The Descriptive Epidemiology of Severe Burn Injury in Australia and New Zealand

Dr. Jason Toppi

BSc, MBBS, Dip Anat

A thesis submitted for the degree of Master of Surgery at

Monash University in 2017

Monash University Institute of Graduate Research

Copyright notice

Abstract

The primary aim of this thesis was to describe the epidemiology, management and outcomes of severe burn injuries presenting to dedicated burn services across Australia and New Zealand. Specifically, this included describing the epidemiology of adult patients with severe burn injury, describing the management and outcomes of these adults with severe burn injury in Australia and New Zealand, describing the predictors of mortality, hospital length of stay and discharge destination in adults with severe burn injury and to compare the management and outcomes of severe burn injury in adults between burn services.

All data used in this thesis was sourced from the Burns Registry of Australia and New Zealand (BRANZ). The BRANZ is a collaboration between the ANZBA and Monash University and is a clinical quality registry of burn injuries, patient demographics, treatments and outcomes of burn injury patients, and captures data about admissions to burn services in Australia and New Zealand. Patients registered to BRANZ were included in this study if they were admitted between August 2009 and June 2013, were adults (aged 18-years or over) and had burns of greater than or equal 20% TBSA.

Ten sites that treated adults presenting with severe burns were included in the final analysis. There were 496 BRANZ registered patients admitted to one of 10 dedicated burn services across Australia and New Zealand who met the inclusion criteria for this study. Over half of the patients were aged between 18 and 40-years and most were male. The median (IQR) %TBSA was 31 (25-47) and ranged from 21 to 100. Three quarters of patients enrolled had burns involving <50% TBSA. The median length of stay was 24 days (including survivors and deaths). Over 80% of patients had a documented time of injury. A total of 84 patients (17%) died in-hospital. Survivors were younger, male and had lower Charlson Co-Morbidity Index (CCI) scores than deceased patients and showed lower rates of self-harm and inhalation injury.

This thesis provides a thorough investigation relating to the demographics, management practices and outcomes of severe burn injuries in adults in Australia and New Zealand. Comparisons with literature from other countries was hampered due to the heterogeneous nature of reporting practices amongst published studies. Thus it was recommended that information relating to patient age and TBSA should always be reported to enable subgroup analysis and that definitions of children, adults and elderly be standardized. Standardised agreements on relevant ways to report incidence, inhalation injury and burn depth were also recommended.

Declaration

This thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

Dr. Jason Toppi

[redacted]

28/01/2017

Acknowledgments

Thank you to Professor Belinda Gabbe of the Monash University Department of Epidemiology and Preventive Medicine and Dr. Heather Cleland of the Victoria Adult Burns Service. Without their passionate participation and input, this thesis could not have been successfully completed. I am extremely grateful for the time and effort spent critically assessing this thesis despite their very busy schedules. The efforts of the practitioners, data collectors and registry staff of the Burns Registry of Australia and New Zealand (BRANZ) are also greatly appreciated. I would also like to thank Dr. Jessica Fairley for offering her time to proof read this thesis.

CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

ABA	American Burn Association
ABSI	Abbreviated Burn Severity Index
ACC	Accident compensation corporation
ADX	Porcine acellular dermal xenograft
ANZBA	Australia and New Zealand Burn Association
BICU	Burn intensive care unit
BOBI	Belgian outcome of burn injury score
BRANZ	Burn registry of Australia and New Zealand
CCI	Charlson Comorbidity Index
CEA	Cultured epithelial autograft
EMR	East Mediterranean Region
EMSB	Emergency management of severe burns
HDI	Human development index
iBID	International Burn Injury Database
ICD-10-AM	The International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification
IQR	Interquartile range
ISBI	International Society for Burn Injuries
LOS	Length of stay
NBR	National Burn Repository
NS	Not stated
PTSD	Post-traumatic stress disorder
RCT	Randomised control trial
SIRS	Systemic inflammatory response syndrome
SDSTPS	Selectively decellularised split-thickness porcine skin
SSG	Split-thickness skin graft
%TBSA	Percent total body surface area
TBSI	Total burn surface index
USA	United States of America
VBSS	Vancouver burn scar score
VSS	Vancouver scar scale
WHO	World Health Organization

1 INTRODUCTION

It has been reported that approximately 1% of all Australians sustain a burn each year, with 50% of these severe enough to affect daily life, though overall the majority of these injuries are not life threatening [1, 2]. It is well established that the percentage of total body surface area (%TBSA) burnt is an important measure of burn severity [3]. Associations between %TBSA and heightened hyper-metabolic and inflammatory reactions are well recognised, with the %TBSA involved representing a critical predictor of clinical outcome [4, 5]. Furthermore, it represents an important measure for burn care research, remuneration of clinical service provision and quality assurance [3, 6, 7].

The care of hospitalised patients with severe burn injuries, defined as 20% or greater total body surface area (TBSA) involved [8], requires input from a variety of specialists and should use a multidisciplinary approach [9]. Whilst severe burn injuries are relatively uncommon, accounting for approximately 8% of burn injury admissions to dedicated burn services across Australia and New Zealand, they represent an important cause of morbidity and mortality [10].

Currently the epidemiology of severe burn injury in Australia is limited to regional cohort studies which have investigated populations based in Victoria, Queensland and New South Wales [1, 11-13]. Whilst the investigation of epidemiological and outcome based factors in specific geographical areas is helpful in evaluating local therapies, broader nation-wide perspectives are still required to help benchmark and improve the quality of care [14].

Detailed information about severe burn injuries, including the underlying event, patient demographics, injury characteristics and management are critical when it comes to understanding the management and outcomes of severe burn injuries. The Burns Registry of Australia and New Zealand (BRANZ) incorporates burn-related epidemiological, quality of care, and outcome data which is focused on monitoring burn injury trends and improving outcomes [10]. This includes implementing evidence-based recommendations which aim to improve patient care capabilities, cost-effectiveness, burn service capacity and outcomes for patients.

As such the primary aims of this thesis were to investigate and describe the epidemiology, management and outcomes of severe burn injuries in Australian adult patients. This also included a thorough review of the current literature to establish what current evidence was available. Specific analyses within this manuscript investigated and described the epidemiology of adult patients with severe burn injury, describing the management and outcomes of these adults with severe burn injury in Australia and New Zealand utilising data from the BRANZ. Predictors of mortality, hospital length of stay and discharge destination in adults with severe burn injury were also investigated and a thorough comparison of the management and outcomes of severe burn injury in adults between burn services was also undertaken.

2 LITERATURE REVIEW

Burn injuries represent an important healthcare issue internationally. In 2004 the number of burn injuries world-wide was estimated to approach 11 million people, and was the fourth most frequently occurring injury type [15, 16].

Within burn injury, severe burns constitute a major cause of mortality and morbidity [17]. Severe burn injuries also represent a major economic liability, with such injuries amongst the most expensive to treat due to long hospital stays, extensive rehabilitation and multiple costly surgical procedures [18].

Low- and middle-income countries (LMICs) represent a disproportionately high level of burn injury incidence and mortality. Data from the World Health Organisation (WHO) estimates that 265,000 deaths result from fire related incidents per year globally [16]. This burden of disease is significantly higher in LMICs, with over 96% of fatal fire-related burn injuries occurring in these countries [16]. A recent WHO report noted that high-income countries have made significant progress in lowering rates of burn deaths through a combination of prevention and care strategies. However, many of these improvements have been incompletely applied in low- and middle-income countries [16].

The international Society for Burn Injuries (ISBI) was founded in the early 1960s and has worked and collaborated closely with the WHO to represent all countries in the field of burns and improve prevention programs [19]. Recently there has been a focus on elevating the standards of burn care worldwide, particularly in low- and middle-countries, by improving education programs and developing cost effective, evidence based, burn care guidelines for low resource regions [19].

Given the mortality and morbidity burden of severe burns worldwide, this is clearly an important area of research. Thus, this literature review summarised data relating to the epidemiology, operative management and outcomes of severe burn injuries in adults to better contextualise the pertinent issues at play, and establish where further research is needed. All references to 'severe burn injury' in this literature review were defined as any burn injury of 20% TBSA or greater, unless otherwise specified.

2.1 EPIDEMIOLOGY OF SEVERE BURN INJURY IN ADULTS

The epidemiology of burn injury in general populations has been extensively described, however the epidemiology of severe burn injuries in adults has not been investigated as thoroughly [20]. Nevertheless, data pertaining to adults with severe burns was found within a number of large reviews, burn registry reports and regional or national cohort studies that included literature from every continent (Figure 1) [18, 20-42]. The primary literature sources used in this epidemiological review are summarised in Figure 1 and Table 1.

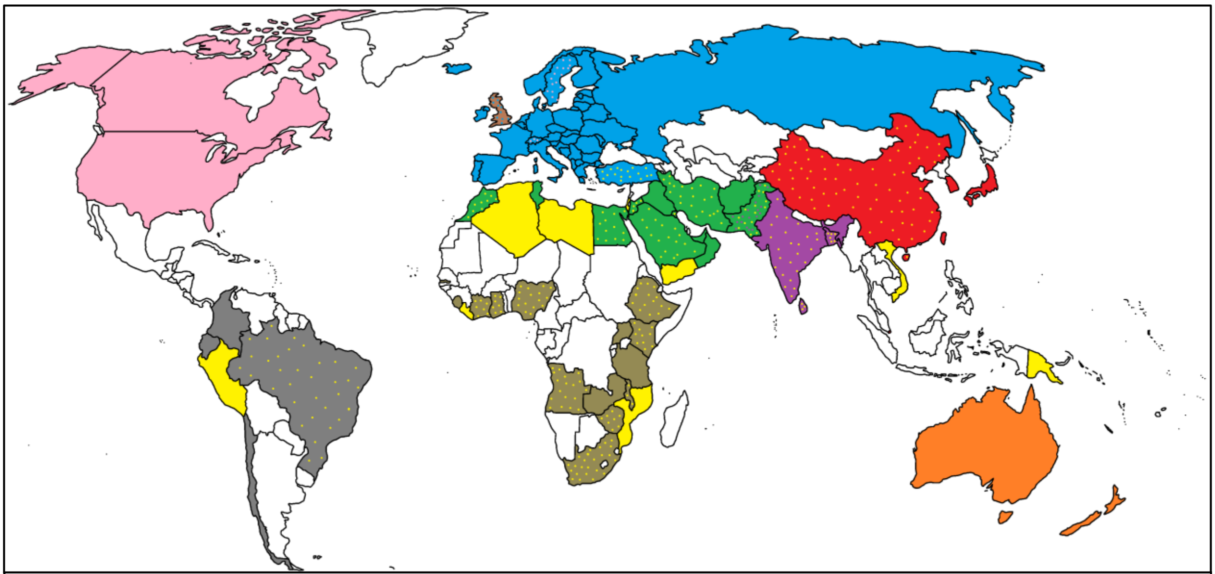
A literature search was carried out from January 1990 to December 2015 using Ovid Medline. The search terms used were: burn$ OR burn injur$ OR thermal injur$ AND epidemiolog$. Only English language studies on humans were included in the search. A total of 1332 articles were then reviewed for inclusion. In the first instance, due to the large number of epidemiological studies available, only systematic reviews were included. There were four systematic reviews that included studies from Europe, South Asia, the East Mediterranean region and a number of low- and middle-income countries (Figure 1 and Table 1). A separate search was also conducted to identify reports or publications from burn injury databases, which added four papers to the study. Burn services in Australia (Burns Registry of Australia and New Zealand- BRANZ), New Zealand (BRANZ), England (International Burn Injury Database- iBID), Wales (iBID), the United States of America (USA) (National Burn Repository- NBR), Canada (NBR), Sweden (NBR) and Switzerland (NBR) contributed to burn injury databases (Figure 1 and Table 1). Regions not represented by publications from the above sources were South America, Africa and a number of countries in East Asia (including China, Japan and South Korea). For these countries separate Ovid Medline searches were conducted using the same terms as above and the country or region name to identify epidemiological studies. An additional 13 studies were found (one systematic review, four multicentre studies and eight single centre studies (Figure 1 and Table 1).

In general, the systematic reviews and burn registries aimed to provide an overview of all burn injuries receiving care in a hospital in a given region [18, 21, 22, 24, 29-32] (Table 1). Reporting methods from the BRANZ, iBID and NBR tended to focus on reporting demographics, general burn characteristics and management trends with subset analysis specifically investigating age, gender and %TBSA in more detail [29-31]. The reviews from Europe, South Asia, the East Mediterranean and Sub-Saharan Africa included multiple, often heterogeneous studies, conducted at different times making direct comparisons difficult and thus tended to provide more general overviews [18, 21, 22, 24, 32] (Table 1). A number of single- and multi-centre regional based studies were also included to provide data on countries not well represented in reviews or by registries [20, 23, 33-42]. These were able to provide more specific information relating to burn injury characteristics, however they were limited mainly in area and patient capture when compared to the larger registries or systematic reviews. The reporting of data pertaining specifically to adults with severe burn injuries was variable given no epidemiological studies exclusively investigating this patient population were found. However, many studies did provide information and, in some cases, subset analysis describing this patient demographic (Table 1).

In LMICs burns in children aged 1 to 14 years were the leading cause of injury death, and as such many studies from these areas focused on paediatric burns [43]. Electrical burns and non-accidental scald and acid injuries were also more common in these regions [42, 43]. This compared with high-income countries where the most common cause of burn death amongst adults was fire in the household, thus literature from these countries had more information pertaining to severe burn injuries in adult populations. These differences in burn characteristics and demographics between regions may have accounted for different data reporting focuses relating to injury incidence, aetiology, outcomes and treatment for the studies below.

2.1.1 Incidence and geography

Brusselaers et al investigated burns literature from 22 European countries [18]. The study reviewed 76 studies encompassing a total of 186,500 patients and found an annual incidence of 0.2-2.9 per 10,000 inhabitants for severe burn injuries. However, Brusselaers et al defined severe burn injury as any burn injury requiring admission to a specialised burn service, and thus included injuries of <20% TBSA. Some regional European studies reported on patients with 20% TBSA or greater, for example Dokter et al reported on an incidence rate approaching 1 per 100,000 person-years in the Netherlands, though this also included paediatric cases [26]. A South American study based in Chile, that reported on severe burn injuries in adults only, estimated the incidence to be 4.6 and 5.6 per 1 million habitants in 2009 and 2010, respectively [20]. Other studies have reported rates of severe burn injuries (20% TBSA or greater) of less than 20% of burn injuries admitted to hospital [11, 38, 44].



