid loss is directly proportional to burn size, leading to the first burn size-based formula for fluid resuscitation; that burn size can be estimated and documented in a systematic fashion, leading to development of the Lund-Browder chart, still in wide use today; that urine output is the most reliable indicator of resuscitation status; that prophylactic antibiotics are not associated with lower rates of burn wound infections; that petroleum-impregnated gauze dressings result in faster healing times and decreased infection rates than the then-commonly used tannic acid or triple dye approach to wound dressings. Perhaps most notably, the surgeons made the first description and characterization of inhalation injury; their observations have since been confirmed in several contemporary studies: (1) that it is more likely among patients exposed to smoke for prolonged periods; (2) that it is more likely among those with burns of the face and mouth; and, (3) that the presence of inhalation injury potentiates burn shock and increases fluid requirements for resuscitation. Today, inhalation injury remains the leading cause of burn-related mortality; 50% of patients with inhalation injury who survive to reach a burn center will die, compared to 5% of patients without inhalation injury.

While the experiences in Boston in 1942 furthered our understanding of the clinical care of burn-injured patients, it also stimulated developments in burn prevention, public safety legislation, and the organization of burn care. Building fire codes, maximum capacities, and minimum number of exits per number of occupants were all instituted after the Cocoanut Grove fire.

1.2 Epidemiology

A burn is an injury to the skin or other tissue that is caused by thermal or other acute trauma; this injury occurs as a result of the skin or other tissues being damaged by flame or hot liquids/solids. Injuries to the skin that occur as a result of radioactivity, friction, electrical current, or contact with chemical substances are also considered burns.

The World Health Organization estimates that over 265,000 deaths result from fire-related burns every year [2]; over 95% of these deaths occur in low- and middle-income countries [3]. The incidence of burn injury worldwide ranks fourth in terms of injury, and is greater than the incidence of HIV and tuberculosis combined. In North America, 486,000 individuals receive treatment for burn injury each year, of which only approximately 30,000 patients are admitted to burn centers [4,5]. Reported annual incidences of burn injuries requiring hospitalization are similar worldwide; 8.4-12.2 per 100,000 in Canada, 15.6 per 100,000 in Sweden, 23 per 100,000 in the United States, 25.3 per 100,000 in Australia and 2.0-29 per 100,000 in the European Union [6–11]. Several studies have demonstrated that burn incidence decreased significantly between the 1970s and the early part of the 21st century [7,9,11,12]; in the US, burn admissions decreased by almost 50% between 1970 and 1990[6]. However, burn incidence has remained relatively stable since the early 2000's [6,8,10,12].

The incidence of burn injury varies greatly with age. The highest age-specific rate of burn injury occurs among children aged 4 years and younger, followed by individuals aged 15-29 years, and then individuals aged 80 years and older [13,14]. In studies that include both children and adults, 40-50% of all patients are children [7,11]. Among studies including only patients aged 18 years and older, the mean age at the time of injury is 30-45 years [10,12,15–17]. In the United States, patients aged 60 years and older represent 13% of all hospital admissions for burn injury [18].

Burns are more common among male children, except below one year of age when approximately equal incidence is observed between sexes [18]. Similarly, among adults, approximately 75% of burn injuries are observed among men [7,10,15–17,19], and the incidence is approximately two-fold higher among men than among women [7,9,15,17]. Among the elderly, the male predominance diminishes somewhat, to about 60% of all injuries [11,12,20,21].

Burn mechanism also varies by age and gender. Children are most commonly injured by scalds, representing more than half of all pediatric burns [11,12,18]. In contrast, adult burns requiring admission are most commonly flame-related [11,12,17,20], although scalds are the most common among patients treated in the emergency department who don't require admission [11]. Among the elderly, the proportion of burns due to scalds increases, but flame injuries still predominate [18,20,21]. Overall, flame burns are more common among men while scalds are more common among women [11]. The majority of burns occur in the home, while 8 to 33% of injuries are work-related [9,11,12,18]. Chemical and electrical injuries each represent only about 3% of all burns [18]. In most studies, the incidence of self-inflicted burn injury is 2-6% [8,11,18,22], while in two studies, perhaps reflecting varying case ascertainment, the incidence was much higher, at 14-16% [9,15].

Socioeconomic deprivation is a well-recognized risk factor for injury worldwide [23–26]. Consistent with this finding, burn injury rates vary significantly based on socioeconomic status, including factors such as income, education, and housing. Burns are more common among individuals living in high poverty neighbourhoods [27,28]. In the United States, 45% of children admitted with burn injury have Medicaid coverage [12]. Data regarding the association between education level and burn injury risk are mixed, with some studies demonstrating that risk is inversely proportional to education level and other studies finding no association [28]. In the North American context, burns are also more common among ethnic minorities [11,12,28].

Inhalation injury-the airway damage caused by smoke inhalation- is much more common in adults than children, reflecting the dominance of flame burns among adults. The reported incidence of inhalation injury ranges from 3-28% [10,12,16,17], reflecting the lack of consensus definition for its detection and classification.

1.3 Classification of burn injuries

Burn injuries are classified according to their anatomic location, extent and depth of skin involvement, and mechanism. Burn size is estimated based on the percent of the body surface area that is involved by burn (% total body surface area, TBSA). This is estimated by health care providers at the time of presentation. Overestimation is common, particularly by non-burn physicians, and significant variation in estimated TBSA occurs even among burn surgeons [29–32]. Accurate burn size estimation is important for the triage of burn injured patients; the American Burn Association recommends that patients with burns of 10% TBSA or greater be referred to a burn center for treatment [33]. Burn size is also an important predictor of fluid resuscitation requirements. Therefore, incorrect estimations of burn size can result in over- or under-triage, and over- or under-resuscitation after injury [30,32,34,35].

Burn depth estimation is also challenging. Despite an increase in technologies aimed at improving the accuracy of depth assessments, clinical evaluation remains the most common practice [36]. The depth of a burn determines its likelihood of healing without intervention, and is therefore an important factor in determining treatment course and need for surgical management [37]. Burn depth is classified in relation to the dermis [37]. Superficial burns, such as sunburns, involve only the epidermis. These burns are not included in the estimation of TBSA. Superficial dermal burns extend through the epidermis into the papillary dermis, while deep dermal burns extend into the reticular dermis. Full thickness burns extend through the dermis and into the subcutaneous tissue. In terms of healing potential, superficial and superficial dermal burns are expected to heal with appropriate wound care, while deep dermal and full thickness burns require surgical excision and grafting [37].

There is no consensus definition as to what constitutes a *severe* burn injury. Definitions are largely based on characteristics of the burn itself, such as size and depth, or are based on resource requirements. By burn size, TBSA of 20% and greater is often considered a cutoff for severe injury [38]. By resource requirements, injuries requiring admission to a burn center are considered severe [19].

1.4 Pathophysiology

1.4.1 Pathophysiology of burn injury

Burn injury induces a profound inflammatory response that results in hypermetabolism, insulin resistance, and muscle catabolism [39]. This response is the most profound of any other type of trauma or critical illness, and in terms of inflammatory and metabolic changes, burn injury can therefore be considered the most severe of all critical illnesses and/or injuries [40].

The first 48 hours following burn injury are characterized by decreased cardiac output and contractility [41]. Beyond two days, however, the physiology of burn shock is distinct from other types of shock. Cardiac output and heart rate increase by 150% compared to unburned individuals, and myocardial oxygen consumption remains elevated at the time of discharge from hospital [41]. The liver increases in size, and is approximately twice the size at discharge as at admission [41,42].

These changes are modulated by the inflammatory cascade provoked by burn injury, largely in an effort to offset the heat loss that occurs through burn wounds [43]. While these inflammatory processes are ultimately aimed at burn wound repair, they also result in three distinct metabolic responses: (1) hypermetabolism, (2) insulin resistance, and (3) muscle catabolism. These responses are accompanied by multi-organ dysfunction, blunted growth, and blunted immunity with increased infection risk [41].

Hypermetabolism is the hallmark of the inflammatory response to burn injury, and results in a 40-80% increase in metabolic rate that is sustained up to one year following the burn [41]. These increases are largely modulated by catecholamines and corticosteroids; a 10 to 50-fold increase in catecholamine levels is observed post-burn [44,45]. Resting energy expenditure is increased alongside increased cardiac work, lipolysis, and liver dysfunction [41]. The energy needs of the burn injured patients are therefore immense, and are largely met by mobilization of amino acids and proteins through increased protein turnover and degradation [39].

The catabolism associated with hypermetabolism results in skeletal muscle wasting [44]. Severely burned patients can lose up to 25% of their total body mass after burn injury [46]. Data from the critical care literature demonstrate that a 20% loss of skeletal muscle mass is associated with increased infection rates; a 30% loss increases risk of pneumonia and pressure sores, and a 40% loss is associated with increased mortality [47]. Concurrent with loss of muscle mass is an increase in total body fat and percent total body fat [44]. This physiological loss of muscle mass, combined with the immobility associated with the initial phases of burn treatment, results in decreased strength and may limit patients' rehabilitation [39]. In children, catabolism is associated with pronounced growth retardation for up to 1 year, and indefinite loss of bone mineral density and bone mineral content [43,48]. Consistent with this finding, reduced lean body mass is observed among burn patients up to 3 years after injury [49].

Muscle catabolism is exacerbated by the insulin resistance that accompanies the stress response to burns. Both central and peripheral insulin resistance are observed, resulting in increased circulating endogenous insulin levels which increase glycogenesis and protein breakdown, resulting in increased circulating triglycerides, free fatty acids, and urea [41,44]. This increase in triglycerides is thought to contribute to fatty infiltration of the liver and organs after burn injury [50]. Peripherally, insulin-mediated uptake of glucose by skeletal muscle and other tissues is attenuated [41]. Hyperglycemia is also associated with poor wound healing and loss of skin grafts [51]. Insulin resistance remains present at the time of discharge from hospital [52], and might persist; one recent study observed significantly increased rates of diabetes-related admissions among burn survivors compared to the general population [53].

The treatment strategies that underpin burn care are centered on reducing or offsetting the hypermetabolic response. Arguably the most important intervention to blunt the stress response is the early excision and coverage of burn wounds. Metabolic rate reduces to 130% of normal following complete closure of the wounds [41]. Furthermore, early excision reduces catabolism and infection risk, while delays in excision can double catabolism [43]. Complete early coverage of all burn wounds is often not achievable, owing to lack of available patient skin for grafts. In this setting, dermal skin substitutes allow immediate restoration of the skin barrier, thereby preventing heat loss and attenuating hypermetabolism [39]. Maintaining ambient temperature in patient rooms and the use of occlusive dressings also contribute to reduced heat and fluid loss through the burn wound [43]. Pharmacologic strategies aimed at blunting or offsetting the hypermetabolic response are also in use; these include beta blockade with propranolol, and anabolic steroids to increase lean muscle mass and improve growth, particularly in children[41]. The role of these pharmacological interventions over the longer term after injury is unknown.

Several studies have demonstrated that hypermetabolism and its physiological effects persist for up to three years after injury, including tachycardia, hepatomegaly and liver enzyme elevation, insulin resistance and hyperglycemia, as well as alterations in several hormonal axes including growth hormone, parathyroid hormone, and sex hormones [44,54]. These findings might offer a biologic rationale for the findings of a few long-term clinical studies that burn survivors have increased risk of admission for fractures, respiratory infections, cardiovascular diseases, and diabetes [53,55–57]. The optimal pharmacological treatment and follow-up for these physiological changes remains to be characterized.

1.4.2 Pathophysiology of inhalation injury

Inhalation injury refers to the airway damage that occurs following deposition of toxic smoke particles in the upper and lower airways and lung parenchyma. The airway damage that results from smoke inhalation is secondary to the toxic smoke particles, rather than a direct thermal injury [58]. Noxious components in these smoke particles induce neurogenic inflammation via the release of neuropeptides; this inflammation increases airway blood flow, resulting in plasma extravasation, airway exudate, and a flux of inflammatory mediators [58]. The direct airway damage caused by the smoke, combined with its inflammatory effects, results in airway narrowing secondary to edema and the formation of casts within the airway; these effects reduce lung compliance and ventilation, resulting in hypoxia [59,60]. The severity of the inhalation injury depends on the concentration of toxic agents in the smoke, the size of the smoke particles, and the duration of the exposure [58]. Some injuries are severe enough to cause respiratory failure and may result in acute respiratory distress syndrome [58].

While the acute impact of inhalation injury on the lungs has been well characterized, its effects on other organs in the short and long-term are poorly understood. A preclinical study demonstrated that smoke inhalation is associated with neuronal and astrocyte dysfunction and/or death [58], suggesting a potential impact of inhalation injury on the neurological system. Given the role of neurogenic inflammation in inhalation injury, this might offer a mechanism to explain the increased risk of readmission for neurological diseases observed in one long-term follow-up study of burn survivors [61].

The persistent physiological response to burn injury long after discharge suggests a need to refine the post-discharge management of burn survivors. It has long been held that the burn injury is ‘over’ once a patient is discharged from the hospital; however, data generated to date suggest that burn injury might be a chronic comorbidity that confers risk of late morbidity and mortality and warrants dedicated longitudinal follow-up.

1.5 Improvements in modern burn care

“The patients in the wards presented the usual clinical picture of large exposed burn wounds, covered by broken-down eschars, with infected granulating areas on anaemic, exhausted, and frightened individuals.” (Jora Janzekovic, reflecting on burn care in 1970) [62]

Many improvements in the management of burn wounds have occurred since the Cocoanut Grove fire in 1942. These improvements have resulted in dramatic reductions in mortality after burn injury over the past several decades. The most significant advancements in burn care have been the development and refinement of early burn wound excision and grafting; the use of topical antimicrobials; recognition and characterization of the importance of nutritional support; refinement of fluid resuscitation strategies; and the diagnosis and treatment of inhalation injury.

Early excision of deep dermal and full-thickness burn wounds, followed by coverage with donor or patient skin, is the cornerstone of modern burn care. In 1947, largely based on experience treating the Cocoanut fire victims, Dr. Cope reported that removal of the burn eschar and immediate wound closure was the most effective strategy for reducing mortality [63]. At that time, this approach was limited by infection rates and blood loss, but advances during the 1950s led to consistently safe excision and grafting of up to 30% of the body surface area on the day of injury without increased risk to the patient [64]. Tangential excision represented a further refinement of this technique, which came into wide use in the 1970s and remains the standard today [62,65]. Studies in the 1980s demonstrated improved mortality, as well as reductions in length of stay and hypertrophic scarring in patients who underwent early excision and grafting compared to conservative treatment [66,67]. In a review of all pediatric burns treated at a single burn center between 1968 and 1986, Tompkins et al. largely attribute the reduction in mortality rates (from 9 to 1%) to the advent of early excision and grafting [68].

As excision techniques were refined, the availability of donor skin for wound coverage became a limiting factor of early excision. This led to techniques that facilitated the cryopreservation of cadaveric skin; in 1971, the first report of the viability of this approach was published [69]. The use of cadaveric skin for allografting remains in wide use today. While dermal substitutes have been available since 1981, their use has been limited by cost and the need for a multi-stage procedure [65]. Therefore, a need for an engineered skin substitute that is cost-effective, can be applied in a single stage, and fulfills the functions of skin still remains, and is a significant focus of ongoing basic science research.

During the advent of early excision and grafting, sepsis resulting from burn wound infections remained a leading cause of mortality [65]. Therefore, agents aimed at preventing bacterial colonization of the burn wound were developed. Three of these agents remain in use today: Dakins solution, a hypochlorite solution; mafenide acetate (sulfamylon); and silver-containing solutions such as silver-sulfadiazine [70,71]. While Dakins and sulfamylon are now largely reserved for invasive burn wound infections, the introduction of silver-based antimicrobials, combined with early excision and grafting of the burn wound, greatly reduced the morbidity and mortality associated with burn injury [65].

Until 1921, many thought that toxins in the burn wound caused mortality; it was then proposed that burn mortality was actually secondary to loss of fluids [65]. This initiated the study of the fluid shifts and losses that occur after burn injury, which were eventually characterized and related to the size of the burn. Several formulae for colloid and/or crystalloid requirements based on patient weight, age, and burn size were proposed; however, the Parkland formula, developed by Charles Baxter and Thomas Shires in 1968, remains in use today: 4cc of crystalloid per kilogram of body weight, per % TBSA, administered in the first 24 hours, the first half of which should be given in the first 8 hours after injury [72]. Characterization of the fluid requirements of burn injured patients, and an understanding of the complications associated with over- and under-resuscitation led to reductions in mortality and morbidity over time [73].

The next improvements in burn care followed the recognition that burn injury is accompanied by hypermetabolism, resulting in profound weight loss [46]. In the 1970s, Wilmore and colleagues described the nutritional needs of burn patients as being as high as 8000 calories per day [74]; in the years since, it has become widely recognized that aggressive enteral feeding, initiated as soon as possible after injury, mitigates catabolism and improves outcomes for burn patients [75,76].

Over the past several decades, burn surgeons have focused on improving outcomes through wound coverage, prevention of burn wound sepsis, and optimizing fluid balance and nutritional status after burns. In contrast, the diagnosis, pathophysiology, and treatment of inhalation injury received little attention until success was achieved with the other clinical sequelae of burn. This was perhaps in part related to the absence of appropriate diagnostic techniques for airway injury. Xenon scanning was first utilized in 1972 to diagnose inhalation injury, and was largely replaced with bronchoscopy in the 1980s [77,78]. The availability of reliable, objective tests for inhalation injury facilitated further study of its pathophysiology and treatment. This led to the discovery that inhalation injury is associated with increased mortality, pneumonia, and increased fluid resuscitation requirements, up to 2cc/kg/%TBSA greater than predicted by the Parkland equation [79,80]. Current treatments for inhalation injury, including inhaled acetylcysteine, bronchodilators, and nitric oxide, are relatively new, having been in use since the mid-

1990s. Ventilatory strategies for inhalation injury have largely been modeled on those used in acute respiratory distress syndrome. However, a recent randomized controlled trial demonstrated that in burn patients with inhalation injury and/or acute respiratory distress syndrome, low tidal-volume ventilation failed to achieve adequate oxygenation and ventilation, and was more likely to require rescue ventilation, compared with high-frequency percussive ventilation[81]. Inhalation injury remains an independent risk factor for mortality in the era of modern burn care; it has been suggested that the next significant improvements in burn-related mortality will follow an improved understanding of the pathophysiology and treatments for inhalation injury.

The ultimate impact of these improvements in burn care has been a significant improvement in burn-related mortality rates. In 1984, the burn size lethal to 50% of patients was 65% [82]; by 2014, this improved to 90% [38]. Therefore, half of all patients with a 90% burn are now expected to survive. Much of this improvement occurred in the 1980s: after risk adjustment, the odds of death were 17% lower in 1980–1984, and 33% lower in 1985–1989 than 1975–1979 [12]. Between 1971 and 1991, the total number of deaths due to burns decreased by about 40% in the US [6]. Only incremental improvements have occurred during the last decade, prompting the suggestion that burn care has reached “the floor of survival” within current treatment paradigms [12,68].

Contemporary inpatient mortality rates are in the range of 2-6% [9,11,12,15,17]; among patients with burns of 20% or greater TBSA, mortality is 14% for patients aged less than 55 years, and 38.5% for those 55 years and older, demonstrating the important impact of age on burn survival [38]. Independent risk factors for mortality include increasing age, female sex, inhalation injury, and increasing burn size [11,38,83,84].

1.6 Organization and delivery of burn center care

The treatment of burn injury is resource-intense, requiring pre-hospital emergency medical services, inter-facility transport, specialized surgical and nursing care, critical care, wound care, and physical and occupational therapy. After discharge, patients may require a variety of multi-disciplinary services, including rehabilitation, wound care, reconstruction, psychotherapy, and physiotherapy. Overall, the mean total cost of treating a burn inpatient ranges from $9550 to $39,594.90 USD [16,85,86], or $4097 per % TBSA burned [87]. The societal cost of burn injury is much larger, estimated at $95,551 when indirect costs such as lost productivity due to premature mortality and temporary or permanent labor incapacity are considered [86].

1.6.1 Development of burn centers

Burn centers were developed to concentrate the specialized resources that burn patients require in one hospital. Prior to World War II, most burn patients were cared for by a general practitioner, given morphine, and sent home to die in the company of their families [88]. The increase in burn injuries during the war necessitated a better approach, and prompted interest in caring for burn victims. A military surgeon in England began to gather burned Royal Air Force pilots in a single hospital in England to facilitate their care; this likely represents the first concentration of burn care [88]. As the number of civilian and military burn victims increased during the war, interest and expertise in burn care began to develop. As a result, the first burn center in the United States (US) opened in 1947 [89].

Between 1967 and 1987, 75% of the burn centers that exist today were established [89]. The rationale for developing specialized units to care for burn patients was that burn wounds were unsuitable for clean surgical wards, and required rooms as clean as an operating room with isolation capacity; to collect patients within the same place to facilitate expertise and research, and allow maintenance of a high treatment standard; and in recognition that the optimal treatment of burn patients requires significant healthcare resources that would be impractical to offer at every hospital [88]. In the 1970's alone, 82 burn centers were established, of which 60 continue to care for burn patients today [89]. As a result of this growth in burn care, in 1976 the American Burn Association (ABA) developed "*Specific optimal criteria for hospital resources for care of patients with burn injury*" [90]. These criteria defined burn centers on the basis of available resources, and outlined two levels of care of the burn injured patient: (1) burn units, comprising in-depth multidisciplinary burn expertise and optimal facilities, and (2) burn programs, which were hospitals with special expertise in burns but lacking dedicated facilities. In 1992, the ABA developed a voluntary process for burn center verification; this involves maintenance of specific resources and programs within burn centers to assure quality burn care and optimal outcomes for burn-injured patients [91]. There are currently 71 verified burn centers, the majority of which are in the US. However, many hospitals worldwide provide specialized burn center care. In the US, 50-60% of all burn patients are cared for in a burn center [89], though only 22% of patients receive care in a verified burn center [92].

Burn centers continue to be defined largely based on their available resources. In order to be verified by the ABA, a burn center must exist within an emergency medical services system that includes communication and protocols for triage, referral, and transport of patients needing burn center care [91]. Burn centers are required to maintain a prospective registry of all burn admissions, and to submit this data in a de-identified manner to the ABA's National Burn Repository (NBR). Evidence of a performance improvement and patient safety program is also required, as is the existence of a research program, burn prevention program, and infection control program. To ensure the care provided in burn centers is of the highest quality, burn centers must admit at least 75 patients with acute burns annually, of which 80% should meet the criteria for referral to a burn center.

1.6.2 Injuries requiring burn center care

The ABA has established criteria outlining the patients who should be referred to a burn center. These include all partial-thickness burns to $\geq$10% of the body surface area; all full-thickness burns, burns to the face, feet, hands, perineum, or major joints; any burn with inhalation injury; electrical and chemical burns; burn injury in patients with pre-existing medical disorders that could complicate management or prolong recovery; burns in patients who require special social, emotional, or long-term rehabilitation intervention;

and any patient with burns and concomitant trauma where the burn poses the greater risk of morbidity and mortality [33].

As a result of the relatively low incidence of burn injury and the concentration of care in burn centers, large geographic regions are often served by a single burn center; therefore, an infrastructure for the safe and efficient transport of burn injured patients over long distances is necessary. In one study, half of all admissions to a burn center were transferred from an outside facility, with an average transfer time of 7.2 hours [35]. Burn transfer programs are centered on stabilization of the patient, airway protection, accurate burn size estimates, initiation of fluid resuscitation, and prevention of hypothermia [35]. To make informed decisions about the necessity of referring a patient to a burn center, and the requirement for intubation and/or fluid resuscitation, referring providers must be able to estimate burn size and determine the likelihood of inhalation injury. While transport of burn injured patients by air or land over long distances has been demonstrated to be safe [93], misestimations of burn size and/or the presence of inhalation injury commonly result in over- or under-resuscitation and incorrect airway management, often where the patient is intubated and ventilated for transport unnecessarily [27,35]. One study found that over half of all intubated patients transferred to a burn center had been extubated within the first 24 hours of admission [35].

Given the resources required to transfer an injured patient to a burn center, effective triage practices are an essential component of a burn care system to minimize unnecessary transfer, or overtriage. Overtriage rates are in the range of 12 to 30% [32,94,95], and are commonly attributed to an overestimation of burn size by referring physicians [32,94,95]. In an effort to mitigate unnecessary transfers, many centers now offer telemedicine assessments of referred patients. In one study, these assessments were found to be accurate and cost-effective, and successful in reducing rates of both over- and under-triage to burn centers [96]. Other point of care tools to improve accuracy of burn size estimation by non-experts have been developed, but are not yet in wide use [97,98].

1.6.3 Characteristics of burn center care

There are four main phases of caring for a burn-injured patient. Initial evaluation and resuscitation occur during the first 72 hours after injury, and consist of evaluating all injuries, commencing appropriate fluid resuscitation, and decompressing the extremities and/or torso if required, as in the case of circumferential burns causing compartment syndrome. The next phase is burn wound excision and closure, which commences within the first week of admission, and involves accurate evaluation of the depth of burn wounds, the likelihood of their healing without surgery, and the surgical excision of full-thickness burn wounds. Excised wounds must be covered, either temporarily with allograft (from cadaveric skin bank) or biologic dressings, or permanently, with grafts from the patient (autograft). Once all burn wounds have been excised and covered, at least temporarily, the next phase is definitive wound coverage with permanent materials, usually autograft. This phase can continue for as long as 6 weeks after injury. The average length of stay is 1.36 days per % TBSA [38]. Patients with full-thickness burns tend to have longer hospital stays, on average 3 days per % full-thickness TBSA [38].

The final phase of burn care, which may continue for years after the injury, is rehabilitation, reintegration, and reconstruction. Early mobilization, splinting, and positioning to avoid permanent deformity are initiated as soon as possible after injury by the physiotherapy and occupational therapy teams. As the wounds are definitively closed, therapy progresses to active mobilization and strengthening. A scar management program begins prior to discharge, and continues throughout the outpatient rehabilitation phase. The patient is prepared to make the transition from the burn unit, to rehabilitation, and finally home and back into the community. This is particularly important for patients with visible injuries. Finally, over the months and years after the injury, patients may require reconstructive procedures, commonly for scar contractures that limit mobility. These phases of burn care illustrate the importance of a collaborative, multi-disciplinary approach to caring for the burn-injured patient.

Burn surgeons work in a multidisciplinary team of nurses, occupational and physical therapists, respiratory therapists, dieticians, pharmacists, and social workers. This team works in close collaboration with other specialties; general surgery, cardiac surgery, neurosurgery, obstetrics/gynecology, ophthalmology, oral surgery, pediatrics, plastic surgery, and urology consult services should be available 24 hours per day in the hospital of the burn center [99]. Furthermore, medical services including infectious diseases, internal medicine, dermatology, rheumatology and psychology must also be available [99].

1.6.4 Evidence for burn center care

Burn center care is costly. The estimated total average cost per inpatient day in a burn center is $2705 USD (Range: 111-11,067), compared to $1959 (range: 585-4314) when burn care is provided in general hospitals [87]. Given the higher cost of treating burn patients in burn centers, evidence for the utility of burn center care is needed. In one study, the mean cost per quality-adjusted life year (QALY) was $686 [86]; generally, interventions that cost less than $50,000-$100,000 per QALY are considered to be reasonable value for health care dollars [100]. By this metric, burn care may well represent a cost-effective intervention.

Most studies have sought to demonstrate a mortality benefit of burn center care. However, these studies are limited to studies of the volume-outcome relationship within burn centers, as data concerning outcomes outside of burn centers are not widely available. In adults, two studies have demonstrated that mortality rates are lowest at mid-volume centers (100-200 patients/year), and highest at the highest volume centers (≥300 patients/year) [101,102]. Similarly, no difference in mortality between ABA-verified and non-verified burn centers was observed in a study from California [103]. In contrast, pediatric studies suggest an association between burn center volume and mortality, such that the highest volume centers have the lowest mortality [104,105].

In our current era of low burn-related mortality rates, markers other than mortality are needed to better understand the utility of burn center care. No studies have currently definitively demonstrated a benefit of burn center care on outcomes other than in-hospital mortality, likely owing to the previously mentioned challenges with measuring outcomes outside of burn centers.

1.7 Post-discharge outcomes of burn injury

1.7.1 Post-discharge healthcare utilization

Many burn patients require rehabilitation, on an inpatient or outpatient basis, following their injury. Overall, about 2% of all hospitalized burn patients are discharged to an inpatient rehabilitation facility, though this varies widely based on injury severity and local resources [18,106]. Older patients are also more likely to be discharged to a rehabilitation facility: each additional year of age increases the likelihood by 2% [106]. The average length of stay in inpatient rehabilitation ranges from 21 to 28 days [107,108]. Inpatient rehabilitation has been demonstrated to improve functional outcomes after burns [107–109]. Most patients are discharged home after rehabilitation. Outpatient rehabilitation programs may be required, irrespective of need for inpatient rehabilitation, for the management of contractures, hypertrophic scarring, joint deformities, hand deformities, paresthesia, and chronic pain [82].