Map legend

Pink: NBR (United States of America and Canada, Sweden and Switzerland)

Brown: Stylianou et al (iBID) (England and Wales)

Orange: BRANZ (Australia and New Zealand)

Purple: Golshan et al (South Asia)

Green: Othman et al (East Mediterranean Region)

Blue: Brusselaers et al (North, East, South and West Europe)

Yellow: Forjuoh (Sub-Saharan Africa, Latin America, the Caribbean, the Middle East, India, the Pacific and China)

Tan: Nthumba (Sub-Saharan Africa)

Red: Jie and Ren (North East China); Ho and Ying (Hong Kong, China); Tang et al (Shanghai, China); Kobayashi et al (Tokyo, Japan); Nakae and Wada (Akita, Japan); Chen et al (Taiwan); Song and Chua (Singapore); Seo et al (South Korea)

Grey: Albornoz et al (Chile); Franco et al (Columbia); Ortiz-Prado et al (Ecuador); De-Souza (Brazil)

Figure 1 Geography of epidemiological studies included in this review

Table 1 Source information for epidemiology review

First author (or database name)	Type of study	Geography	Inclusion/exclusion criteria	Total number of cases	Time
National Burns Repository (NBR) (2015)[29]	Burn injury database	United States of America	Included: All cases received from contributing hospitals that met data structure requirements Excluded: Re-admitted patients, admission for reconstruction, rehabilitation, elective admission, outpatients, duplicate encounters, and other acute non burn admission. Records excluded if data on gender not available and length of stay is less than total ICU stay	203, 422	2005-2014
NBR (international contributors) (2015)[29]	Burn injury database	Canada, Sweden and Switzerland	As above	3, 054	2004-2014
International Burn Injury Database (iBID) (2015)[30]	Burn injury database	England and Wales	Included: All patients who have visited or been admitted to a specialised burn service in England and Wales between 2003 and 2011. Excluded: Patients with incomplete records	81, 181	2003-2011
Burns Registry of Australia and New Zealand (BRANZ) (2014)[31]	Burn injury database	Australia and New Zealand	Included: All first admissions (within 28 days of injury) to an Australian or New Zealand burn service. All transfers from another hospital to a burn service (irrespective of time from injury). Admission to hospital for greater than 24 hours or the patient is admitted for less than 24 hours but requires a burns management procedure in theatre; or the patient dies within 24 hours of presentation to BRANZ hospital. All readmissions to the burn service within 28 days of the date of discharge from the first admission Excluded: Those not meeting the above criteria	12, 920	2009-2014
Brusselaers (2010)[18]	Systematic review	Europe	Included: All studies reporting on aetiology, incidence, prevalence, and/or outcome of severe burn injuries as the major topic. All hospitalized burn populations. Papers in English, French, and Dutch Excluded: Studies only considering deceased patients	~186, 500	1985-2009
Golshan (2013)[22]	Systematic review	South Asia	Included: All studies investigating unintentional burns	24, 527	1970-2011

			Excluded: Articles from grey literature and non-English articles. Papers that did not differentiate between intentional and unintentional burns		
Othman (2010)[21]	Systematic review	East Mediterranean Region (EMR)	Included: Cross sectional surveys, retrospective/prospective studies, systematic reviews and case-control studies (all languages) Excluded: Articles about specific aspects of burn management, methodologies apart from those mentioned above, military and war related burns, and articles repeating data from articles already included. Studies which were not about EMR countries or the main topic was not about burns	24, 613	1997-2007
Nthumba (2015)[32]	Systematic review	Sub-Saharan Africa	Included: English publications on burns from countries in sub-Saharan Africa published between 1989 and 2014 Excluded: Case reports and series involving ≤10 patients, any study that did not provide 'adequate data' and all subset data publications	32, 862	1989-2014
Forjuoh (2006)[24]	Systematic review	Africa, Latin America, Caribbean, Middle East, India, the Pacific and China	Included: Papers based on empirical studies Excluded: Review papers based on empirical studies	NS	1974-2003
Kobayashi (2005)[35]	Retrospective multicentre study	Tokyo, Japan	Included: All patients hospitalised with burns treated in one of the 13 burn services registered with the Tokyo Burn Unit Association between 1983 and March 2003 Excluded: Patients lacking adequate epidemiological data	6, 401	1983-2003
Nakae (2001)[36]	Retrospective multicentre study	North Eastern Japan	Included: Epidemiological data collected from regional fire department headquarters. Included all patients with acute burn injuries requiring ambulance transport to hospitals within the Akita Prefecture of Japan between January 1996 and December 1999 Excluded: Cases in which the patient died during transport	342	1996-1997
Chen (2014)[37]	Retrospective multicentre study	Taiwan	Included: Inpatient and outpatient cases of new burn injury. Cases were identified based on ICD-9-CM codes from a random sample of 1 million cases from the National Health Research Database in Taiwan. Excluded: Any patient with a diagnosis of burns in the previous year (to ensure only new burns were included)	7, 630	2009-2010

Jie (1992)[23]	Retrospective multicentre study	North Eastern China	Included: Burn injury patients that presented to burn services of the Dong Bei area in North Eastern China Excluded: All patients who did not meet the above criteria	12, 606	1980-1989
Tang (2006)[34]	Retrospective single centre study	Shanghai, China	Included: All patients with acute burns discharged from the Rui Jin Hospital regional burn service between March 2002 and April 2003 Excluded: Incomplete data records and patients admitted for conditions other than acute burn injury	302	2002-2003
Ho (2001)[33]	Retrospective single centre study	Hong Kong, China	Included: All patients admitted to the burn service of the Prince of Wales Hospital (regional burn service) between March 1993 and February 1999 Excluded: All patients who did not meet the above criteria	1, 063	1993-1999
Seo (2015)[39]	Retrospective single centre study	South Korea	Included: All patients with 'major burns' admitted to the burn intensive care unit (BICU) at Hangang Sacred Heart Hospital burn service between January 2003 and December 2012. 'Major burns' necessitating BICU admission were: ≥20%TBSA burned; ≥10%TBSA burned in children <10-years old or adults >60-years old; full-thickness burns ≥10%TBSA; all burns involving the face, hands, feet or perineum; high voltage electrical burns; associated major trauma or inhalation injury; 'poor-risk' patients with burns Excluded: All patients who did not meet the above criteria	4, 481	2003-2012
Song (2005)[38]	Single centre study	Singapore	Included: All acute burns requiring admission to the Singapore General Hospital burn service between January 1997 and December 2003	2, 019	1997-2003
Ortiz-Prado (2015)[41]	Single centre study	Ecuador	Included: Patients ≥16-years with burn injuries requiring hospitalisation at the Eugenio Espejo burn service between January 2005 and January 2014 Excluded: Deaths or discharges prior to admission	1, 106	2005-2014
Albornoz (2011)[20]	Single centre observational study	Chile	Included: Patients ≥16-years with 20%TBSA or greater burn injuries and Garces severity score over 70 requiring hospitalisation at the Alejandro del Rio Public Assistance Hospital burn service between February 27th to June 27th, 2010 (4 months following a major earthquake) and February 27th to June 27th, 2009 (one year before the Earthquake) Excluded: Children or patients with <20%TBSA burn injuries or a Garces severity score <70	135	2009 & 2010

Franco (2006)[40]	Single centre study	Columbia	Included: All burn injuries requiring hospitalisation at the Hospital Univeritario San Vicente De Paúl burn service between 1994 and 2004 Excluded: All patients who did not meet the above criteria	2, 319	1994-2004
De-Souza (1998)[42]	Single centre study	Brazil	Included: All burn injuries hospitalised in the burn service of the Faculty of Medicine of Ribeirão Preto between January 1990 and April 1995 Excluded: Those treated as outpatients, patients admitted for later reconstructive surgery, and patients who did not complete treatment with the service	229	1990-1995

2.1.2 Age and gender

Similar age distributions were seen throughout the USA, Europe, Australia and New Zealand with adults accounting for 40 to 50% of burn injuries [18, 29-31]. In the USA patients aged between 20 and 30-years were the most prevalent age group, representing 15% of cases [29]. The definition of elderly patients was variable and generally included patients older than 60 to 75-years. Elderly patients made up 7 to 16% of cases in the USA, Australia, New Zealand and Europe [18, 29-31].

Amongst burns in South Asian low- to middle-income countries (LMICs), including India, Pakistan, Sri Lanka and Bangladesh, gender trends closely followed age patterns [22]. Burns in younger patients tended to be associated with male gender, whilst burns in females predominated during adolescence and adulthood [22]. This same trend was also demonstrated in a number of Iranian studies [21]. This was contrasted by populations in Europe, China and South America where males tended to predominate across most age groups [6, 18, 29, 31, 33, 34, 41, 42]. Golshan et al postulated the reason for this shift in gender distribution in some South Asian countries was related to young women being brought into the kitchen to help their mothers cook [22]. In doing so they were exposed to faulty appliances, kerosene stoves and hot liquids whilst wearing loosely fitting and flammable garments [22]. Of sixteen studies included in the review by Golshan et al, five implicated loose/flammable clothing and a further twelve identified kitchen cooking as separate contributing factors [22]. Self-immolation was overrepresented in severe burn injuries, particularly amongst women in LMICs [21, 24].

2.1.3 Burn aetiology

Flame burns were the most frequent cause of burn injury in adults, with higher %TBSA associated with this type of burn. Over 80% of cases in the United States were caused by either flame (43%), scald (35%) or contact injuries (8.9%). Scald injuries were more common in elderly patients, which was consistent with data from Australia, New Zealand, England, Wales, South Asia and the East Mediterranean [21, 22, 29-31]. In LMICs the incidence of work-place burns, particularly those involving electricity, were higher than other regions, likely due to differences in safety regulations and poorer infrastructure [24, 32].

Scald injuries were not always the most frequently observed injury type in the elderly. The majority of a Shanghai cohort of patients aged over 64-years had mostly flame injuries (73%) related to domestic tasks [34]. Of Chinese adults, the majority had flame type burns (41% and 46% of patients admitted to regional burn services in Hong Kong and Shanghai, respectively) [33, 34]. The highest rate of flame injuries in China were seen in the countries North East (51% of patients admitted to a number of regional burn services) and was thought to be related to firework injuries during the Spring Festival [23]. In adults with severe burns in Chile and Brazil, close to 80% were related to fire or flame [20, 42]. Alcohol was implicated in over 50% of the flame injuries observed in the Brazilian study [42].

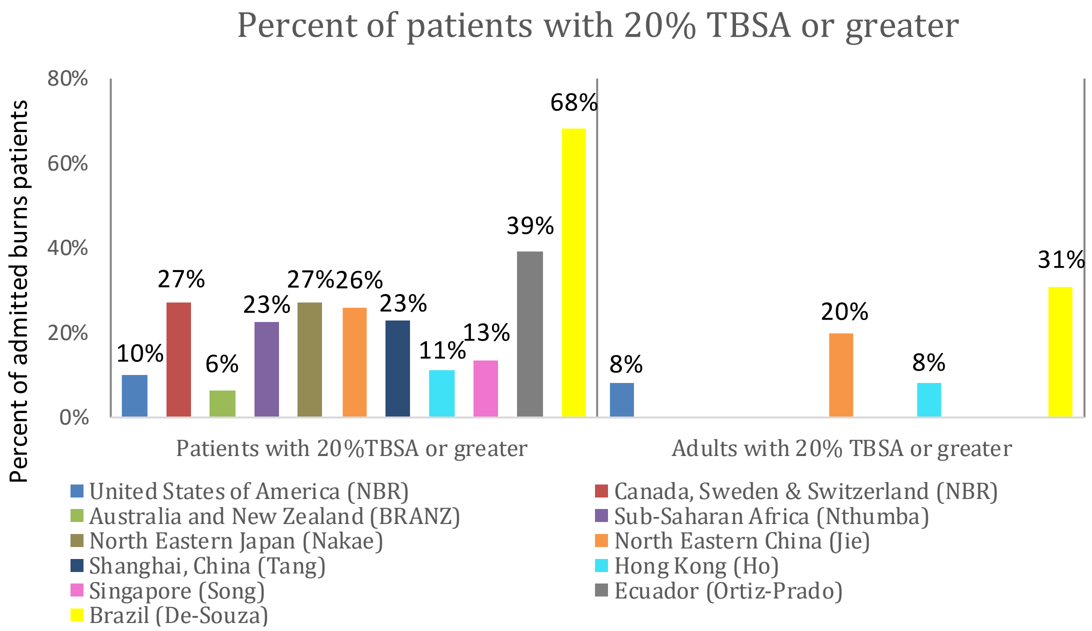
Flame was identified as a major cause of severe burn injury in a number of LMICs in South Asia [22]. For example, Ahuja et al reported an average %TBSA of 42% amongst flame burns caused by liquid petroleum gas in India. The authors identified constrained living conditions in single room dwellings and preventable gas leaks from faulty rubber tubing or gas stoves as contributing factors [22, 45].

In sub-Saharan Africa scald burns predominated amongst the total population (which included paediatric cases and non-severe burn injuries) accounting for 59% of cases, as compared with flame burns which accounted for 33% [32]. Amongst adults with severe burn injuries, flame was the most common burn cause in South Africa [28]. Rates of flame injury approached 75% for adults with a %TBSA of 20% or greater, whilst scald, electrical and chemical accounted for less than 25% of such cases [28]. Flame burns also accounted for 81% of adult fatal burns, with most occurring in patients with a %TBSA of 30% or greater [28]. A large number of injuries related to petroleum products included illegal petrol siphoning and accidents from kerosene lamps and stoves [32, 46, 47]. Othman et al identified intentional self-harm burns corresponded with a greater %TBSA resulting in higher rates of mortality [21]. They tended to be flame burns in young (mean age range 17 to 27 years) female victims (74% to 99%) [21]. The most common motives were marital problems or quarrels with husbands or other family members [21, 24].

2.1.4 Total body surface area

The relative incidence of severe burn injury within each study cohort varied greatly amongst regions [23, 29, 31-34, 36, 38, 41] (Figure 2). A number of studies failed to differentiate patients with 20% TBSA or greater burns [18, 21, 22, 24, 30, 35, 37] and two only analysed patients with severe burn injuries (excluding those without) [20, 39].

Australian and New Zealand populations demonstrated the lowest rate of severe burn injury amongst admitted patients (6.4%), closely followed the USA (10%), Hong Kong (11%) and Singapore (13%) [29, 31, 33, 38]. This compared with much higher rates observed in Ecuador (39%) and Brazil (68%) [41, 42]. Cohorts from Canada, Sweden, Switzerland, sub-Saharan Africa, North Eastern Japan, and mainland China had rates ranging between 23 and 27% [23, 29, 32, 34, 36]. Possible reasons for the higher rates of severe burn injury seen in Brazil and Ecuador include high numbers of suicide attempts by adult women (particularly in Brazilian women from low socioeconomic backgrounds and poor living conditions), high rates of occupational flame injuries, poorly regulated/unsafe working conditions and inadequate safety equipment [41, 42]. Mean %TBSA was consistently lower amongst survivors when compared with deceased patients. For the East Mediterranean Region, the mean %TBSA ranged from 10 to 27% for survivors vs. 48 to 80% for deceased patients [21]. In North Eastern China, 7.1% of all patients had a %TBSA ≥50% [23]. This compared with Australian and New Zealand rates of 1.2% of admitted patients. The rates in Australia and New Zealand may be lower because of higher rates of smaller %TBSA burns being admitted when compared to other countries or missing data from hospitals that did not contribute to the registry.



Measured ≥21% TBSA: Sub-Saharan Africa (Nthumba), Ecuador (Ortiz-Prado et al), North Eastern China (Jie & Ren); Adult defined as ≥15-years: Hong Kong (Ho et al), North Eastern China (Jie and Ren); Adult defined as ≥16-years: United states of America (NBR); Adult defined as ≥18 years: Brazil (De-Souza); %TBSA estimated from graph: Ecuador (Ortiz-Prado)

Figure 2 Patients (all ages) with ≥20% TBSA burns and adults with ≥20% TBSA burns

Describing the epidemiology of burn injury on a global scale was challenging because dedicated burn registries, such as the BRANZ, NBR and iBID, have not been established in many countries. Despite this, a number of conclusions could be made regarding the epidemiology of burns and included a male predominance and strong risk factors for burn mortality such as increased age and %TBSA [18, 21, 25, 31, 48]. Amongst high-income countries, both the incidence and mortality of burn injuries was decreasing. Factors identified as contributing to this were safer working conditions, better access to appropriate healthcare centres and vigorous educational campaigns to help prevent burns [18].

2.2 SURGICAL MANAGEMENT OF SEVERE BURN INJURY IN ADULTS

Severe burns constitute life threatening injuries with a wide range of physiological and psychological sequelae for patients. However, developments within critical care and resuscitation techniques over the last 50-years have resulted in substantial improvements in mortality and burn injury outcomes [17].

A variety of skin replacement techniques exist today, and whilst autograft is considered the best replacement for skin loss, it is limited in use in large burns where there may be concerns with the physiological condition of the patient, or limited donor sites available [49-51].

Available temporary and permanent skin substitutes include allograft, xenograft and bioengineered skin products. Xenografts and allografts provide an alternative for temporary skin coverage but are limited by availability, graft rejection, disease transfer and other ethical considerations [49]. Thus, bioengineered skin substitutes provide a viable alternative for both permanent and temporary skin coverage.

There is a large amount of heterogeneity regarding burn injuries and their treatment. Furthermore, extensive, deep burn wounds are relatively uncommon and often require complex management pathways. This sometimes involves utilising several treatment products, which differ between patients. This makes conducting large randomised control trials assessing skin substitutes difficult [49]. To investigate this issue further a review of the literature was undertaken to better understand the safety and efficacy of various surgical grafting options for severe burn injuries in adults.

A search of the literature was carried out from January 1990 to March 2015 using a combination of search terms (Adult AND severe OR major OR extensive OR large OR massive OR 20% TBSA AND burn$ OR thermal$ AND surg$ OR operat$ OR graft$ OR debride$ OR Biobrane OR Integra OR CEA OR cultured epithelial autograft). The following databases were searched: Ovid Medline, Embase and the Cochrane central register of control trials. All references of included studies were then reviewed for potential inclusion. All studies directly comparing treatment modalities in adult patients (18-years of age or older) with severe burn injury (TBSA of 20% or greater) were included in this literature review (Table 2).

2.2.1 Autologous split-thickness skin graft

The notion of early tangential excision and immediate grafting of burns was first introduced by Douglas Jackson and colleagues in 1960 [52]. Further research in the coming years then focused on investigating the safety, feasibility and efficacy of early excision [53, 54]. The current paradigm involves early excision of necrotic areas of the burn wound whilst preserving as much of the underlying viable tissue as possible. This is followed by coverage with split-thickness skin grafts [55, 56]. Prior to this, the traditional care of deep and full thickness burn injuries involved awaiting eschar separation. In the interim dressings and topical antimicrobials were often used (despite antimicrobials delaying eschar separation) [55]. Split-thickness skin grafts would then be used to cover underlying granulating tissue. This process was long, often taking several weeks, and was associated with high levels of joint contracture, hypertrophic scaring, wound infection, sepsis, systemic inflammatory response syndrome (SIRS) and death [55].

The rationale behind early excision and grafting is that there is a reduction in the release of inflammatory mediators and bacterial colonisation with an associated down-regulation of the systemic inflammatory reaction and reduced rates of metabolic derangements, sepsis and organ failure [55]. Thus early wound debridement and closure has been shown to be associated with decreased mortality, length of stay and complication rates [54-58]. Furthermore, split-thickness skin grafts are not limited by host rejection. For these reasons, early tangential excision followed by autologous split-thickness skin graft has become the gold standard of care for severe burn injuries.

The technique however does have a number of limitations, including limited donor-site availability (especially in large surface area injuries), scaring and contracture [49, 55, 59-61]. Thus, newer research has focused on alternative skin replacement techniques including biological skin substitutes (i.e allograft and xenograft) and a variety of bioengineered skin substitutes.

2.2.2 Biological skin substitutes

Biological dressings have the capacity to provide adequate coverage in large surface area burn injuries without the cost, expertise or infrastructure associated with bioengineered skin. Biological dressings include the use of cadaveric allograft and porcine heterograft [62-65]. There are three types of commonly used porcine skin options available (living, fresh and lyophilised); all of which have demonstrated similar results [62].

Porcine skin products possess a number of desirable properties which include the ability to adhere to clean wounds (thus reducing infection and heat, protein and electrolyte losses), cover nerve endings (decreasing pain), accelerate skin healing to reduce scar formation, and exhibiting relatively low rates of rejection [62]. Disadvantages are the theoretical risk of zoonosis, patient rejection based on culture, religious or ethical beliefs and product availability.

Cadaveric allograft has been shown to be effective as a temporary skin replacement in large surface area severe burn injuries [66]. It has also been recommended as a definitive wound dressing for partial thickness burns, and as a wound bed preparation in excised full thickness burns [8]. The process of cryopreservation was pioneered by Webster and Matthews in the 1940's [67, 68] as they were able to successfully use refrigerated allograft after three to eight weeks of preservation [66]. In 1968 the process was further refined by Cochrane who was able to store viable skin below 100°C [69]. Today the process of cryopreservation and distribution of cadaveric allograft is managed by dedicated skin banks, which allows early excision and wound coverage in patients with massive burn injuries before their condition further deteriorates [66]. Another common method of cadaveric allograft preservation is 85% glycerol. Unlike cryopreserved skin, 85% glycerol has antiviral and antimicrobial effects which may be associated with decreased risk of disease transmission and reduced antigenicity [8]. Furthermore, cryopreserved skin, when compared with 85% glycerol, is more labour intensive, less cost-effective and thus more difficult to distribute [8]. Skin cells preserved in glycerol are nonviable which may impact their clinical utility, though they do maintain their normal morphology and structural integrity [70]. More research comparing preservation techniques is still required [8].

Human cadaveric allograft provides an important treatment tool when managing complex life threatening severe burns. Disadvantages in its use include limited availability and the high costs associated with running and maintaining tissue banks [8, 66]. For example, the Donor Tissue Banks of Victoria and Queensland are the only operational skin banks in Australia [8]. Thus, bioengineered skin substitutes can provide a more accessible alternative.

2.2.3 Bioengineered skin substitutes

Bioengineered skin substitutes are of most relevance in the treatment of severe burns. Management of smaller burns is generally straightforward using autograft. Many authors have investigated the use of different biological skin substitutes however most of these comparisons are limited in quality due to the diversity of products available, heterogeneous patient populations, different management methods for burns and a lack of standardised outcome measures [49-51, 63-65, 71-88]. Furthermore, complex severe burn injuries are less common and are often treated with a number of different management pathways based on the particular patient.

Biobrane™ *(Dow Hickam/Bertek Pharmaceuticals, Sugar Land, Texus, USA)* is a bilaminate biosynthetic temporary dressing used as a covering over meshed autografts or to cover clean debrided superficial and mid-dermal burns and donor sites. It has also been used as a temporary cover over freshly excised full thickness burns [50]. It is composed of a nylon mesh fabric coated with porcine peptides that is bonded to a thin, semi-permeable, silicone layer [49-51]. Biobrane™ has demonstrated comparable rates of wound healing and infection when compared with silver sulfadiazine and TransCyte® and similar rates of adherence, fluid collection and autograft take when compared with cryopreserved allograft. A significantly reduced requirement for dressing changes and pain medications has also been demonstrated for Biobrane™ when compared with silver sulfadiazine [49-51, 71, 72, 83-85, 89].

Integra® *(Integra Life Science Corporation, Plainsboro, New Jersey, USA)* is a bilayer structure that consists of cross-linked bovine collagen, and a glycosaminoglycan layer coated with a silicone membrane on one side, which peels off [49-51]. Peck et al compared Integra with Biobrane™ or allograft in a within-patient control trial that was prematurely ceased due to high infection rates with Integra® use. Heimbach et al conducted a prospective, within-patient randomised control trial comparing Integra® with autograft, allograft, xenograft and a synthetic dressing. It included 139 burn sites in 106 patients from 11 different centres [50, 77]. The median take of Integra® was 80%, compared to 95% for all other sites. The authors noted less hypertrophic scarring and higher patient satisfaction with Integra® at 1-year follow-up [50, 77].

Cultured epithelial autograft (CEA) involves using sheets of keratinocytes grown in vitro from patient biopsy samples, and applying them to wounds such as burns. A systematic review investigating the use of CEA by Wood et al in 2006 identified a number of issues with CEA, including time taken to culture cells and the preparation of the wound bed [90]. The time required to grow confluent sheets has decreased over time, from 5 weeks initially to 3 weeks throughout the 1980's and early 1990's [90]. Stark et al were able to demonstrate a time to clinical use of 14 days using a keratinocyte fibrin glue suspension on a patient with 88% TBSA burns, with a total of 22% TBSA closed using this method [90, 91]. Wood et al also cited a number of case series that identified the importance of a clean, debrided wound bed, preferably with a dermal element. Studies assessing the graft take rate of CEA have shown a wide range of results from 0% to 100% [90]. Though Wood et al noted variations regarding the exact definition of 'take' and inconsistency amongst the time at which 'take' was assessed.

Evidence from two studies by Boyce et al (with possible patient overlap) that used within-patient comparisons reported on a variety of clinically based outcomes comparing CEA with conventional split-thickness autograft (neither study excluded children) [49, 80, 92]. This included reepithelialisation rates of 50 to 60% for CEA compared with >80% for autograft ($P<0.05$) [80]. Reepithelialisation rates of 71.5% for CEA and 90.8% for autograft at day 14 were also noted in the subsequent 2002 study [92]. Higher regrafting rates were also found to be associated with CEA (65%) when compared with autograft (0%; $p<0.05$) [80]. Again, these findings were replicated in a later study by Boyce et al which demonstrated significantly higher regrafting rates associated with CEA as compared with autografting (36% vs. 2%, respectively; $p<0.05$) [92]. The authors noted the increased rate of regrafting in CEA to be related to a decreased percentage of initial engraftment. The ratio of closed wound:donor site areas for CEA was significantly greater than that for split-thickness autograft (4:1 meshed), suggesting a reduction in donor skin harvesting when CEA was used [92].

There is still a lack of high quality comparative studies investigating bioengineered skin substitutes within the literature. This hampers any ability to make meaningful conclusions regarding their use. Only Integra® and CEA were investigated in any meaningful way in the comparative studies discussed. Other products including Biobrane™, Apligraf®, and Dermagraf® have predominantly been investigated with lower level evidence study designs such as large case series, or in patients with smaller %TBSA burns [49]. Thus the surgical management of adults with severe burn injury (≥20% TBSA) is primarily based on low level evidence from heterogeneous patient cohorts.

2.2.4 Comparative studies investigating the surgical management of severe burns in adults

Table 2 summarises studies that directly compared different surgical interventions in adults with severe burns [63-65, 78, 93, 94]. Of the papers identified, there were two retrospective observational studies, two prospective within-patient control trials, one randomised within-patient control trial and one randomised control trial (RCT). Interventions investigated included xenografts, CEA, Integra®, cadaveric allografts and conventional SSG. Four of the studies assessed LOS and infection and all but one study investigated mortality [63-65, 78, 93, 94].

Table 2 Description of surgical management studies

First author	Study type	Burn aetiology and comorbidities	Baseline Characteristics	Intervention	Control	Outcomes and follow-up
Xiao (2014)	Randomised control trial	*Burn aetiology:* "Severe" inhalation injuries excluded *Comorbidities:* NS	*N*=52 *Mean age (range):* 44.8 (18-65) *Mean %TBSA (range):* 56 (40-70)	Delayed microskin autograft & Vaseline-based moisture dressing	Microskin autograft & cadaveric allograft	*Outcomes:* Graft take area % at 3 weeks; scar assessment (VBSS); mortality; LOS; organ dysfunction; infection *Follow-up:* 6 months
Chen (2013)	Prospective within-patient control study	*Burn aetiology:* All thermal injury types, inhalation injuries included *Comorbidities:* No serious organ/blood system complications	*N*= 30 *Age range:* 18-60[a] *%TBSA range:* 25-60[a] *Maximum %TBSA full-thickness:* 40%	Porcine acellular dermal xenograft (ADX)	SSG	*Outcomes:* Graft take area % at 2 weeks; Scar assessment (VSS); Histology *Follow-up:* 0.5-2 years
Sun (2011)	Prospective within-patient control study	*Burn aetiology:* Inhalation injuries excluded *Comorbidities:* Patients with "basic diseases" excluded; "elderly" patients excluded	*N*=31 *Mean age (range):* 37 (21-60) *Mean %TBSA (range):* 65.5 (45-90) *Minimum %TBSA full-thickness:* 30%	Microskin autograft with selectively decellularised split-thickness porcine skin xenograft	Microskin autograft and cadaveric allograft	*Outcomes:* Graft take area % at 3 weeks; graft rejection; mortality; ulceration or scaring; pain; itching; functional deficit *Follow-up:* 18 months
Ryan (2002)	Retrospective observational study	*Burn aetiology:* Inhalation injuries included *Comorbidities:* NS	*N*=270 *Mean age (range):* 46.6 (18-94) *Mean %TBSA (range):* 43.3 (20-97%) *Mean full thickness % (range):* NS	Integra®	No Integra®	*Outcomes:* Mortality; LOS *Follow-up:* Up to 4 years
Peck[b] (2002)	Randomised within-patient control trial	*Burn aetiology:* Electrical injuries excluded, inhalation injuries included Severe exfoliating skin conditions excluded	*N*=7 *Mean age (range):* 41.1 (19-54) *Mean %TBSA (range):* 63.1 (47-80) *Mean full thickness % (range):* 35.6 (13-93)	Integra®	Biobrane™ or Cadaveric allograft	*Outcomes:* Mortality, infection; LOS *Follow-up:* Up to 5 months
Munster (1990)	Retrospective observational study	*Burn aetiology:* Inhalation injuries included *Comorbidities:* NS	*N*=25 *Mean Age:* 29.4[c] *Mean %TBSA (range):* 62.7 (40-96) *Mean full thickness % (range):* 35.6 (13-93)	CEA	SSG	*Outcomes:* Graft take area %; LOS; Mortality; Number of procedures; Major complications; Cost *Follow-up:* 6-26 months

[a]Mean NS; [b]study terminated (high infection rate in the Integra® group); [c] Range NS (minimum age 18-years); %TBSA: Total body surface area; ADX: Porcine acellular dermal xenograft; SSG: Autologous split-thickness skin graft; CEA: Cultured epithelial autograft; VBSS: Vancouver Burn Scar Score; VSS: Vancouver scar scale; LOS: length of stay; NS: Not stated

2.2.5 Comparison of investigated surgical managements

A 2014 randomised control trial by Xiao et al compared the efficacy of conventional aggressive early excision and debridement followed by microskin-allograft complex coverage vs. a delayed micro-grafting technique (Table 3) [65, 95]. The delayed technique involved eschar excision 3-5 weeks after the burn and was performed using liquefaction on the interface between eschar and the wound bed. The rationale being that the delayed technique allowed grafting onto raised granulation tissue with less bleeding, no requirement for general anaesthesia and the ability to stabilise physiologically compromised or elderly patients prior to a definitive grafting procedure. The delayed technique yielded a significantly better Vancouver Burn Scar Score (VBSS) (2.1) than the conventional group (3.9, $p<0.05$). Gross subjective assessments of movement at the elbow and knee joint were also noted to be better in the delayed group. Other measures including reepithelialisation rate, the need for regrafting, burn complication rates and bacterial culture profiles were similar in both groups. The authors fail to discuss the lack of differences between the two groups in any significant detail. Given the lower study numbers (26 patients in each treatment arm) this result may have reflected a lack of power. This study set out to explore the treatment of older patients who may have multiple co-morbidities and be unfit for a general anaesthetic. This physiologically compromised patient cohort appeared to tolerate the delayed technique without any significant drawbacks in terms of burn wound treatment. However, whilst not seen in this population, increased hospitalisation time (which was higher in the delayed group) can be associated with higher risks of infection [65, 96]. Furthermore, older at risk patients may also be more predisposed to SIRS, sepsis and death in the setting of delayed complete wound debridement [96]. The authors noted no deaths after surgery in both groups, though it was not specifically mentioned if, or how many patients died prior to admission to the burns service. A recent meta-analysis by Ong et al comparing early excision and immediate grafting with treatment with dressings only followed by delayed grafting after eschar separation found a significant decrease in mortality and LOS with immediate grafting [55]. The only drawback found by the authors in patients undergoing early excision and immediate grafting was an increased volume of blood loss [55].

Chen et al investigated the efficacy of an acellular porcine allograft in combination with autologous SSG [64]. The co-grafting technique involved debridement of the wound to viable tissue and the application of the co-graft to the wound bed following adequate haemostasis. The acellular dermal matrix (ADX) involved a process to decellularise and deepidermise porcine skin, thereby maintaining the extracellular structure of the dermis whilst removing components that may elicit an immunological host response [97]. When compared to traditional SSG, the co-grafting technique yielded significantly improved scar outcomes at 3, 6 and 12 months (Table

3). Histological examination at 22 months demonstrated skin structure resembling normal skin in the ADX treated areas, whilst SSG treated areas showed disordered collagen.