The post-acute care utilization of health care resources by burn-injured patients has not been well described or quantified in the literature. Presumably, many patients who suffer minor injuries do not require any further burn-related healthcare beyond their initial treatment. However, the variety of potential impacts that major burn can have on an individual may necessitate multi-disciplinary care after discharge. The utilization of healthcare resources by burn survivors can be categorized into those directed at rehabilitation, mental health, physical health, or reconstructive needs. In one Dutch study of 429 burn survivors 12-24 months after injury, 76.5% had sought medical help for burn-related problems within two years after injury [110].

Age is an independent predictor of resource utilization after burn injury. Elderly patients have increased length of stay, increased rates of discharge to rehabilitation facilities, and an increased need for home health nursing [111]. This is of particular importance given the aging of the "baby boomer" generation; anticipation of their future needs after burn injury may minimize the overall burden on the healthcare system.

In addition to patient-level factors such as age, injury factors may also influence the utilization of health care resources by burn survivors. The physical changes caused by burns often require patients to undergo reconstructive procedures aimed at improving appearance and/or function. In one study, 38% of patients underwent at least one reconstructive procedure after discharge (range 1-45) [112]. The need for reconstruction is often related to the functional impact of a burn, which is most often a function of burn site [112,113]. For example, patients with upper extremity burns are more likely to undergo reconstructive procedures, reflecting the functional significance of burns to the hands [112]. Patients whose injuries require reconstructive surgery are more likely to be unemployed, have poor sexual and extended family relationships, and poor social environments [113], reflecting the implications of functional impairment after burn.

1.7.2 Physical and social impact of burn injury

Burn injuries occur suddenly and unexpectedly, with the potential to leave a lasting impact on individuals of all ages. They can affect the physical, mental, and social health of an individual in a variety of ways, over both the short and long-term. In-hospital sequelae of burn injury may include admission to the intensive care unit, mechanical ventilation, sepsis, multi-organ failure, multiple operations, amputation, and severe pain [11,38,114], each of which might have long term sequelae of their own [115–117]. Small, single-centre studies have demonstrated decreased health-related quality of life over the months and years after burn injury [118–120].

Following the acute care phase, patients must adapt to their injury and its many potential implications. Survivors may return home or be transferred to a rehabilitation or long-term care facility. Those who return home may require assistance with activities that they were previously able to perform independently, and may be unable to return to their previous level of activity [119,121]. They may find themselves no longer able to fulfill all conditions of their previous employment, or be unemployed [122,123]. Their sense of self and personal relationships may suffer as a result. Burn injuries may also result in changes in physical appearance and/or changes in physical function that are distressing to the patient. Common complaints include scar contractures, disfigurement, and deformity due to partial or complete loss of body parts [113]. Through the few studies conducted to date, we are beginning to understand the far-reaching, multi-factorial effects of burn injury and it's potential to affect all aspects of a survivor's quality of life − physical functioning, independence, mental health, societal contributions, and relationships.

The long-term personal impact of major burn injury has not been well characterized. In 2008, under 2% of all of the published burn literature addressed post-discharge outcomes [124]. Moreover, there is no consensus on core outcomes to assess, and at what interval after injury.[125]. Studies conducted to date have focused on the evaluation of patient-centered outcomes. In one systematic review, the most commonly studied outcomes after burn injury were education and work status, mental function, self-care, mobility, and interpersonal interactions and relationships [126]. The study of long term outcomes after burn injury has been limited by small cohorts with great variability in size and extent of burns, making generalizability difficult and comparisons across studies almost impossible.

Most data that exist regarding burn outcomes are derived from prospectively maintained databases. The ABA maintains the National Burn Repository (NBR), which collects data from 96 hospitals in the United States, as well as 6 international burn centers (4 in Canada, and 2 in Sweden) [18]. The NBR includes data on all burn admissions, but does not capture patient outcomes after discharge. The National Institute on Disability and Rehabilitation Research (NIDRR) established a prospective database in 1994 in order to provide a model for tracking long-term outcomes after burn injury. NIDRR includes data on the outcomes of 3449 individuals with major burn across four centers, including patient demographics, injury characteristics, and various outcome assessment tools [127].

Given the potential for both mental and physical health issues after burn injury, many patients will require social support after their injury and a temporary or indefinite period of time off work [123]. Based on NIDRR data, 54% of patients have returned to work or school at 6 months after injury [127]. However, the majority of patients in the NIDRR cohort suffered less than 20% TBSA burn. The extent of burn injury, prior psychiatric history, and involvement of the extremities are all predictors of employment status after burn injury [123]. Unemployment is the greatest predictor of decreased quality of life in burn-injured patients [128].

Burn survivors have decreased quality of life (QOL) and increased emotional distress relative to non-burned controls [129]. One study determined an average loss of quality-adjusted life years of 0.078 at 2 years for adult burn survivors [130], with overall decrease in QOL of 9-25% depending on TBSA. The decrement in quality of life after major burn injury is comparable to patients who have sustained traumatic brain injury [130].

1.7.3 Psychological impact of burn injury

Following the Cocoanut Grove fire, reports began to emerge regarding the mental and emotional distress experienced by survivors. Psychiatric interviews and questionnaires were conducted to identify psychopathology in the one year after the tragedy. Of 46 patients available for follow-up, 26 (57%) suffered from at least one “psychiatric complication”, described then as general nervousness characterized by restlessness, irritability, fatigue, nightmares, and sudden recollections of events of the fire [131]. This likely represents the first description of post-traumatic stress disorder (PTSD) among burn injured patients, and an early recognition that burn injury might have sequelae unrelated to the burn wound itself.

Emerging data suggests that there might be an association between mental illness and the risk of burn injury The prevalence of pre-injury affective disorders, alcohol dependence, and substance misuse is higher among burn patients than in the general population [132]. The pre-injury prevalence of mental illness has been reported to be as high as 75% [132–137], compared to 48% in the general population. This might be explained through several shared socio-demographic risk factors for both burn injury and mental illness, such as low socioeconomic status and belonging to a minority group [138]. Psychiatric morbidity itself is a risk factor for being burned; many burns occur as a result of intentional injuries, often with suicidal intent [139].

Mood disorders and alcohol abuse most commonly affect burn patients prior to their injury [132]. In one prospective study, 41% of patients admitted for treatment of burn injury had pre-injury alcohol abuse or dependence, while 31% had a pre-injury mood disorder [140]. Axis II diagnoses such as antisocial personality disorder and borderline personality disorder are also over-represented in the burn population [141]. The burden of psychiatric illness can be significant, with 6% of patients having 3 or more psychiatric diagnoses prior to their injury [132]. This pre-injury psychiatric morbidity is important to recognize because it can have a profound impact on the outcomes of burn survivors.

Patients with existing mental illness are more likely to have a longer length of stay in hospital, to experience increased pain, and to encounter difficulty adjusting to their injury [141]. Patterson hypothesized that hospitalization causes patients to resort to dysfunctional modes of adaptation, such as regression, depression, and poorly controlled hostility [139]. These dysfunctional processes interfere with patients' ability to adapt, adjust, and participate in rehabilitation and reintegration into their family, community, and livelihood following a burn injury. Adjustment after burn injury is typically measured using patient reported measures of health-related quality of life, such as the Burn Specific Health Scale. Maladjustment following major burn injury is a risk factor for psychiatric sequelae and poor quality of life [132,134,138], and might be an important mediator of how comorbid mental illness affects post-burn psychiatric morbidity.

New onset of psychiatric morbidity after injury is also common, particularly among those with a pre-injury history of mental illness. In one prospective study, 41% of patients with a pre-existing mental illness developed a new Axis I diagnosis during their admission [133], most commonly adjustment disorder and substance withdrawal. Comparatively, these diagnoses were observed in only 27% of patients without a lifetime psychiatric diagnosis. After discharge, a pre-burn diagnosis of anxiety is a risk factor for depression, while pre-burn affective and substance use disorders increase the risk of PTSD [134]. Overall, affective disorders, alcohol and substance abuse are associated with the greatest psychiatric morbidity after injury. High rates of PTSD are observed in patients with pre-burn affective disorder [132] and adjustment disorder during hospitalization.

New onset mood and anxiety related disorders are also prevalent among burn survivors without a psychiatric history [135,136]. The overall prevalence of a post-burn psychiatric diagnosis is 31-51% [135,136]. Mood and adjustment disorders are common, as are acute stress disorder (ASD) and PTSD. Psychological distress often becomes apparent during the inpatient phase, often manifested through symptoms of anxiety and alienation. This inpatient distress is a risk factor for subsequent, chronic psychological distress [142]. The prevalence of post-burn onset anxiety disorders is 12-27%, while up to one third of patients may suffer from PTSD [134,136,143,144]. The prevalence of post-burn depression ranges from 10-28%, compared to 8% in the general population [134–136,145]. Other than pre-existing mental illness, risk factors for post-burn mental illness include female sex, younger age, and neuroticism personality trait [136,144].

Injury characteristics have not been reliably associated with subsequent development of mental illness, although one study found a weak association between extent of burn injury and development of depression [144]. The pain associated with burn injury might also be associated with mental health outcomes. Studies have found an association between the severity of inpatient pain and depressive and PTSD symptoms at 1 and 2 years after injury [146]. This influence of inpatient pain on longer-term psychological adjustment was found to be greater than the influence of burn size, length of stay, or pre-injury mental illness[146]. Similarly, in a prospective study, anxiety related to acute burn pain was associated with persistent posttraumatic stress symptoms at one year[147]. Pain might also affect self-harm; in one study, severe pain at discharge was the only significant predictor of suicidal ideation at both 6 months and 1 year after discharge, even after accounting for existing psychiatric comorbidity[148]. Psychiatric morbidity is not confined to the immediate post-burn period; rather, it persists after injury, with a prevalence of 31% after two years [136]. Much of this late morbidity can be attributed to PTSD.

PTSD is the most commonly observed anxiety disorder after burn injury [149]. PTSD is characterized by persistent mental and emotional stress that occurs as a result of injury or severe psychological shock, and typically involves sleep disturbance and constant vivid recall of the experience, as well as symptoms of hyperarousal [150]. A recent systematic review and meta-analysis described a prevalence of PTSD of 9-45% in the first year after burn, and 7-25% among patients beyond two years after their injury [151]. The strongest predictors of PTSD after burn injury are patient perception of a threat to life, acute intrusive symptoms, and pain. Injury characteristics are not reliably associated with development of PTSD. Acute stress disorder may be a pre-cursor to PTSD, though not all patients with ASD develop PTSD [138]. Scores on ASD questionnaires at discharge are highly predictive of the development of PTSD up to two years after injury [138].The symptomatic burden of PTSD does not change meaningfully over the first 2 years after injury, and affects survivors on an ongoing basis [138]. The presence of PTSD has been demonstrated to increase use of mental health services among those affected [138].

Psychological stress in general, particularly of chronic duration, elicits greater health care utilization [152]. Palmu et al found that 28% of burn survivors had contact with psychiatric services within 6 months of their injury [135]. Of these, 20% received medication, and 13% required ongoing psychiatric care. The most significant finding of this prospective study was that only half of the patients who had an unequivocal need for psychiatric care (eg. psychosis, PTSD, suicidal intent) received such care. Patients with pre-burn mental health disorders and greater than 20% total body surface area burn injury were most likely to receive psychiatric care. In another study with longer follow-up, 25% of patients had sought help for mental health problems within two years after their injury [110]. The high prevalence of mental health disorders among burn-injured patients suggests a high rate of utilization of health care services after discharge.

1.8 Existing knowledge gaps

While the mortality from acute burn injury has plateaued over the last 10 years, very little is known of the impact that burn injury has on an individual's long-term morbidity, mortality, and utilization of the health care system. Specifically, the long-term complications of major burn injury, and associated resource utilization, are poorly understood.

To date, few studies have examined the health care needs of burn survivors after discharge. In a recent study, Van Loey et al found that 68% of burn survivors expressed interest in a burn-specific outpatient clinic [110], suggesting a gap between the services currently offered and those required by this unique group of patients. Recently, several Australian studies have demonstrated that burn survivors have increased readmission rates for cardiovascular, gastrointestinal, infectious, and neurological diseases compared to matched controls [57,61,153,154]. However, these studies included patients injured in the early 1980s; given the improvements that have occurred in burn care over the last 30 years, these findings might not be generalizable to modern burn survivors. The few other studies that have been conducted to date of long-term burn outcomes are characterized by small cohort sizes and varying outcome measures, both of which limit the generalizability and comparability of results.

In summary, current data regarding long-term outcomes and resource utilization after major burn injury are sparse, and are insufficient to inform interventions and allocate resources to ultimately meet the needs and improve the outcomes of patients who survive major burn injury.

CHAPTER 2: RESEARCH AIMS AND HYPOTHESIS

2.1 Rationale

As summarized in Chapter 1, all but the most severe burn injuries are now survivable, with resultant increases in the prevalence of burn survivors worldwide. These patients represent a unique cohort whose injuries might have long-lasting physical, physiological, and psychiatric sequelae. As a result, they are likely to be high utilizers of the health care system. To adequately plan for the current and future healthcare needs of these patients and improve the quality of their care, the impact of burn injury on an individual's long-term morbidity, mortality, and utilization of the health care system needs to be evaluated.

We will utilize several epidemiological study designs and statistical methods to gain a comprehensive understanding of the trajectory faced by burn patients after discharge. Large administrative databases will allow longitudinal follow-up of a population-based cohort of burn-injured patients, providing an opportunity to assess long term morbidity, health care utilization and incidence of premature mortality after burn injury.

A comprehensive understanding of the trajectory faced by patients after discharge will help inform discussions between the physician, patient, and patient's families. This information will be useful when considering goals of care, establishing patient and family expectations, and planning for discharge. The multi-disciplinary team will be better equipped to prepare patients and families for discharge because they will have a better understanding of patient needs post-discharge, and of the reasons patients return to hospital shortly after discharge. Furthermore, through an understanding of the reasons why patients return to hospital or are admitted over the months and years after discharge, we can begin to inform interventions aimed at reducing emergency department visits and hospital admissions, with benefit to both the patient and the healthcare system. These interventions may occur during the first admission, or on an ongoing basis in the community. In addition to informing new interventions to improve long-term outcomes in burn survivors, our work will inform resource planning and allocation; ultimately, this can improve the efficiency with which we care for burn-injured patients.

Through an evaluation of the association between burn injury and mental illness, our work will characterize the mental healthcare needs of burn survivors, providing a comprehensive understanding of the physical and psychological morbidity that might follow burn injury. The literature clearly demonstrates a significant burden of mental illness among burn-injured patients. Unfortunately, studies to date are limited by small sample sizes, short follow-up intervals and high rates of loss to follow-up. Furthermore, pre-injury mental illness is not objectively measured in these studies, typically relying on patient recall. Our population-based approach will overcome many of the challenges faced by single center, retrospective cohort studies, as it will allow longitudinal follow-up and capture of pre- and post-injury healthcare utilization across all areas of the healthcare system.

An understanding of the complex relationship between mental illness and burn injury will inform the design and implementation of a number of new initiatives to ultimately mitigate the long-term psychological impact of burn injury at both the individual and the system level. This will include minimizing the impact that injury has on pre-existing mental illness, and determining how best to care for these individuals. In individuals without pre-existing mental illness, our study will inform potential screening and guide early interventions for mental illness.

Characterization of the typical predictors and onset of mood and anxiety disorders following burn injury will inform development of screening programs that might have a benefit at both the individual and systems levels. At the individual level, timely recognition of mental illness might result in earlier treatment, less severe symptoms, and reduction in self-harm events; ultimately dampening the impact of mental illness on the individual's recovery after burn injury. At the system level, screening might result in more efficient use of limited mental health resources, particularly emergency mental health services. The diagnosis and treatment of mental illness might also reduce overall health care utilization, as depression and disability are known to be predictors of high utilization [152].

As a whole, our work will inform improvements in the existing burn care infrastructure in Ontario, and allow development of a template for tracking long-term outcomes across burn centers in Ontario. We anticipate that this will allow for ongoing evaluation of the effectiveness of new interventions, and will facilitate the benchmarking of outcomes across burn centers in North America.

2.2 Hypothesis

Several studies have demonstrated that the pathophysiologic response to burn injury persists up to three years after the burn[50,54,155]. We hypothesize that the persistence of this response will result in high rates of long-term acute healthcare consumption related to altered cardiovascular and endocrine physiology and metabolism. Given data suggesting a high prevalence of mental health disorders among these patients both pre- and post-burn, we hypothesize that the pre-injury utilization of both inpatient and outpatient mental health services is greater in burned individuals than the general population. We expect that burn injury and its sequelae will further increase the risk of mental health-related utilization after injury. Finally, we anticipate that the hypothesized increased rates of healthcare utilization and mental illness among burn survivors will be associated with an increased risk of late mortality compared to uninjured controls.

2.3 Aims

Specific aim 1: To evaluate population-based rates of major burn injury in Ontario

The burden of major burn injury at the population-level is poorly understood. An understanding of the incidence of major burn injury, and how this has changed over time, is essential to inform future delivery of healthcare services to these patients. Furthermore, data regarding mortality rates and how these have changes over time are essential to identify opportunities for improvement and inform discussions with patients and their families. These data will be generated through the following sub-aims:

Sub-Aim 1.1 – To determine the incidence and case fatality rate of major burn injury

Sub-Aim 1.2 – To evaluate temporal trends in rates of major burn injury requiring admission to hospital

Specific aim 2: To evaluate post-acute care utilization of health services by survivors of major burn injury

The utilization of the health care system by patients following their initial hospitalization is unknown. We will evaluate the usage patterns of various inpatient services among a large population of burn survivors. Through this work, we will gain an understanding of how these patients utilize the health care system with a view to informing future resource allocation. This aim will be explored through the following sub-aims:

Sub-Aim 2.1 –To determine rates, principal causes, and risk factors for emergency department visits after discharge

Sub-Aim 2.2 – To determine rates, principal causes, and risk factors for unplanned readmissions after discharge

These data will provide a broad understanding of the morbidity faced by burn survivors over the longer term following discharge. We will then focus on understanding the mental health morbidity of burn survivors through Specific Aim 3:

Specific Aim 3: To evaluate the association between burn injury and mental illness

Mental health disorders are prevalent both before and after burn injury. The impact of injury on an existing mental-health disorder, and its association with subsequent mental health in these patients is unknown. Through this work, we will gain an understanding of the prevalence of mental health disorders after burn injury in comparison to before, and we will begin to characterize the nature of the relationship between burn injury and mental health. The incidence of mood and anxiety disorders and substance abuse will be estimated, and risk factors for development of mental health disorders following injury will be identified in Sub-Aim 3.1:

> **Sub-Aim 3.1** – To estimate the rate of mental health disorders before and after major burn injury

Having estimated the rate of mood disorders, Sub-Aim 3.2 will focus on self-harm events in order to understand this potentially preventable source of morbidity and premature death:

> **Sub-Aim 3.2** – To evaluate the rate of, and risk factors for, self-harm behaviours before and after major burn injury

To complete our study with an evaluation of the long-term impact of burn injury:

Specific aim 4: To estimate long-term mortality after major burn injury

The effect of sustaining a major burn injury on long-term life expectancy is unknown. Emerging data from the critical care literature suggests that survivors of critical illness have shorter life expectancy than matched controls(4-6). A determination of the magnitude of this potential effect in burn survivors, and evaluation of associated risk factors will allow the identification of at-risk patients and inform future interventions aimed at reducing this impact.

CHAPTER 3: GENERAL METHODS

3.1 Overview

The work described in this dissertation was conducted at Sunnybrook Health Sciences Centre and at the Institute for Clinical Evaluative Sciences (ICES), in Toronto, Ontario, Canada. Research ethics approval for the thesis was obtained from the Sunnybrook Health Sciences institutional review board, as well as the University of Toronto Office of Research Ethics.

3.2 Data Sources

This thesis was conducted using data derived from several linked health administrative databases held at ICES. ICES is a section 45 prescribed entity under the Province of *Ontario's Personal Health Information Privacy Act*; as such, ICES collects and holds a large proportion of the administrative health data collected in Ontario for the purposes of health system planning and management[156]. Under this law, patients do not have to consent to the collection of their health data. In the absence of patient consent, ICES must uphold strict procedures to maintain patient privacy and confidentiality. These procedures include data encryption, physical security measures, anonymization of data, strict policies regarding access to data and dissemination of results, and regular audits[156]. These policies and procedures are implemented internally and enforced by the ICES privacy officer. Additionally, the Information and Privacy Commissioner of Ontario conducts regular audits of ICES' privacy practices[156].

Similar to other Canadian provinces, the Ontario government administers a single-payer system that universally funds all hospital, laboratory, and necessary physician services for eligible residents; therefore, these data sources include records for virtually all residents in the province. Non-residents of Ontario, and individuals with lapsed healthcare coverage are not captured. Healthcare coverage lapses when individuals fail to renew their health card (required every 5 years), or move out of the province. Ontario census data estimates that less than 5% of Ontarians moved out of the province over a 5-year period[157]. These databases can be deterministically linked using an encrypted unique identifier based on each patient's Ontario Health Card Number. The specific ICES holdings used in this dissertation are described below; the holdings utilized for each specific aim are presented in **Table 3.1**.

The Registered Persons Database (RPDB) contains demographic and vital statistics information for all individuals eligible for the Ontario Health Insurance Plan. Data include age, sex, vital status, postal code, and census dissemination area. The RPDB also captures the date of last contact with the healthcare system.

The Discharge Abstract Database (DAD) captures all acute care hospitalizations in the province of Ontario after the year 1991. The DAD contains information regarding the admitting hospital, admission source (ED, elective, other hospital, same-day surgery) the admission diagnosis, in-hospital interventions and length of stay, diagnoses contributing to the hospital stay, and discharge disposition.

The National Ambulatory Care Reporting System (NACRS) records all ambulatory visits, including emergency department and outpatient visits. Similar to the DAD, NACRS contains information for each ED visit including the presenting complaint, interventions, triage category, and discharge disposition.

The Ontario Mental Health Reporting System (OMHRS) captures data regarding all admissions to a mental health facility in the province, starting in 2005. Data contained in OMHRS include DSM-IV axis I and axis II diagnoses at admission and discharge, marital and employment status, presence of specific psychiatric symptoms, information regarding self-harm attempts and their intent, and information regarding substance use.

The Ontario Register General-Death (ORGD) database contains data regarding all deaths in the province, including the date, location, and immediate, antecedent and underlying cause of death.

The Ontario Marginalization Index (ONMARG) database contains data for each census subdivision of the province. ONMARG was created by researchers at the Centre for Research on Inner City Health (now the Centre for Urban Health Solutions) in Toronto to facilitate exploration of how multiple dimensions of social marginalization are concentrated at the local level, and how these factors are associated with health outcomes[158]. ONMARG is derived from 2006 census data and includes 4 dimensions of marginalization: residential instability, material deprivation, ethnic concentration, and dependency. Each dimension is operationalized in quintiles from least to most marginalized. The ONMARG for individuals is derived based on their census subdivision (smallest geographical unit), dissemination area, or local health integration authority (largest geographical unit). As such, the ONMARG does not represent individual-level data.

3.3 Data Validation

The Canadian Institute for Health Information utilizes a variety of measures to ensure accuracy and consistency in its databases[159]. In 2010, CIHI conducted a re-abstraction study which demonstrated 86% accuracy in reporting of the most responsible diagnosis for admission in the DAD[160]. Several other validation studies have demonstrated the accuracy of diagnoses codes in the DAD for the identification of inflammatory bowel disease, stroke, chronic obstructive pulmonary disease, and spinal cord injury[161–163]. The accuracy of the DAD in identifying procedures such as kidney transplantation and carotid artery revascularization has also been demonstrated[164,165].

The ICD-10 diagnosis codes for burn injury are listed in **Appendix A**. Given that these codes are used to derive the study cohort in this thesis, we undertook a validation study to ascertain the accuracy of burn-specific diagnoses codes in the DAD. The findings of that study are reported in **Appendix B**. Briefly, we found that TBSA codes were highly sensitive and specific in identifying patients with ≥10 and ≥20% TBSA injuries (89/93% sensitive and 95/97% specific), with excellent agreement (κ, 0.85/κ, 0.88). Codes were weakly sensitive (68%) in identifying ≥10% TBSA *full-thickness* burn, though highly specific (86%) with moderate agreement (κ, 0.46). The diagnoses codes had limited sensitivity (43%) to identify inhalation injury, but high specificity (99%) with moderate agreement (κ, 0.54). Burn mechanism had excellent coding agreement (κ, 0.84).

The findings of this validation study indicate that ICD-10 diagnoses codes can be reliably utilized to identify patients with burn injury on the basis of burn size or mechanism. However, these codes are less reliable in characterizing patients based on burn depth or the presence of inhalation injury.

3.4 Tables for Chapter 3

Table 3.1. Datasets used in each specific aim of thesis

Specific Aim	Data Sources
1: To evaluate population-based rates of major burn injury in Ontario	RPDB, DAD, NACRS
2: To evaluate post-acute care utilization of health services by survivors of major burn injury	RPDB, DAD, NACRS, ORGD
3: To evaluate the association between burn injury and mental illness	RPDB, DAD, NACRS, OMHRS, ORGD
4: To estimate long-term mortality after major burn injury	RPDB, DAD, NACRS, ORGD, ONMARG

CHAPTER 4: TEMPORAL TRENDS IN THE EPIDEMIOLOGY OF MAJOR BURN INJURY

The purpose of this chapter is to:

1) Evaluate temporal trends in the incidence of burn injury over 2003-2013

2) Describe where patients with burn injury receive their care, and evaluate how this has changed over 2003-2013

3) Evaluate trends in in-hospital mortality rates over 2003-2013

Acknowledgement: Parts of Chapter 4 are reproduced from the following, with permission from Lippincott Williams & Wilkins:

Mason SA, Nathens AB, Byrne JP, Gonzalez A, Fowler R, Karanicolas PJ, Moineddin R, Jeschke MG. Trends in the epidemiology of major burn injury among hospitalized patients: a population-based analysis. J Trauma Acute Care Surg. Epub 2017 May 22.

4.1 Summary

Background: Burn-related mortality has decreased significantly over the past several decades. While often attributed in part to regionalization of burn care, trends in burn case-fatality rates and burn care regionalization have not been evaluated at the population level

Methods: We conducted a retrospective, population-based cohort study of all patients with $\geq$ 20% total burned surface area (TBSA) burn injury in Ontario, Canada. Adult ($\geq$16y) patients injured between 2003-2013 were included. Deaths in the emergency department were excluded. Logistic generalized estimating equations were used to estimate adjusted 30-day mortality. Mortality trends were compared at burn and non-burn centers.

Results: 772 patients were identified at 84 centers. Patients were 74% (n=570) male, of median age 46 (IQR 35-60) years and median TBSA 35% (IQR 25-45). Mortality at 30 days was 19% (n=149). The proportion of patients treated at a burn center increased from 57% to 71% between 2003 and 2013 (p=0.07). Average risk-adjusted 30-day mortality rates decreased over time; there were significantly reduced odds of death in 2010-2013 compared to 2003-2006 (OR 0.39, 95% CI 0.25-0.61). Burn centers exhibited significantly reduced mortality from 2003-2006 to 2010-2013 (OR 0.36, 95% CI 0.34-0.38) while mortality was not significantly reduced in non-designated centers (OR 0.41, 95% CI 0.13-1.24).

Conclusions: Mortality rates have decreased over time; significant improvements have occurred at burn centers while mortality rates at non-designated centers vary widely. A high proportion of patients continue to receive care outside of burn centers. These data suggest there are further opportunities to regionalize burn care and in so doing, to potentially lower burn-related mortality.

4.2 Introduction

Mortality following burn injury has dropped over the last twenty years such that most burn injuries are now survivable[19,166]. These improvements have been attributed, in part, to a dedicated, multidisciplinary approach to the care of burn injury, prompting efforts to develop regional systems for the care of burn-injured patients[89,167]. While there is evidence in other areas of surgery and medicine that regionalization or concentration of care improves outcomes, there are limited data available relevant to the patient with major burn injury [168–173].

Efforts to characterize trends in regionalization, and its effect on the outcomes of burn injured patients, have been hindered by the lack of a consensus definition for what constitutes a burn center and a lack of data regarding care at non-burn centers [89,173]. The only recognized mechanism for assessing and confirming the quality of care provided in a burn center is verification by the American Burn Association (ABA)[174]. However, in the US, non-verified (self-designated) burn centers outnumber verified burn centers [173], and half of all patients are treated outside of burn centers altogether [92]. Additionally, outside of the US, there are only 4 ABA verified burn centers [175].

A further factor precluding efforts to study regionalization is that data regarding burn care and outcomes are largely derived from the National Burn Repository (NBR), a database maintained by the ABA. Participation in the NBR is voluntary for non-verified burn centers; as a result, the NBR only captures the 36% of burn patients who are treated at a participating center[16]. While the NBR is a rich data resource for the study of outcomes among participating centers, it does not allow the study of processes of care or outcomes outside of NBR centers. A comprehensive evaluation of the benefits related to the regionalization of burn care requires data from all centers caring for burn-injured patients – both burn centers and non-burn centers, similar to the approach evaluating the benefits of trauma systems and/or trauma center care[170,176]. As a result, there is limited information on the benefits of regionalization in burn care.