Sun et al also investigated the use of decellularised porcine skin in a prospective within-patient controlled trial [63]. Their method of graft preparation involved applying microskin autografts to either selectively decellularised split-thickness porcine skin (SDSTPS) or cryopreserved cadaveric allogeneic split-thickness skin [98]. There were no significant differences ($P>0.05$) in terms of area epithelialised 3 weeks post graft between skin xenografts and allografts (87±21% vs. 83±41%, respectively). The time to rejection and exfoliation was significantly higher in the skin xenograft area (17±3 days) when compared to the skin allograft area (14±2 days, $p<0.05$). Other clinical parameters investigated also showed no significant differences between skin xenografts and allografts (Table 3). The authors reported no deaths in their study cohort, though it was not clear if this excluded patients who died prior to or on arrival to the burns service.

Two studies investigated the use of Integra® [78, 93]. In a study by Ryan et al patients treated with Integra® were older, had more extensive burns and a higher incidence of associated inhalation injury compared with patients treated without Integra® (i.e. standard treatment with SSG) [93]. There were no significant differences between the two groups in terms of mortality. The length of stay of survivors in the no Integra® group (64±23 days) was significantly less than the Integra® group (47±47 days, $p<0.001$). However, upon subgroup analysis that included only those patients with two or more mortality risk factors (age> 60-years, burn size> 40% TBSA, or inhalation injury) the trend was reversed (Integra®: 63±18 days vs. no Integra®: 107±60 days, $p=0.014$)[93].

Peck et al used a randomised within-patient controlled trial protocol to compare the use of Integra® with either Biobrane™ or cadaveric allograft. Treatment of all patients involved sequential excisions of burn eschar ensuring that all deeply burned skin was removed within 2 weeks of injury. Two mirror-image sites, for example bilateral upper arms or bilateral thighs, were then randomised by site to either Intergra® or one of the researchers' standard wound coverings (Biobrane™ or cadaveric homograft). Other wound burn sites not included in the direct comparison were managed with tangential excision and meshed split-thickness skin graft. Each treatment covered between 1 and 9% TBSA. Temporary wound coverings were used on control sites: In the first phase of the study Biobrane™ was used and secured with staples with overlying mafenide acetate dressings applied. In the second phase of the study the control sites were covered with allograft that had been meshed at a 1:1 ratio. The control areas were then covered with gauze soaked silver nitrate. The experimental sites were covered with sheets of

Integra®. Mafenide acetate dressings were also applied in the first phase, with silver coated dressings applied in the second phase of the study. The trial was terminated early due to the significantly higher rate of graft site infections in the Integra® group (71%) as compared to the no Integra® group (29%) [78].

Munster et al compared the use of CEA and SSG. CEA, when compared with SSG, yielded a non-significant reduction in terms of mortality (0% vs. 33%, respectively) and major complications (i.e. septicaemia, pneumonia and organ failure) (28% vs. 61%, respectively). Graft take was more favourable in the SSG group (92%) when compared with the CEA group (75%).

Table 3 Summary of surgical interventions

First Author	Groups	Baseline characteristics	Mortality N (%)	Mean LOS	Infection N (%)
Xiao (2014) [65]	Delayed microskin autograft & Vaseline based moisture dressing	N= 26 Mean age: 47.1 Male gender: 10 (38%) %TBSA: 55% Inhalation: 3 (11.5%)	0	98 days	1. No pathogen 5 (19.2%) 2. Single isolate 20 (76.9%) 3. Multiple isolates 1 (3.9%)
	Microskin autograft & cadaveric allograft	N= 26 Mean age: 42.5 Male gender: 7 (27%) %TBSA: 57% Inhalation: 2 (7.7%)	0	68 days	1. No pathogen 8 (30.8%) 2. Single isolate 18 (69.2%) 3. Multiple isolates 0
Chen (2013) [64]	ADX with SSG co-graft	N= 30 Age range: 18-60[a] %TBSA range: 25-60%[a] Maximum %TBSA full-thickness: 40%	-	-	-
	SSG	As above (within patient controls)	-	-	-
Sun (2011) [63]	Microskin autograft with SDSTPS xenograft	N= 31 Mean age: 37 Age range: 21-60 %TBSA: 65.5% %TBSA range: 45-90%	0	-	0
	Microskin autograft & cadaveric allograft	As above (within patient controls)	As above	-	0
Ryan (2002) [93]	Integra®	N= 43 Mean age: 50 Age range: 19-83 %TBSA: 50%† %TBSA range: 25-90% Inhalation: 31 (72%)†	13 (30%)	64[a]† days	-
	No Integra®	N= 227	69 (30%)	47[a]† days	-

		Mean age: 46 Age range: 18-94 %TBSA: 42%† %TBSA range: 20-97% Inhalation: 67 (30%)†			
Peck (2002) [78]	Integra®	N=7 Mean age: 41.1 Age range: 19-54 %TBSA: 63.1% %TBSA range: 47-80% % Full thickness: 35.6% Inhalation: 2 (29%)	3 (43%)	77 days	<u>Infected graft sites:</u> 5 (71%)
	Biobrane™ or Cadaveric allograft	As above (within patient controls)	As above	As above	<u>Infected graft sites:</u> 2 (29%)
Munster (1990) [94]	CEA	N= 7 Mean age: 31.0 Male gender: 6 (86%) %TBSA: 69.6% TBSA range: 54-91% % Full-thickness: 31.4% Inhalation: 4 (57%)	0	60 days	<u>Major complications (i.e. septicaemia, pneumonia, and multiple-organ failure)</u> 2 (28%)
	SSG	N= 18 Mean age: 28.8 Male gender: 15 (83%) %TBSA: 60.0% %TBSA range: 40-96% % Full-thickness: 37.2% Inhalation: 73 (39%)	6 (33%)	54 days	<u>Major complications(i.e. septicaemia, pneumonia, and multiple-organ failure)</u> 11 (61%)

Dagger (†) – p<0.05 between groups; %TBSA: Total body surface area; ADX: Porcine acellular dermal xenograft; SSG: Autologous split-thickness skin graft; CEA: Cultured epithelial autograft; LOS: length of stay; SDSTPS: Overlaid selectively decellularized split-thickness porcine skin; [a]Calculated from survivors only

2.3 OUTCOMES FOLLOWING SEVERE BURN INJURY IN ADULTS

Severe burn injuries constitute a significant burden in terms of morbidity, mortality and healthcare cost [16]. Establishing a standardised, easily measured set of short to long term outcome measures for severe burn injury is difficult [14, 99]. This is because there are many different outcomes which can be used [10, 14, 99]. Furthermore, there are also a variety of ways one can measure and report on different parameters [100].

This review focused on three well established clinically relevant in-hospital outcomes (mortality, length of stay and positive blood cultures). These outcomes have been commonly used to assess the performance of burn services over time and have been cited as important measures of burn injury outcome [10, 14, 99]. Longer term patient related factors, including functional capability, psychological recovery and scar outcome have also been recognised as important outcome measures [99, 101].

2.3.1 Short-term in-hospital outcomes

Mortality

Mortality rates amongst adults with severe burn injuries widely varies depending on geography, burn related factors (e.g. injury method, cause and severity) and patient related factors (e.g. age, gender and co-morbidities). In high-income countries the mortality rates amongst general populations have tended to decrease over the last decade with general trends towards increased mortality associated with older age, increased %TBSA, inhalation injury and flame type burns [18, 29, 31]. In the United States of America, the mortality rate for adults with severe burn injuries (≥20% TBSA) between 2005 and 2014 was 27% [29]. This decreased to 19% in adults aged between 16 and 60-years of age but was higher for adults aged 60 and older (56%) [29]. These mortality rates were in keeping with others reported from different high-income regions in Europe, Australia and New Zealand [18, 31]. Similar results have also been demonstrated in South America, with one Brazilian study demonstrating a mortality rate of 33% amongst hospitalised adults with severe burns [42]. Jie and Ren reported on 12,606 burn injuries from nine hospitals over a decade in North Eastern China [23]. Subset analysis was carried out on 2,496 adults (patients aged 15-years and older) with severe burn injuries. The mortality rate amongst adults with 20% TBSA burns or greater was 4.6%. Younger adults with severe burns were less likely to die than older adults. The mortality rate for patients aged from 15 to 59-years was 4.1%, as compared to 15% for patients aged 60-years and above [23]. The authors noted a relatively low number of older patients (4% of admissions were 60-years or older), advances in medical and surgical care and governmental initiatives as factors contributing to the lower mortality rate [23]. Though there were no clear reasons to account for the considerably lower mortality rates observed in this study when compared with other reported data [18, 20-42]. One possibility may have been that patient deaths prior to arriving to hospital were higher, though pre-hospital death rates would be needed to exclude this as a possibility.

Length of stay

Length of hospital stay (LOS) was not well reported, and amongst those that did report this outcome, many failed to specify whether the LOS was for survivors only or all patients. In general European populations, the mean and median LOS ranged from between 7 to 33 days and 3 to 18 days, respectively [18]. This was compared with a mean LOS range of 12 to 16 days and 17 to 28 days for reporting studies from the East Mediterranean and South Asia Regions, respectively [21, 22]. Length of stay was shown to increase with %TBSA, with one study demonstrating an average LOS of 2 days/%TBSA for burns greater than 50%TBSA in adults [28]. For burns of 20-49% TBSA the average LOS was generally 1 day/%TBSA [28]. These results were consistent with data published elsewhere. Johnson et al analysed 52,712 records from the National Burn Repository (USA) over a six year period between 2002 and 2007 [102]. The authors demonstrated a consistent LOS of 1 day/%TBSA for patients who survived burns of up to 60% TBSA [103].

Bacteraemia

The presence of bacteraemia as demonstrated with a positive blood culture result provides an important investigative tool as it may be used as both a prognostic factor which can influence other outcomes (such as mortality or LOS) and can also be viewed as an outcome in its own right [104-106]. In Australian burn services blood cultures were more often performed in more severe injuries, with 56% of adult in-patients with severe burns having at least one culture taken [31]. A positive result was reported in 5% of adult burn cases in Australia between 2013 and 2014, similar to the number of positive results in 2011/12 and 2012/13 (7% and 8%, respectively) [31]. Keen et al have argued that blood cultures represent an over-used investigation which can be expensive, invasive and often afflicted by false-positive results [104]. Keen et al found no substantial changes in patient length of stay, ventilator days or mortality despite reducing the number of blood cultures taken by 50% after implementing a utilisation protocol [104]. The total number of bacteraemic patients decreased, from 51% pre utilisation protocol to 30% post utilisation protocol (p=0.04), and was associated with a decrease in the yield of positive blood cultures (15% true positives prior to utilisation protocol vs. 9% post utilisation protocol, p=0.06). The authors postulated that the decrease may have reflected a true decline in bacteraemia incidence or possibly broader antibiotic coverage of the average patient in 1997 [104].

Nevertheless, bacteraemia and burn wound colonisation have been shown to be important prognostic factors [104-107]. The presence of gram-negative bacteraemia has been shown to significantly increase the risk of mortality in burn injuries [105]. As an outcome measure, positive blood cultures have also been shown to be more likely in higher acuity patients or those with an indwelling urinary catheter [104].

2.3.2 Long-term post-discharge outcomes

Relationships between major trauma and episodes of depression, anxiety, fear, moodiness, frustration and other neuroses have been previously described [108, 109]. Fauerbach et al also demonstrated a greater difference between burn trauma patients and a normative sample when investigating personality at the time of discharge [110]. Adult severe burn injury survivors can often be faced with protracted recovery times and many go on to suffer from post-traumatic stress disorders (PTSD) and depression [111]. However long term data suggests reactive changes in adult burn injuries may plateau, with one study demonstrating a return to baseline premorbid psychological traits for many patients after three to 19-years [108]. This was in keeping with other studies which suggest that many hospitalised burns patients did not suffer from long-term major psychopathology [112]. However there was limited data investigating long-term outcomes in patients with more severe burns exceeding 70%TBSA [112]. Furthermore, adults with severe disfigurement may not achieve social reintegration post injury, and thus such patients may not be well represented in long-term follow-up literature [112].

Pavani et al prospectively studied a population of 50 adults with 40% TBSA burns or greater who required ICU admission and ventilator support [111]. Of the 50 patients enrolled, 27 died prior to discharge, two died during follow-up and two were unreachable, leaving 19 patients who were evaluated one year post discharge from ICU using the 5-level EQ-5D questionnaire [111, 113]. Sixty-eight percent of patients reported problems with mobility, though no patients reported extreme problems with mobility at one year [111]. Pain/discomfort and anxiety/depression were reported by 79% of patients and 58% of patients had problems with self-care [111]. No patients had returned to work at one year, with 37% having retired and 63% remaining unemployed [111]. Every patient also had a poorer level self-perceived health status at one year post injury when compared to their pre-injury level [111]. Nevertheless, there was literature to suggest severe burn injury survivors may have a good quality of life without major psychopathology [108, 112, 114]. There were many reasons for these discrepancies, including small sample sizes, poor follow-up rates, different time points for follow-up, different inclusion criteria and different outcome measurement tools [111, 115-117].

2.3.3 Independent predictors of mortality

Predictive models are important and aid researchers in a number of ways including estimating the likelihood of death for research purposes and monitoring burn service performance. Establishing good epidemiological datasets for patient populations also enables a strong foundation for clinical benchmarking, the development of better management protocols and identifying factors that influence mortality [101]. Clinically, predictive models can also be used by practitioners to inform on the course of (or risk of developing) illness and to help guide patients, clinicians and families in joint decision-making regarding further treatment. However, there are a number of limitations in the use of prediction models in clinical use [118]. For example, prognostic models are often too complex to be used in the clinical setting [118]. Many models also lack both independent verification on different patient populations and appropriate validation [101, 118]. Severe burns may also produce a wide array of different physiological and pathological sequelae. Such injuries often require specific treatments based on individual patient circumstances which further complicates the use of predictive models.

Whilst a variety of complex burn injury prediction models exist within the literature [101, 119, 120], with as many as 45 different published models cited, they tend to only focus on mortality and many are yet to be independently validated [25, 101]. Models have been used since the early twentieth century, with more sophisticated models using multivariate logistic regression developed in the 1980s [5, 48]. Predictive models such as the Abbreviated Burn Severity Index (ABSI) and modified Baux Score were developed to identify independent risk factors for burn injury mortality, assess the effects of changes in treatment, and to benchmark outcomes over time [101].

Total body surface area

The %TBSA is a well-established and validated predictor of mortality, with all burn injury mortality prediction models including it [101, 119, 121]. Brussalares et al demonstrated patients were 6.6 times as likely to die with a %TBSA of 40% or more when compared to those with a %TBSA lower than 40% [122]. This correlation persisted when analysing %TBSA as a continuous variable. Stylianou et al demonstrated a 2.1 increase in the log odds of mortality with every standard deviation increase in %TBSA [25]. Harats et al demonstrated patients with burns of 20 to 29% TBSA had 14 times the risk of mortality than those with burns of <10%

TBSA. This increased to 119 times greater for patients with a %TBSA of 30% or more when compared to those with <10% TBSA burns [27].

Age

Age, like %TBSA, has been included in virtually all burn mortality prediction models [123]. Whilst age is a strong independent risk factor for burn mortality, it does not necessarily show a linear relationship. Most early burn models incorporated the entire spectrum of age whilst recent research has aimed to stratify predictive models based on age groups to enable higher levels of accuracy [25, 48, 101, 119, 123].

Taylor et al investigated over 100,000 cases from the National Burns Repository (NBR), stratifying them into clinically meaningful age groups (<18 (children), 18 to 60 (adults) and >60 (elderly)) [123]. Using predictive models based on these age groups, a linear increase in mortality was found with increasing age in adults and the elderly, but not for children. Taylor et al found similar increases in impact of burn size in children and adults, but larger effects on mortality in those aged over 60-years. For patients 60-years and older, age-specific modelling showed a greater mortality increase per 1% TBSA and one-year increase in age than with younger patients. The mortality rate for these patients (≥60-years) was 17% [123]. Inhalation injury also significantly increased mortality in all age groups, but the effect was larger in children [123].