In this study, we aimed to evaluate temporal trends in 30-day mortality over a period characterized by increasing regionalization of burn care in Ontario, Canada's most populous province. Our population-based approach allows the capture of burn-injured patients across all centers, overcoming the limitations of previous studies. We postulated that the concentration of burn care had increased over time and associated with this, was a significant improvement in survival.

4.3 Methods

Study Design & Setting

We conducted a population-based retrospective cohort study of patients living in Ontario, Canada who were admitted to hospital for treatment of acute major burn injury between April 1, 2003 and March 31, 2014. Ontario has a population of greater than 13 million in a geographic area of 415,598 miles, and is served by two adult regional burn centers, one of which is verified by the ABA. Similar to other Canadian provinces, the Ontario government administers a single-payer system that universally funds all hospital, laboratory, and physician services for eligible residents. This study was approved by the institutional review board at Sunnybrook Health Sciences Centre, Toronto, Canada.

Data Sources

Data were derived from three sources: (1) the Discharge Abstract Database (DAD) – a population-based administrative database which records all acute care hospitalizations in the province of Ontario after the year 1991; (2) the Registered Persons Database (RPDB) – an administrative database of all residents of the province of Ontario who are alive and eligible for coverage under the Ontario Health Insurance Plan (OHIP); and (3) the National Ambulatory Care Reporting System (NACRS) – a population-based administrative database which records all emergency department visits in Ontario. These data were made available through the Institute for Clinical Evaluative Sciences (ICES). ICES is a prescribed entity under the Province of Ontario's privacy law and holds a large proportion of the administrative health data collected in Ontario. Databases held at ICES contain health and sociodemographic information on residents of Ontario. These datasets were linked using unique encoded identifiers and analyzed at ICES.

Study Population

All individuals aged 16 years or older, living in the province of Ontario, Canada, and admitted to hospital for treatment of acute burn injury involving a total body surface area (TBSA) of 20% or greater between April 1, 2003 and March 31, 2014 were included. Patients lacking a valid health card number and non-residents of Ontario were excluded. In order to focus on a cohort of patients likely to benefit from burn center care, we excluded patients who sustained other concurrent major injuries, including brain injury, major torso trauma, or long bone fractures. To limit the analysis to patients who might benefit from in hospital care, whether at a burn center or not, we excluded patients who died in the ED.

Eligible patients were identified from the DAD by the presence of an ICD-10CA diagnosis code in the range T31.20-T31.99. Patient characteristics were abstracted from the RPDB, and injury characteristics and admitting center were abstracted from the DAD. Age- and gender-stratified population estimates were derived from a database of yearly Ontario intercensal population estimates held at ICES.

Burn center care and regionalization

Our goal was to characterize trends in mortality alongside trends in regionalization, defined as the proportion of patients receiving care in a regional burn center. A regional burn center was defined in accordance with the province's 'Burns Center Consultation Guidelines'[177]. These guidelines were developed by the Ontario Trauma Advisory committee and Critical Care Services Ontario, the entity responsible for oversight of burn care in the region, and serve to guide the transfer of patients to designated burn centers –

of which there are three in Ontario (2 adult, 1 pediatric). Attribution of burn center care was determined by the location of initial burn care. If a transfer from a non-burn center to a burn center occurred beyond 3 days after admission, the care was attributed to the non-burn center, recognizing that patients transferred after 3 days were likely initially admitted with the intent of definitive, rather than preliminary care.

Outcomes

The primary outcome in this study was 30-day mortality, including both in-hospital and post-discharge deaths within 30 days of injury. Discharge disposition in the DAD was used to capture in-hospital deaths, and post-discharge deaths were identified in the RPDB.

Covariates

Baseline patient characteristics including sex, comorbidity burden, urban versus rural residence, and income quintile were considered potential confounders, and therefore included in multivariable analyses. Comorbidity burden was represented based on the Johns Hopkins Adjusted Clinical Groups case mix system[178], which assigns patients to one of six morbidity categories based on prior healthcare utilization. Income quintiles based on each patient's postal code were used as a marker of socioeconomic status. Patient residence was classified as urban or rural on the basis of the Rurality Index of Ontario (RIO)[179]; this takes into account the population density of the city/town of the patient's residence, as well as the distance to the nearest basic and advanced referral center. A RIO $\geq$45 is considered rural[179]. We also considered the following injury characteristics to be potential confounders: TBSA, burn mechanism, and inhalation injury, as defined by ICD-10 diagnoses codes in the DAD. We have previously validated the use of ICD-10CA codes for identifying and estimating burn size[180].

Statistical Analysis

A descriptive analysis of patient demographics and injury characteristics across the study period was performed. Annual age- and gender-specific incidence rates were estimated using annual Ontario population estimates, and compared across all years. Incidence rates were directly standardized for age and sex to the 2015 Canadian population[181]. The Cochran-Armitage test was performed to test for temporal trends, stratified by age and gender.

Logistic generalized estimating equations were used to derive risk-adjusted odds ratios for 30-day mortality across each year of the study. Least squares means were then used to estimate risk-adjusted mortality rates for each year. A second multivariable model was used to estimate the odds of mortality in the last 4 years of the study (2010-2013) compared to the first 4 years (2003-2006). We considered that in-hospital deaths occurring within 24 hours of admission might not be modifiable by regionalization; thus, we conducted two analyses, one including deaths within 24 hours, and one excluding these deaths. Stratified analyses were used to determine whether there was any effect modification, allowing for the determination of whether the secular trends in burn mortality differed by burn center status. Given the smaller sample size at non-burn centers, only age, comorbidity, TBSA, and inhalation injury were included in the analysis of outcomes at non-burn centers for model parsimony. Model concordance was assessed by determining the area under receiver-operating curves. All statistical analyses were performed using SAS 9.4 (Cary, NC). In all analyses, $p < 0.05$ was considered significant.

4.3 Results

During the study period, 803 patients with acute major burn injury were identified, who received definitive care at 84 different centers (2 burn centers, and 82 non-burn centers). Of these, 31 patients died in the emergency department and were excluded from further analysis; the vast majority of these deaths (>90%) occurred in EDs at hospitals without a burn center. The proportion of patients treated at a regional burn center increased from 57% in 2003 to 71% in 2013 (p=0.07).

The overall age- and gender-standardized incidence of major burn injury across the study period was 1.15 per 100,000 person years. The highest incidence of major burn injury was observed in males aged 45-54 years (1.26/100,000). In contrast, the incidence of major burn injury in females was highest among those aged 75 years and older (1.10/100,000), while males ≥75 years represented the second highest incidence group (1.19/100,000). The overall rate of major burns increased from 2003 to 2006, then peaked and subsequently declined, before reaching a plateau in 2010. The age- and gender-stratified rates of major burn injury between 2003 and 2013 are presented in **Figures 4.1** and **4.2**. Rates were higher in males (0.85 per 100,000 person-years) than females (0.30 per 100,000 person years), yielding an incidence rate ratio of 2.83 (95% CI 2.47-3.25). No significant trends in rates were observed across age strata.

Patient characteristics

Patients were 74% (n=570) male, with a median age of 46 years (IQR 35-60) (**Table 4.1**). The majority of patients were urban-dwelling (80%, n=620). A quarter of patients (n=202, 26%) were in the lowest income quintile and only 8% (n=58) were in the highest quintile.

There were few changes in patient characteristics over 2003-14. Gender, age distribution and rurality were unchanged over time. However, there were significant changes in the distribution of patients across income quintiles over the interval of study; the proportion of patients in the lowest income quintile decreased from 35% to 16%, while the proportion of patients in the middle two quintiles (2-3) increased from 29% to 55%. The proportion of patients in the highest two quintiles (4-5) did not change significantly, representing approximately 25-30% of all patients each year.

A comparison of the patient and injury characteristics between 2003-2006 and 2010-2013, stratified by burn center status, is presented in **Table 4.2**. No changes were observed in age, income quintile, or comorbidity. The proportion of female patients treated outside of burn centers increased over time, while the proportion of rural residents treated outside of burn centers decreased over time.

Injury Characteristics

Baseline injury characteristics are presented in **Table 4.1**. The median %TBSA was 35 (IQR 25-45), and the incidence of inhalation injury was 9% (n=70). Most injuries were secondary to flame (66%, n=510), or contact (31%, n=238) burns while a small proportion (3%, n=24) were electrical in nature. Cause of burn remained relatively stable over time. No significant temporal trends were observed in either burn extent or incidence of inhalation injury.

In both 2003-2006 and 2010-2013, burn centers admitted significantly more patients with inhalation and electrical injuries compared to non-burn centers (**Table 4.2**). The proportion of patients with flame injuries treated outside of burn centers increased over time.

Resource utilization and discharge disposition

Median (IQR) hospital length of stay was 12 (18) days. The majority of patients were discharged home (58%, n=350); of these, most (33%, n=205) were discharged home with support, such as in-home nursing visits for wound care, while 145 (n=24%) patients were discharged home without support. One-third (31%, n=189) of patients were discharged to a rehabilitation or long-term care facility. The proportion of patients discharged home decreased significantly between 2003 and 2014 (68% to 46%, p <0.001); concomitantly, there was a significant increase in the proportion of patients discharged to inpatient rehabilitation facilities or long-term care (9% to 36%, p<0.001).

Mortality

The overall 30-day mortality rate was 19% (n=149); excluding deaths within 24 hours of admission, the 30-day mortality rate was 10% (n=68).

After adjustment for patient and injury characteristics, the odds of death in 2010-2013 were significantly lower than 2003-2006, both including (OR 0.39, 95% CI 0.25-0.61) and excluding (OR 0.34, 95% CI 0.20-0.58) 24-hour deaths. The area under receiver operating characteristic curve (AUC) for these models was 0.87 (95% CI 0.81-0.92) and 0.92 (0.89-0.95), respectively. On stratified analysis including only burn centers, there was a significant reduction in mortality at burn centers between 2003-2006 and 2010-2013, both when including 24-hour deaths (OR 0.36, 95% CI 0.34-0.38) and when excluding them (RR 0.34, 95% CI 0.29-0.40) (**Table 4.3**). The AUC for these models was 0.90 (95% CI 0.85-0.96) and 0.94 (95% CI 0.91-0.97), respectively. In contrast, at non-burn centers, mortality did not change significantly when comparing 2010-2013 to 2003-2006, either including (OR 0.41, 95% CI 0.13-1.24) or excluding (OR 0.99, 95% CI 0.20-4.91) deaths within 24 hours (**Table 4.3**). The AUC for these models was 0.75 (95% CI 0.53-0.97) and 0.88 (95% CI 0.79-0.97), respectively.

Trends in risk-standardized mortality rates are presented in **Figure 4.3**. Greater variation in year on year mortality was observed at non-designated centers as compared to burn centers.

4.5 Discussion

This population-based analysis characterizes the burden of major burn injury in the province of Ontario, providing critical epidemiologic data for future resource planning and injury prevention efforts. We characterized the concentration of care in our geographical region, and examined trends in regionalization over time. Overall, the proportion of patients treated at a burn center increased from 57% to 71%; thus, almost 30% of patients with major burn injury continue to receive care outside of regional burn centers. Our data suggest that 30-day mortality rates have improved significantly over the last ten years. While these improvements were observed at burn and non-burn centers, consistent improvements were observed at burn centers, particularly over the last three years. At non-burn centers, mortality varied greatly from year to year. The overall incidence and severity of burn injury, in terms of both burn extent and the incidence of inhalation injury, has remained stable over time.

We have identified a significant opportunity to further centralize the care of majorly burn-injured patients, and in so doing, to potentially improve their outcomes. While burn care did become increasingly concentrated over time, 30% of patients continue to receive care outside of a burn center. Few data sources exist to facilitate the study of trends in regionalization of burn care, limiting our ability to compare local trends in regionalization to other areas. Some data exist to suggest regionalization has occurred throughout the United States. Kastenmeier et al found that admissions to five regional burn centers in the United States increased by 31% over 1998 to 2006[182]; given reports of stable, or decreasing incidence of burn injury overall, this increase in admissions likely reflects improved regionalization of care. Similarly, in New York, the proportion of patients receiving burn center care increased from 33% to 77% between 1985 and 2006[167]. While difficult to quantify, many authors attribute recent improvements in mortality and health care utilization to the concentration of care in burn centers (23,24). Our study endorses this finding, as mortality rates decreased alongside increasing concentration of care in burn centers.

The factors that may contribute to reductions in mortality remain to be definitively characterized. The observed differences in mortality trends on the analyses stratified by burn center status suggest that the effect of time on mortality is modified by treatment in a burn center. Burn centers employ a resource-intensive, multidisciplinary approach to burn care that is patient-oriented and rooted in processes of care aimed at improving the quality and outcomes of burn care. Prior efforts to demonstrate an association between burn center care and improved outcomes have largely focused on burn center volumes, rather than burn versus non-burn center care. This work has not conclusively demonstrated better survival in *high-volume* burn centers[101,102]. Our study compared trends in mortality at two regional burn centers to eighty-two non-burn centers, irrespective of patient volumes. The definition of a burn center in our region is largely based on available resources; one of the two burn centers is an ABA-verified center. Thus, direct comparisons with our study are limited, as this is the first study to compare burn and non-burn center outcomes using a population-based approach. The failure of previous studies to link burn center volumes and mortality might be explained in several ways. Mortality might be an insensitive marker of burn center care, due to confounding by varying illness severity, immortality time bias, or other unmeasured factors. It may be that centers have not met the volume threshold at which a mortality benefit exists, or that all centers studied have actually exceeded this critical volume. Another possibility is that the benefit of regionalized burn care is best represented by outcomes other than mortality, such as inpatient and post-acute care health resource utilization, health-related quality-of-life, and functional recovery. These outcomes have not traditionally been studied in the burn literature[126,183,184], though one study has demonstrated that burn center care is associated with reduced length of stay and inpatient costs[185]. The next improvements in the structures of burn care will follow characterization of these outcomes, an understanding of the patients most likely to benefit from specialized care, a consistent definition of what constitutes specialized care, and further characterization of the infrastructure required to support a centralized burn care system. Furthermore, an understanding of triage practices is also necessary; that 30% of patients with major burn injury do not reach a burn center might reflect a conscious decision on the part of community surgeons who feel burn care is within their scope of practice, versus an infrastructure problem, where differences exist in access to care. A characterization of these barriers will inform future efforts to achieve fully concentrated care, with resultant improvements in outcomes following major burn injury.

Efforts to further regionalize care and improve outcomes for burn-injured patients are justified, given that the overall incidence of major burn injury in our geographical region has remained stable over the last eleven years. This finding is similar to that reported in a non-population-based Canadian study which reported stable incidence between 1995 and

2004[10]. In contrast, Australian and European studies have reported a decreased incidence of overall burn admissions[9,11]. These observed differences might reflect differences in inclusion criteria and study periods, as well as increased awareness of patients that can be successfully managed as outpatients, regional case mix variations, and local cultures of care and resource availability.

To date, few studies have published population-based rates of burn injury. We have estimated an overall incidence of 1.15 admissions per 100,000 person-years; this is not directly comparable to other published rates, as we have included only patients with ≥20% TBSA injury, and no other population-based rates exist for this specific cohort. While the overall incidence of major burn injury is relatively low compared to other causes of injury[186], these patients have significant health resource needs, with inpatient length of stay regularly approaching two weeks, and the majority requiring inpatient rehabilitation following discharge; only one-quarter of patients are discharged home without support. The incidence of major burn injury is particularly high among the elderly; among females, incidence is highest among those aged ≥75, and among males those aged ≥75 represent the second highest incidence. Resource planning efforts must acknowledge that as the population grows, particularly alongside aging of the baby boomer generation[187], the volume of patients requiring burn care may increase.

We recognize several limitations of this study. The use of administrative data precludes our ability to perform comprehensive risk adjustment. Furthermore, significant variation in burn size estimation exists among physicians[188], which may result in incorrect documentation of burn size. Overestimation of burn size may introduce misclassification bias, such that patients with <20% TBSA may be included. Ultimately, this may lead to an overestimation of the number of centers providing care to major (≥20% TBSA) burns, and an underestimation of regionalization and mortality. Another limitation concerns our definition of burn centers. We considered a patient to have received burn center care if they were transferred within 3 days of their injury; this may have underestimated the number of patients who received definitive care in a burn center. However, this likely has resulted in an underestimation of the true association between burn center care and mortality. If we assume a benefit to burn center care, then attributing the outcomes of patients transferred beyond 3 days to the non-burn center likely biases our comparison towards the null. The optimal interval within which burn patients should receive definitive care has not been defined. Errors in the estimation of burn size and depth by inexperienced practitioners can result in under- or over-resuscitation, with well described negative sequelae, including compartment syndrome, acute kidney injury, and shock[189,190]. Thus, patients transferred more than 3 days after their injury might not have modifiable outcomes to the same extent as those transferred in a timely manner. Our conclusions are also limited by the sample size of patients treated in non-burn centers; as a result, we are likely underpowered to detect significant trends in mortality at non-burn centers. Significant variations in mortality were observed at non-burn centers compared to burn centers, and future work should characterize whether this variation truly reflects varying processes of care. Our analysis of the health resource needs of burn survivors has not extended beyond the inpatient phase; it is likely that these patients continue to require regular contact with the healthcare system that we have not captured.

In conclusion, we have characterized the burden of major burn injury at the population level in a geographical region of more than 13 million, and have demonstrated that burn injury is a consistent source of morbidity and mortality year after year. Significant improvements in mortality have occurred following major burn injury. These improvements were most significant at burn centers, while mortality rates vary widely outside of burn centers. A considerable opportunity to further regionalize care exists. Future work should focus on identifying barriers to regionalization of burn care and delineating the outcomes most valid to patients.

4.6 Tables for Chapter 4

Table 4.1. Baseline patient and injury characteristics

	Overall N=772	**Burn center N=490**	**Non-burn center N=282**	**P value**
Patient characteristics				
Median age (IQR)	46 (35-60)	48 (35-63)	46 (34-58)	0.09
Male (%)	570 (74)	373 (76)	197 (70)	0.11
Comorbidity (%)				0.31
1 - None	55 (7)	32 (7)	23 (8)	
2	82 (11)	55 (11)	27 (10)	
3	321(42)	209 (43)	112 (40)	
4	164 (21)	108 (22)	56 (20)	
5 - Highest	148 (19)	84 (17)	64 (23)	
Income Quintile (%)				0.31
1- Lowest	202 (26)	120 (24)	82 (29)	
2	174 (23)	119 (24)	55 (20)	
3	134 (17)	82 (17)	52 (18)	
4	137 (18)	84 (17)	53 (19)	
5- Highest	58 (8)	19 (16)	39 (14)	
Rural (%)	152 (20)	78 (16)	74 (26)	0.001
Injury characteristics				
Median TBSA (IQR)	35 (25-45)	35 (25-45)	25 (25-45)	0.05
Inhalation injury (%)	70 (9)	56 (11)	14 (5)	0.003
Burn Mechanism (%)				0.10
Flame	510 (66)	324 (66)	65-70%	
Contact	238 (31)	146 (30)	30-35%	
Electrical	24 (3)	20 (4)	1-5%	
Outcomes				
24-hour mortality (%)†	81 (10)	50 (10)	31 (11)	0.73
30-day mortality (%)‡	149 (19)	101 (21)	48 (17)	0.22

Counts <6 suppressed so as to remain compliant with privacy regulation

IQR, interquartile range

TBSA, total body surface area

†within 24 hours of admission; excluding deaths in the emergency department

‡including deaths within 24 hours of admission

Table 4.2. Patient and injury characteristics, by time period

	2003-2006			2010-2013		
	Burn Center N=193	**Non-Burn Center N=121**	**p-value**	**Burn Center N=171**	**Non-Burn center N=79**	**p-value**
Patient characteristics						
Median age (IQR)	45 (34-59)	45 (35-63)	0.39	47 (34-58)	52 (34-67)	0.13
Male (%)	143 (74)	89 (74)	0.92	135 (79)	48 (61)	0.006
Comorbidity (%)			0.19			0.83
1 None	16 (8)	12 (10)		13 (8)	1-5%	
2	20 (10)	12 (10)		19 (11)	5-10%	
3	78 (40)	37 (31)		74 (44)	45-50%	
4	48 (25)	26 (21)		36 (21)	15-20%	
5 Highest	31 (26)	34 (28)		25 (15)	15-20%	
Income Quintile (%)			0.13			0.74
1 Lowest	48 (25)	40 (33)		43 (25)	22 (28)	
2	39 (20)	19 (16)		43 (25)	16 (20)	
3	26 (13)	20 (17)		29 (17)	28 (23)	
4	41 (21)	29 (24)		24 (14)	9 (11)	
5 Highest	38 (20)	13 (11)		28 (17)	14 (18)	
Rural (%)	25 (13)	33 (27)	0.002	34 (20)	15 (19)	0.61
Injury Characteristics						
Median TBSA (IQR)	35 (25-45)	25 (25-45)	0.09	35 (25-45)	25 (25-35)	0.05
Inhalation injury (%)	21 (11)	6 (5)	0.07	23 (13)	<6	0.05
Mechanism (%)			0.05			0.39
Flame	130 (67)	71 (59)		107 (63)	70-75%	
Electrical	10 (5)	<6		8 (5)	1-5%	
Contact	53 (27)	48 (40)		56 (33)	25-29%	
Outcomes						
24-hour mortality (%)†	21 (11)	11 (9)	0.61	19 (11)	<6	0.12
30-day mortality (%)‡	47 (24)	18 (15)	0.04	31 (18)	7 (9)	0.06

Counts <6 suppressed so as to remain compliant with privacy regulation
IQR, interquartile range
TBSA, total body surface area
†within 24 hours of admission; excluding deaths in the emergency department
‡ including deaths within 24 hours of admission

Table 4.3. Trends in 30-day Mortality

	All deaths		Excluding deaths within 24h of admission	
	OR (95% CI) ***2010-2013 vs 2003-2006***	**p-value**	**OR (95% CI)** ***2010-2013 vs 2003-2006***	**p-value**
All centers	0.39 (0.25-0.61)	<0.001	0.34 (0.20-0.58)	<0.001
Burn centers	0.36 (0.34-0.38)	<0.001	0.34 (0.29-0.40)	<0.001
Non-burn centers	0.41 (0.13-1.24)	0.09	0.99 (0.20-4.91)	0.35

Hierarchical Logistic regression model accounting for age, sex, comorbidity, %TBSA, inhalation injury burn mechanism, and correlated outcomes within centers. OR, odds ratio; CI, confidence interval

4.7 Figures for Chapter 4

Figure 4.1: Trends in age-standardized incidence by gender.

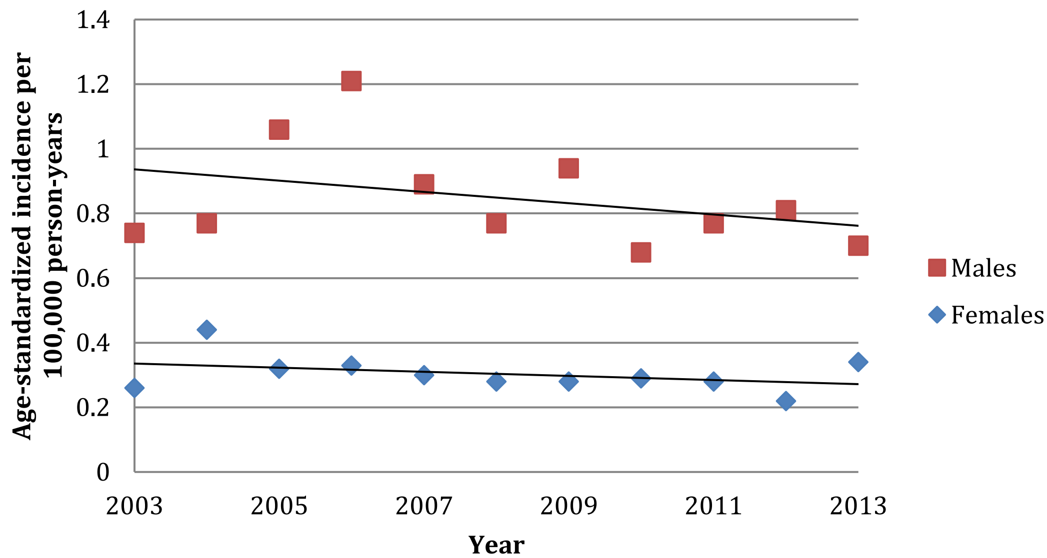


Figure 4.2: Trends in sex-standardized incidence by age group.

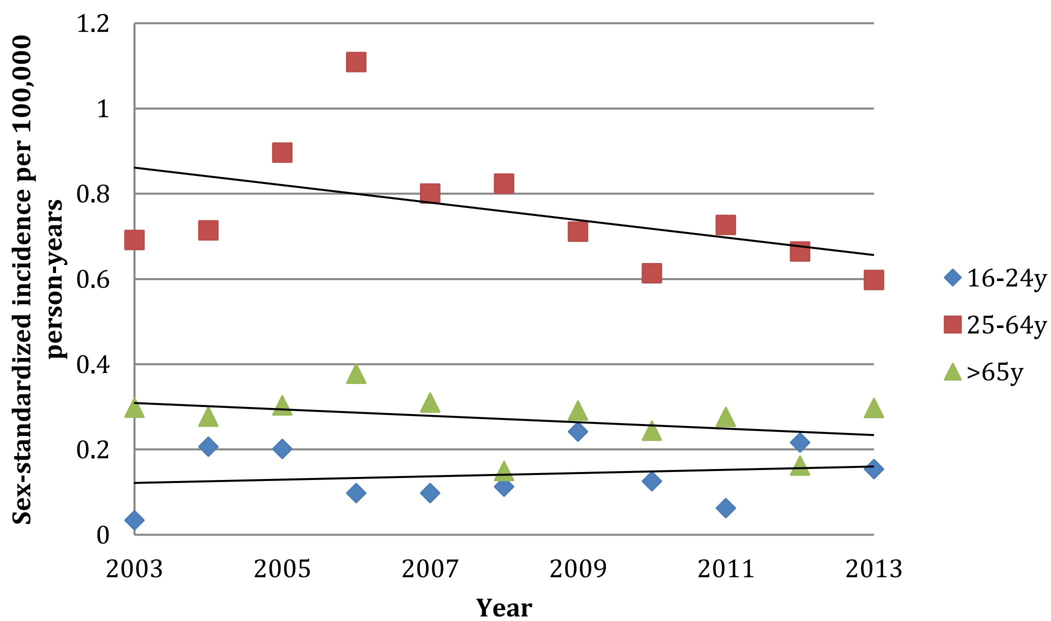
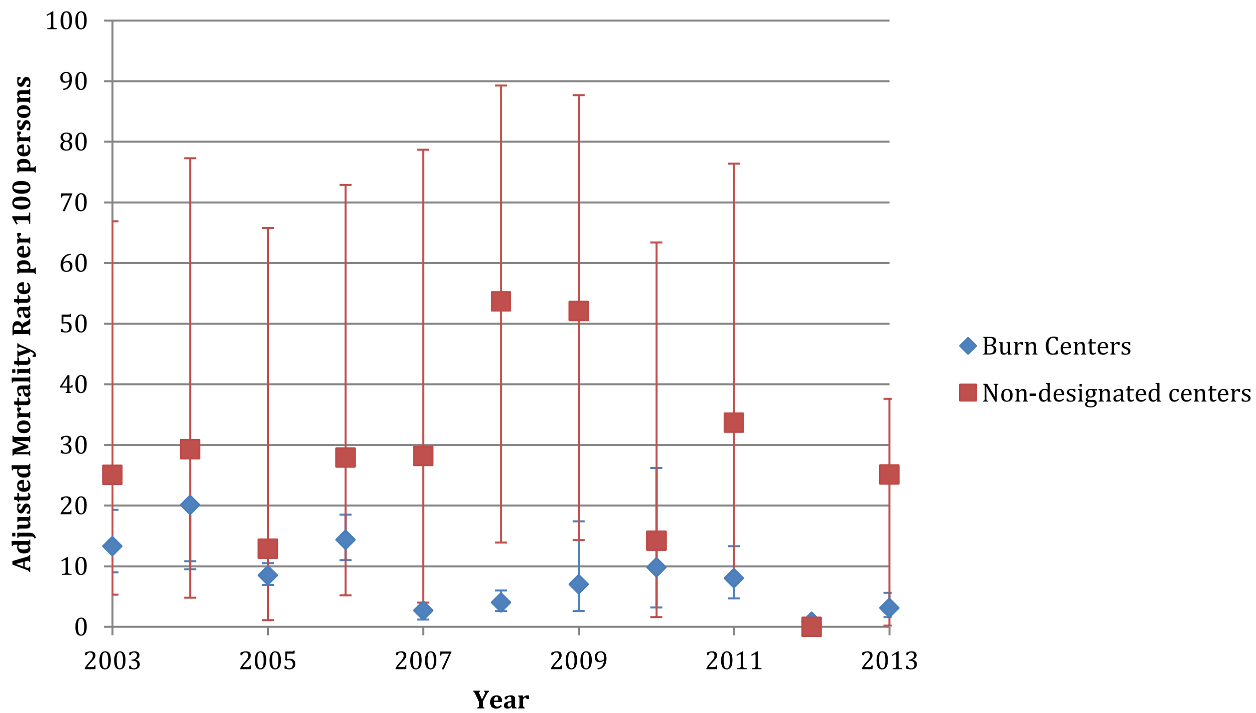


Figure 4.3: Trends in adjusted 30-day mortality by burn center status. Yearly mean adjusted rates derived from multivariable hierarchical logistic regression model adjusted for patient and injury characteristics. Error bars represent 95% confidence intervals. The table demonstrates the number of yearly admissions. BC, burn center; NBC, non-burn center; N, total yearly admissions.



N											
BC	43	43	55	52	38	46	42	37	51	41	42
NBC	32	24	27	38	26	27	29	25	20	17	17

CHAPTER 5: POST-ACUTE CARE HEALTHCARE UTILIZATION FOLLOWING MAJOR BURN INJURY

The purpose of this chapter is to:

1) Describe the rate and principal reasons for emergency department visits in the five years following burn injury

2) Describe the cumulative incidence and principal reasons for unplanned readmissions in the five years following burn injury

3) Evaluate factors associated with emergency department visits and unplanned readmissions

Acknowledgement: Parts of Chapter 5 were reprinted from the following:

Mason SA, Nathens AB, Byrne JP, Fowler RA, Karanicolas PJ, Moineddin R, Jeschke MG. Burn center care reduces acute healthcare utilization after discharge: a population-based analysis of 1895 survivors of major burn injury. Surgery. Epub 2017 July 13.

5.1 Summary

Background: Improvements in survival after burns have resulted in more patients being discharged home after severe injury. However, the post-discharge healthcare needs of burn survivors are not well understood. We aimed to determine the rate and causes of unplanned presentation to acute care facilities in the five years after major burn injury.

Methods: Data derived from several population-based administrative databases were used to conduct a retrospective cohort study. All patients aged ≥16 years who survived to discharge following a major burn injury in 2003-2013 were followed for 1-5 years. All ED visits and unplanned readmissions were identified and classified by cause. Factors associated with ED visits were modeled using negative binomial generalized estimating equations; factors associated with readmission were modeled using multivariable competing risk regression.

Results: We identified 1895 patients who survived to discharge; 68% of patients had at least one ED visit and 30% had at least one readmission. Five-year mortality was 10%. The most common reason for both ED visits and readmissions was traumatic injury. After risk adjustment, patients who received their index care in a burn center experienced significantly less need for subsequent unplanned acute care - fewer ED visits (RR 0.61, 95% CI 0.52-0.72) and fewer hospital readmissions (HR 0.77, 95% CI 0.65-0.92).

Conclusions: Acute healthcare utilization is frequent following burn injury, and is most commonly related to traumatic injuries. Burn-related events are uncommon beyond 30

days after discharge, suggesting low rates of burn recidivism. Patients treated at burn centers have significantly reduced unplanned healthcare utilization after their injury.

5.2 Background

Despite an overall reduction in burn incidence, hundreds of thousands of patients continue to be admitted to hospital each year for the treatment of major burn injury[18]. Improvements in burn-related mortality have occurred such that most patients survive to discharge[191,192,166]. While the nature of burn injury suggests that some patients will have ongoing complex care needs after discharge, the post-acute healthcare needs of burn survivors are not well understood.

Burn care is largely provided in specialized burn centers[92,167], despite a lack of evidence to suggest that care in these centers results in lower mortality[101,102]. However, burn centers might have resources that facilitate improved care transitions, resulting in reduced post-acute healthcare use. Given that readmissions and emergency department (ED) visits might represent gaps in the transition of care from the hospital setting, they are increasingly being utilized as quality indicators[193]. Rates of these events might therefore be an indicator of the utility and quality of burn center care. Furthermore, an understanding of the rate and causes of acute healthcare use after discharge might inform the development of targeted interventions to improve long-term outcomes after burn injury.

The objective of this study was to determine the rate and principal causes of unplanned readmissions and emergency department visits in the five years following major burn injury. Further, we sought to identify the patient and/or injury factors associated with each of these events. We hypothesized that treatment at a burn center would be associated with lower rates of post-acute unplanned healthcare utilization.

5.3 Methods

Study design

We conducted a population-based, retrospective cohort study in Ontario, Canada using health administrative data. This study was approved by the Research Ethics Board at Sunnybrook Health Sciences Centre.

Data sources

Data were derived from several administrative databases: (1) the Discharge Abstract Database (DAD), which contains demographic, diagnostic (including burn injury characteristics), procedural, hospital and discharge information for all hospital admissions in the province of Ontario; (2) the National Ambulatory Care Reporting System (NACRS), which captures demographic, diagnostic, hospital and discharge information for all emergency department visits in the province of Ontario; (3) the Registered Persons Database (RPDB), which contains vital statistics data for all residents of the province of Ontario who are alive and eligible for health care coverage; (4) the Office of the Register General – Deaths (ORGD) database, which contains information on date and cause of death for all residents eligible for health care coverage in Ontario. These datasets were linked using unique encoded identifiers and analyzed at the Institute for Clinical

Evaluative Sciences. Similar to other Canadian provinces, the government of Ontario administers a single payer health care system that universally funds all hospital, laboratory, and physician services for eligible residents. Therefore, these datasets include information for all eligible residents in the province. Diagnostic information in these datasets is recorded according to the Canadian version of the tenth revision of the *International Classification of Diseases and Related Health Problems* (ICD-10-CA). We have previously validated diagnoses codes for the identification and characterization of major burn injury[180].

Study population

We used the DAD to identify all patients aged 16 years and older who were admitted to hospital for the treatment of major burn injury between April 1, 2003 and March 31, 2013, and survived to discharge. Major burn injury was defined in accordance with the American Burn Association criteria for referral to a burn center[33]: any burn resulting in (1) 10% total body surface area (TBSA) burn, or (2) full-thickness burns to the face, feet, hands, and perineum, or (3) any burn with inhalation injury. Individuals lacking a valid Ontario health card or who sustained concurrent major trauma with their burn were excluded.

Exposure of interest

We hypothesized that patients who received their initial burn care at a regional burn center might have reduced post-discharge acute healthcare utilization compared to those treated outside of burn centers. In Ontario, specialized burn care is provided at two adult regional burn centers, one of which is verified by the American Burn Association. We have previously demonstrated that in Ontario, approximately 30% of patients receive care outside of burn centers[194].

Outcomes

The primary outcomes of interest were emergency department (ED) visits and unplanned readmissions during the five years following discharge from the index burn admission. Emergency department visits were identified in NACRS and categorized according to the main reason for the visit. All readmissions were identified in the DAD, where each readmission is categorized as urgent or elective. To focus on modifiable events, we included only unplanned readmissions, recognizing that elective readmissions are often an appropriate management strategy for burns in the course of burn reconstruction. Similarly, we hypothesized that ED visits and readmissions occurring within 72 hours of discharge might be distinct from those occurring later after discharge, in that they likely represent ongoing sequelae of the index admission, so these were excluded. To mitigate overlap between ED visits and readmissions, ED visits leading to readmission were considered only as a readmission and not counted as ED visits. All patients had a minimum follow-up of one year.

We considered deaths occurring during the five years after discharge as a secondary outcome. All deaths were captured through ORGD and classified as in-hospital if associated with a DAD record, as in ED if associated with a NACRS record alone, and as occurring out of hospital if there was no associated DAD or NACRS record.

Covariates

We considered several patient characteristics as potential confounders. These included age, sex, pre-injury comorbidity burden, socioeconomic status, and urban/rural residence. Comorbidity burden was estimated using the resource utilization band of the Johns Hopkins Adjusted Clinical Groups case mix system, which assigns patients to one of six morbidity categories based on the rate and severity of prior healthcare utilization[195]. For the purposes of our analysis, we collapsed categories 0 and 1, representing non- and healthy users, into a single category. Using each patient's postal code, the median neighbourhood income was determined; income quintiles were then used as a marker of socioeconomic status. Patient residence was classified as urban or rural based on the Rurality Index of Ontario (RIO), where a RIO$\geq$45 is considered rural; this considers population density as well as the distance each patient must travel to the nearest basic and advanced referral center[179].

We also considered several injury-specific variables as potential confounders. These were derived from diagnoses codes in the DAD pertaining to the index admission, and included total body surface area (TBSA) burned, presence of inhalation injury, and mechanism of the burn (flame, electrical, or contact). We also considered the disposition of each patient's index admission, classified as discharge to: home, home with homecare, another inpatient facility, rehabilitation or long-term care facility, or other. Patients discharged home with homecare receive in-home nursing visits for wound or other care (e.g., intravenous antibiotics). We were unable to differentiate between discharge to a rehabilitation or long-term care facility in these datasets.

Statistical analysis

Descriptive statistics were calculated for the entire study population. We compared patient and injury characteristics between patients with and without an ED visit, as well as with and without a readmission. The Wilcoxon rank-sum test was used to compare non-normally distributed continuous variables, while the chi-square test was employed for categorical variables. Crude rates of ED visits and readmissions per 100 person years were estimated.

Separate modeling approaches were undertaken to determine the factors associated with the risk of ED visits and readmission. Given the greater frequency of ED visits relative to readmissions, and the rarity of death preceding ED visits, these were modeled as a count outcome, using negative binomial generalized estimating equations. A negative binomial distribution was utilized given the significant overdispersion in the ED visit count. To account for varying follow-up times, each patient's total follow-up time was log-transformed and included in the model as an offset term. Follow-up time was calculated as the time from index discharge to the end of follow up; follow-up ended at March 31, 2014 or death, whichever came first. Generalized estimating equations were used to account for the clustering of patient outcomes at the hospital level. Variables were chosen *a priori* for inclusion in the model, based on clinical relevance and differences identified on univariate analysis.

In choosing the best approach to model readmissions after discharge, we considered the presence of the competing risk of death, and the likelihood that readmissions and mortality are not independent events, which limits application of traditional survival analysis. A competing risk is an event whose occurrence precludes the occurrence of the event of interest[196]. As such, readmission hazards were estimated using a time-to-event approach that explicitly accounted for the competing risk of death. The cumulative incidence of readmission by 5 years was estimated, and factors associated with the time to first readmission were identified using Fine and Gray multivariable risk regression[197]. Patients were censored at the end of follow-up or five years, whichever came first. To determine the impact of accounting for the competing risk, the subdistribution hazards were compared to cause-specific hazards derived from a Cox Proportional hazards model. Variables were chosen *a priori* for inclusion in the model, based on clinical relevance and differences identified in the cumulative incidence of readmission among patient and injury subgroups. Proportionality of hazards was confirmed by visually examining the cumulative hazards versus time plot, and by using interaction terms. Where the proportionality assumption was violated, interaction terms were included in the model and re-examined.

All analyses were conducted using SAS version 9.4 (Cary, NC).

5.4 Results

We identified 1895 patients who survived to discharge following a major burn injury. Patients were most commonly young, urban-dwelling males, of lower median income with moderate pre-injury comorbidity (**Table 5.1**). The median TBSA burned was 15% (Interquartile range, 5-25). Most sustained flame burns, and 9% sustained an inhalation injury. Approximately half of all patients were treated at a burn center, and the majority were discharged home; 39% with homecare, and 39% without.

The cumulative incidence of readmission, ED visits, and mortality during follow-up are presented in **Figure 5.1**. After discharge, we identified 8210 ED visits among 1290 patients; overall, 68% of patients had at least one ED visit (Interquartile range, 0-5). Eleven percent of patients had 5 or more ED visits per year. The overall rate of ED visits during follow-up was 104 per 100 patient years. Sixteen percent of all ED visits (n=6899) resulted in readmission. Compared to patients without an ED visit, those with a visit also had higher levels of pre-injury health care use and fewer received burn center care (49 vs 57%) (**Table 5.1**).

Of all ED visits, 23% were related to traumatic injury, 11% were related to mental illness, and 11% were related to post-treatment complications (**Table 5.2a**). Among traumatic injury visits, only 4% were burn-related.

We identified 1473 readmissions among 571 patients; overall, 30% of patients had at least one unplanned readmission during the five years post-discharge (range, 1-61). The rate of unplanned readmissions during follow-up was 19 per 100 patient years. Compared to patients without a readmission, those readmitted were significantly older, of lower socioeconomic status, and had higher levels of pre-injury comorbidity (**Table 5.1**). The cumulative incidence of readmission by age group is presented in **Figure 5.2**. Fewer readmitted patients received care at a burn center compared to those not readmitted (43 vs 55%) **(Figure 5.3**), and readmitted patients were less likely to have been discharged home after the index admission (66 vs 83%).

Consistent with ED visits, traumatic injury was also the leading cause of unplanned readmissions. The other common causes were cardiovascular, respiratory, and gastrointestinal disease (**Table 5.2b**). Among the admissions attributed to injury, 24% were burn-related.

Mortality at five years was 10%; most patients had both an ED visit (86%) and readmission (72%) prior to death.

After adjustment for patient and injury characteristics, patients treated at a burn center experienced significantly fewer ED visits (RR 0.61, 95% CI 0.52-0.72) than patients treated at non-burn centers (**Table 5.3**). Factors associated with a greater number of ED visits included discharge to a rehabilitation or long-term care facility after the index burn admission, and younger age. Patients with the highest level of pre-injury comorbidity had a 9-fold higher rate of ED visits than those with minimal comorbidity. No injury-specific factors were significantly associated with ED visits.

Similarly, burn center patients were 23% less likely to experience an unplanned readmission during follow-up (HR 0.77, 95% CI 0.65-0.92) compared to those treated at non-burn centers (**Table 5.4**). Factors associated with an increased risk of readmission were increasing age, lower socioeconomic status, and discharge to a rehabilitation or long-term care facility after the index admission (**Table 5.4**). Patients with the highest level of pre-injury comorbidity had a four-fold greater risk of readmission during follow-up compared to patients with minimal comorbidity, as illustrated in **Figure 5.4**.

5.5 Discussion

In this population-based, longitudinal cohort study of burn survivors, we found that more than 70% of patients had an ED visit and 30% experienced an unplanned readmission after their burn admission. Traumatic injuries, mental illness, and respiratory disease were common causes for both ED visits and readmissions, while burn-related ED visits and readmissions were uncommon beyond 30 days after discharge. The infrequency of burn-related visits beyond 30 days after discharge suggests a low rate of burn recidivism. Patients who received their burn care in a burn center experienced 40% fewer ED visits, and were almost 25% less likely to have an unplanned readmission, compared to patients treated outside of burn centers.

Few studies have examined the healthcare utilization of burn survivors after discharge, reflecting the challenges associated with capturing these events and following patients long-term. As a result, most studies, in both burn and other cohorts, have focused on reporting 30-day readmission rates[193,198–200]. Health administrative databases offer an opportunity for longitudinal examination of healthcare utilization, and are increasingly used for this purpose[57,153,201]. Using one such database, Mandell et al followed burn survivors for two years and found that principal causes of readmission were rehabilitation, sepsis, and mental illness, and that burn-related readmissions were uncommon beyond 30 days[202]. Forty-five percent of patients in their study experienced a readmission, compared to 30% of patients in our study. Two differences in study design likely explain this difference: (1) we included all adult patients, while Mandell et al included only those 45 years and older, representing an older cohort who might be expected to have higher hospitalization rates related to chronic illness[203]; and (2) we included only unplanned readmissions, while Mandell et al included all types of readmission, including planned reconstruction, likely accounting for the observed differences in admission reasons – chiefly, that rehabilitation was the principal reason for readmission in their study. Several population-based studies using administrative data in Australia, with more than 15 years follow-up, have demonstrated high rates of readmissions after burn injury, related to cardiovascular, infectious, and gastrointestinal diseases[57,153,204]. This group identified significantly increased readmissions for each of these diseases compared to an age- and sex-matched uninjured cohort, consistent with our findings that medical readmissions are common over the longer term after discharge.

The key strength of our study is the utilization of administrative data, which offers the ability to follow patients longitudinally after discharge with minimal loss to follow-up. Patients are lost to follow-up only if they become ineligible for health coverage or move out of the province; census data estimates that less than 5% of Ontarians moved out of the province over a 5-year period[157]. Furthermore, Ontario's single-payer healthcare system facilitates capture of all healthcare visits for all insured persons. As a result, our data represent near complete follow-up during the five years after burn injury. Furthermore, the availability of data regarding timing and causes of death allowed us to account for the competing risk of death in the readmission analyses; failure to account for this competing risk can result in overestimation of the hazard ratio[205].

Our findings are limited by the lack of an uninjured comparator group; as a result, we are only able to report absolute, rather than relative rates of healthcare use. The use of administrative data limits our ability to understand the factors that contribute to a lower risk of emergency health services use among patients who received their care in a burn center. Furthermore, factors that might be important in risk of readmission or ED visits, such as functional status, home supports, and access to a family physician, are unavailable in administrative data. We have not captured whether or not patients had outpatient visits prior to their ED visit and/or readmission, which limits our ability to determine whether or not events may have been preventable. Similarly, while we have accounted for pre-injury comorbidity in our analyses, we have not specifically accounted for the type of comorbidity present; as a result, we are unable to determine whether visits related to medical illness represent the development of new disease after injury. Ultimately, we feel these unmeasured factors are unlikely to be differentially distributed at burn versus non-burn centers, and as such, are unlikely to bias our observation that burn center care was associated with reduced rates of ED visits and readmissions.

Many quality improvement programs have identified the transition from inpatient to outpatient care as a target for improving outcomes, given the costs associated with avoidable ED visits and readmissions[206]. However, evidence regarding the effectiveness of interventions aimed at reducing readmissions and ED visits is mixed, and no single intervention has consistently been demonstrated to be effective[207–209]. In contrast, multifaceted interventions have been successful in reducing readmissions among medical patients [207,210,211]. Our data suggest that perhaps these care transitions occur more successfully in burn centers, as evidenced by reduced rates of acute healthcare utilization after discharge. Though most post-burn healthcare utilization in our study was not directly burn-related, our observation that patients treated in a burn center had lower rates of acute healthcare use after discharge suggests that at least some of these visits might be preventable. This might reflect a combination of early discharge planning, patient education, multidisciplinary input in disposition decisions (social work, nursing, physiotherapy, etc), and direct access to a burn nurse by telephone or to same or next-day clinic. Future work should characterize the specific processes of care that facilitate successful care transitions and reduced post-acute healthcare utilization, in order to inform future quality improvement and post-burn healthcare delivery.

Transitions to outpatient care should be focused on helping patients achieve the best possible level of health and functioning after burn. In our study, more than one-third of patients had a high comorbidity burden at the time of their injury, and readmissions for medical diseases were common. Future investigation should focus on identifying whether opportunities for primary or secondary health prevention measures might exist during the index hospitalization or transition to outpatient care that might ultimately improve long-term health. For example, the index burn admission might represent an extended opportunity for patients to be connected with primary care providers or specialists, or to have their home medications reassessed. The high rate of ED use in our study suggests that some patients might be using the ED for primary care; 11% of patients had 5 or more ED visits per year. Prior work has identified that 4 or more visits per year is the most common threshold to consider patients ‘high-users’[212]. Therefore, efforts to ensure patients have a primary care provider at the time of discharge are warranted.

Ultimately, our data expand our knowledge of the longer-term healthcare needs of burn survivors. These patients require longitudinal follow-up for potential burn sequelae, such as wound contractures, but also require ongoing management of chronic diseases, including mental illness and prevention of subsequent trauma-related injury. Our findings suggest that burn centers may be best positioned to help transition patients to this complex and multi-disciplinary follow-up care. Ultimately, the role of burn centers in the delivery of care following the acute phase remains to be characterized; nonetheless, our data suggest that further efforts regionalize burn care might reduce post-burn acute healthcare utilization.

In conclusion, burn survivors have high rates of post-acute care health utilization that persist up to five years following discharge. Patients treated in burn centers have a significantly reduced rate of unplanned healthcare utilization. These data demonstrate the potential benefits of burn center care, and can inform the delivery of post-acute health service delivery for burn survivors.

5.6 Tables for Chapter 5

Table 5.1: Patient and injury characteristics by status at five years

	All	ED* Visit not leading to admission		P value	Readmission		P value	Death
		>1	None		>1	None		
Number of patients (%)	1895	1290 (68)	605 (32)		571 (30)	1324 (70)		185 (10)
Median age, years (IQR†)	44 (30-56)	44 (29-55)	45 (34-57)	0.006	52 (40-66)	41 (28-51)	<0.001	68 (54-76)
Male (%)	1408 (74)	956 (74)	452 (75)	0.74	394 (69)	1014 (77)	<0.001	113 (61)
Income Quintile (%)				0.07			0.003	
1-Lowest	464 (25)	337 (26)	127 (21)		149 (27)	315 (24)		64 (35)
2	413 (22)	286 (22)	127 (21)		147 (26)	266 (20)		46 (25)
3	346 (18)	224 (18)	122 (20)		104 (19)	242 (18)		23 (13)
4	379 (20)	249 (20)	130 (22)		95 (17)	284 (22)		22 (12)
5-Highest	275 (15)	179 (14)	96 (16)		67 (12)	208 (16)		26 (14)
Rural (%)	346 (18)	251 (19)	95 (16)	0.05	104 (18)	242 (18)	0.97	22 (12)
Comorbidity Band (%)				<0.001			<0.001	
1-Lowest	130 (7)	72 (6)	58 (10)		16 (3)	114 (9)		<5%
2	246 (13)	145 (11)	101 (17)		46 (8)	200 (15)		<5%
3	836 (44)	546 (42)	290 (48)		197 (34)	639 (48)		15-20%
4	383 (20)	290 (23)	93 (15)		128 (22)	255 (19)		20-25%
5-Highest	295 (16)	234 (18)	61 (10)		184 (32)	111 (8)		50-55%
Median % TBSA‡ (IQR†)	15 (5-25)	15 (5-25)	15 (5-25)	0.26	15 (5-25)	15 (5-25)	0.10	15 (5-15)
Burn mechanism (%)				0.71			0.19	
Flame	1002 (53)	679 (53)	323 (53)		298 (52)	704 (53)		55-60%
Contact	780 (41)	537 (42)	243 (40)		246 (43)	534 (40)		<5%
Electrical	112 (6)	73 (6)	39 (6)		26 (5)	86 (7)		40-45%
Inhalation injury (%)	167 (9)	117 (9)	50 (8)	0.56	49 (9)	118 (9)	0.82	15 (8)
Index burn center care (%)	981 (52)	638 (49)	343 (57)	0.003	247 (43)	734 (55)	<0.001	62 (34)
Discharge disposition (%)				0.15			<0.001	
Home	747 (39)	505 (39)	242 (40)		185 (32)	562 (42)		25-30%
Homecare	737 (39)	516 (40)	221 (37)		195 (34)	542 (41)		35-40%
Rehab or LTC§	290 (15)	183 (14)	107 (18)		143 (25)	147 (11)		25-30%
Other inpatient	82 (4)	56 (4)	26 (4)		29 (5)	53 (4)		<5%
Other	39 (2)	30 (2)	8 (1)		19 (3)	19 (1)		<5%

Counts <6 suppressed so as to remain compliant with privacy regulation
*ED, Emergency department
†IQR, Interquartile range
‡TBSA, Total body surface area
§LTC, Long-term care

Table 5.2a: Principal causes* of emergency department (ED) visits

	N (%)
ED visits not resulting in admission	6899
External cause of injury	1604 (23)
Accidents	989
Self-harm	24
Assault	103
Poisoning	19
Burns, frostbite, corrosions	64
Visit related to prior surgical treatment	790 (11)
Attention to sutures & dressings	280
Repeat prescription	184
Intravenous antibiotics	133
Examination for surgical follow up	106
Complication of surgical procedure	87
Mental health	734 (11)
Disorders related to psychoactive	431
substance use	139
Neurotic and stress-related disorders	80
Mood disorders	

* As defined by ICD-10CA diagnosis codes (NACRS)

Table 5.2b: Principal causes* of readmissions

	N (%)
Unplanned readmissions	1473
External cause of injury	234 (16)
Accidents	77
Burns, frostbite, corrosions	55
Self-harm	20
Assault	15
Poisoning	14
Respiratory disease	185 (13)
Chronic lower respiratory diseases	106
Influenza & pneumonia	40
Cardiovascular disease	162 (11)
Ischemic heart disease	56
Heart failure	36
Gastrointestinal disease	149 (10)
Liver and biliary disease	59

* As defined by ICD-10CA diagnosis codes (DAD)

Table 5.3: Factors associated with emergency department visits

	Adjusted Rate Ratio (95% CI*)
Index burn center care	0.61 (0.52-0.72)
Age group	
16-29 years	Ref
30-44 years	0.67 (0.58-0.76)
45-59 years	0.70 (0.58-0.83)
60-75 years	0.54 (0.43-0.68)
75+ years	0.55 (0.38-0.81)
Female	0.96 (0.81-1.13)
Comorbidity Band†	
1-Lowest	Ref
2	1.55 (1.11-2.17)
3	2.03 (1.51-2.72)
4	4.08 (3.00-5.56)
5-Highest	9.17 (6.53-12.89)
% Total Body Surface Area Burn	
<20	Ref
20-39	0.86 (0.76-0.98)
40-59	1.16 (0.79-1.70)
60+	0.89 (0.71-1.12)
Inhalation injury	0.97 (0.83-1.14)
Burn Mechanism	
Flame	Ref
Contact	0.78 (0.70-0.88)
Electrical	0.72 (0.52-1.00)
Index Discharge Disposition	
Home	Ref
Home with support	0.96 (0.81-1.15)
Rehabilitation or long-term care	1.28 (1.05-1.55)
Other inpatient	1.21 (0.91-1.60)
Other	1.32 (0.84-2.08)

*Confidence interval

†Measure of comorbidity burden based on healthcare utilization in 2 years prior to injury

Table 5.4: Factors associated with unplanned readmissions

	Subdistribution Hazard Ratio (95% confidence interval)†	Hazard Ratio (95% confidence interval)‡
Index burn center care	0.77 (0.65-0.92)	0.76 (0.64-0.90)
Female sex	0.99 (0.82-1.19)	0.98 (081-1.18)
Age group		
16-44 years	Ref	Ref
45-64 years	1.39 (1.14-1.70)	1.40 (1.14-1.71)
65-74 years	1.92 (1.43-2.59)	2.07 (1.54-2.77)
75+ years	2.67 (1.95-3.65)	2.82 (2.06-3.85)
Income Quintile		
1- Lowest	Ref	Ref
2	1.20 (0.95-1.51)	1.18 (0.94-1.48)
3	0.98 (0.76-1.26)	0.94 (0.74-1.21)
4	0.83 (0.64-1.08)	0.81 (0.62-1.05)
5- Highest	0.71 (0.53-0.96)	0.72 (0.53-0.96)
Comorbidity Band§		
1- Lowest	Ref	Ref
2	1.60 (0.89-2.85)	1.62 (0.91-2.90)
3	1.84 (1.09-3.10)	1.87 (1.11-3.15)
4	2.50 (1.46-4.28)	2.55 (1.49-4.36)
5- Highest	4.71 (2.75-8.08)	5.10 (2.97-8.73)
% TBSA‖ burn (per % increase)	1.00 (0.99-1.01)	1.00 (0.99-1.01)
Index discharge disposition		
Home	Ref	Ref
Home with Support	0.95 (0.77-1.16)	0.94 (0.77-1.15)
Rehabilitation or Long-term care	1.74 (1.37-2.22)	1.77 (1.39-2.25)
Other inpatient	1.23 (0.79-1.91)	1.39 (0.91-2.12)
Other	1.47 (0.96-2.24)	1.43 (0.93-2.19)

* Confidence interval
† Derived from Fine and Gray competing risk regression model
‡ Derived from Cox Proportional Hazards model
§ Measure of comorbidity burden based on healthcare utilization in 2 years prior to injury
‖ TBSA, total body surface area

5.7 Figures for Chapter 5

Figure 5.1: Cumulative incidence of readmission, emergency department (ED) visits, and death during follow-up. ED visits include visits leading to readmission