Inhalation injury

A number of studies have demonstrated a significant increase in mortality with an associated inhalation injury [124-126]. However, the effects of inhalation injury can be difficult to measure as the definition is not universal, with some studies defining inhalation injury based on ventilation requirement, and others on parameters such as positive clinical findings or a suggestive history [101].

In their analysis of mortality risk factors carried out on a cohort of 4,927 patients admitted to a regional burn service in Dallas, Texas, O'Keefe et al defined inhalation injury based on specific criteria [126]. This included bronchoscopic evidence of an inhalation injury, or a history of a fire in an enclosed space; radiographic evidence of diffuse chest oedema; and hypoxia [126]. O'Keefe et al demonstrated a significant increase in mortality when an inhalation injury was present (OR: 3.4; 95% CI: 1.9, 6.0) and noted it to be an important measure that should be incorporated into mortality prediction models (along with %TBSA, full-thickness burn area, age and gender) [126].

Burn depth

Greater burn depth, and surface area, results in an increased loss to the protective skin barrier leading to fluid loss, hypothermia, increased risk of infection and pain. Previous studies have reported on the greater risk of mortality with increased full thickness burn area [121, 126-128]. Specifically, a 7% increased risk of mortality with each unit increase in the area of full thickness burn [128]. Patients with full thickness injury demonstrate a more profound physiological insult and require more extensive debridement and grafting procedures as compared with patients without full thickness burns [128].

Physiology and comorbidities

The Acute Physiology and Chronic Health Evaluation (APACHE) measure is an internationally recognised, well validated and widely used physiological disease scoring system [129]. The points system is based on a variety of factors, including age, physiological parameters and clinical measurements within the first 24-hours of admission to an intensive care unit (ICU) [129]. A higher score designates an increased chance of death. Both increased APACHE II and APACHE III scores have been shown to be associated with higher mortality rates amongst burn injury patients [128, 130-132].

Diabetes, hypertension and cardiac disease have been associated with higher complication rates after burn injuries [5, 133]. Increased mortality has also been shown in patients with pre-existing cardiac conditions as well as increased treatment times and morbidity in drug and alcohol users, and patients with neurological conditions [5, 133-135]. Patients with pre-existing cardiac conditions tend to have a reduced physiologic reserve and capacity to compensate, which would likely explain this phenomenon. Reasons for increased morbidity amongst neurological patients include reduced mobility, leading to longer burn exposure and more severe injury as well as more difficult rehabilitation [5].

Intent of injury

Self-immolation is a common method of suicide in a number of areas including the Middle East, Africa and South Asia [136]. Self-immolation was reported to account for 7 to 9% of suicides in India, and 71% in some regions of Iran [136]. In Europe and North America rates of between 2 to 14% have been demonstrated [137]. Self-harm burns are mostly flame injuries that tend to be more severe in nature and have higher mortality rates when compared with accidental burns [5, 138]. Self-inflicted burns have significantly higher %TBSA, burn depth, inhalation injury and mortality when compared with accidental flame burns [137-139]. Dousing and setting alight an accelerant is the most common method of self-immolation and is the main contributor to increased burn depth, %TBSA and thus is a significant contributor to the higher mortality rates seen in this patient population [139].

Studies investigating self-inflicted burn injury characteristics and outcomes, such as mortality, have generally consisted of small sample sizes (<50 patients) from single burn centres [137]. This has resulted in contradictory descriptions of the characteristics and outcomes in these patients [137]. Whilst self-immolation results in increased mortality, few studies have evaluated mortality after adjusting for important confounders such as co-morbidities, %TBSA and burn depth [137]. Duarte et al investigated a cohort of 114 self-inflicted burn injuries admitted to a regional burn service in Porto Alegre, Brazil between 2003 and 2012. Intentional self-inflicted burns were associated with a 59% higher risk of in-patient death when compared with accidental injuries after adjusting for burn severity, co-morbidities, inhalation injury, age and previous psychiatric disorders [140]. Duarte et al recognised the challenge of understanding why this phenomenon arises, and speculated that changes in biological and social interactions may occur after self-immolation. Higher rates of post-traumatic stress disorder, depression and self-injurious behaviour are found in these patients, which can worsen the course of mood disorders and hamper patient recovery [140]. They can also contribute to poor motivation, non-compliance with treatment and ongoing self-harm which may also contribute to poorer outcomes independently of injury severity [137, 140]. Negative attitudes towards patients with self-inflicted injuries from medical staff, including irritation, a decreased willingness to help, and ambivalence, has been documented previously [137, 141, 142]. However, the role these attitudes play in mortality outcomes is unknown [137].

Thombs et al reported on an adult population of 593 self-inflicted burns across 70 burn centres in the USA using data from the NBR [137]. They found no increased risk of mortality amongst self-inflicted burns when compared with patients with similar demographic, health and injury characteristics (including %TBSA) [137]. The notion that self-inflicted injury is not an independent predictor of death has been reported elsewhere [139]. Duarte et al utilised a smaller patient population from one burn service, thus these results may have reflected the characteristics of one practice rather than a definitive phenomenon. Nevertheless, other studies have demonstrated an association between self-harm and death independent of other mortality risk factors [143, 144]. These contradictory results were most likely related to the heterogeneous nature of burn injuries, the relatively small sample sizes of studies investigating self-immolation and differences in how papers define a self-immolation injury.

Gender

Previous authors have identified an association between female gender and higher rates of mortality [18, 21, 22, 126, 145, 146]. However gender is rarely used in predictive models [101]. O'Keefe et al demonstrated a two-fold increase in mortality for women aged between 30 and 59-years as compared with men of the same age [126]. Moore et al investigated a cohort of 348 women and 1,367 men admitted to intensive care units across eight regional burn services in Australia [147]. Women were found to have had more than double the risk of death when compared to their male counterparts after adjusting for confounding factors [147].

Nevertheless, other authors have reported conflicting results. A large European based review of burn injury epidemiology found seven studies that reported greater mortality rates in women, although seven other studies from the same review found no association between gender and mortality, and others found an increased mortality rate in men [18]. No clear explanation exists as to why women would be at greater risk of mortality. Differences in body composition, hormonal factors and immunological responses have been postulated but more research is required to help guide future targeted therapies [126, 145-147].

Lactic acid

Higher serum lactic acid levels have been shown to be associated with increased rates of mortality [148]. Tahir et al showed that lactic acid, when compared to the ABSI, showed higher sensitivity to correctly predict deaths within the first week of admission (62% of all deaths) [149]. This decreased to 38% when looking at deaths between the second and fourth weeks of death.

Burn service Volume

The benefits of a national burns registry are generally well accepted [10, 150, 151]. Evidence-based care implementation requires centralised systems to collect and correlate data which can be used for benchmarking.

The notion of volume dependent outcomes is a well-researched area in other fields of medicine. McCrum et al established a 27% higher risk of death amongst patients receiving care at low quintile hospitals as compared with those at high quintile hospitals [152]. The study included inpatients who underwent one of five of the most commonly performed surgical procedures within the United States and reported on the 30-day post-operative mortality rate. In contrast, the importance of dedicated burn services and burn centre case volume is a less researched area.

Light et al investigated mortality rates amongst low, moderate and high volume burn services, with results suggesting lower mortality rates within medium and high volume hospitals after controlling for patient and facility characteristics [151]. Light et al concluded that a strong relationship existed between the annual number of burn admissions and burn related deaths. Dedicated burn services seeing between 100 and 300 patients per annum had consistently higher rates of survival, suggesting a strong association between clinical expertise developed within dedicated services that see high patient volumes [151]. Similar research by Pacella et al demonstrated significantly higher rates of home discharges and lower rates of transfer to other hospitals amongst lower severity burns when comparing high and medium volume centres with low volume centres, despite similar mortality rates [153]. Comparable data from other jurisdictions, including Australia, is lacking and no predictive models have ever incorporated burn centre volume as a factor.

2.3.4 Common predictive models

The Abbreviated Burn Severity Index (ABSI)

The ABSI was derived from a dataset of 590 burn patients admitted to two burn services in 1982 [121]. It was developed as a simple system to measure burn severity based on a five-variable scale (gender, age, presence of inhalation injury, presence of full thickness burn and %TBSA) and has demonstrated high levels of sensitivity and specificity for mortality prediction [121, 149]. The ABSI has been independently verified, and has demonstrated correct classification of 98% of survivors and 82% of deaths [101]. Despite the ABSI being conceived and validated over 30 years ago, Forster et al in 2011 were able to show that the calculated mortality rates based on a cohort of 2,813 patients using the ABSI score were well within the mortality estimate defined by the ABSI [154]. The study's primary aim was to re-asses the ABSI score in the setting of changes in patient demographics and advances in burn injury care since its initial conception [154]. Forster et al concluded that the ABSI scoring system was still a highly accurate and useful clinical tool for predicting mortality in burn injury patients [154].

The Modified Baux Score

The Baux score was described by a non-burn academic in the thesis *"Contribution a l'etude du traitement local des brulures thermiques etendues"* in 1961. In its original form, the Baux score used the sum of age and %TBSA to predict the futility of care, with a total score of 75 generally considered a lethal burn. The score was subsequently modified to reflect the higher levels of survival seen with modern day burn care, and to take into account the presence of inhalation injury [120]. Whilst the modified Baux score is well validated and useful tool, its calculation can be difficult and the Revised Baux Score nomogram allows a quick calculation of risk of mortality [155]. Recent studies have shown the modified Baux score to be of greatest use predicting mortality in elderly patients (≥60-years). Wibbenmeyer et al demonstrated the modified Baux score to be superior to the ABSI in a cohort of 308 elderly patients [156].

Total burned surface index (TBSI)

The TBSI is based on a cohort of 562 patients retrospectively analysed between 1970 and 1976 by Bhatia and Mukherjee [157]. This index used the presence or absence of burns on 11 different body sites and was incorporated into a multiple logistic model that predicted survival. The model showed a 79% correct classification rate however lacks adequate independent validation [101].

Belgian outcome of burn injury score (BOBI)

The BOBI score was based on a multicentre prospective trial of six burn services conducted between 1999 and 2004 in Belgium (Belgian outcome in burn injury study group) [101, 158]. Clinical parameters including age, %TBSA and the presence of an inhalation injury were investigated and a multivariable regression model was developed based on data extracted from 5,246 patients. A mortality score between 0-10 (with a higher value designating an increased risk of mortality) was given based on: the percentage of %TBSA burned where <20=0, 20-39=1, 40-59=2, 60-79=3 and 80 and above=4; the age where under 50=0, 50-64=1, 65-79=2 and 80 or above=3 and; the presence of an inhalation injury= 3. The definition of inhalation injury was any injury requiring ventilation. The multivariable regression model has shown good accuracy on ROC analysis (0.94) and has been externally validated [158].

This literature review has included an in-depth investigation, discussion and summary of the most up-to-date evidence with regards to severe burns in adults with regards to epidemiology, management and outcomes. Burn injuries, regardless of where they occur, represent a significant healthcare burden affecting patients of all ages and genders. However, there appears to be a limited number of high quality comparative studies specifically investigating the epidemiology, and management, of severe burn injuries in adults. This is an important issue, particularly given the high mortality and morbidity seen with these types of injuries. This lack of high quality comparative data hampers any ability to make meaningful conclusions regarding the management of these injuries.

2.4 STUDY RATIONALE

The majority of epidemiological data pertaining to burn injuries requiring hospitalisation investigates general populations; including analysis of paediatric and adult cases without a specific severity focus. Whilst this data is a critical aspect of burns research, more focused investigations regarding severe burn injury (≥20% TBSA) in adults remains an important area of attention for low, middle and high-income countries where these injuries continue to represent a significant cause of mortality and morbidity.

There is a continuing need for research into the epidemiology, management and outcomes of severe burn injuries. In particular, there is a lack of definitive literature examining outcomes based on different surgical therapies for severe burn injuries in adults.

Limitations of current literature investigating severe burn injuries in adults include: a lack of consistent epidemiological reports focused on this patient population, few high quality comparative studies investigating the surgical management of large area (≥20% TBSA) burns in adults, and a lack of a standardised reporting methods with regards to burn injury outcomes and quality measures. Thus, this study addresses the descriptive epidemiology, treatment and outcomes of adults with severe burn injury admitted to dedicated burn services within Australia and New Zealand.

3 AIMS

The primary aim of this thesis was to describe the epidemiology, management and outcomes of severe burn injuries presenting to dedicated burn services across Australia and New Zealand. The specific aims were to:

1. Describe the epidemiology of adult patients with severe burn injury.
2. Describe the management and outcomes of these adults with severe burn injury in Australia and New Zealand.
3. Describe predictors of mortality, hospital length of stay and discharge destination in adults with severe burn injury.
4. Compare the management and outcomes of severe burn injury in adults between burn services.

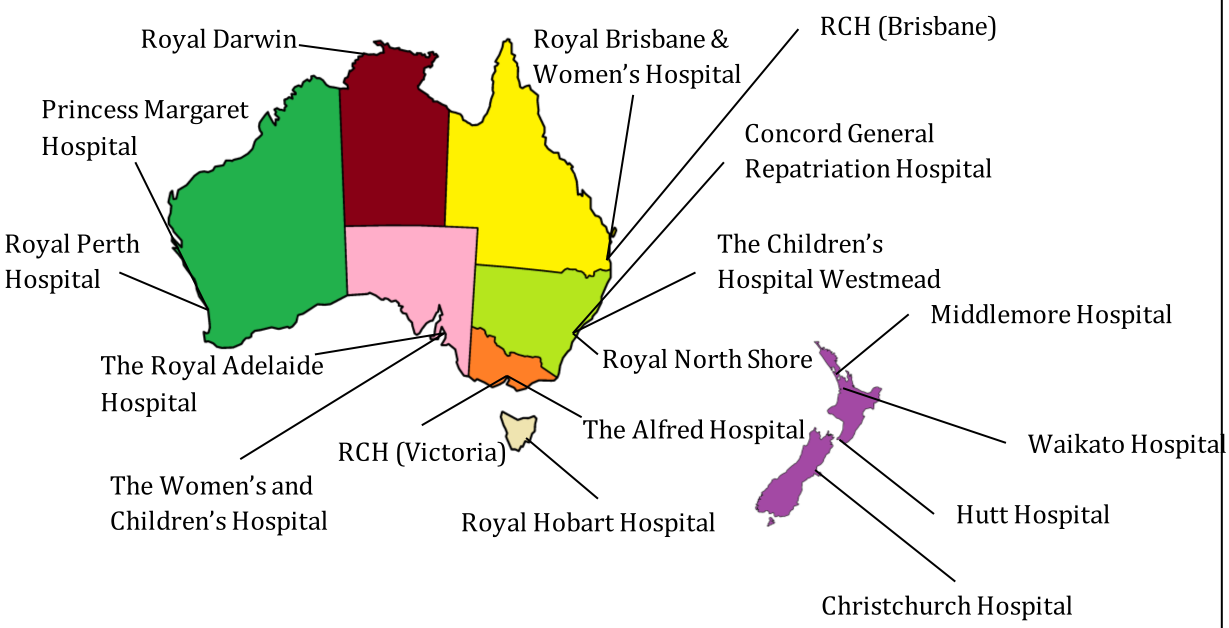
4 METHODOLOGY

4.1 SETTING

4.1.1 Australia and New Zealand burn services

Australia and New Zealand comprise a total population of over 28 million people with approximately 50,000 burn related injuries requiring admission to hospital each year in Australia alone [159-161]. The Australia and New Zealand Burns Association (ANZBA) was established in 1976 with the principal aim to improve standards of care through research and education [159]. It is a not for profit organisation and is the peak body for health professionals who care for burn injury patients in Australia and New Zealand [159]. Across the 17 specialist burn services in Australia and New Zealand (Figure 3), over 2,500 patients are managed every year [159]. These dedicated burn services provide regional expertise for communities and health professionals as well as treating and managing more severe burn trauma. Many burn injuries are superficial in nature and can be managed in the community or at non-dedicated burn services, while more specialised units are required to manage more complex or severe burns [159].