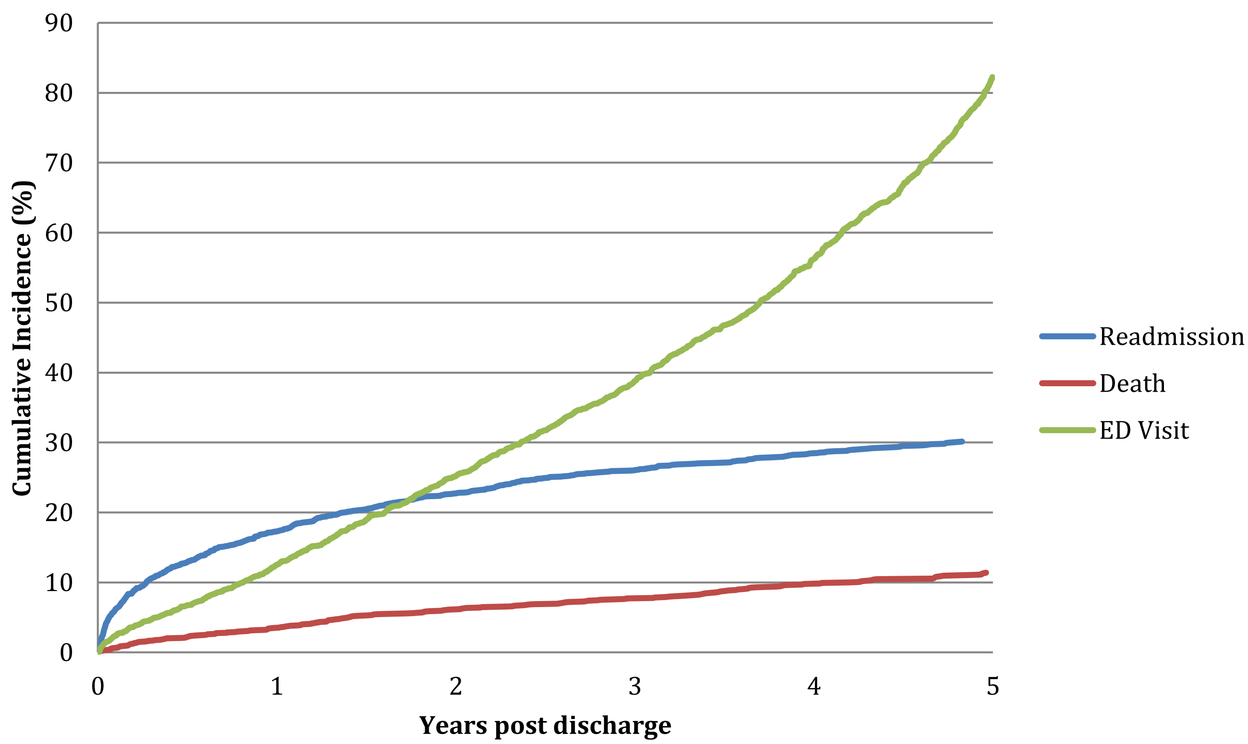


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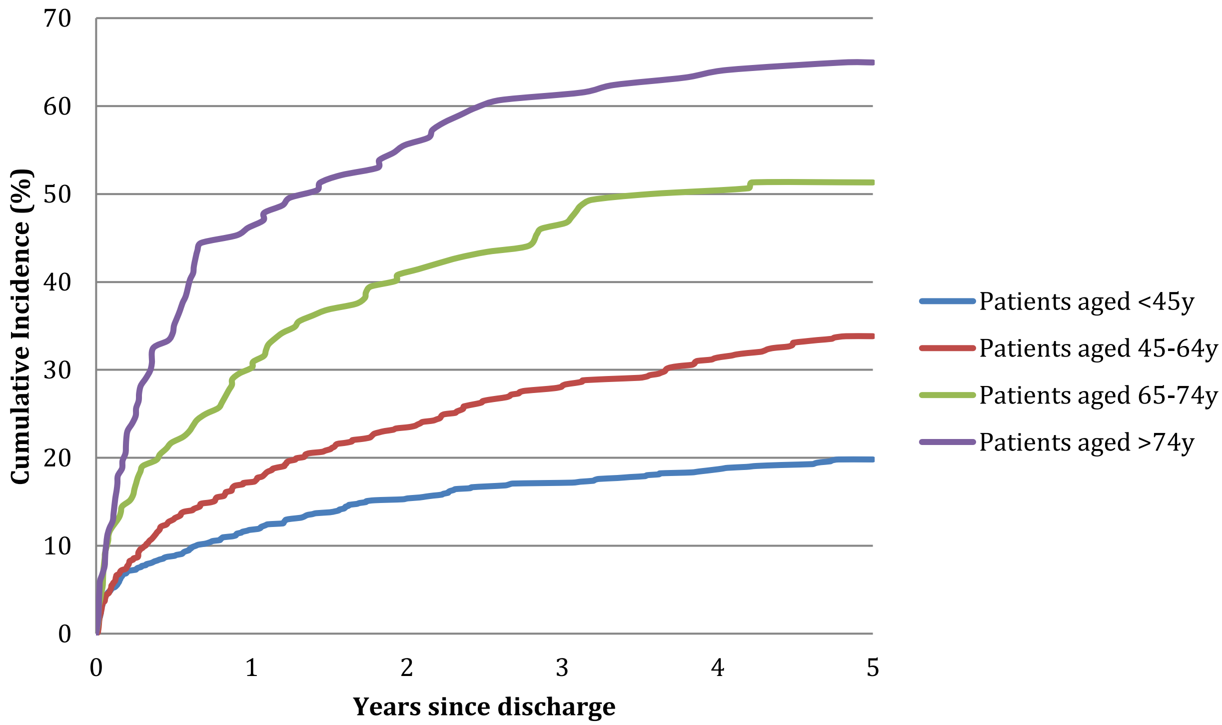
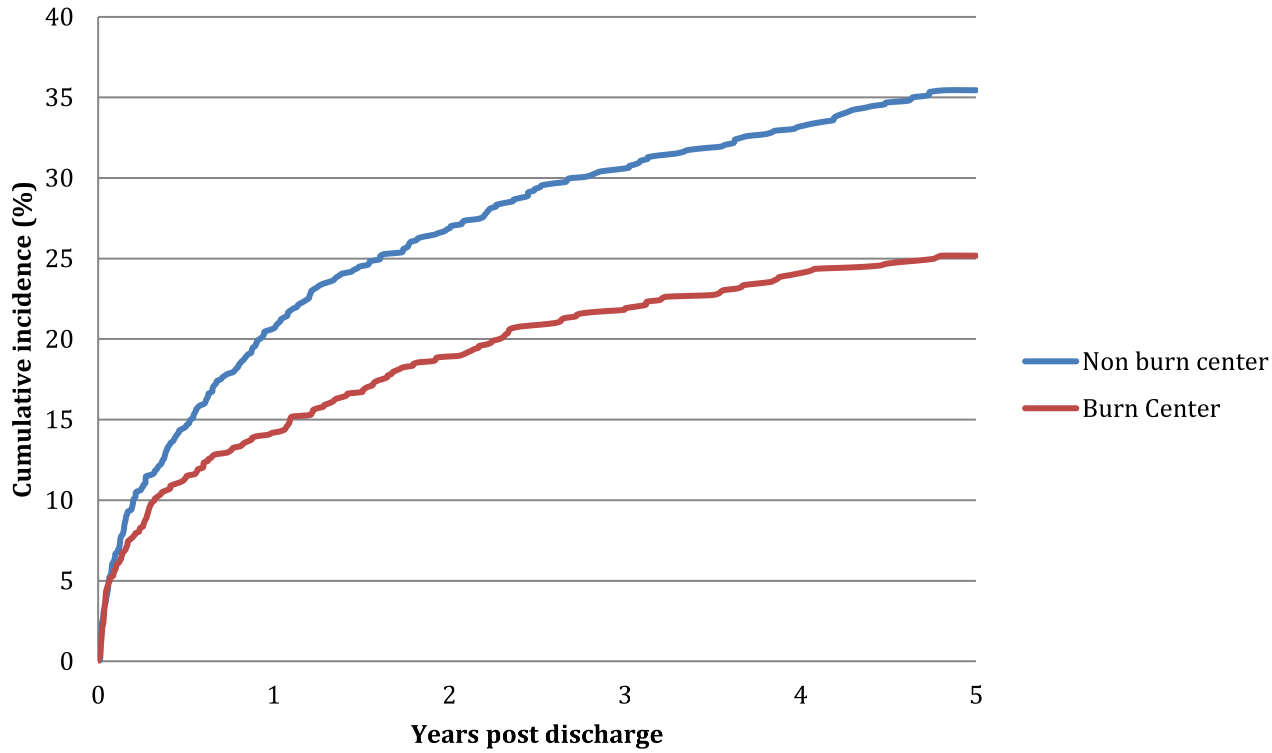
Figure 5.2: Cumulative incidence of readmission by age group



Number at risk:

<45 y	949	833	797	778	763	748
45-64 y	677	551	505	469	446	428
65-74 y	152	100	80	70	64	61
≥75 y	117	59	44	33	32	30

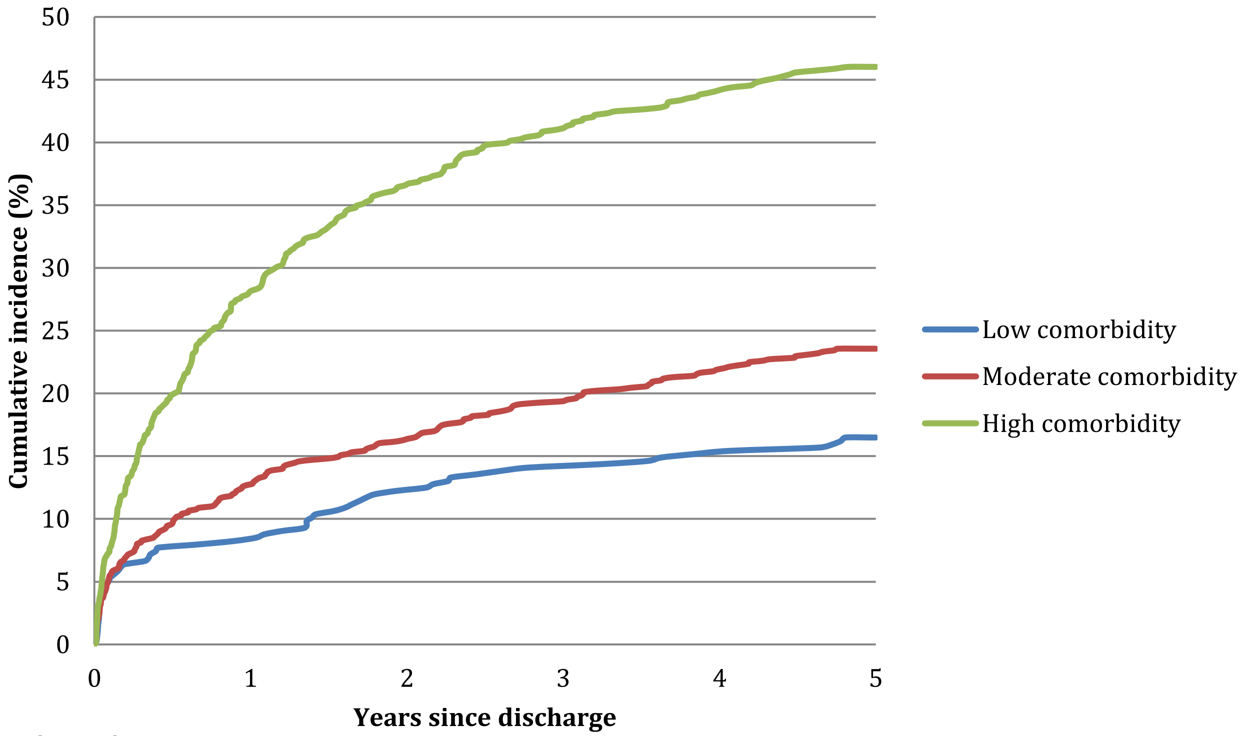
Figure 5.3: Cumulative incidence of readmission by location of index burn care



Number at risk:

Burn center	981	833	778	743	721	709
Non burn center	914	710	648	610	585	562

Figure 5.4: Cumulative incidence of readmission, by pre-injury comorbidity



Number at risk:

Comorbidity						
Low	376	344	328	318	314	309
Moderate	836	726	693	665	643	626
High	678	468	400	365	344	331

CHAPTER 6: THE ASSOCIATION BETWEEN MENTAL ILLNESS AND BURN INJURY

The purpose of this chapter is to:

1) Describe the overall rate of mental illness, as measured by emergency department visits for mood disorder, anxiety, substance abuse, self-harm, and schizophrenia, in the three years both preceding and following burn injury

2) Evaluate the rate of overall and specific mental illnesses after burn injury compared to before burn injury

3) Identify patient and injury factors associated with risk of mental illness after burn injury

Acknowledgement: Parts of Chapter 6 were reprinted from the following:

Mason SA, Nathens AB, Byrne JP, Ellis J, Gonzalez A, Fowler RA, Karanicolas PJ, Moineddin R, Jeschke MG. The association between burn injury and mental illness among burn survivors: a population-based self-matched longitudinal cohort study. Journal of the American College of Surgeons. Epub 2017 Jun 28.

6.1 Summary

Background: Mental health disorders are prevalent before and after burn injury. The impact of burn injury on risk of subsequent mental health disorders is unknown.

Methods: We conducted a population-based, self-matched longitudinal cohort study using administrative data in Ontario, Canada between 2003- 2011. All adults who survived to discharge following major burn injury were included, and all mental health-related emergency department visits were identified. Rate ratios for mental health visits in the three years after burn, compared to the three years prior, were estimated using negative binomial generalized estimating equations.

Results: Among 1530 patients with major burn injury, mental health visits were common both before (141 per 1000 person years) and after (154 per 1000 person years) injury. Mental health visits were most common in the 12 weeks immediately preceding injury. No significant difference in the overall visit rate was observed after burn (RR 0.97, 95% CI 0.78-1.20), though among patients with ≤1 pre-injury visit, mental health visits tripled (RR 3.72, 95% CI 2.70-5.14). Among all patients, self-harm emergencies increased two-fold (RR 1.95, 95% CI 1.15-3.33).

Conclusions: Mental health emergencies are prevalent amongst burn-injured patients. Although the overall rate of mental health visits is not increased after burn, the rate increases significantly among patients who were not high utilizers pre-injury. Self-harm risk increases significantly after burn injury, underscoring the need for screening and

targeted interventions after discharge. An increased rate immediately prior to burn suggests an opportunity for injury prevention through mental healthcare.

6.2 Background

Burn injury is a devastating event, exposing survivors to extreme stressors that may have significant physiological, aesthetic, and psychological consequences. After discharge, recovery may be limited by several factors: new functional limitations, visible scarring or deformity, chronic pain, and traumatic stress related to the initial injury[126,144,213,214]. Taken together, these stressors might have a detrimental impact on the mental health of burn survivors.

Many studies have attempted to describe the burden of mental illness in burn survivors, and suggest that mood and anxiety-related disorders are prevalent[132,133], while up to one-third of patients suffer from post-traumatic stress disorder[134]. Unfortunately, the interpretation of these studies is limited by small sample sizes, short follow-up intervals and high rates of loss to follow-up. More importantly, existing studies were unable to explicitly account for pre-burn mental illness; many did not collect any pre-injury data, or relied on potentially biased self-reporting of prior psychiatric morbidity.

The objective of this study was to determine whether the rate of mental health visits increases after burn injury, and to identify risk factors for post-burn mental health visits. To overcome the limitations of prior studies, we employed a population-based approach that facilitates capture of a large cohort of burn-injured individuals and their pre-injury mental healthcare utilization. These data are critical to identify opportunities for prevention through screening, and to inform the design and implementation of new initiatives to mitigate the long-term impact of burn injury on the mental health of burn survivors.

6.3 Methods

Study Design

After obtaining Research Ethics Board approval, we conducted a population-based, self-matched longitudinal cohort study in Ontario, Canada, using information from several linked administrative databases. We used an exposure crossover design such that each patient acted as their own control[215]; this approach minimizes confounding due to personality, genetics, socioeconomic status, and other stable characteristics that can be difficult to measure.

Data Sources

Data were derived from four sources: (1) the Discharge Abstract Database (DAD), which captures demographic, diagnostic, procedural, and discharge information on all acute care hospitalizations in the province of Ontario; (2) the Registered Persons Database, comprising vital statistics for all residents of the province of Ontario who are alive and eligible for coverage under the Ontario Health Insurance Plan; (3) the National Ambulatory Care Reporting System (NACRS), which captures demographic, diagnostic, and discharge information for all emergency department visits in Ontario, and (4) the Ontario Mental Health Reporting System (OMHRS), which records demographic, diagnostic, and discharge information for all individuals receiving mental health services in Ontario; up to 3 diagnoses per visit are recorded, according to the *Diagnostic and Statistical Manual of Mental Disorders,4th edition* (DSM-IV). These datasets were linked using unique encoded identifiers and analyzed at the Institute for Clinical Evaluative Sciences. Similar to other Canadian provinces, the Ontario government administers a single-payer system that universally funds all hospital, laboratory, and necessary physician services for eligible residents; therefore, these data sources include records for virtually all residents in the province. The diagnoses codes for burn injury in these datasets have previously been validated[180].

Study Patients

The study population included all patients aged 16 years and older who were admitted to hospital for treatment of major burn injury between April 1, 2003 and March 31, 2011 in Ontario, Canada. In order to ensure complete follow-up, only patients who remained alive and eligible for health coverage for three years after their discharge were included. Similarly, to ensure the identification of all pre-injury visits, only patients eligible for health coverage during the three years prior to the burn admission were included. Individuals lacking a valid Ontario health card or those who sustained concurrent major trauma with their burn were excluded. Major burn injury was defined as any burn injury resulting in (1) $\geq$10% total body surface area (TBSA) burn, (2) full-thickness burns to the face, feet, hands, or perineum, or (3) any TBSA burn with inhalation injury. These criteria were chosen as they represent injuries that are severe enough to warrant referral to a burn center, and might be most associated with subsequent mental health events[33].

Outcomes

The primary outcome was the composite rate of mental health visits (related to mood disorder, anxiety, self-harm, substance abuse, and schizophrenia) in the three years after burn injury, compared to the three years before injury. All emergency department (NACRS) or mental health (OMHRS) visits with an ICD-10 or DSM-IV main diagnosis code designating these disorders, or those with an ICD-10 external cause of injury code designating intentional self-harm (range X61-X84) were identified. Secondary outcomes included individual rates of visits for mood disorders (ICD-10 diagnosis codes F30-39), anxiety (F40-42, 44-48), schizophrenia (F20-29), substance abuse (F10-F19) and self-harm (X61-84).

Covariates

Patient-specific variables included age, sex, comorbidity, socioeconomic status, and urban/rural residence. Comorbidity burden was estimated using the Johns Hopkins Adjusted Clinical Groups case mix system[178], which assigns patients to one of six morbidity categories based on prior healthcare utilization. To simplify the analysis, we collapsed categories 0 and 1, representing non-users and healthy users, into a single category. Income quintiles based on the median neighbourhood income of each patient's postal code were used as a marker of socioeconomic status. Patient residence was classified as urban or rural on the basis of the Rurality Index of Ontario (RIO)[179], which takes into account the population density of the city/town of the patient's residence as well as the distance to the nearest basic and advanced referral center. A RIO $\geq$45 is considered rural[179]. Injury-specific variables were derived from diagnoses codes in the DAD and included %TBSA, presence of inhalation injury, and burn mechanism.

Statistical Analysis

Descriptive statistics were calculated for the entire study population. The patient and injury characteristics of patients with pre-injury visits were compared to those with post-injury visits using Student's t-test for normally distributed continuous variables, the Wilcoxon rank-sum test for non-normally distributed continuous variables, and the chi-square test for categorical variables. Rates of mental health visits per 1000 person years were estimated for each of the pre- and post-injury periods. Time intervals were divided into segments of 13 weeks to describe the distribution of visits over time. We used negative binomial generalized estimating equations to compute rate ratios of mental health visits for the post-injury period compared to the pre-injury period, accounting for the paired nature of the observations. Negative binomial models were used because there was significant over-dispersion in the outcome counts. Incident rate ratios for relevant patient (age, sex, socioeconomic status, comorbidity) and injury (burn size, presence of inhalation injury, burn mechanism) subgroups were estimated.

We postulated that the severity of pre-injury mental illness, as represented by the rate of emergent healthcare use, might modify the effect of burn injury on the rate of post-injury mental health visits. Therefore, we performed a second analysis, stratifying on the pre-injury emergent mental healthcare utilization. Patients with 1 or fewer visits in the 3 years prior to injury were considered low-utilizers, while patients with 2 or more visits were considered high-utilizers.

In all analyses, a two-sided p-value of <0.05 was considered significant. All statistical analyses were performed using SAS version 9.4 (Cary, NC).

6.4 Results

We identified 1530 patients eligible for inclusion in the study. Baseline characteristics of the cohort are presented in **Table 6.1**. The mean age was 44 years and most were male, urban dwelling and from lower income quintiles. The median total body surface area burned was 15% (IQR, 5-25), 52% of injuries were flame burns, 8% involved inhalation injuries, and 3% (n=43) were acts of deliberate self-harm.

There were a total of 1358 mental health visits before (n=644) and after (n=714) burn injury. The proportion of patients with a mental health visit increased from 10% (n=153) to 12% (n=184) after injury (p<0.001). The incident rate of mental health visits pre-burn was 141 per 1000 patient years, compared to 154 per 1000 patient years post-injury (crude IRR 1.09, 95% CI 0.87-1.37).

The rates of specific mental health visits are presented in **Table 6.2.** Substance abuse-related visits were most common, both before and after injury. No significant difference in the rate of substance abuse visits was observed after burn injury. No significant differences were observed in the overall rate of visits after burn, or in visits with a principal diagnosis of mood disorders, anxiety or schizophrenia.

The majority of patients (94%) had one or fewer visits in the three years prior to burn injury; 89 patients (6%) had 2 or more visits prior to injury. Significant differences in the rate of mental health visits after burn injury were identified between these two groups of patients (**Table 6.3**). Among low-utilizers, there was a greater than 3-fold increase in the rate of mental health visits after burn injury; significant increases in the individual rates of anxiety, mood disorder, substance abuse, self-harm, and schizophrenia visits were also observed. In comparison, among high-utilizers, the rate of mental health visits decreased after burn injury, as did individual rates of mood disorder and substance abuse. The rates of schizophrenia, anxiety, and self-harm among high-utilizers were similar before and after injury.

Overall, there was almost twice the rate of self-harm emergencies after burn injury (**Table 6.4**), while among pre-injury low-utilizers, self-harm emergencies increased four-fold (**Table 6.3**). The association between burn injury and self-harm events was strongest among females, individuals from higher income quintiles, and those with a high level of pre-injury comorbidity (**Table 4**).

The greatest number of visits overall was observed in the 12 weeks immediately preceding the burn injury (**Figure 6.1a**); the number of visits was relatively constant during the first 2 years of the pre-injury period, and then increased steadily throughout the year prior to the burn. After the burn injury, the number of visits remained consistent throughout follow-up. Similarly, the number of self-harm events increased throughout the year prior to the burn, and peaked in the 12 weeks immediately preceding the burn injury (**Figure 6.1b**). In contrast, after burn injury, self-harm events occurred consistently throughout follow-up.

Incident rate ratios did not differ significantly among any patient or injury subgroups, with the exception of the previously mentioned differences based on pre-injury utilization.

6.5 Discussion

In this population-based, self-matched, longitudinal cohort study, we demonstrated a high frequency of mental illness-related emergent healthcare utilization both before and after burn injury. Healthcare visits for substance abuse were most common, followed by visits related to mood and anxiety disorders. While the overall rate of mental health visits did not increase significantly after burn injury, the rate of self-harm emergencies almost doubled, and rates of emergency visits related to anxiety increased by 63%, perhaps related to traumatic stress. Furthermore, among pre-injury low-utilizers, the overall rate of mental health visits more than tripled after burn injury; similar significant increases were observed for visits related to substance abuse, mood disorders, schizophrenia, self-harm, and anxiety.

Our findings are consistent with the results of prior studies demonstrating a high prevalence of both pre- and post-injury mental illness among burn patients[132–137,145,216], with rates that are higher than the general population[132,137]. The rate of mental health-related emergency visits among burn survivors is approximately 7-fold higher than the general population. The average rate in the general population is 16-23 per 1000[217–219], compared to 154 per 1000 after burn injury. Similarly, self-harm emergencies occur after burn injury at a rate that is several fold higher than the Canadian national rate, estimated at 1.2 per 1000[220].

We did not observe an increase in the overall rate of emergent mental health visits compared to the pre-injury rate. Few studies have directly compared the rates of mental health disorders after burn injury to pre-injury rates. However, our results are consistent with previous work that found no significant increase in mental health visits in the two years after burn injury compared to two years before[137]. In contrast, among pre-injury low utilizers, we observed significantly increased rates overall and for visits related to mood and anxiety disorders, self-harm, schizophrenia, and substance abuse visits after injury. To the best of our knowledge, ours is the first study to report self-harm rates following burn injury.

We observed the greatest number of mental health emergencies in the three-month period immediately preceding the burn; this is similar to the finding of Palmu et al that 40% of patients had received an Axis I diagnosis in the month preceding their injury[216]. Mental illness is an independent risk factor for unintentional injury and injury recidivism[221]. That these patients have been engaged with the healthcare system in the months prior to their burn suggests that an opportunity for intervention exists. Taken together, these data suggest that the treatment of mental illness might be an important target for burn prevention efforts. The high rate of mental health visits in the three months immediately prior to burn injury also has implications for inpatient burn management. Patients with premorbid mental illness are more likely to experience delirium, have poor coping, and experience delayed wound healing[142,222,223]. These patients are also more likely to have dysfunctional adaptation to their injury, resulting in poor adherence to care plans and negative impacts on physical recovery[139,222]. Perhaps reflecting these care challenges, multiple studies have demonstrated increased length of stay among those with premorbid mental illness[139,222,223], and injured patients with mental illness are less likely to be discharged home[221].

After discharge, we found that the rate of self-harm events approximately doubles, with the largest increase in self-harm observed among patients with minimal pre-burn emergent mental healthcare use. Consistent with other cohorts, self-harm rates in our study were higher among females and those with a high comorbidity burden[224]. Risk factors for self-harm in our study that have not previously been described include middle age (45-64 years), residence in an urban setting, and higher socioeconomic status. Patients with flame burns, and those with smaller burns (<20% TBSA) also had higher rates of self-harm.

The key strength of our study is its design; the exposure-crossover method facilitates comparisons of pre- and post-burn mental health rates within individuals. This approach minimizes confounding due to personality, genetics, socioeconomic status and other stable characteristics that can be difficult to measure[215]. Furthermore, the use of administrative data facilitated capture of a large cohort of burn-injured individuals with complete longitudinal follow-up over time. Using administrative data to identify pre-injury mental health visits also mitigates any recall bias that might be associated with patient self-reporting of prior mental health problems.

While administrative data offer many advantages, they also limit our ability to assess the severity of mental health conditions or to understand what treatment may have been undertaken. We have not included outpatient mental health visits in our analysis, and our study includes only those patients who sought or were able to access treatment in an emergency setting. While we observed increased schizophrenia rates among pre-injury low utilizers, it is unlikely that burn injury is associated with the onset of schizophrenia. It is more likely that these patients have received a diagnosis as a result of their prolonged contact with health care providers during their burn hospitalization. A further limitation is that many self-harm visits might not be disclosed as intentional by the patient, or may not be recognized as such by the physician; a prior study using similar data found that for every two deliberate self-harm events, there is one event of undetermined intent[220]. Therefore, it is likely that we have underestimated the true rate of self-harm emergencies, and we may also have underestimated the proportion of burn injuries that were secondary to self-harm. Finally, while post-traumatic stress disorder (PTSD) has recently emerged as a topic of great interest, its identification in administrative data is challenging; PTSD is associated with a number of symptom patterns, and emergent visits might be attributed to other mental health disorders, such as substance abuse, depression or anxiety[225]. As a result, we were not able to specifically report rates of PTSD.

We have demonstrated a significant burden of mental illness among survivors of major burn injury. The high rate of emergency mental health services use suggests that multiple opportunities for intervention exist, with the potential to improve patient outcomes and reduce costly emergency room use. Of greatest concern is that intentional self-harm emergencies double after burn injury. Self-harm is the single most important predictor of subsequent suicide, with hazard ratios for subsequent death ranging from 2.4-12 depending on psychiatric comorbidity, age, and sex[226]. Therefore, self-harm visits represent an important opportunity to prevent subsequent suicide.

Effective treatments exist for mood disorders, anxiety, schizophrenia and substance abuse. Identifying at-risk individuals through screening programs would facilitate earlier intervention. Early intervention has been demonstrated to improve outcomes across a wide range of metrics, including mortality, quality of life, and community reintegration[227,228]. However, the high rate of emergent healthcare utilization in our study suggests that a barrier exists to accessing effective help from outpatient mental health services. An urgent need to characterize these barriers exists. Both burn inpatient and follow-up care provide multiple occasions to screen for psychiatric symptoms, provide integrated psychosocial care and/or refer for psychiatric care.

Conclusions

Burn-injured patients have high rates of emergent health care utilization related to mental illness. The highest rate of events occurs in the weeks immediately prior to burn injury, suggesting an opportunity for injury prevention through improved identification of those at risk and targeted mental health care. Self-harm emergencies double after burn injury, highlighting the need for screening during follow-up. Given that effective treatments are available, and early intervention improves outcomes, efforts to increase awareness and improve access to outpatient mental health services for burn-injured patients are warranted.