The ANZBA designates the following indications for burn service referral: >10%TBSA burns (or >5% TBSA in children), full thickness burns >5% TBSA, burns affecting special areas (face, hands, feet, genitalia, perineum, major joints and circumferential limb or chest burns), burns with inhalation injury, electrical burns, chemical burns, burns with pre-existing illness, burns associated with major trauma, burns at the extremes of age (elderly and young children), burns in pregnant women, and non-accidental burns [159].



Map legend

Orange (Victoria): The Alfred Hospital and Royal Children's Hospital (RCH Victoria)

Lime (New South Wales): Royal North Shore, The Children's Hospital Westmead and Concord General Repatriation Hospital

Pink (South Australia): The Royal Adelaide and Women's and Children's Hospital

Burgandy (Northern Territory): The Royal Darwin Hospital

Green (Western Australia): Princess Margaret and Royal Perth Hospital

Purple (New Zealand): Middlemore, Waikato, Hutt and Christchurch Hospital

Yellow (Queensland): Royal Brisbane & Women's Hospital and The Royal Children's Hospital (RCH Brisbane)

Tan (Tasmania): Royal Hobart Hospital

Figure 3 Burn services in Australia and New Zealand

4.1.2 The Burns Registry of Australia and New Zealand

The Burns Registry of Australia and New Zealand is a collaboration between the ANZBA and Monash University. It is a clinical quality registry of burn injuries, patient demographics, treatments and outcomes of burn injury patients, and captures data about admissions to burn services in Australia and New Zealand. Currently, 16 of 17 BRANZ sites contribute data. The remaining site was the Royal Brisbane and Women's Hospital, the adult burn service for

Queensland, which received ethics approval to contribute data to the registry in late 2015 and commenced submission of data in July 2016. Table 4 summarises participating sites included in this study. Individual hospitals have been de-identified and relabelled as sites A to J.

Patients are included on the registry if admitted to hospital for over 24 hours, admitted for less than 24 hours but required surgical management or died prior to discharge. In order to be included in the registry patients must have been admitted within 28 days of injury or transferred from another hospital (irrespective of the time from injury) [10].

Table 4 Participating BRANZ Hospitals included in this study

Hospital	Adults/paediatrics
Hospital A	Adults
Hospital B	Adults
Hospital C	Adult/Paediatrics
Hospital D	Adults
Hospital E	Adults
Hospital F	Adults
Hospital G	Adult/Paediatrics
Hospital H	Adult/Paediatrics
Hospital I	Adult/Paediatrics
Hospital J	Adult/Paediatrics

4.2 ETHICS APPROVAL

The registry was approved by the Human Research Ethics Committees of each participating site. This project was approved by the Ethics Committee of The Alfred Hospital (approval number: 59/13) and Monash University (approval number: CF14/2383 – 2014001302).

4.3 INCLUSION AND EXCLUSION CRITERIA

Patients registered to BRANZ were included in this study if they met the following criteria:

i. Admission between August 2009 and June 2013;
ii. Adults (aged 18-years or over);
iii. with greater than or equal 20% TBSA affected.

4.4 DATA EXTRACTION

The variables extracted and data completeness are summarised in Table 5. Variables were then grouped based on the data type.

Table 5 Completeness of variables extracted

Variables extracted	**Completeness N= 496**
Demographic variables	
Age	496 (100%)
Gender	496 (100%)
Co-morbidities	489 (98.6%)
Hospital campus	496 (100%)
Geographic location	496 (100%)
Insurance fund source	495 (99.8%)
Admission source	496 (100%)
Burn injury event	
Place of burn injury	473 (95.4%)
Action when burn injury occurred	475 (95.8%)
Primary cause of burn	495 (99.8%)
Associated inhalation injury	496 (100%)
Alcohol or drugs involved	407 (82.1%)
Severity of burn injury	
%TBSA involved	496 (100%)
Burn depth	341 (68.8%)
Body regions involved	418 (84.3%)
Burn management	
Operative management	493 (99.4%)
Type of first operation	417 (84.1%)
Length of stay	495 (99.8%)
Time from injury to admission	364 (73.4%)
Time from admission to surgeon assessment[a]	213 (65.7%)
Time from admission to graft surgery[b]	218 (63.9%)
Blood cultures taken	478 (96.3%)
Blood culture result[c]	336 (100%)
Disposition	
Discharge destination	495 (99.8%)
Treatment withdrawn/withheld[d]	70 (83.3%)

[a]Percentage of patients assessed by a surgeon (N=324); [b]Percentage of patients who were grafted (N= 341); [c]Percentage of patients who had blood cultures taken (N= 336); [d]Percentage of patients who were deceased (N= 84)

4.5 DATA MANAGEMENT

Demographic data

Median and IQR were used to describe the age distribution given the skewed nature of this variable. Co-morbidities were based on the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM). The ICD-10-AM is a coding scheme for diseases and external causes of injury. Developed and published by the World Health Organization (WHO), the ICD-10 is used to assist clinicians, researchers and clinical coders in translating diseases, injuries and procedures into alphanumeric codes. Using these codes a Charlson Co-morbidity Index (CCI) was calculated. The CCI predicts the 10-year mortality for patients based on the presence of certain co-morbid conditions. Patients were assigned a score of 0, 1, 2, 3, or 6 based on the conditions present, with a higher score representing the risk of less favourable outcomes. In this study the 19 Charlson conditions were mapped from ICD-10-AM codes to assign CCI scores to each patient as described by Gabbe et al [162].

There were a number of possible funding sources for treatment provided for hospitalised patients. These included: Australian public healthcare (i.e. Commonwealth state funding agreement), private health insurance (Australia), self-funding (Australia), workers compensation (Australia), motor vehicle third party personal claims (Australia), Department of Veterans Affairs (Australia), reciprocal health care agreements (with other countries), other sources (e.g. travel insurance), motor vehicle compensation (Australia), Accident Compensation Corporation (no-fault personal injury cover in New Zealand), surgical services contract and other private insurance (New Zealand).

Burn injury event

The place where the burn injury occurred was defined as the physical location of the person when the injury occurred and numeric codes were assigned to the following locations: home (usual place of residence), residential institution (i.e. nursing home, orphanage, hospice, reform school or prison), school or other public administrative area (buildings or grounds used by the general public), sports or athletics areas, street or highway, industrial or construction area, farms, places of recreation (e.g. parks, forests, campsites etc.), other residence (e.g. a friend's home) or another specified place (e.g. abandoned or derelict house, parking lot or military training ground etc.).

The action being taken by an individual when the burn occurred was coded numerically for the following tasks: sports activity (physical exercise with a described functional element), leisure activity (e.g. hobbies or activities with an entertainment element that excluded sport), working for income, cooking/preparing food or drink, cleaning, gardening, household maintenance (unpaid duties excluding cooking, cleaning or gardening), near a person cooking, vehicle maintenance, bathing, eating/drinking, sleeping/resting, education, driving/passenger, self-harming, suspected illegal activity, other vital activities (e.g. personal hygiene), other types of unpaid work (unpaid domestic duties like caring for children) or other specified activities not elsewhere classified. The primary burn cause was classified as chemical, contact, scald, electrical, flame, friction, pressurised gas/air, radiant heat, cooling or other specified burn cause.

Burn severity

The %TBSA was the %TBSA assessed using the 'rule of nines'[163] by the most senior burns clinician within 72-hours of admission. Categorisation based on quartiles (20-25%, 26-30%, 31-49% and ≥50%) was used to describe the %TBSA given the skewed distribution of this variable. Burn depth was also assessed clinically and was classified as superficial dermal, mid-dermal, deep dermal and full thickness burns [159]. These assessments were then re-classified into three groups to simplify the reporting of results: superficial partial thickness burns (superficial or mid dermal), deep partial thickness/full thickness burns (deep dermal or full thickness) and combination burns (where a patient had been assessed as having areas of superficial partial thickness burns *and* deep partial/full thickness burns). The mean body area affected by each type of burn depth was also presented using the same nomenclature as above (i.e. superficial partial thickness or deep/full thickness burns).

Body regions were categorised into 12 areas and reported with either a 'yes' or 'no' based on which body area was affected by burn injury. The body regions were: scalp, face, eye(s), neck, breast/chest, trunk, buttock, perineum, hand(s), foot/feet, lower limb(s), and upper limb(s).

Burn management

Operative management was defined as the patient going to the operating theatre at least once for a burn wound management procedure (this excluded dressing changes). The 'type of operation' data captured was for the first trip to theatre for each different procedure a patient had, and included the following: debridement and grafting (i.e. SSG), debridement and temporary skin closure (e.g. Biobrane™), debridement and dermal reconstructive product (e.g. Integra®), debridement and skin cell product (e.g. CEA) or other wound management procedures (e.g. escharotomy, fasciotomy, amputation or other specified procedures). This data provides information about surgery types performed for each patient, but not details for each surgical episode. Detailed information regarding all surgeries was deemed likely to constitute a data collection burden not justified by its value given resources available to participating burn units.

The LOS was calculated from the admission date/time to hospital and discharge date/time, and was categorised into four groups based on quartiles (0-10 days, 11-20 days, 21-40 days and ≥41 days) due the highly skewed distribution. The time from injury to admission was calculated from the difference in time (hours) between the date/time of injury and the date/time of admission. The time from admission to surgeon assessment was calculated from the difference in time (hours) between hospital admission and assessment by either a head of unit, a burns surgeon with 2 years' experience in a major burn service with emergency management of severe burns (EMSB) certification or a burns nurse practitioner with EMSB certification. Time from admission to graft surgery was calculated using the difference in time (hours) between hospital admission and first operative debridement and graft (SSG) procedure.

Discharge destination

Discharge destinations were coded into one of the following: transfer to another hospital, a psychiatric unit, another health care accommodation (e.g. nursing home if this was not the usual residence prior to admission), inpatient rehabilitation centre, patients absconding or discharging against medical advice, death, usual residence/home, and hospital in the home (HITH) or another specified destination. Deaths were further categorised as unexpected (death despite ongoing active treatment), treatment withheld (upon admission) and treatment withdrawn (during admission).

4.6 DATA ANALYSIS

Descriptive statistics were used to summarise the characteristics of the included patients. Frequencies and percentages were used for categorical variables and an assessment of normality was undertaken for all continuous variables. For normally distributed variables, the mean and standard deviation (SD) was reported. Chi Square tests were used to compare categorical variables, and Fisher's Exact where assumptions of Chi-Square tests were violated (I.e. small cell sizes). Mann-Whitney U tests (two groups) or Kruskal Wallis tests (more than two groups) were used to compare the means of continuous variables where data were not normally distributed. Tables and graphs were generated using Microsoft Excel to assist in interpretation of results. Figures included illustrative figures, pie charts and bar graphs.

The primary outcomes of interest were mortality, length of stay and discharge destination. Both univariate and multivariate analyses were performed for all outcomes. For each model multivariate analysis was undertaken.

Mortality

A Cox Proportional Hazards regression model was used to model time to death. This type of survival model relates the time that passes before the designated event (i.e. death) occurs [164]. In simple terms, the hazard ratio was a measure of how often an event (i.e. death) occurred in one group compared to another over time. The times from injury to admission, injury to initial burn wound assessment, admission to surgeon assessment and admission to first graft procedure were assessed and reported in hours. For survival analysis the time of admission was designated the time of origin (t0). Potential risk factors for mortality were analysed using univariate analysis and included age, gender, co-morbidities, cause, injury intent (self-harm vs. unintentional), %TBSA, the presence of an inhalation injury, body area involved, blood culture result, hospital volume, and whether an operation was performed. Those with a significant association (p-value<0.05) with univariate analysis were subsequently included in the multivariate model.

Subgroup analysis was performed on all deceased patients to investigate differences between early (≤24-hours after admission) and late deaths (>24-hours). Logistic regression was undertaken to identify differences between the two groups. Any variables where a significant difference was identified (p-value <0.05) were included in a multivariate analysis.

Length of stay (LOS)

Length of stay was log-transformed as the variable was highly skewed and a natural log transformation resulted in a more normal distribution of this outcome. Linear regression, with the log transformed LOS, was used to identify predictors of LOS [165]. The ratio of geometric means was obtained which represents the percentage increase or decrease in mean LOS relative to the reference group. Age, gender, co-morbidities, cause, self-harm, %TBSA, the presence of an inhalation injury, body area involved, blood culture result, hospital volume, whether an operation was performed, and if patients were discharged with HITH, were considered as potential predictors of LOS. Factors demonstrating a p-value of <0.05 on univariate testing were included in the multivariable model. As HITH was an in-home nursing service aimed at reducing LOS, it was also included in the model. In-hospital deaths were excluded from the LOS analyses.

Discharge destination

Multinomial logistic regression enables the prediction of probabilities of different possible outcomes of a categorically distributed dependent variable for a given set of independent variables [165]. Multinomial logistic regression was used to identify predictors of discharge destination. Relative risk ratios (and 95% CI) were calculated based on factors considered predictors of discharge destination. These included age, gender, co-morbidities, cause, injury intent, %TBSA, the presence of an inhalation injury, body area involved, blood culture result, hospital volume and whether an operation was performed. Variables with a p-value <0.05 on univariate testing were included in the multivariate model. As noted for the LOS outcome, in-hospital deaths were excluded.

Comparison of burn services

Burn services in Australia and New Zealand were compared in terms of demographic data, burn injury event, burn severity, burn management, discharge destination and outcomes including mortality and length of stay. Only burn services with 50 or more cases over the study period were included in this analysis. Where individual categorical frequencies were less than five, categories were collapsed to avoid statistical disclosure. A p-value of less than 0.05 was chosen as the level of significance. All statistical analyses were carried out using STATA (version 13).

5 DESCRIPTIVE EPIDEMIOLOGY OF SEVERE BURN INJURIES

5.1 PATIENT DEMOGRAPHICS

Ten sites that treated adults presenting with severe burns were included in the final analysis. There were 496 BRANZ registered patients admitted to one of ten dedicated burn services across Australia and New Zealand who met the inclusion criteria for this study (Table 6). Over half of the patients were aged between 18 and 40-years and most were male. The majority of patients were treated in one of three Australian burn services (56%) (Table 6).

Table 6 Demographics of the entire population

Characteristics	All patients N= 496
Age	
Median (IQR)- years	38 (18-85)
Range- years	18-97
Age Quartiles	
18-25 years	113 (22.8%)
26-40 years	168 (33.9%)
41-55 years	107 (21.6%)
≥56 years	108 (21.8%)
Gender	
Male	374 (75.4%)
Female	122 (24.6%)
Hospital Campus	
Hospital A	109 (22.0%)
Hospital B	105 (21.2%)
Hospital C	63 (12.7%)
Hospital D	62 (12.5%)
Hospital E	57 (11.5%)
Hospital F	53 (10.7%)
Hospital G	15 (3.0%)
Hospital H	13 (2.6%)
Hospital I	12 (2.4%)
Hospital J	7 (1.4%)
Insurance fund source[a]	
Commonwealth state funding agreement (Australia)	331 (66.9%)
Workers compensation	51 (10.3%)
Other[b]	131 (22.9%)
Admission source	
Inter-hospital transfer	279 (56.3%)
Via ambulance from scene of injury	189 (38.1%)
Other referral source[c]	28 (5.6%)

[a]Insurance fund source data missing for n=1; [b]Funded by self, motor vehicle compensation, private insurer, ministry of health or ACC (NZ), reciprocal health care or department of veterans affairs; [c]From general practitioner, self presentation or burn service

5.2 BURN INJURY EVENT

Most patients sustained their injuries in the home (Table 7). The most common activities resulting in severe burn injuries included: intentional self-harm, leisure activities, working and preparing food/drink. Most cases were flame burns with 40% of patients also sustaining an associated inhalation injury. Scald burns accounted for a minority of cases (Table 7). Contact, chemical, friction, electrical, non-flame and radiant heat burns together accounted for less than 5% of cases. In a quarter of patients, there was documentation suggesting the patient was affected by alcohol and/or drugs at the time of injury.