6.6 Tables for Chapter 6

Table 6.1: Baseline patient and injury characteristics

	All patients N=1530	**Patients with >1 visit** **Pre-Burn** N=153	**Post-burn** N=184	**P value**
Male (%)	1142 (75)	96 (63)	124 (67)	0.37
Mean age (SD)	44 (17)	45 (14)	42 (15)	
Income Quintile (%)				0.96
1 - Lowest	378 (25)	47 (32)	50 (28)	
2	339 (22)	32 (22)	40 (22)	
3	277 (18)	30 (20)	37 (21)	
4	311 (20)	21 (14)	26 (15)	
5 - Highest	211 (14)	17 (12)	25 (14)	
Home location (%)				0.82
Urban	1256 (82)	130 (86)	152 (83)	
Rural	272 (18)	22 (14)	31 (17)	
Comorbidity burden†				0.07
(%)	107 (7)	<6%	<6%	
1 - Lowest	202 (13)	<6%	5-10%	
2	679 (44)	25-30%	30-35%	
3	307 (20)	20-25%	25-30%	
4	232 (15)	45-50%	35-40%	
5 - Highest				
Median TBSA (IQR)	15 (5-25)	15 (5-25)	15 (5-25)	0.61
Inhalation injury (%)	128 (8)	19 (12)	28 (15)	0.46
Burn Mechanism (%)				0.15
Flame	792 (52)	60-65%	112 (61)	
Electrical	96 (6)	<6%	7 (4)	
Contact	642 (42)	30-35%	65 (35)	
Burn center care	780 (51)	67 (44)	77 (42)	0.72

Counts <6 suppressed so as to remain compliant with privacy regulation

†As measured by the Johns Hopkins Adjusted Clinical Groups case mix system based on prior healthcare utilization.

SD, standard deviation

TBSA, total body surface area

IQR, interquartile range

Table 6.2: Rates of mental health visits

	Rate per 1000 person years		Adjusted RR (95% CI)
	Pre-Injury	**Post-injury**	
Any	141	154	0.97 (0.78-1.20)
Mood disorder	26.4	26.4	0.99 (0.70-1.40)
Substance abuse	86.7	80	0.86 (0.63-1.18)
Schizophrenia	17.9	24.4	1.26 (0.68-2.31)
Anxiety	10.5	18.3	1.64 (0.97-2.77)
Self-Harm	6.3	13.3	1.95 (1.15-3.33)

RR, rate ratio, estimated using negative binomial generalized estimating equations accounting for clustering of events within quarters and paired observations before and after burn

CI, Confidence interval

Table 6.3: Rates of mental health visits by rate of pre-injury utilization

	Low Utilizers†			High Utilizers‡		
	Rate per 1000 person years		Adjusted RR (95% CI)	Rate per 1000 person years		Adjusted RR (95% CI)
	Pre-injury	Post-injury		Pre-injury	Post-injury	
Any	45.10	170.71	3.72 (2.70-5.14)	6516.90	5179.8	0.72 (0.55-0.94)
Mood disorder	6.25	37.47	6.01 (2.84-12.70)	1258.43	752.81	0.58 (0.38-0.89)
Substance abuse	22.90	80.50	3.46 (2.29-5.21)	4104.12	2820.22	0.66 (0.45-0.98)
Schizophrenia	3.47	23.59	6.73 (2.42-18.69)	865.17	876.40	0.91 (0.43-1.96)
Anxiety	12.49	25.68	2.02 (1.04-3.90)	337.08	528.09	1.45 (0.68-3.09)
Self-Harm	0.69	11.80	17.01 (2.25-128.65)	314.61	494.38	1.48 (0.81-2.70)

† ≤1 pre-injury visit
‡ >1 pre-injury visit
RR, Rate ratio, estimated using negative binomial generalized estimating equations accounting for clustering of events within quarters and paired observations before and after burn
CI, Confidence interval

Table 6.4: Self-harm events by patient and injury subgroups

	Rate per 1000 Person Years		**Rate Ratio (95% CI)**
	Pre-injury	Post-Injury	
All patients	6.3	13.3	1.95 (1.15-3.33)
Sex			
Male	3.1	5.7	1.76 (0.72-4.33)
Female	3.3	7.6	2.26 (1.29-3.96)
Age Group			
16-44 years	2.5	5.7	1.98 (0.76-5.16)
45-64 years	3.3	7.2	2.07 (1.14-3.77)
>65 years	0.4	0.4	1.00 (0.09-11.03)
Income Quintile			
1-3 Lowest	5.0	9.6	1.72 (0.91-3.25)
4-5 Highest	1.1	3.5	3.20 (1.13-9.05)
Home location			
Urban	6.1	10.2	1.78 (1.02-3.10)
Rural	0.2	1.1	5.00 (0.58-42.71)
Comorbidity			
1-3 Lowest	0.7	2.2	3.33 (0.89-12.47)
4-5 Highest	5.7	10.1	1.82 (1.03-3.22)
TBSA			
<20%	4.4	9.4	2.03 (1.07-3.85)
≥20%	2.0	4.0	1.92 (0.71-5.19)
Inhalation injury	0.4	1.7	3.99 (0.82-19.48)
No inhalation injury	5.9	11.5	1.74 (0.99-3.05)
Burn Mechanism			
Flame	5.0	10	1.94 (1.08-3.46)
Electrical	0	0	-
Contact	1.3	3.3	2.27 (0.68-7.63)
Index admission			
Burn center	2.8	6.3	1.86 (0.90-3.83)
Non burn center	3.5	7.0	1.97 (0.92-4.24)

CI, confidence interval
TBSA, total body surface area

6.7 Figures for Chapter 6

Figure 6.1a: Distribution of all mental health visits. Each interval represents a 13-week time period; error bars represent 95% confidence intervals. Dashed line represents time of burn injury.

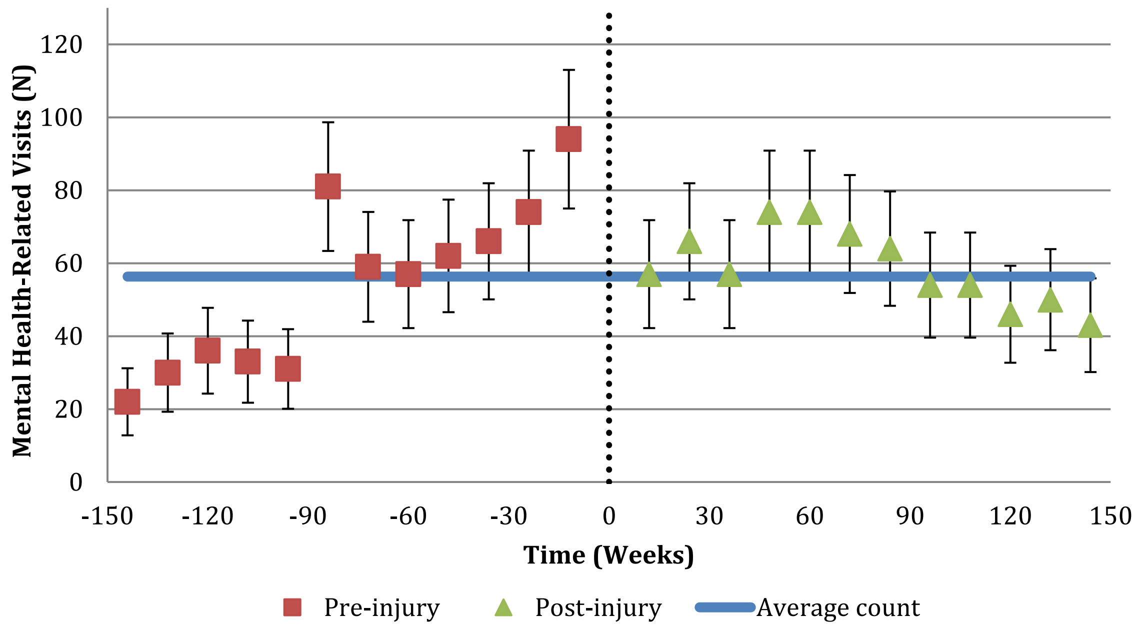
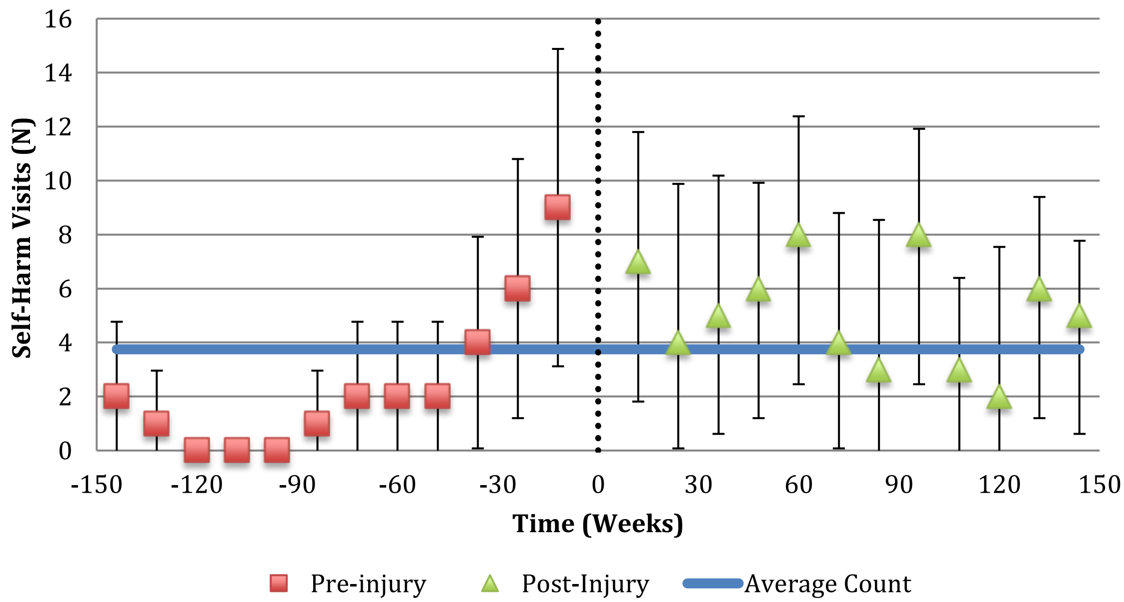


Figure 6.1b: Distribution of self-harm visits. Each interval represents a 13-week time period; error bars represent 95% confidence intervals. Dashed line represents time of burn injury.



CHAPTER 7: THE IMPACT OF BURN INJURY ON LONG-TERM SURVIVAL

The purpose of this chapter is to:

1) Estimate 5-year survival among patients who survived to discharge after burn injury, compared to matched, uninjured controls

2) Characterize causes of death among burn survivors as compared to matched controls

3) Identify patient and injury factors associated with a higher risk of premature mortality

7.1 Summary

Introduction: The effect of sustaining a major burn injury on long-term life expectancy is poorly understood. We aimed to estimate long-term mortality following major burn injury compared to matched controls.

Methods: Using health administrative data, all adults who survived to discharge after major burn injury between 2003-2013 were matched to between 1 and 5 uninjured controls on age, sex, and the extent of both physical and psychological comorbidity. To account for socioeconomic factors such as residential instability and material deprivation, we also matched on marginalization index. The primary outcome was five-year all-cause mortality, and all patients were followed until death or March 31,2014. Cumulative mortality estimates were estimated using the Kaplan-Meier method. Cox proportional hazards modeling was used to estimate the association of burn injury with mortality.

Results: 1965 burn survivors of mean age 44 (standard deviation 17) years with median total body surface area burn of 15% (interquartile range (IQR) 5-15) were matched to 8671 controls and followed for a median 5 (IQR 2.5-8) years. Five-year mortality was significantly greater among burn survivors (11 vs 4%, $p<0.001$). The hazard ratio was greatest during the first year (4.15, 95% CI 3.17-5.42), and declined each year thereafter, reaching 1.65 (95% CI 1.02-2.67) in the fifth year after discharge. Burn survivors had increased mortality related to trauma (mortality rate ratio, MRR 9.8, 95% CI 5-19) and mental illness (MRR 9.1, 95% CI 4-23).

Conclusions: Burn survivors have a significantly higher rate of long-term mortality than matched controls, particularly related to trauma and mental illness. Burn follow-up

should be focused on injury prevention, mental healthcare, and detection and treatment of new disease.

7.2 Background

Advances in the care of burn-injured patients have occurred over the past several decades, such that in-hospital mortality rates have markedly declined[19,68,192]. Despite an increasing prevalence of burn survivors worldwide and data suggesting persistent physiological changes up to three years after burn[54], the effect of sustaining a major burn injury on long-term life expectancy is poorly understood.

Emerging data from the critical care literature suggest that survivors of critical illness, such as septic shock and acute respiratory distress syndrome, have a shorter life expectancy than matched controls[201,229–231]. The few studies of life expectancy after burn injury demonstrate mortality rates in the range of 3-12% during follow-up periods of up to 18 years[232–235]. These studies are limited by the absence of appropriate controls and adjustment for other factors that might confound the relationship of burn with late mortality. As such, it is unclear whether published mortality rates are higher than age-matched controls. There are some limited data suggesting that burn survivors have a 1.4 to 2-fold increased risk of death during follow-up compared to age- and sex-matched controls[234,235]. However, these studies did not match on other factors that might be associated with background risk of death, such as comorbidity or socioeconomic factors. Therefore, the generalizability of these findings is unknown.

The objective of this study was to estimate the relative rate of five-year, all-cause mortality following major burn injury, compared to uninjured members of the general population.

7.3 Methods

Study design and setting

We conducted a population-based, retrospective matched cohort study in Ontario, Canada of all patients who survived to discharge following major burn injury. Ontario is Canada's most populous province, with a population of more than 13 million. Our objective was to evaluate the rate and causes of 5-year mortality among burn survivors, compared to uninjured, matched controls. This study was approved by the Research Ethics Board at Sunnybrook Health Sciences Centre.

Data sources

Data were derived from several linked administrative databases. The Canadian Institute for Health Information (CIHI) Discharge Abstract Database (DAD) captures demographic, diagnostic, procedural, hospital and discharge information for all hospital admissions in the province. The DAD was linked to the National Ambulatory Care Reporting System (NACRS), which captures all emergency department visits; to the Registered Persons Database, which contains vital statistics data; and to the Office of the Register General – Deaths (ORGD) database, containing information on date and cause of death for all residents eligible for health care coverage in Ontario. These datasets were linked using unique encoded identifiers and analyzed at the Institute for Clinical Evaluative Sciences. The government of Ontario administers a single payer health care system that universally funds all hospital, laboratory, and physician services for eligible residents. Therefore, together these datasets include health data regarding the initial hospitalization and post-discharge health trajectory of all patients who sustain a burn injury in Ontario. Diagnostic information in these datasets is recorded according to the tenth revision of the *International Classification of Diseases and Related Health Problems* (ICD-10). We have previously demonstrated the validity of these codes in identifying and characterizing major burn injury[180].

Study subjects

We used the DAD to identify all patients aged 16 years and older who survived to discharge following a major burn injury between April 1, 2003 and March 31, 2014. For the purposes of the study, major burn injury was defined consistent with the American Burn Association criteria for referral to a burn center[33]: any burn resulting in (1) 10% total body surface area (TBSA) burn; or, (2) full-thickness burns to the face, feet, hands, and perineum; or (3) any burn with inhalation injury. Individuals lacking a valid Ontario health card or who sustained concurrent major trauma with their burn were excluded.

For each patient who survived to discharge after their injury, we randomly selected up to five patients from the general population who had not sustained burn injury, matching on age (± 1 year), sex, comorbidity score (defined as the total number of distinct Johns

Hopkins aggregated diagnosis groups (ADGs) in which subjects had diagnoses), presence of a major physical comorbidity (defined using ADGs), presence of a major psychological comorbidity (defined using ADGs), and on all four dimensions of the Ontario marginalization index. The Johns Hopkins case mix system was developed to predict healthcare utilization by considering duration, intensity, and severity of service use related to both inpatient and outpatient resource use[195]. ADGs consist of 32 diagnosis clusters, each having similar clinical criteria and expected health resource needs; individuals can have comorbidities belonging to between zero and 32 ADGs[236]. The Ontario marginalization index is based on census data and postal code, and was developed to quantify differences in marginalization between persons across four dimensions: material deprivation, ethnic concentration, residential instability, and dependency[158]. Several studies have demonstrated that the marginalization index is associated with health behaviors and outcomes[237–241]. For the purposes of our study, burn survivors were matched to controls on each dimension of the marginalization index; each dimension is stratified by quintile (first=least deprived, fifth=most deprived). Controls were assigned the index discharge date corresponding to their matched case.

In order to assess whether matching on the marginalization index resulted in groups balanced in terms of rural residence, we used the Rurality Index of Ontario. This measure of rurality takes into account population density and distance to the nearest basic and advanced referral center for each patient, based on their postal code[179].

Outcomes

The primary outcome of interest was post-discharge all-cause mortality. All deaths that occurred during the five-years after discharge were identified in in the DAD if they occurred in hospital, in NACRS if death occurred in the ED, and in the ORGD if death occurred outside of hospital. Deaths were classified based on the underlying cause of death using Becker's groupings of leading causes of death [242].

Statistical analysis

Descriptive statistics were calculated for the entire study population. Standardized differences were used to confirm balance between the case and control cohorts after matching, and a standardized difference greater than 10% was considered significant[243]. All patients were followed from discharge until death or March 31, 2014, and censored at five years. Overall and cause-specific mortality rates were estimated. Mortality rate ratios for specific causes of death were derived using Poisson generalized estimating equations to account for the matched nature of the data.

We obtained cumulative all-cause mortality estimates using the Kaplan-Meier method, comparing survival curves using the log-rank test. Survival among burn survivors and matched controls was also compared to the expected general population survival for men and women of the average cohort age, obtained from Ontario life-table data[244]. To assess potential effect modification by age and sex, stratified survival analyses were performed on the basis of sex and age less than or greater to 65 years. Cox proportional hazards modeling was used to estimate the association of burn injury with mortality. The sandwich covariance estimator was used to account for the correlated failure times within matched cases and controls. The proportional hazards assumption was verified graphically and using interaction terms.

All statistical analyses were performed using SAS version 9.4 (Cary, NC).

7.4 Results

We matched 1965 burn survivors of mean age 44 years (standard deviation 17) with median total body surface area burn of 15% (interquartile range (IQR), 5-25) to 8671 controls. No significant post-matching differences between cases and controls were identified in terms of age, sex, rurality, marginalization index, or comorbidity (**Table 7.1**). Subjects were 74% male and most were urban-dwelling. At the time of injury, a major physical comorbidity was present among 57% of the burn survivors and 55% of controls, while a major psychological comorbidity was present among 44% of burn survivors and 42% of controls. Burn patients and their matched controls represented a marginalized population, with more than one-quarter of burn survivors in the most marginalized quintile of residential instability and material deprivation.

The median follow-up time was 4.9 (IQR 2.3-7.8) years among burn survivors, and 5.4 (2.6-8.1) among controls. Overall mortality rates during follow-up were 28.7 per 1000 person years among burn survivors, and 12.1 per 1000 person years among controls. At five years, 11% of burn survivors and 4% of controls had died (**Figure 7.1**). Median time to death was 1.6 years (IQR 0.7-3.4) among burn survivors and 2.4 years (IQR, 1.4-3.8) among controls (log rank $p<0.001$). The largest differences in late mortality rates between burn survivors and controls were observed among patients aged younger than 65 years at the time of injury (**Figures 7.2 and 7.3**).

The most common causes of death among both burn survivors and controls were cancer and ischemic heart disease (**Table 7.2**). However, cause-specific mortality rates for trauma (mortality rate ratio (MRR) 9.8, 95% confidence interval (CI) 5-19), mental illness (MRR 9.1, 95% CI 3.7-22.6), and cirrhosis (MRR 3.8, 95% CI 1.2-12.5), were significantly higher among burn survivors.

The hazard associated with burn injury decreased with time and thus violated the proportionality assumption. Therefore, we estimated hazard ratios for each individual year of follow up (1 through 5 years). The hazard ratio was greatest during the first year (4.15, 95% CI 3.17-5.42), and declined each year thereafter, reaching 1.65 (95% CI 1.02-2.67) in the fifth year after discharge (**Table 7.3**). This represents a 4-fold increased risk of death compared to matched controls during the first year of follow-up, and a 1.5-fold increased risk of death in the fifth year after injury.

7.5 Discussion

In this population-based matched cohort study, we found that survivors of major burn injury have a substantially increased rate of subsequent all-cause mortality, which persists at least to 5 years after discharge. The use of a non-injured comparison cohort matched on age, sex, comorbidity, and social marginalization accounts for much of the background risk of death regardless of injury. Trauma and mental illness-related deaths were particularly common compared to the uninjured general population, even after matching for pre-injury psychological comorbidity.

Few studies have examined the association between burn injury and late mortality. Duke et al. observed a two-fold increase in the adjusted risk of late death among Australian young adult and middle-aged burn survivors compared to age- and sex-matched controls[234], while we observed a four-fold increase. The greater risk of death in our study might be related to varying follow-up times; we observed that the hazard ratio decreased over time, and Duke et al.'s study had median follow-up time of 16 years. If the hazard associated with burn truly does decrease with time, it would be expected that longer follow-up periods might attenuate the hazard ratio. Our finding that mental illness-related deaths are more common among burn survivors is consistent with Duke et al., though they did not find significant differences in the rates of injury or cancer-related deaths. However, a recent Norwegian study found that accidental deaths were the 2nd most common cause of death after burn injury; most accidental deaths in that study were related to alcohol intoxication and suicide

In our study, suicide was 4 times more common among burn survivors than matched controls. This is in stark contrast to the findings of a recent study of combat burn survivors in the United States, in which zero suicide deaths were observed after discharge[245]. While their findings might be related to misclassification bias, differences in suicide risk between civilian and military burn survivors might be related to several factors, including variation in the availability and provision of mental health supports to military personnel compared to civilians, and a pre-existing network of peer support within the military that might help to mitigate psychological stress. Characterization of the differences in health service delivery and resilience traits between military and civilian burn survivors might identify future targets for reducing self-harm and suicide risk among all burn survivors.

In addition to increased rates of suicide deaths, we also observed increased rates of deaths due to unintentional injuries. While some of the observed injury deaths might have been misclassified intentional injuries, further work is needed to understand the factors that might be associated with increased injury risk among burn survivors. Some of this vulnerability to injury might be explained by altered executive functioning that increases an individual's likelihood of participating in risky behavior, and therefore, of sustaining injury. Executive functioning refers to emotional and behavioral regulation by the frontal lobe, including judgment, impulse control, self-monitoring and planning[246]. The Centers for Disease Control and Prevention has identified several risky behaviors that are associated with intentional and unintentional injury, including driving without a seatbelt, driving over the speed limit, carrying a weapon, driving while drinking alcohol, violent or aggressive behavior, and substance use[247]. These behaviors are more common among trauma patients than the general population, and particularly among patients with chronic alcohol use[248]. However, risky behaviors have not yet been characterized in burn-injured patients. Other factors, such as mental illness and substance abuse, might also underscore injury risk[221,249,250]. These interrelated factors may represent important targets for injury prevention after burn injury. Brief interventions for alcohol in trauma centers have had some success in reducing injury recidivism[250], and therefore might have a role in preventing injury deaths among burn patients.

The high rates of death due to traumatic injury and mental illness observed in our study are likely interrelated. Previous work has demonstrated a significant burden of mental illness among burn survivors[135,138,142], and mental illness is an independent risk factor for traumatic injury[221]. Our data suggest that an unrealized opportunity to improve burn outcomes through targeted injury prevention efforts and improved mental healthcare may exist. There is an urgent need to understand the mental healthcare needs of burn survivors, and to characterize barriers to accessing care. Our results highlight the need for screening for psychological symptoms during follow-up, given that effective treatments are available for mental health disorders[227,228]. Earlier intervention may prevent these premature deaths, while also reducing risk of unintentional injury.

Burn survivors are also at significantly increased risk of non-traumatic death: deaths related to cancer, ischemic heart disease, diabetes, respiratory disease, and cirrhosis were all more common among burn survivors. Prior work has demonstrated that burn injury causes sustained changes to immune responses and is associated with high levels of oxidative stress[54,251,252]. These changes are implicated in the persistent physiological and metabolic changes observed after burn, including insulin resistance, hepatomegaly, increased cardiac output and cardiac index, tachycardia, cardiac stress, and hormonal abnormalities including elevations in epinephrine, norepinephrine, and cortisol[41,42,50,54,153,155]. Altered systemic responses have been observed after both minor and major burn injury, suggesting that even minor burns have the capacity to induce more long-lasting changes. Much of this work has been conducted on pediatric patients, and the generalizability of these findings to the adult population has not yet been demonstrated. However, the hypothesis that burn injury induces persistent physiological changes is supported by recent work demonstrating increased readmission rates for infectious, neurological, and cardiovascular diseases after burn injury compared to the general population[57,61,253]. Future work should focus on elucidating the association between the persistent hypermetabolic response to burn injury and post-burn development of disease.

One key strength of our study is the ability to capture all deaths occurring after burn injury among a large cohort of burn survivors, and to compare their mortality rates to individuals who share similar demographics and comorbidity burden, as well as similar degrees of socioeconomic marginalization related to factors such as material deprivation and residential instability. Burn risk is higher among low-income individuals, immigrant populations, and those with mental illness[28,133,134,140,254,255], as evidenced by the baseline characteristics of our cohort. These factors are also independently associated with poor health outcomes[255]; in our study, 5-year survival was lower among the uninjured cohort than would be expected for individuals of similar age and sex. This underscores the importance of explicitly accounting for both the physical and social determinants of health when evaluating long-term outcomes after burn.

We recognize several limitations of our work. While we have accounted for the presence of pre-injury comorbidities, we are unable to account for variation in illness severity, compliance with treatment, or quality of care received, each of which might modify the mortality risk associated with these comorbidities. Similarly, we are unable to account for differences in lifestyle factors such as smoking status, alcohol and substance use, and obesity. However, these behaviors have previously been demonstrated to be associated with the marginalization index[239,240], and might therefore be similar between burn survivors and controls, perhaps limiting the impact of this unmeasured confounding.

In conclusion, burn survivors are at increased risk of all-cause mortality for at least five years after discharge, compared to uninjured controls. Taken together, our data suggest a long-term physiological and psychological impact of burn injury that increases the rate of late mortality. As such, burn injury should be considered akin to a chronic disease, rather than as a discrete event in an individual’s life. Longitudinal follow-up is warranted, and should be focused on the prevention of injury, provision of mental healthcare, and detection and treatment of new disease.

7.6 Tables for Chapter 7

Table 7.1: Patient characteristics

	Burn Survivors N=1965	**Matched controls N=8671**	**Standardized Difference**
Mean age, years (standard deviation)	44 (17)	44 (17)	0.03
Males (%)	1459 (74)	6494 (75)	-0.03
Major physical ADG† (%)	1111 (57)	4730 (55)	0.04
Major mental ADG† (%)	870 (44)	3613 (42)	0.05
Number of distinct ADGs† (%)			0.07
0-2	349 (18)	1652 (19)	
3-5	577 (29)	2674 (31)	
6-8	502 (26)	2214 (26)	
≥9	537 (27)	2131 (25)	
Residential instability (%)			0.03
1 *Least marginalized*	267 (14)	1200 (15)	
2	334 (18)	1440 (18)	
3	380 (19)	1585 (20)	
4	372 (19)	1610 (20)	
5 *Most marginalized*	498 (27)	2266 (28)	
Material deprivation (%)			0.02
1 *Least marginalized*	253 (14)	1115 (14)	
2	350 (19)	1534 (19)	
3	355 (19)	1511 (19)	
4	377 (20)	1616 (20)	
5 *Most marginalized*	516 (28)	2325 (29)	
Ethnic concentration (%)			0.02
1 *Least marginalized*	377 (20)	1663 (21)	
2	428 (23)	1839 (23)	
3	333 (18)	1416 (17)	
4	349 (19)	1527 (19)	
5 *Most marginalized*	364 (20)	1656 (20)	
Dependency (%)			0.02
1 *Least marginalized*	343 (19)	1518 (19)	
2	360 (19)	1610 (20)	
3	371 (19)	1583 (20)	
4	383 (19)	1635 (20)	
5 *Most marginalized*	394 (21)	1755 (22)	
Rurality Index (%)			0.10
0-24 *Most urban*	1475 (76)	6707 (78)	
25-49	306 (16)	1390 (16)	
50-74	109 (6)	333 (4)	
≥75 *Most rural*	38 (2)	116 (2)	

†Aggregated diagnosis groups; based on the Johns Hopkins adjusted clinical groups case-mix system

Table 7.2: Causes of death among burn survivors and matched controls

	Burn survivors N=1965		Matched controls N=8671		Mortality rate ratio (95% confidence interval)
	N	Cause specific mortality (%)	N	Cause specific mortality (%)	
Mental health	14	0.7	7	0.1	9.1 (3.7-22.6)
Trauma	21	1.3	12	0.1	9.8 (5-19.2)
Cirrhosis	<6	0.2	6	0.1	3.8 (1.2-12.5)
Cardiac	7	0.4	9	0.1	3.6 (1.3-9.6)
Ischemic heart disease	21	1.1	32	0.4	3.2 (1.8-5.6)
Chronic respiratory disease	8	0.4	12	0.1	3.0 (1.2-7.4)
Cancer	36	1.8	88	1.0	2.1 (1.3-3.4)
Diabetes	<6	0.2	12	0.1	2.2 (0.6-7.5)
Dementia	<6	0.2	8	0.1	1.7 (0.5-6.4)
Stroke	<6	0.2	11	0.1	1.3 (0.3-4.8)

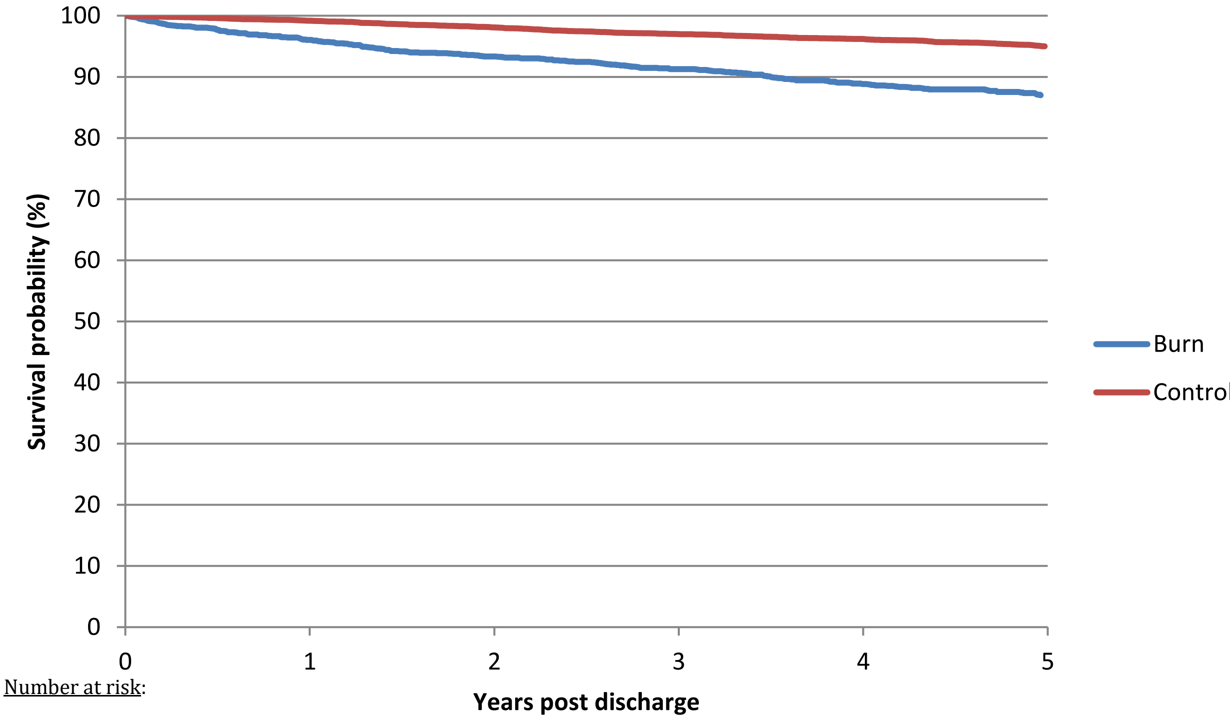
Counts <6 suppressed so as to remain compliant with privacy regulation

Table 7.3: Hazard ratios by year post-discharge

Year	Hazard Ratio (95% Confidence Interval)
1	4.15 (3.17-5.42)
2	2.44 (1.78-3.36)
3	1.84 (1.28-2.65)
4	3.0 (1.98-4.54)
5	1.65 (1.02-2.67)

7.7 Figures for Chapter 7

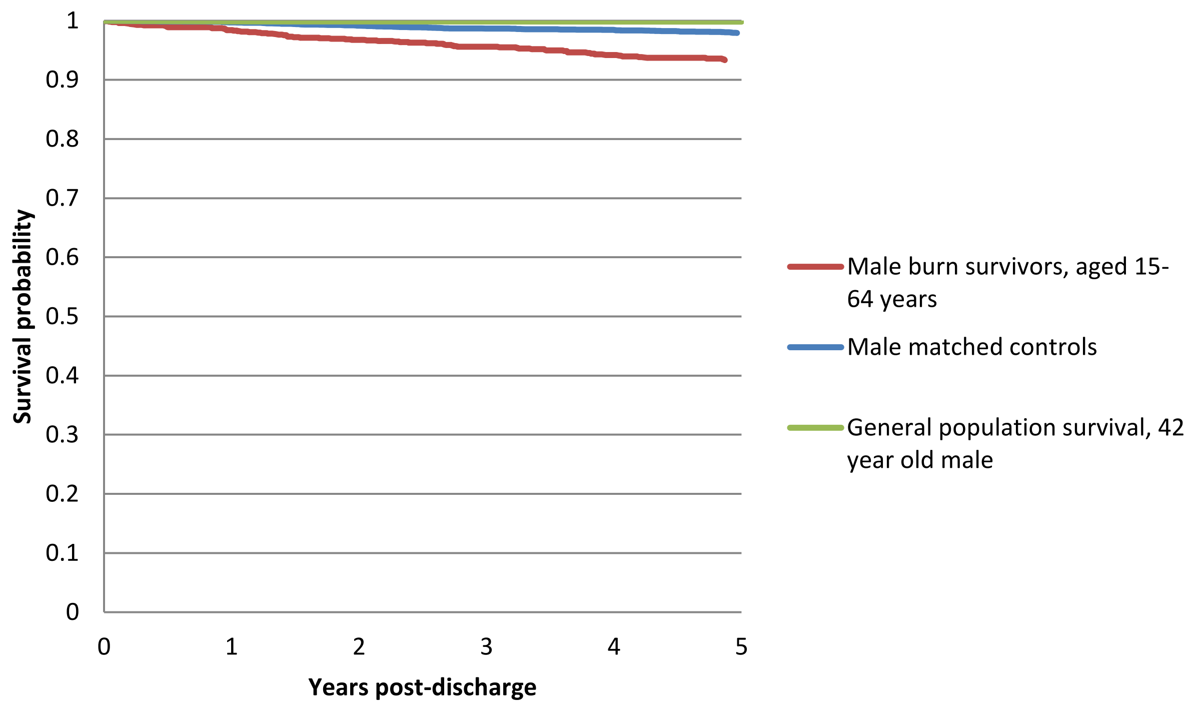
Figure 7.1: Kaplan-Meier survival curve comparing burn survivors to matched controls



Number at risk:

Burn	1965	1726	1517	1342	1149	970
Control	8671	7819	6970	6216	5394	4606

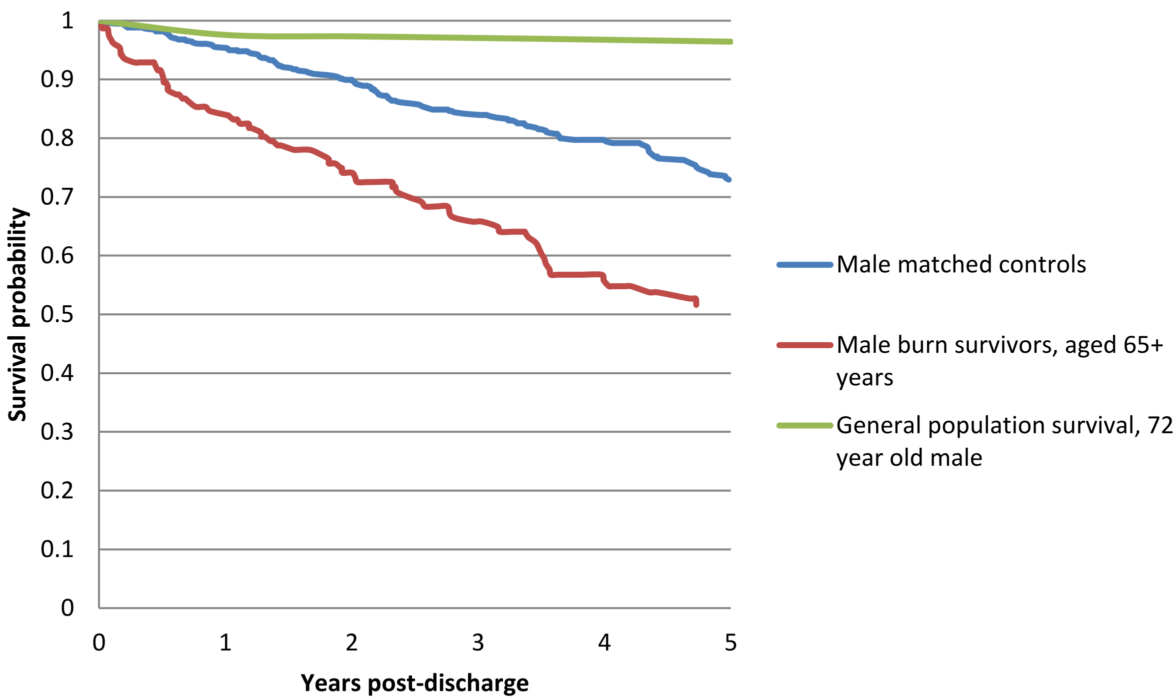
Figure 7.2a: Kaplan-Meier survival curves comparing male burn survivors aged <65 years to matched controls. General population survival represents expected survival for a male in Ontario, Canada of the average cohort age (42 years).



Number at risk:

Burn	1301	1181	1047	940	815	702
Control	5869	5380	4794	4333	3793	3279

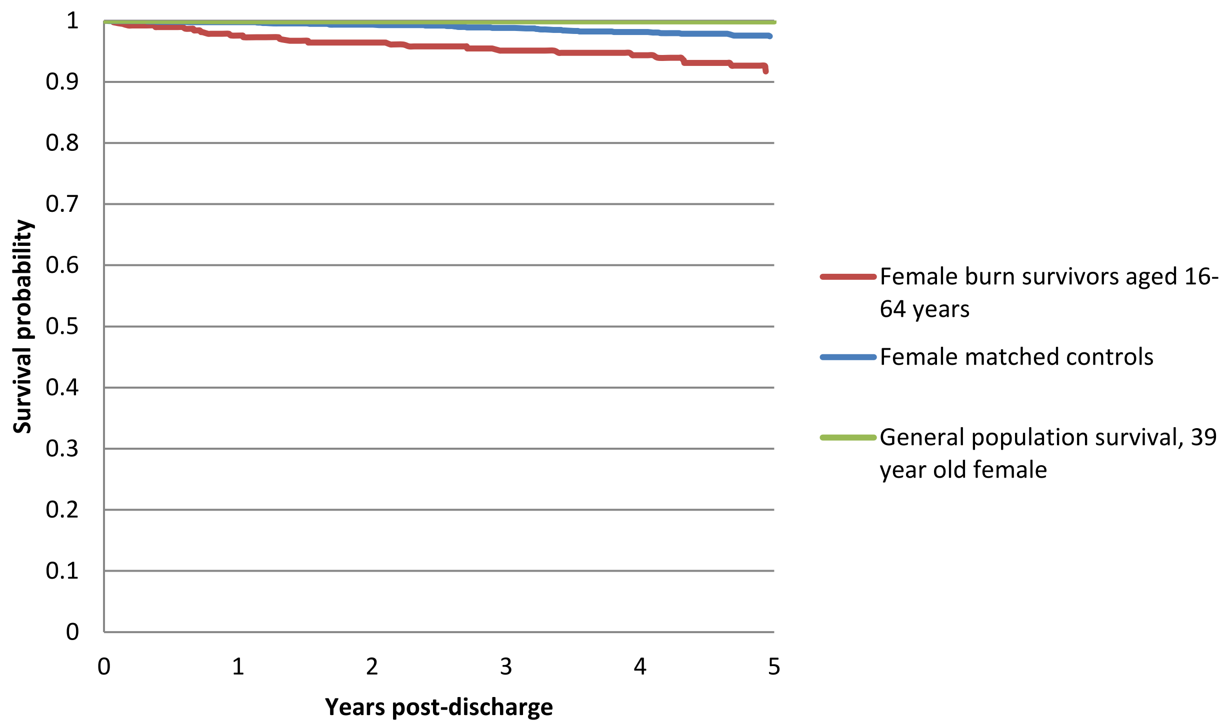
Figure 7.2b: Kaplan-Meier survival curves comparing male burn survivors aged 65 years and older to matched controls. General population survival represents expected survival for a for a male in Ontario, Canada of the average cohort age (72 years).



Number at risk:

Burn	158	120	95	78	58	47
Control	625	527	447	369	296	236

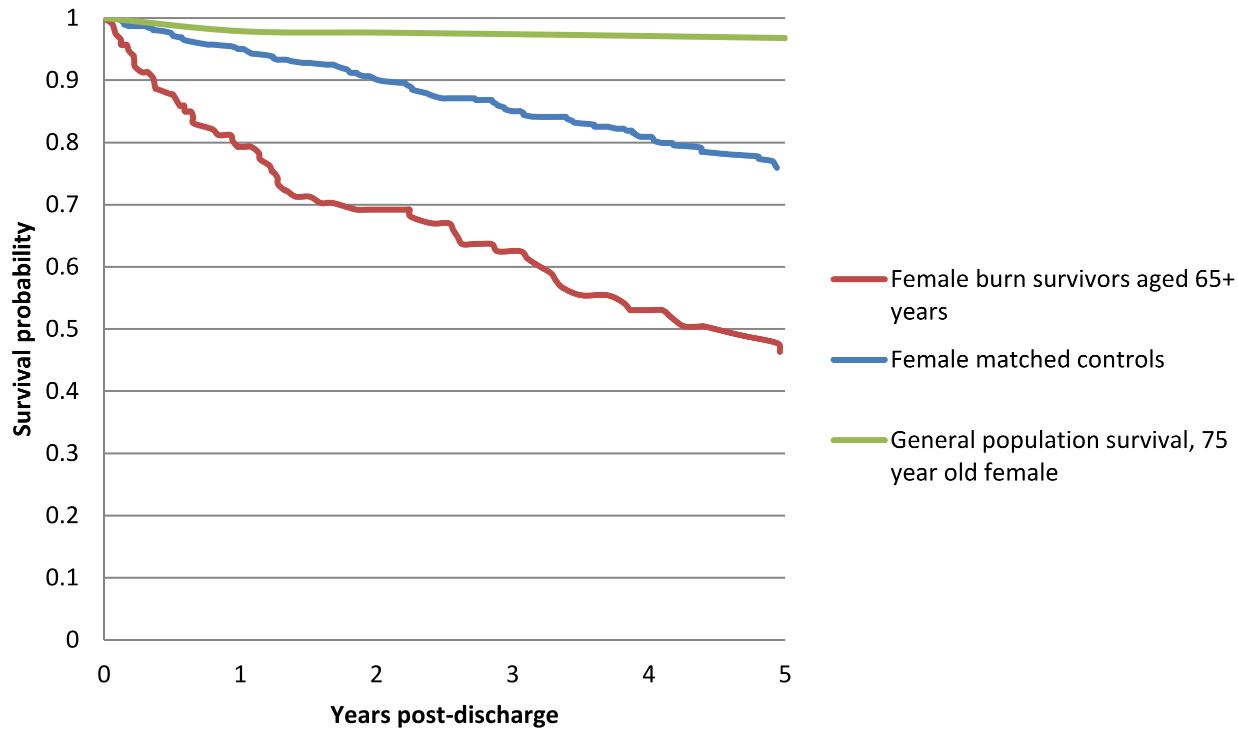
Figure 7.3a: Kaplan-Meier survival curves comparing female burn survivors aged <65 years to matched controls. General population survival represents expected survival for a male in Ontario, Canada of the average cohort age (39 years).



Number at risk:

Burn	390	346	314	273	236	190
Control	1704	1181	1047	940	815	702

Figure 7.3b: Kaplan-Meier survival curves comparing female burn survivors aged 65 years and older to matched controls. General population survival represents expected survival for female in Ontario, Canada of the average cohort age (75 years).



Number at risk:

Burn	116	83	66	55	44	35
Control	473	396	335	284	245	210

CHAPTER 8: GENERAL DISCUSSION

The purpose of this chapter is to:

1. Summarize the findings of the four studies comprising the thesis.
2. Discuss the limitations of these studies.
3. Outline the implications of the thesis findings for burn and non-burn care providers and policy makers.

8.1 Conclusions

Burns are a devastating event in an individual's life, with the potential for permanent physical, functional, and psychological implications. The immediate consequences of burn injury have been well-described and these as well as burn-related mortality rates have improved significantly over time. Despite the fact that all but the most severe injuries are now survivable and patients with previously fatal injuries are being discharged home, our understanding of the long-term implications of burn injury is limited. The four studies presented within this dissertation demonstrate how various epidemiological study designs and analytic techniques can be applied to administrative data in order to understand the long-term healthcare needs of burn survivors. We have shown that burn injury is associated with morbidity and mortality that continues well beyond the acute care hospitalization.

First, we demonstrated that the incidence of burn injury in Ontario has remained stable between 2003 and 2013. While the overall incidence is greatest among males aged 45-54 years, the greatest incidence among women was observed for those aged 75 years and older; among men, this was the age group with the second-highest incidence. The majority of patients with a burn size of 20% TBSA or greater received their care in one of Ontario's two burn centers, and this proportion increased over time, from 57 to 71%. In-hospital mortality rates improved significantly during 2003-2013; on stratified analyses, we observed that mortality rates improved among patients treated at burn centers, but were highly variable among patients treated outside of burn centers. Overall, 81% of patients survived to discharge. Of these, most were discharged home, of which 59% required homecare resources; one-third of patients were discharged to a rehabilitation or long-term care facility.

Having gained an understanding of the inpatient burden of burn injury in Ontario, we then evaluated healthcare utilization after discharge, as represented by emergency department (ED) visits and unplanned readmissions. ED visits are very common, experienced by 70% of patients after discharge. These visits are largely related to unintentional (non-burn) injuries, though burn-related visits are common during the first 30-days after discharge. Unplanned readmissions are experienced by approximately one-third of burn survivors, and are also largely related to unintentional injuries, though medical readmissions (cardiovascular, respiratory, and gastrointestinal) are also common. The infrequency of burn-related ED visits and readmissions beyond 30 days suggests a low rate of burn recidivism. We found that patients who received their index burn care in a burn center experienced significantly fewer ED visits and readmissions. Other risk factors for acute healthcare utilization after discharge included older age, more comorbidities, and lower socioeconomic status. No injury-specific factors were associated with healthcare utilization.

Healthcare utilization related to mental illness was common after burn injury. To understand whether this was related to pre-existing mental illness, or to the burn itself, we performed a self-matched longitudinal cohort study. We found that the overall rate of ED visits for mental illness did not increase in the three years after burn injury, as compared to the three years prior. However, the rate of self-harm visits doubled. Self-harm risk was greatest among women, middle-aged individuals, and those with the highest socioeconomic status. The pre-injury rate of mental illness was significantly greater than in the general population, suggesting a high level of psychiatric comorbidity among burn-injured patients. The impact of burn injury on mental health was most evident among patients who had experienced one or fewer ED visits for mental illness prior to their injury. Among these patients, the rate of ED visits for mental illness increased four-fold after burn injury; significant increases were observed in the rates of self-harm, substance abuse, depression, and anxiety.

In addition to the increased risk of acute healthcare utilization after discharge, burn survivors have an increased risk of five-year mortality compared to matched, uninjured controls. Five-year mortality after burn injury was 11%, compared to 4% among matched controls. While the increased risk of death compared to controls was highest during the first-year after discharge, and decreased each year thereafter, the overall hazard ratio associated with burn injury was 4.51 (95% CI 3.38-6.03). This represents a four-fold increased risk of death compared to controls, during each day of follow-up in the five years after burn injury. Although the commonest causes of death were ischemic heart disease and cancer in both burn survivors and matched controls, deaths related to unintentional injury and mental illness were 9-fold more common among burn survivors. The association between burn injury and late mortality was strongest among women, middle-aged patients, patients with pre-existing psychological comorbidity, and, unexpectedly, among the least marginalized patients.

Overall, the findings of this dissertation demonstrate that the healthcare utilization and mortality risk associated with burn injury are not limited to the acute phase, and may persist for at least five years following discharge. Much of this post-burn healthcare utilization is related to unintentional injury and mental illness. Mental illness is common among burn-injured patients both before and after injury, and therefore represents a risk factor not only for burn, but also for ongoing healthcare utilization and mortality after burn injury. Even after accounting for the background risk of death among a matched comparison group, burn survivors have an increased risk of all-cause five-year mortality. Taken together, our findings demonstrate a physical and psychological impact of burn injury that persists up to 5-years after discharge. As such, long-term follow-up and the identification of strategies that might minimize this impact are warranted.

8.2 Limitations

The work presented in this dissertation has a number of limitations.

8.2.1 Limitations of available data

The limitations of the work presented in this dissertation are largely related to the use of administrative data. Administrative data offer many advantages, chief among them the ability to capture all burn-injured patients in the province and follow their healthcare utilization over time with minimal loss to follow-up. However, these data also offer many limitations, as these data are not collected for research purposes. As a result, many clinically important variables are not available in the datasets used. Specific unmeasured variables of interest are discussed below.

Patients not captured by administrative data

The datasets used in this thesis are linked by means of an encrypted identifier that is derived from each patient's health card number. Therefore, there are select patients who may not have been captured by these datasets as a result of not having a health card. These include individuals who are homeless, non-residents of Ontario, and First Nations residents. Given that these represent relatively small populations, their exclusion is unlikely to have significantly influenced our findings.

Absence of information regarding burn severity

We are unable to characterize the severity of burn injury beyond the size of the burn. Burn-specific factors captured in the datasets used include burn size, burn depth, burn mechanism, and presence of inhalation injury. However, our validation study demonstrated that burn depth and inhalation injury are not reliably coded. Data regarding physiological parameters, laboratory measurements, and physical findings are unavailable. Therefore, we are unable to evaluate whether these specific factors might be associated with long-term outcomes. Furthermore, burn size estimations in the DAD reflect the burn size recorded in the patient chart; we are unable to ascertain the accuracy of these estimations. It has previously been demonstrated that burn size estimations can vary widely, even among burn care providers[32,34,188]. Therefore, our results may be subject to misclassification bias as a result of misestimations of burn size.

Absence of information regarding processes of care at burn and non-burn centers

A common theme throughout this dissertation is that many patients did not receive burn center care. We are unable to characterize the reasons underlying this undertriage; specifically, we do not know if non-burn centers made attempts to transfer patients, and were denied, or if transfers were abandoned due to delays in transfer or unavailable resources. Similarly, we are unable to ascertain whether emergency physicians and other care providers are familiar with the guidelines for referral to a burn center. In Chapters 4, 5, and 7, we describe the improved outcomes observed among patients treated at burn centers. However, we are unable to characterize the specific processes of burn center care that underscore these improvements.

Absence of information regarding patient health behaviours

Beyond receiving care in a burn center, many factors might be important predictors of healthcare utilization and mortality after discharge. Important potential modifiers of the outcomes described in Chapters 5 and 7 are patient lifestyle factors such as smoking, alcohol use, and physical inactivity. These factors have well-recognized associations with premature mortality[256,257], and it has been demonstrated that these behaviors are more common among individuals of lower socioeconomic status[258,259]. Given that 47% of our burn cohort are in the lowest two income quintiles, these behaviors are likely prevalent, and may contribute to the healthcare utilization and premature mortality observed after burn injury. However, in Chapter 7, we matched burn patients to uninjured controls on each dimension of the marginalization index, thereby creating a comparison group similar in socioeconomic status, who perhaps share similar lifestyle behaviors. We observed a four-fold increased risk of 5-year mortality among burn survivors compared to matched controls, which is unlikely to be due to lifestyle factors alone.

Absence of information related to access to specific forms of mental healthcare

Psychologist services in Ontario are not insured; as a result, their utilization is not captured in the administrative datasets. Furthermore, outpatient services provided by a psychiatrist in a private setting are not insured. We have therefore likely underestimated the rate of healthcare utilization related to mental illness, both before and after burn injury, in Chapters 5 and 6. Similarly, our inability to capture the utilization of these uninsured services limits our ability to determine how these services might be associated with emergent mental healthcare utilization after burn injury, and whether patient factors such as marginalization might be associated with their use.

Outcomes not captured by administrative data

This thesis used post-discharge healthcare utilization and mortality to describe the long-term outcomes associated with burn injury. However, these outcomes may not represent those that are considered most valuable by patients. Functional recovery, physical appearance, the ability to return to work, and social reintegration are all outcomes that patients perceive to be of the greatest importance[260,261]. These outcomes contribute to the social costs of burn injury, which have been estimated to account for 56% of the cost of burn injury[86]. Data regarding the factors associated with these social outcomes would be of great relevance to patients and policy makers alike. Unfortunately, examination of such outcomes using administrative data is not currently feasible.

8.2.2 Limitations of data analysis

In Chapter 4, we used logistic regression to derive risk-adjusted estimates of 30-day mortality at burn centers and non-burn centers. It is possible that patient and injury characteristics not be captured in the datasets used might have significantly influenced our findings, resulting in residual confounding. Specifically, burn-specific data, such as burn depth, are important risk factors for mortality. It is possible that these factors differ systematically between burn and non-burn centers. Patients with the same size burn, but of varying depths, might have distinct physiological responses that influence the decision regarding whether or not to transfer to a burn center. However, as burn centers would be expected to receive the patients who are the most unwell, incomplete risk adjustment for injury severity would be expected to bias our results towards the null. Despite this, we observed significant improvements in mortality at burn centers, but not at non-burn centers.

The focus of Chapters 5-7 of this thesis is the post-discharge healthcare utilization and mortality of burn survivors. We assumed that post-burn health is strongly associated with pre-burn physical and psychological health, and therefore that risk-adjustment for pre-injury health status was critical in order to estimate meaningful estimates of post-burn healthcare utilization. We used several approaches to risk adjustment.

In Chapter 5, multivariable Poisson and Fine and Gray competing risk models were used to derive risk-adjusted estimates of post-discharge ED visits and readmissions. Pre-injury comorbidity was operationalized using the resource utilization band of the Johns Hopkins ACG system, which arranges patients into 6 groups on the basis of their past resource utilization, both inpatient and outpatient. As such, this approach accounts only for those comorbidities for which patients received care. We cannot account for comorbidities that might be present among individuals who, for whatever reason, did not have prior contact with the healthcare system. While this might result in an underestimation of the extent of comorbidity present in the cohort, we would expect this to be limited to minor comorbidities, given that more severe comorbidities would require some form of contact with healthcare providers, either on an outpatient or inpatient basis, and would therefore be captured. Furthermore, there is no reason to infer that unmeasured comorbidity differs systematically between burn and non-burn centers. Therefore, we believe that the observed differences in healthcare utilization among patients treated at burn centers compared to non-burn centers are valid.

In Chapter 7, we matched burn survivors to uninjured members of the general population on a number of factors that might confound the association between burn injury and late mortality. These included age, sex, each of the 4 dimensions of the marginalization index, the total number of comorbidities present, the presence of a major physical comorbidity, and the presence of a major psychological comorbidity. As described above, the comorbidity variables utilized in this analysis are based on pre-injury healthcare utilization, and thus are limited to those conditions for which patients accessed healthcare. Therefore, there may be unmeasured differences in the comorbidity burden between the burn survivors and matched controls. Similarly, residual confounding due to unmeasured lifestyle factors might be present. However, given that we have matched patients on age, sex, and marginalization, and prior work has demonstrated an association between marginalization and smoking and alcohol consumption[239,240], we believe that any unmeasured differences in comorbidity or lifestyle factors between burn survivors and controls are unlikely to explain the observed four-fold increase in mortality.

In Chapter 7, we also compared cause-specific death rates between burn survivors and matched controls using Poisson generalized estimating equations. A potential limitation of this approach, as evidenced by the wide confidence intervals surrounding each mortality rate ratio, is the low event rate of each type of death. This limits our ability to draw conclusions about the association of burn injury with specific causes of death. Nonetheless, despite greater uncertainty around our estimates, we observed significant increases in trauma and mental health related deaths that, when considered in the context of our findings in Chapters 5 and 6, we believe are unlikely to be spurious.

Finally, the focus of Chapter 6 is the association between burn injury and mental illness. While the use of a self-matched study design overcame the need to adjust for stable patient characteristics that can be difficult to measure, there remains the possibility of misclassification bias, particularly as relates to self-harm case ascertainment. It can be challenging to determine the intent behind injury for several reasons: it may not be disclosed as intentional by the patient, or detected as such by the physician, and patients may not present to the emergency department after a self-harm attempt[220]. While this misclassification would result in underestimation of the true self-harm rate in the cohort, there is no reason to infer that the magnitude would differ in the pre-injury period compared to the post-injury period, and therefore is unlikely to influence the relative rates described in our study.

Another possibility is that the burn injury itself represented an undiagnosed self-harm attempt; in these cases, the pre-injury self-harm rate would be underestimated. However, given that only 1-4% of all burns are self-inflicted[18,262,263], and patients with self-inflicted burns are more likely to die compared to unintentional burns[264] (and would therefore be excluded from our cohort), we believe that this potential underestimation is unlikely to have significantly influenced our results.