Table 7 Burn injury event characteristics of entire population

Place, action and primary cause that resulted in severe burn injury	All patients N= 496
Place of burn injury[a]	
Home	272 (57.5%)
Place of recreation	35 (7.4%)
Other residence	31 (6.6%)
Trade or service area	30 (6.3%)
Street or highway	29 (6.1%)
Industrial or construction area	29 (6.1%)
Farm	17 (3.6%)
Other specified place[b]	30 (6.3%)
Action when burn injury occurred[c]	
Intentional self-harm	85 (17.9%)
Leisure activity (excludes sport)	69 (14.5%)
Working for income	68 (14.3%)
Preparing food/drink	53 (11.2%)
Sleeping/resting	35 (7.4%)
Suspected illegal activity	30 (6.3%)
Household maintenance	24 (5.1%)
Vehicle maintenance	23 (4.8%)
Gardening	21 (4.4%)
Other specified activities[d]	67 (14.1%)
Primary cause of burn injury[e]	
Flame	427 (86.3%)
Scald	44 (8.9%)
Other specified cause[f]	24 (4.9%)
Associated inhalation injury	
Yes	200 (40.3%)
No	296 (59.7%)
Alcohol or drugs involved[g]	
Yes	102 (25.1%)
No	305 (74.9%)

[a]Place of burn injury data missing for n=23; [b]Residential institution, school or public administrative area, sports or athletics area, farm; [c]Action when burn injury occurred data missing for n=21; [d]Sports activity, cleaning, near person preparing food/drink, driving, bathing, vehicle/household; [e]Primary cause of burn injury data missing for n=1; [f]Contact, chemical, friction, electrical, pressurised gas/air (non-flame), radiant heat; [g]Alcohol or drugs involved data missing for n=89 maintenance, gardening

5.3 SEVERITY OF BURN INJURY

The median (IQR) %TBSA was 31 (25-47) and ranged from 21 to 100. Three quarters of patients enrolled had burns involving <50% TBSA. Lower %TBSA burns tended to be more superficial in nature, with 31% of %TBSA 20-25% burns being superficial partial thickness (Figure 4). This decreased to less than 10% in patients with burns affecting ≥50% TBSA, where close to half had deep partial/full thickness burns. Mixed type burns predominated, ranging from 46% to 56% throughout all %TBSA categories. A total of 89 patients (18%) had no burn depth information recorded.

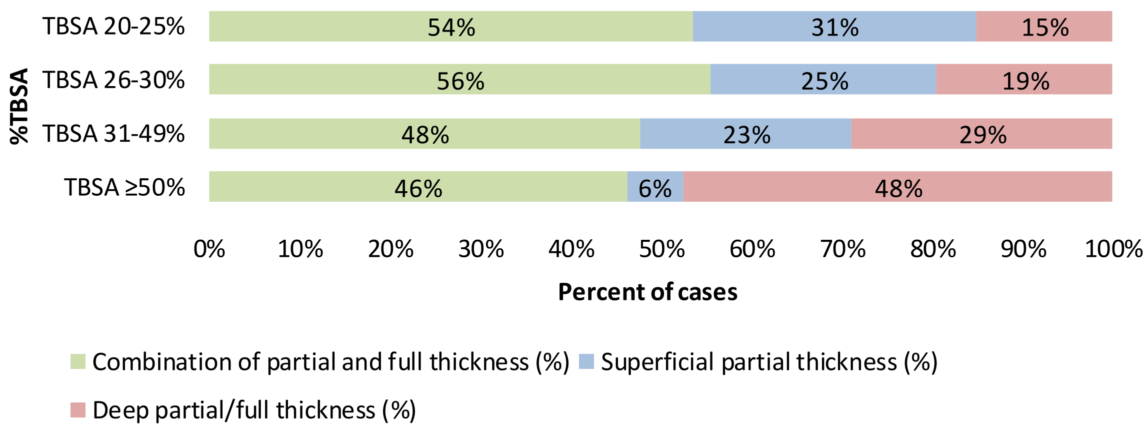


Figure 4 Burn injury depth

The mean percentage of burn injury that was assessed as being either superficial partial thickness or deep partial/full thickness was also investigated (Figure 5). Larger area burns (≥50% TBSA) had much higher mean areas of deep partial and full thickness (mean area of burn of 57%) than smaller area burns (mean area of burn of 40%) (Figure 5).

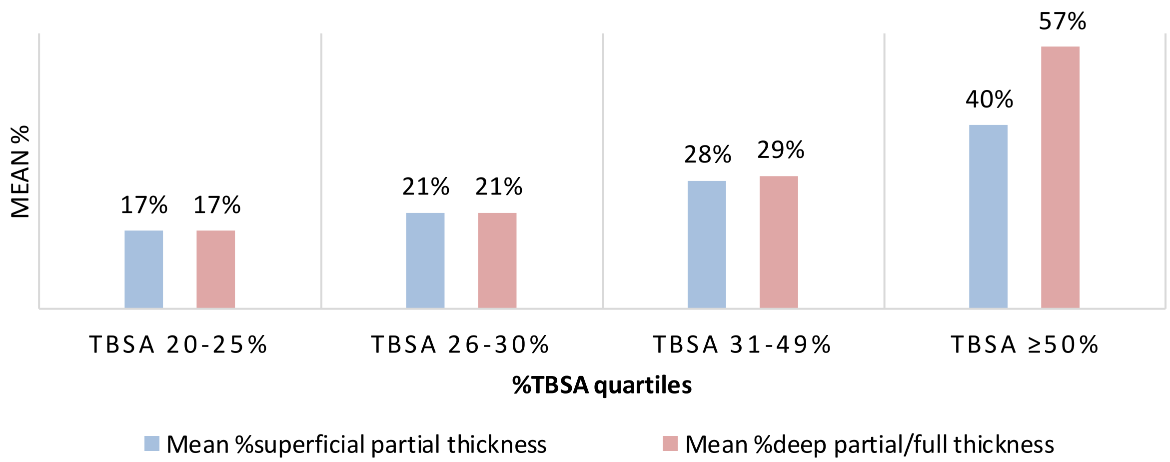


Figure 5 %TBSA of burn by mean area of depth

The most common body areas involved were the upper limbs, lower limbs, face, trunk and hands, each being involved in over 50% of cases respectively (Figure 6). Two thirds (66%) of patients had burns involving regions both above and below the waist. Seventeen per cent of patients had burns involving regions solely above the waist, and 1.2% had burns only below the waist.

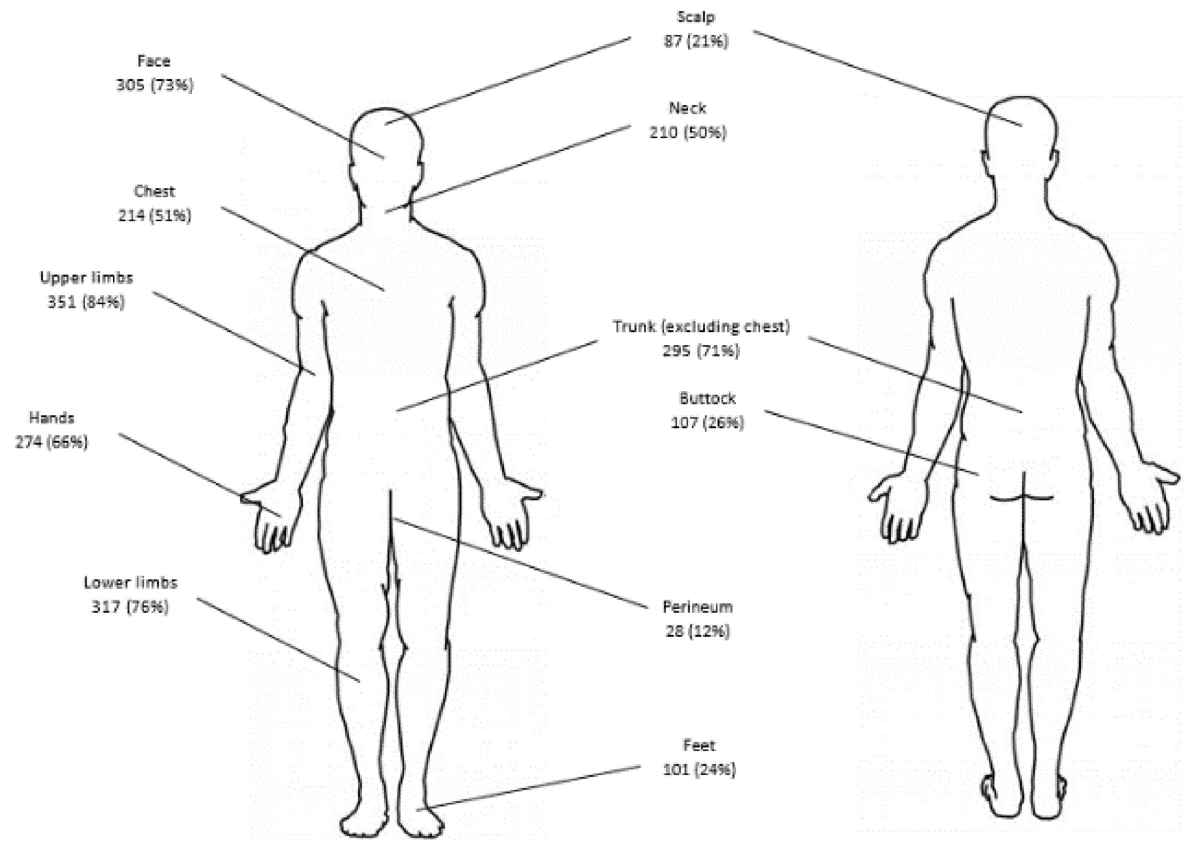


Figure 6 Body regions involved

5.4 CARE CHARACTERISTICS

Almost a third of patients with burns ≥50% were managed non-operatively compared to 16% of patients with burns <50% TBSA (Figure 7). Non-operative management was used the least in patients with a %TBSA between 26-30% (5.6%).

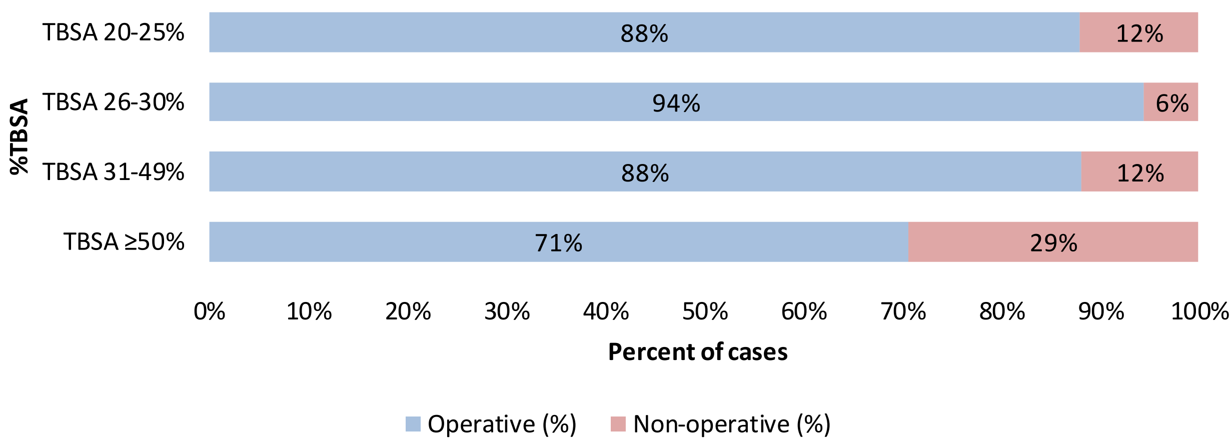


Figure 7 Operative vs. non-operative management

Autologous grafting was the most widely used procedure in all %TBSA categories (Figure 8). This was followed by temporary skin closure and standalone debridement procedures. The proportion of patients treated with Biobrane increased with %TBSA. Close to a third of patients with 50% TBSA burns or greater were managed with Biobrane. The use of Integra was also more prevalent in patients with a %TBSA ≥50% (Figure 8).

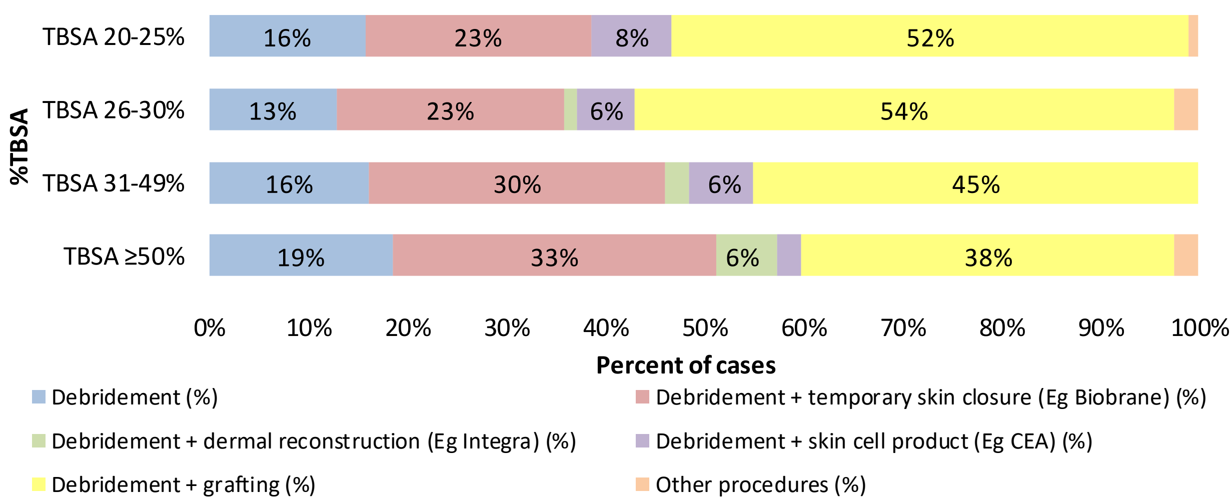


Figure 8 Most common unique operations

Table 8 summarises care characteristics. The median length of stay was 24 days (including survivors and deaths). Over 80% of patients had a documented time of injury. The median time to admission from injury was 5.1 hours (Table 8). The median time from admission to surgeon assessment and graft surgery was 9.6 hours and 118 hours, respectively (Table 8).

Table 8 Care characteristics of entire population

Characteristics	All patients N= 496
Length of stay[a]	
Range- days	0.1-237.5
Median (IQR)- days	24 (12-44)
Length of stay quartiles	
0-10 days	114 (23.0%)
11-20 days	102 (20.6%)
21-40 days	141 (28.5%)
≥41 days	138 (27.9%)
Time frame (Hours)- median (IQR)	
Injury to admission[b]	5 (2-8)
Admission to surgeon assessment[c]	10 (2-19)
Admission to graft surgery[d]	118 (60-188)

[a]Length of stay data missing for n=1; [b]Injury to admission data missing for n=132; [c]Admission to surgeon assessment data missing for n=283; [d]Admission to graft surgery data missing for n=2

Most patients had at least one set of blood cultures taken (68%) (Figure 9). Of these 30% were positive.