8.3.3 Limitations of external generalizability

The 30-day and 5-year mortality rates, and rates of post-discharge healthcare utilization presented in this thesis, may not broadly generalizable to burn injured cohorts in other jurisdictions. Although Ontario is served by two regional burn centers, one of which is verified by the ABA, and therefore likely offers similar care to that received in other ABA centers, Canada has a single-payer, universally accessible health care system. As such, patterns of healthcare utilization after burn injury might be very distinct from those that would be expected in regions without a universally-available, publicly-funded system. A recent American study found that burn patients with workers compensation insurance were four times more likely to be readmitted than patients with private insurance[255]. Therefore, the healthcare utilization rates described in Chapter 5 may be higher than would be expected in the US. While the specific rates may not generalizable, our findings can provide insight into the types of morbidity faced by burn survivors after discharge.

8.3 Implications of dissertation findings

The analyses presented in this dissertation have a number of implications related to burn care, health policy, and methodology. We have demonstrated several approaches to the use of administrative data to evaluate risk-adjusted long-term outcomes and health services use after burn injury at the population level. Although few studies of long-term outcomes after burn injury have been conducted, common limitations cited in these studies are small sample sizes, high rates of loss to follow-up, and an inability to capture healthcare use at centers other than the treating center. The use of administrative data overcomes many of these challenges.

Our analyses identified that undertriage to burn centers is a significant problem in Ontario. Although the proportion of patients who received burn center care increased over the study period, as of 2013, one-third of patients with $\geq$20% TBSA burn injuries were not treated in a burn center. According to both the Critical Care Services Ontario and ABA guidelines, these patients should unequivocally be referred to a burn center [33,265]. Our data demonstrate that patients treated in burn centers have significantly lower rates of healthcare utilization after discharge. Therefore, efforts to improve concentration of burn care might result in improved outcomes for patients while perhaps generating cost-savings to the healthcare system.

A common theme throughout this dissertation is the burden of mental illness, both before and after burn injury, that is associated with significant acute healthcare utilization. Self-harm events double after burn, and the rate of mental health-related deaths was 9-fold higher among burn survivors than in a group of matched, uninjured controls. Taken together, these findings suggest the need for revised mental healthcare policy, and a characterization of the barriers associated with accessing mental health care. Improved mental healthcare has the potential to significantly improve outcomes after burn injury, to prevent premature death and further injury, and to reduce acute healthcare utilization. Furthermore, our finding in Chapter 6 that mental health visits spike in the 12 weeks prior to burn injury suggests that improved mental healthcare might also have a role in burn prevention.

Our findings have a number of other implications for burn prevention efforts. In Chapter 4, we found that the incidence of burn injury among women is highest in the 75 years and older age group, and second-highest in men aged 75 years and older. Although not significant, we observed a trend towards increasing incidence in this age group. Given the anticipated increase in ‘baby boomers’, it is likely that the proportion of elderly burn injured patients will continue to increase. This age group represents an important target for injury prevention campaigns, and our work can be used to inform their development. There also exists an opportunity for targeted injury prevention efforts aimed at burn survivors, given that non-burn unintentional injury was the commonest cause of healthcare utilization after burn, and a common cause of late mortality.

CHAPTER 9: FUTURE DIRECTIONS FOR RESEARCH

The work presented in this dissertation suggests a number of opportunities for future investigation.

9.1 Evaluation of burn triage practices in Ontario

Further investigation is needed to understand the factors that contribute to undertriage to burn centers in Ontario. This work should focus on evaluating awareness of burn triage guidelines among emergency medicine physicians, as well as among general and plastic surgeons at non-burn centers who admit patients with major burn injury. Perhaps many surgeons feel care of the burn-injured patient is within their scope of practice, and therefore opt to admit rather than refer a patient to a burn center. Some portion of this undertriage might also be related to barriers in referring or transferring patients, including unavailable resources at burn centers or logistical challenges related to the potential long-distance transfer of patients. Furthermore, patient preferences regarding care are unknown, and patient preference for treatment closer to home, particularly among the elderly, might have an important impact on triage decisions.

Future work should characterize whether or not Ontario's two burn centers would have the resources to increase their capacity by 30% (the proportion of patients currently not receiving burn center care). We identified several non-burn centers that treat relatively high volumes of burn patients each year throughout the province, perhaps suggesting a role for "Level 2" burn centers similar to those that exist for the care of trauma patients. In Canada's trauma system, Level 2 trauma centers provide major trauma care, and have some trauma and outreach programs, but do not have academic and research programs[266]. Future work should aim to understand whether a role for similar types of burn centers might exist in Ontario, and if so, patients who can be optimally treated outside of Level 1 burn centers should be identified. An understanding of the geographical distribution of burn injuries would help to inform the most optimal locations for such Level 2 centers.

Finally, although we demonstrated that burn center care reduces post-discharge healthcare utilization, and is likely therefore associated with reduced cost of post-discharge care, the cost-effectiveness of burn center care has not been demonstrated. Burn center care is resource-intense, and therefore costly. Given that granular cost data are available in the administrative datasets used throughout this dissertation, an opportunity exists to conduct cost-effectiveness analyses of burn center care; this would facilitate identification of the most cost-effective processes of burn care, and inform further refinements to the delivery of burn care in Canada. This would also provide a baseline comparison for future evaluation of the cost-effectiveness of proposed new interventions. Similarly, many patient-reported outcome measures are now available to permit the conduct of cost-utility analyses[267]; these would facilitate identification of the interventions associated with the greatest improvements in quality-adjusted life years for burn survivors.

9.2 Delineating the best processes of mental healthcare for burn survivors

Much of the morbidity after burn injury is related to mental illness. The increased rate of self-harm after burn injury demonstrated in Chapter 6 underscores the need for screening during follow-up. Our findings should be used to inform the design and evaluation of a screening program aimed at earlier detection of mental illness, with the goal of improving patient outcomes and preventing premature deaths related to suicide. However, a screening program will only be effective if access to the appropriate interventions is available for all patients. One approach might be the integration of a dedicated psychiatrist and/or psychologist within the burn center team, which might overcome some of the challenges associated with accessing this care outside of the burn center. However, this is likely to be of benefit only to those patients who reside in the vicinity of the burn center. Ultimately, an evaluation of the barriers to accessing mental health care after burn injury is required. This should involve a mixed-methods approach with the capture of qualitative data from patients, family physicians, psychiatrists, and burn care providers. This approach would enable investigators to understand, from a variety of perspectives, the challenges faced in attempting to access mental healthcare. This work would generate practical, actionable data to inform policy interventions aimed at ensuring equal access to these critical services for all burn survivors, thereby helping to ensure that earlier identification through screening leads to earlier intervention.

9.3 Further characterization of the association between the pathophysiological response to burn injury and long-term morbidity and mortality

While we have identified that a large portion of the healthcare utilization and late mortality after burn injury is related to mental illness, burn survivors also have high rates of cardiovascular, respiratory, and gastrointestinal diseases. While previous studies in burn-injured children have demonstrated that the physiological changes induced by burn injury persist up to three years after burn injury, no similar studies have been conducted in adult burn survivors. Therefore, it is not clear whether the incidence of medical comorbidity among burn survivors truly represents sequelae of the pathophysiological response to burn injury. Future work should aim to characterize the persistence of this response in adults, and to demonstrate associations between the specific aspects of this response and the development of new disease. Through this work, opportunities for new interventions might be identified to further improve burn outcomes in future.

9.4 Evaluation of access to and receipt of primary healthcare among burn survivors

In our cohort of adult burn survivors, 36% of patients were classified as having 'high' or 'very-high' levels of comorbidity at the time of their injury, according to the Johns' Hopkins ACG case-mix system. We also found that one in every four burn patients lives in an area with the greatest degree of marginalization related to material deprivation and residential instability, while one in every five burn patients lives in an area with the greatest degree of marginalization related to ethnic concentration and dependency. Therefore, burn patients represent a marginalized cohort at risk for poor health outcomes, even prior to their burn injury.

Given that background health and marginalization might be important modifiers of outcomes after burn injury, the pursuit to improve burn outcomes cannot ignore the background health and health behaviors of burn injured patients, particularly for those from marginalized communities. Therefore, future work should characterize the role that burn care providers and burn centers might have in advocating for the provision of primary care, either within the burn center or in the community. Such efforts might begin with an evaluation of the existing number of burn patients who have a family physician. The uptake of recommended practices for cardiovascular, diabetic, and cancer screening among these patients should also be evaluated. Administrative data has previously been used for similar evaluations in other cohorts[268,269]. Such work might generate data to inform policy or other interventions aimed at improving the background health of burn survivors with a view to improving their overall long-term outcomes.

Ultimately, burn injury should be considered through the lens of a chronic, multi-morbid disease, rather than as a discrete, singular event. This perspective will ultimately facilitate the development of new interventions and policies to improve the delivery and outcomes of burn care in Canada and beyond.

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APPENDIX A: ICD-10 DIAGNOSIS CODES FOR BURN INJURY

ICD-10 codes for extent and depth of burn

ICD-10CA code	TBSA (%)	Proportion full-thickness (%)
T31.10	10-19	0 or unspecified
T31.11	10-19	<10
T31.12	10-19	10-19
T31.20	20-29	0 or unspecified
T31.21	20-29	<10
T31.22	20-29	10-19
T31.23	20-29	20-29
T31.30	30-39	0 or unspecified
T31.31	30-39	<10
T31.32	30-39	10-19
T31.33	30-39	20-29
T31.34	30-39	30-39
T31.40	40-49	0 or unspecified
T31.41	40-49	<10
T31.42	40-49	10-19
T31.43	40-49	20-29
T31.44	40-49	30-39
T31.45	40-49	40-49
T31.50	50-59	0 or unspecified
T31.51	50-59	<10
T31.52	50-59	10-19
T31.53	50-59	20-29
T31.54	50-59	30-39
T31.55	50-59	40-49
T31.56	50-59	50-59
T31.60	60-69	0 or unspecified
T31.61	60-69	<10
T31.62	60-69	10-19
T31.63	60-69	20-29
T31.64	60-69	30-39
T31.65	60-69	40-49
T31.66	60-69	50-59
T31.67	60-69	60-69
T31.70	70-79	0 or unspecified
T31.71	70-79	<10
T31.72	70-79	10-19
T31.73	70-79	20-29
T31.74	70-79	30-39

T31.75	70-79	40-49
T31.76	70-79	50-59
T31.77	70-79	60-69
T31.78	70-79	70-79
T31.80	80-89	0 or unspecified
T31.81	80-89	<10
T31.82	80-89	10-19
T31.83	80-89	20-29
T31.84	80-89	30-39
T31.85	80-89	40-49
T31.86	80-89	50-59
T31.87	80-89	60-69
T31.88	80-89	70-79
T31.89	80-89	>80
T31.90	>90	0 or unspecified
T31.91	>90	<10
T31.92	>90	10-19
T31.93	>90	20-29
T31.94	>90	30-39
T31.95	>90	40-49
T31.96	>90	50-59
T31.97	>90	60-69
T31.98	>90	70-79
T31.99	>90	>80

ICD-10 Codes for Mechanism of Burn

Mechanism	**ICD-10 code**
Exposure to smoke/fire/flames	X00-X09
Exposure to electric current	W85-W87
Contact with heat/hot substances	X10-X19

APPENDIX B: THE ACCURACY OF BURN DIAGNOSIS CODES IN ADMINISTRATIVE DATA

Acknowledgement: Parts of Appendix B were reprinted from the following, with permission from Elsevier:

Mason SA, Nathens AB, Byrne J, Fowler R, Gonzalez A, Karanicolas PJ, Moineddin R, Jeschke MG. The accuracy of burn diagnosis codes in health administrative data: A validation study. Burns. 2017 Mar; 43(2): 258-64.

B.1 Summary

Background: Health administrative databases may provide rich sources of data for the study of outcomes following burn injury. We aimed to determine the accuracy of International Classification of Diseases diagnoses codes for burn injury in a population-based administrative database.

Methods: Data from a regional burn center's clinical registry of patients admitted between 2006-2013 were linked to administrative databases. Burn total body surface area (TBSA), depth, mechanism, and inhalation injury were compared between the registry and administrative records. The sensitivity, specificity, and positive and negative predictive values were determined, and coding agreement was assessed with the Kappa statistic.

Results: 1215 burn center patients were linked to administrative records. TBSA codes were highly sensitive and specific for $\geq$10 and $\geq$20% TBSA (89/93% sensitive and 95/97% specific), with excellent agreement (κ, 0.85/ κ, 0.88). Codes were weakly sensitive (68%) in identifying $\geq$10% TBSA *full-thickness* burn, though highly specific (86%) with moderate agreement (κ, 0.46). Codes for inhalation injury had limited sensitivity (43%) but high specificity (99%) with moderate agreement (κ, 0.54). Burn mechanism had excellent coding agreement (κ, 0.84).

Conclusions: Administrative data diagnosis codes accurately identify burn injury by burn size and mechanism, while identification of inhalation injury or full-thickness burns is less sensitive but highly specific.

B.2 Background

The care of the burn-injured patient has evolved over the past several decades, such that all but the most devastating injuries are survivable[192]. Alongside these improvements, a need to understand the long-term outcomes of burn patients has emerged to inform development of interventions to mitigate long-term morbidity following burn injury. However, a paucity of data regarding the long-term burden of burn injury exists [123,126].

Our current knowledge of outcomes after burn injury derives from studies hampered by small cohort sizes and loss to follow up with limited data available beyond 2 years after injury[14,119,126]. Many of these challenges can be overcome through population-based studies that utilize health administrative data. These data facilitate the long-term study of burn-injured individuals through the analysis of health care utilization data. Such data has been successfully utilized to study long-term mortality following major burn injury[234,235]. In other cohorts, these data have been used to evaluate self-harm risk, cancer risk, and to describe long-term health trajectories[201,229,230,235,270,271].

A key limitation of administrative data is the potential for misclassification bias. The identification of patients with specific conditions, such as burn injury, depends on the accuracy with which these conditions are coded within administrative databases. In

Canadian administrative databases, diseases are coded using the tenth revision of the International Classification of Diseases (ICD-10)[272]. While the validity of these codes has been demonstrated for many conditions[162,164,165,273,274], the accuracy of codes for burn size, depth, body region, mechanism and inhalation injury is unknown. Prior to the use of administrative databases to study the long-term outcomes of burn-injured patients, it is important that these diagnosis codes are evaluated and proven sufficiently accurate. Therefore, the objective of this study was to determine the accuracy of ICD-10 diagnosis codes for burn injury and inhalation injury in a provincial health administrative database, using comprehensive clinical data from the same patients in a second regional clinical database.

B.3 Methods

Study Design

This study is reported in accordance with the guidelines for diagnostic and validation studies of health administrative data[275]. Records derived from a clinical burn registry reflecting the acute care of burn patients admitted to the largest burn center in Canada were linked to administrative discharge data to validate ICD-10 diagnosis and external cause codes for burn injury. This study was approved by the Research Ethics Board of Sunnybrook Health Sciences Centre.

Data Sources

Two distinct healthcare datasets were used for the study: (1) a provincial health administrative database, and (2) a comprehensive regional clinical registry. The clinical burn registry contains data regarding patient demographics, injury characteristics, and inpatient complications for all patients admitted to the burn center. Data were entered into the registry by a trained burn registrar and collected in accordance with the National Burn Repository data standard[276]. TBSA estimations were derived from the Lund and Browder chart completed by the admitting burn surgeon on admission. Presence of inhalation injury was documented on admission based on bronchoscopic evaluation performed by the admitting burn surgeon. Mechanism of injury was recorded in the medical record based on the admission history taken by the surgeon (self-reported by patient or collateral history from witnesses).

To determine the accuracy of burn diagnosis codes in administrative data, the burn registry was linked to the Registered Persons Database (RPDB). The RPDB contains demographic information on all residents of Ontario, and is linked by unique identifier to the Discharge Abstract Database (DAD), a population-based administrative database that records all discharges from acute care hospitals in the province of Ontario after the year 1991. Diagnoses responsible for admission are coded in the DAD according to a modification of the 10th revision of the International Classification of Diseases, and each admission can contain up to 25 recorded diagnoses. The Canadian Institute for Health Information coding standards require that data abstractors assign burn diagnosis codes according to each affected body area, along with codes reflecting the TBSA and external cause of injury[277]. These data were made available through the Institute of Clinical and Evaluative Sciences (ICES). ICES is a prescribed entity under the Province of Ontario's privacy law and holds a large proportion of the administrative health data collected in

Ontario. These datasets were linked using unique encoded identifiers and analyzed at ICES.

Validation Cohort

We used the clinical registry to identify all patients aged 16 years and older who were admitted to the burn center for the treatment of acute burn injury between January 1, 2006 and December 31, 2013. Patients were excluded if data regarding their burn extent, presence of inhalation injury, or mechanism of injury were missing in the clinical burn registry. The TBSA estimation, % full-thickness burn estimation, mechanism of burn injury, and diagnosis of inhalation injury from the burn registry were considered the reference standard.

Administrative data and record linkage

Once the validation cohort was assembled, each patient record was linked to administrative data through both deterministic and probabilistic linkage. Deterministic linkage was performed based on hospital health record number and date of birth. Where deterministic linkage was not possible, probabilistic linkage on patient name was used.

Validation

The ICD-10 diagnosis codes related to the identification of burn injury, characterization of burn extent, depth and mechanism, and identification of inhalation injury were defined *a priori* and used to derive case definitions for validation (**Table 1**).

We compared case definitions derived from the DAD to those derived from the reference standard. Diagnoses were coded as binary variables for each patient; for example, inhalation injury was coded as present or absent in the clinical registry and as positive or negative based on DAD diagnoses. For each case definition, each patient was classified as true positive (registry present, DAD positive), true negative (registry absent, DAD negative), false positive (registry absent, DAD positive), and false negative (registry present, DAD negative).

We sought to determine whether the administrative data were accurate in identifying patients with ≥10% TBSA, ≥20% TBSA, ≥10% full-thickness burn, and inhalation injury, as compared to the clinical registry. These TBSA cutoffs were chosen as they identify patients who meet criteria for referral to a burn centre (≥10% TBSA)[33] and major burn injury (>20% TBSA). This was assessed in two ways: (1) by determining the agreement for each case definition between the clinical registry and administrative data using the kappa coefficient, and (2) by calculating the sensitivity, specificity, and positive and negative predictive values (PPV, NPV). Accuracy in burn mechanism between the clinical registry and administrative data was assessed by exact agreement. For each mechanism (flame, electrical, contact), coding agreement was assessed using the kappa coefficient. To understand how accurately TBSA estimates are coded, we evaluated agreement between TBSA estimates within each decile of % TBSA between the clinical registry and administrative data using the kappa coefficient.

For our purposes, accuracy of 80% or greater and a kappa coefficient of 0.60 or greater were considered targets for validation [278,279]. Based on prior studies of the validity of other diagnoses codes in the same database, we expected these codes to have sensitivity in excess of 75% and specificity in excess of 90%[162,164,273,280–282].

Statistical Analysis

Descriptive statistics were used to describe the validation cohort. Means and standard deviations, or medians and interquartile ranges were calculated for continuous variables, as appropriate. For discrete variables, absolute frequencies were measured. Sensitivity, specificity, PPV, NPV, accuracy (% exact agreement) and the kappa coefficient were calculated for each case definition. Agreement was considered excellent where kappa was greater than 0.81; substantial where kappa ranged between 0.61-0.80 and moderate where kappa was between 0.41-0.60 [283]. All analyses were conducted on de-identified data using SAS Version 9.4 (Cary, NC).

B.4 Results

We identified 1252 patients in the burn registry meeting inclusion criteria. Of these, 17 were excluded prior to linkage due to missing data. We were able to deterministically link 89% (n=1099) patients to administrative data; the remaining 11% (n=136) were linked probabilistically (**Figure B.1**).

The patient and injury characteristics of the validation cohort are presented in **Table B.2**. Most patients (73%, n=890) were men, and the median age of patients was 50 years. The median TBSA was 7.8%, with the most frequent mechanism being flame burns (61%, n=731).

In the burn registry, the prevalence of ≥10% TBSA burn injury was 41% (n=502); the prevalence of ≥20% TBSA burn injury was 20% (n=245). 17% of patients had ≥10% TBSA full-thickness burns. The prevalence of inhalation injury was 16% (n=196).

Burn Size

The diagnosis codes in the administrative data identified both ≥10% TBSA and ≥20% TBSA with high sensitivity and specificity (**Table B.3**). In identifying patients with ≥10% TBSA, administrative data were 89% sensitive and 95% specific; for ≥20% TBSA, administrative data were 93% sensitive and 97% specific. Agreement between the clinical registry and administrative data in discriminating between ≥ and <10% and 20% TBSA injury was excellent (κ=0.85 and 0.88 respectively). Accuracy (exact agreement) between TBSA estimates within each decile of % TBSA was 87%. Coding agreement by TBSA decile ranged from moderate to excellent (κ, 0.58-0.86), and generally increased with increasing burn size (**Table B.4**).

We also evaluated the sensitivity of diagnosis codes to identify patients with full-thickness burns of ≥10% TBSA. These codes were moderately sensitive (68%) and highly specific (86%), with moderate agreement between the burn registry and administrative data (κ, 0.46).

Inhalation Injury

The administrative data diagnoses codes were poorly sensitive (43%) but highly specific (99%) for inhalation injury. Agreement between the clinical registry and administrative data was moderate (κ=0.54).

Burn Mechanism

We first sought to determine overall agreement between the clinical registry and administrative data for burn mechanism, and then to determine coding accuracy for flame, contact, and electrical burns. An external cause of injury code was missing in the administrative data for 9 patients (0.7%). Among the remaining patients, overall agreement was excellent (κ, 0.84). Diagnoses codes were highly sensitive for flame and contact burns (93% and 89%), while moderately sensitive for electrical burns (76%). Specificity for all 3 mechanisms was excellent (91-99%, **Table B.3**).

B.5 Discussion

We conducted a retrospective validation study of the accuracy of burn diagnosis codes in a health administrative database in Ontario, Canada. Our findings demonstrate that diagnoses codes were highly sensitive and specific for burn size and mechanism, while burn depth and inhalation injury were less sensitive and specific. The high accuracy of diagnoses codes for burn extent and burn mechanism suggests that administrative data can be reliably used to identify cohorts of burn-injured patients on the basis of either TBSA or mechanism. The diagnoses codes had the greatest sensitivity and specificity in discriminating between greater and less than 20% TBSA injury, with lower but strong agreement below this threshold. We observed greater reliability with increasing deciles of % TBSA, consistent with prior studies demonstrating that the accuracy of burn size estimations increases with increasing burn extent [29].

The diagnoses codes for inhalation injury had poor sensitivity; despite high specificity, only 43% of patients with inhalation injury were identified as such in the administrative data. The significant difference in prevalence of inhalation injury between the burn registry and administrative data (16% vs. 7%) suggests that inhalation injury is not coded as commonly during routine medical records abstraction for administrative purposes. This may reflect low clinical suspicion and confirmatory diagnostic testing, poor documentation of inhalation injury in the medical record, or incomplete coding of inhalation injury as a secondary diagnosis by the data abstractor. As a result, these codes cannot be reliably used to identify burn-injured patients with inhalation injury.

We found that diagnoses codes for ≥10% full-thickness burns were weakly sensitive and highly specific, with moderate agreement. The characterization of patients based on the extent of full-thickness burn is limited by the nature of ICD-10 diagnosis codes for burn depth. This is expressed in deciles, such that both 0% and 9% full-thickness have the same diagnosis code; this same code is used when burn depth is unspecified. As a result, for patients with <10% TBSA, it is impossible to discriminate between patients with and without full-thickness burns. This limits the ability of researchers to distinguish patients with potentially significant functional burns that will very likely require surgery, i.e. full-thickness burns to the face, feet, or hands, from those with more minor burns.

A key limitation of this work is its generalizability to administrative databases in other settings. Furthermore, data derived from the largest regional burn center in Canada were used as the reference standard. Diagnoses codes in administrative data are assigned based on abstraction from the medical record. Therefore, the accuracy of TBSA estimations in administrative data depends on the accuracy of estimations in the medical record. While we demonstrated high accuracy of these codes in our study, this reflects comparison to estimations performed by expert burn surgeons. TBSA estimations have previously been demonstrated to vary widely, even among burn surgeons [27,30,284]. It is reasonable to assume that TBSA estimations might be less accurate outside of regional burn centers. This will be a limitation of future studies utilizing health administrative data to identify burn-injured patients, and might result in misclassification of patients based on their burn extent. To the best of our knowledge, this is the first validation study of burn diagnosis codes, limiting our ability to compare our results to studies in other settings.

Conclusion

This validation study linked a clinical burn registry to population-based health administrative database in order to assess the validity of diagnoses codes for burn size, depth, mechanism, and inhalation injury. We have demonstrated that diagnosis codes for TBSA and burn mechanism are highly sensitive and specific, with excellent reliability between the administrative data and burn registry. Our findings suggest that patients with major burn injury can be reliably identified in administrative data. This should encourage investigators to consider the potential advantages of using health administrative data to further contribute to our understanding of burn injury and its impact at both the patient and health care system levels.

B.6 Tables for Appendix B

Table B.1: Case definitions for validation	
	ICD-10CA Diagnosis Code(s)
≥10% TBSA	T31.10-T31.99
≥20% TBSA	T31.20-T31.99
Inhalation injury	T27.0-T27.3
TBSA[†]	
0-10	T31.0
11-20	T31.1
21-30	T31.2
31-40	T31.3
41-50	T31.4
51-60	T31.5
61-70	T31.6
71-80	T31.7
81-90	T31.8
>90	T31.9
≥10% full-thickness TBSA[†]	T31.12, T31.22-23, T31.32-34, T31.42-45, T31.52-56, T31.62-67, T31.72-78, T31.82-89, T31.92-99
Burn Mechanism	
Flame	X00-X09
Contact	X10-X19
Electrical	W85-W87

ICD-10CA, International Statistical Classification of Diseases and Related Health Problems,10th Revision, Canada
TBSA, total body surface area

Table B.2: Patient and injury characteristics of validation cohort	
Patient characteristics	
Median Age, years (IQR)	50 (35-62)
Male (%)	890 (73)
Injury Characteristics	
Median % TBSA (IQR)	7.8 (3.1-16.5)
Median % full-thickness TBSA (IQR)	0.5 (0-5)
Inhalation Injury (%)	195 (16)
Mechanism (%)	
Flame	731 (61)
Contact	385 (32)
Electrical	90 (7)
Median APACHE II Score (IQR)	3 (1-7)
In-hospital mortality (%)	12 (1)

IQR, Interquartile Range
TBSA, total body surface area
APACHE, Acute Physiology and Chronic Health Evaluation

Table B.3: Estimates of diagnostic accuracy of administrative data

	Sensitivity (%, 95%CI*)	Specificity (%, 95% CI*)	Positive Predictive Value (%, 95% CI*)	Negative Predictive Value (%, 95% CI*)
≥ 10% TBSA	89 (86-92)	95 (93-97)	93 (90-95)	93 (91-95)
≥ 20% TBSA	93 (89-96)	97 (95-98)	88 (84-92)	98 (97-99)
≥ 10% full-thickness TBSA	68 (61-74)	86 (83-88)	49 (43-55)	93 (91-95)
Inhalation injury	43 (36-50)	99 (98-100)	93 (88-98)	90 (88-92)
Burn Mechanism				
Flame	93 (87-92)	91 (88-93)	94 (92-95)	85 (82-88)
Contact	89 (85-92)	93 (91-95)	86 (82-89)	95 (93-96)
Electrical	76 (65-84)	99 (99-100)	93 (85-98)	98 (97-99)

CI, Confidence Interval
TBSA, Total body surface area

Table B.4: Prevalence and accuracy of specific injury characteristics

	Prevalence (%)				
	Burn registry	**Administrative data**	**Accuracy (%)**	**Kappa (95%CI)**	**Agreement**
≥10% TBSA	41	40	93	0.85 (0.82-0.88)	Excellent
≥20% TBSA	20	21	96	0.88 (0.84-0.91)	Excellent
≥10% full-thickness TBSA	17	23	83	0.46 (0.40-0.52)	Moderate
Inhalation injury	16	7	90	0.54 (0.47-0.61)	Moderate
Mechanism			88	0.84 (0.81-0.87)	Excellent
Flame	61	60	92		
Contact	32	34	93		
Electrical	7	6	98		
%TBSA			87		
0-10	58	60	92	0.83 (0.80-0.86)	Excellent
11-20	21	19	92	0.74 (0.70-0.79)	Substantial
21-30	9	10	96	0.77 (0.70-0.83)	Substantial
31-40	4	4	98	0.77 (0.68-0.87)	Substantial
41-50	3	3	99	0.73 (0.60-0.86)	Substantial
51-60	2	2	99	0.72 (0.57-0.86)	Substantial
61-70	1	2	99	0.58 (0.38-0.78)	Moderate
71-80	0.9	0.8	99.5	0.70 (0.47-0.93)	Substantial
81-90	0.3	0.7	99.7	0.67 (0.36-0.97)	Moderate
>90	0.7	0.5	99.8	0.86 (0.66-1)	Excellent

CI, Confidence Interval
TBSA, Total body surface area

B.7 Figures for Appendix B

Figure B.1: Derivation and linkage of validation cohort. ICD-10, International Classification of Diseases, 10th edition.