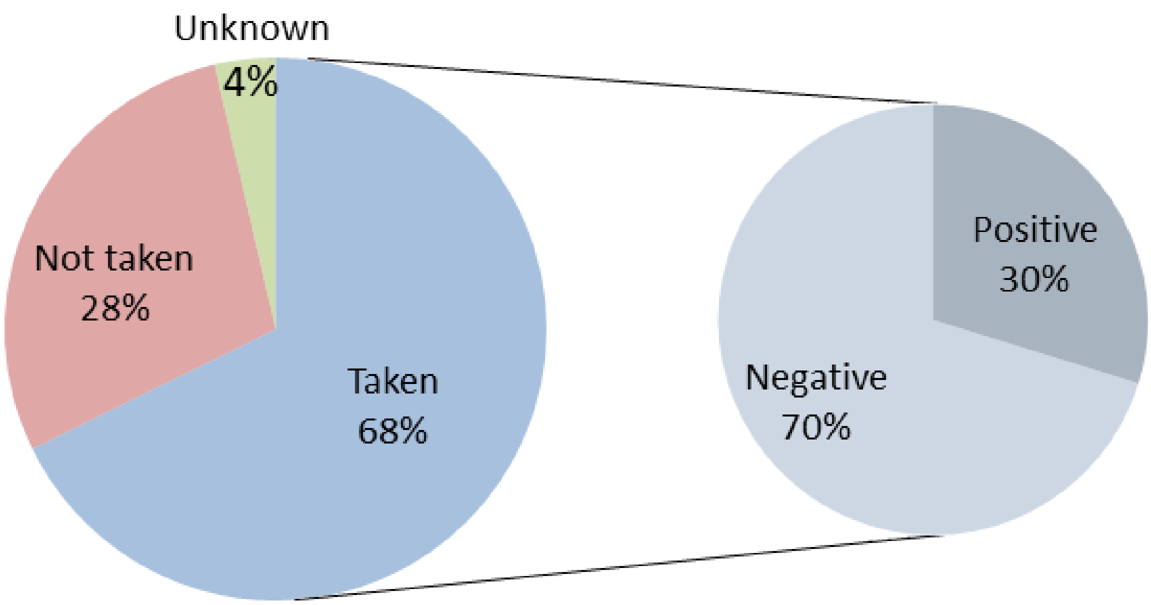


Figure 9 Blood cultures: Cases with blood cultures taken and not taken (left) and percent of positive and negative results from those with cultures taken (right)

5.5 DISPOSITION

More than half of patients were discharged back to a place of residence and there were 84 (17%) in-hospital deaths (Figure 10). Of the deaths, 49 (58%) had treatment withdrawn (active treatment commenced but stopped), 13 (15%) had treatment withheld (considered palliative upon admission), 8 (10%) died unexpectedly and 14 (17%) did not have data available. Time from admission to death was seen as an important surrogate marker for palliation on admission, as most patients where treatment was withheld died within 24-hours of admission (29% of patients) as compared to those who died after 24-hours (8%; p-value 0.02).

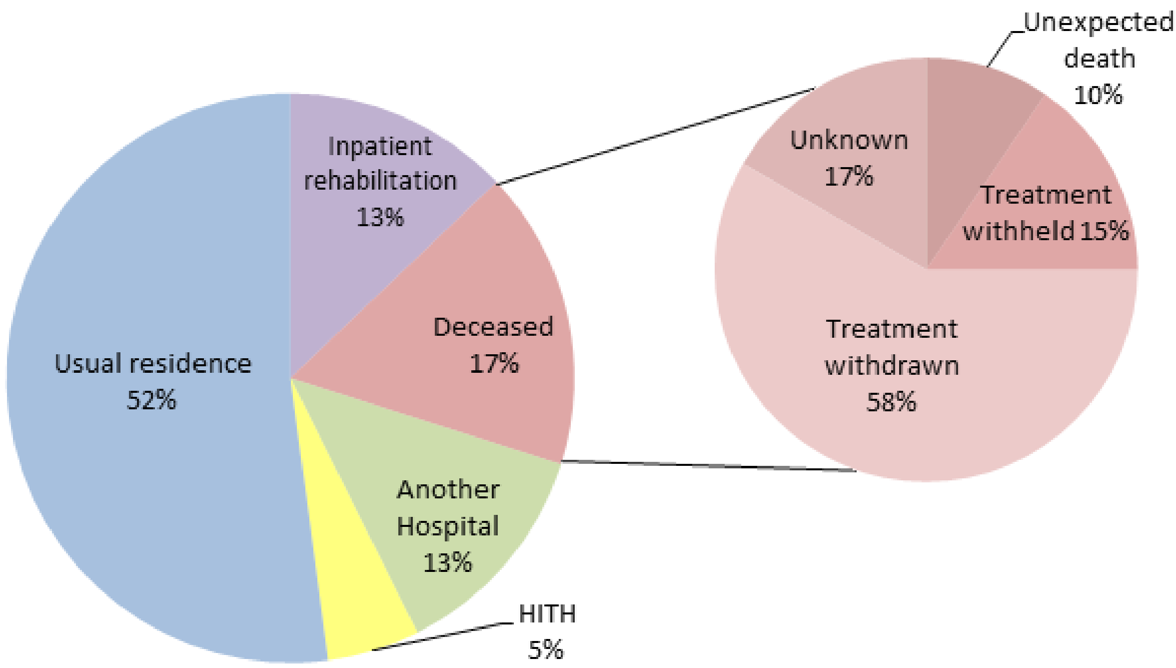


Figure 10 Disposition at time of discharge and decision pathways for deceased patients

6 MORTALITY, LOS AND DISCHARGE DESTINATION

6.1 SURVIVORS VS. DEATHS

A total of 84 patients (17%) died in-hospital. Survivors were younger, male and had lower CCI scores than deceased patients and showed lower rates of self-harm and inhalation injury (Table 9). Deceased patients had fewer blood cultures taken when compared with survivors.

Table 9 Survivors vs. deaths

Characteristics	Survivors N= 411	Deaths N= 84	P-value
Age			
Median (IQR)- years	36 (18-81)	53 (19-97)	<0.01
Range- years	18-84	19-97	
Gender			
Male	323 (78.6%)	50 (59.5%)	<0.01
Female	88 (21.4%)	34 (40.5%)	
Charlson Co-morbidity Index[a]			
0	281 (68.4%)	54 (64.3%)	<0.01
1	76 (18.5%)	7 (8.3%)	
≥2	47 (11.4%)	23 (27.4%)	
Primary cause of burn injury[b]			
Flame	350 (85.4%)	76 (90.5%)	0.22
Other specified cause[c]	60 (14.6%)	8 (9.5%)	
Intentional self-harm[d]			
Yes	50 (12.6%)	35 (45.5%)	<0.01
No	347 (87.4%)	42 (54.6%)	
%TBSA quartiles			
20-25%	136 (33.1%)	5 (6.0%)	<0.01
26-30%	101 (24.6%)	5 (6.0%)	
31-49%	115 (28.0%)	13 (15.5%)	
>50%	59 (14.4%)	61 (72.6%)	
Associated inhalation injury			
Yes	135 (32.9%)	65 (77.4%)	<0.01
No	276 (67.2%)	19 (22.6%)	
Body area[e]			
Above and below waist	270 (76.7%)	56 (86.2%)	0.09
Above or below waist	82 (23.3%)	9 (13.9%)	
Face involved[f]			
Yes	256 (72.7%)	49 (75.4%)	0.66
No	96 (27.3%)	16 (24.6%)	
Hospital case volume			
<100	236 (57.4%)	45 (53.6%)	0.52
≥100	175 (42.6%)	39 (46.4%)	
Blood cultures[g]			
Positive	81 (20.3%)	19 (24.7%)	<0.01
Negative	220 (55.0%)	16 (20.8%)	
None taken	99 (24.8%)	42 (54.6%)	
Operative management[h]			
Yes	377 (92.2%)	42 (50.6%)	<0.01
No	32 (7.8%)	41 (49.4%)	

[a]Charlson Co-morbidity Index data missing for n=7; [b]Primary cause missing for n=1; [c]Scald, contact, chemical, friction, electrical, pressurised gas/air (non-flame), radiant heat; [d]Intentional self-harm data missing for n=7; [e]Body area missing for n= 18; [f]Face involved missing for n= 18; [g]Blood culture data missing for n=6; [h]Operative management data missing for n=3

6.2 MORTALITY RISK

Table 10 summarises the results of the univariate Cox Proportional Hazards Regression analysis for in-hospital mortality. All in-hospital deaths within one day were excluded from the analysis. Increased age, female gender, intentional self-harm, increased %TBSA and inhalation injury were associated with an increased risk of in-hospital mortality (Table 10). These factors were included in a multivariable model and higher age and %TBSA, self-harm and inhalation injury were associated with increased rates of mortality, after adjusting for confounders (Table 11).

Table 10 Mortality risk (univariate analysis)

Factor	Hazard Ratio (95% CI) N= 495	P-value
Age	1.04 (1.03, 1.05)	<0.01
Gender		
Male (reference)	1.00	
Female	2.00 (1.29, 3.10)	<0.01
Charlson Co-morbidity Index[a]		
0 (reference)	1.00	1.00
1	0.45 (0.20, 0.98)	0.05
≥2	1.61 (0.98-2.65)	0.06
Primary cause of burn injury[b]		
Flame (reference)	1.00	
Other	0.67 (0.33, 1.40)	0.29
Intentional self-harm[c]		
No (reference)	1.00	
Yes	4.01 (2.54, 6.32)	<0.01
%TBSA quartiles		
20-25% (reference)	1.00	
26-30%	1.30 (0.38, 4.49)	0.68
31-49%	2.70 (0.96, 7.57)	0.06
>50%	15.47 (6.18, 38.73)	<0.01
Inhalation injury		
No (reference)	1.00	
Yes	4.99 (2.98, 8.35)	<0.01
Body area[d]		
Above waist only (reference)	1.00	
Above and below waist	1.82 (0.87, 3.82)	0.11
Below waist only	2.10 (0.26, 16.82)	0.49
Face involved[e]		
No (reference)	1.00	
Yes	1.11 (0.63, 1.95)	0.73
Case Volume		
≥100 (reference)	1.00	
<100	0.89 (0.58, 1.37)	0.59
Blood Cultures[f]		
Not taken (reference)	1.00	
Positive	0.26 (0.14, 0.48)	<0.01
Negative	0.14 (0.08, 0.25)	<0.01
Operative management[g]		
No (reference)	1.00	
Yes	0.08 (0.05, 0.12)	<0.01

[a]Charlson Co-morbidity Index data missing for n=7; [b]Primary cause of burn injury data missing for n=1; [c]Intentional self-harm data missing for n=21; [d]Body area data missing for n= 78; [e]Face involvement data missing for n= 78; [f]Blood culture data missing for n= 18; [g]Operative management data missing for n=3

Table 11 Mortality risk (multivariate analysis)

Factor	Hazard Ratio (95% CI) N=468	P-value
Age	1.06 (1.05, 1.08)	<0.01
Gender		
Male (reference)	1.00	
Female	1.21 (0.75, 1.95)	0.43
Charlson Co-morbidity Index[a]		
0 (reference)	1.00	
1	0.44 (0.19, 1.00)	0.05
≥2	0.47 (0.27, 0.81)	<0.01
Intentional self-harm[b]		
No (reference)	1.00	
Yes	3.24 (2.00, 5.24)	< 0.01
%TBSA quartiles		
20-25% (reference)	1.00	
26-30%	1.20 (0.32, 4.52)	0.79
31-49%	2.58 (0.88, 7.60)	0.09
>50%	16.13 (6.12, 42.52)	<0.01
Inhalation injury		
No (reference)	1.00	
Yes	2.51 (1.43, 4.42)	<0.01

[a]Charlson Co-morbidity Index data missing for n=7; [b]Intentional self-harm data missing for n=21

6.3 EARLY DEATHS VS. LATE DEATHS

Table 12 summarises all deaths based on length of stay (LOS). This analysis included all patients (I.e. those who died within 24-hours and those who died after 24-hours. The age and gender distributions of both groups were similar. Deaths after one day in-hospital had a higher CCI score than those who died within 24-hours. In-hospital deaths within 24-hours of admission had higher rates of inhalation injury, burns involving the face, flame burns, treatment withheld patients and non-operative management courses (Table 12). Of the in-hospital deaths within one day, 68% had treatment withdrawn after a period of active treatment (Table 12).

Table 12 Early deaths (≤1 day) vs. late deaths (>1 day)

Characteristics	**Death ≤1 day from arrival at burn service N= 40**	**Death >1 day from arrival at burn service N= 43**	**P-value**
Age			
Median (IQR)- years	51 (19-97)	53 (21-86)	0.77
Range- years	19-97	21-86	
Gender			
Male	26 (65.0%)	24 (55.8%)	0.39
Female	14 (35.0%)	19 (44.2%)	
Charlson Co-morbidity Index[a]			
0	35 (87.5%)	18 (41.9%)	<0.01
≥1	5 (12.5%)	25 (48.1%)	
Primary cause of burn injury[b]			
Flame	39 (97.5%)	36 (83.7%)	0.03
Other specified cause[c]	1 (2.5%)	7 (16.3%)	
Intentional self-harm[d]			
Yes	20 (57.1%)	15 (36.6%)	0.07
No	15 (42.9%)	26 (63.4%)	
%TBSA quartiles			
20-25%	2 (5.0%)	3 (7.0%)	0.22
26-30%	1 (2.5%)	4 (9.3%)	
31-49%	4 (10.0%)	9 (20.9%)	
>50%	33 (82.5%)	27 (62.8%)	
Associated inhalation injury			
Yes	36 (90.0%)	28 (65.1%)	<0.01
No	4 (10.0%)	15 (34.9%)	
Body area[e]			
Above and below waist	28 (87.5%)	28 (84.9%)	0.76
Above or below waist	4 (12.5%)	5 (15.2%)	
Face involved[f]			
Yes	29 (90.6%)	20 (60.6%)	<0.01
No	3 (9.4%)	13 (39.4%)	
Hospital case volume			
<100	16 (40.0%)	28 (65.1%)	0.02
≥100	24 (60.0%)	15 (34.9%)	
Operative management[g]			
Yes	6 (15.4%)	36 (83.7%)	<0.01
No	33 (84.6%)	7 (16.3%)	
Decision pathways			
Treatment withdrawn	23 (67.7%)	26 (72.2%)	0.02
Treatment withheld	10 (29.4%)	3 (8.3%)	
Unexpected death	1 (2.9%)	7 (19.4%)	

Survivors excluded from analysis; [a]Charlson Co-morbidity Index data missing for n=7; [b]Primary cause of burn injury data missing for n=1; [c]Scald, contact, chemical, friction, electrical, pressurised gas/air (non-flame), radiant heat; [d]Intentional self-harm data missing for n=7; [e]Body area data missing for n= 18; [f]Face involvement data missing for n= 18; [g]Operative management data missing for n=1

6.4 PROFILE OF PATIENTS BY LOS

All in-hospital deaths were excluded from analyses of LOS. The median LOS increased with age and %TBSA and was higher in women, those who had at least one operative procedure and self-harm injuries (Table 13). The LOS for patients with a positive blood culture or inhalation injury was also higher than those without (Table 13).

Table 13 Median LOS (IQR) by demographic and injury characteristics

Characteristics	Median (IQR) LOS of survivors N= 411
Age quartiles	
18-25 years	23.1 (15.3-33.4)
26-40 years	24.8 (15.7-41.5)
41-55 years	30.7 (19.8-48.7)
≥56 years	40.8 (23.8-63.6)
Gender	
Male	26.3 (16.8-42.0)
Female	36.8 (22.2-61.1)
Charlson Co-morbidity Index[a]	
0	24.2 (15.6-38.6)
1	31.8 (20.4-55.5)
≥2	53.1 (2.9-21.2)
Primary cause of burn injury[b]	
Flame	27.1 (18.5-47.5)
Other specified cause[c]	27.7 (11.0-43.2)
Intentional self-harm[d]	
No	26.2 (17.1-43.5)
Yes	40.0 (15.8-50.8)
%TBSA quartiles	
20-25%	21.3 (15.2-29.0)
26-30%	23.8 (15.8-36.2)
31-49%	33.1 (22.5-50.8)
≥50%	67.5 (36.9-91.0)
Associated inhalation injury	
No	23.1 (15.0-38.0)
Yes	41.7 (23.6-65.0)
Body area[e]	
Above and below waist	27.4 (18.02-51.0)
Above or below waist	26.1 (16.1-39.8)
Face involved[f]	
No	26.2 (16.1-43.2)
Yes	27.0 (18.1-50.7)
Hospital case volume	
≥100	29.1 (19.8-48.5)
<100	25.8 (15.8-46.6)
Blood cultures[g]	
Positive	56.4 (37.6-84.0)
Negative	27.7 (19.6-42.4)
None taken	15.5 (6.0-20.9)
Operative management[h]	
No	10.2 (5.1-15.6)
Yes	28.8 (19.0-48.7)

Deceased patients excluded; [a]CCI data missing for n=7; [b]Primary cause missing for n=1; [c]Scald, contact, chemical, friction, electrical, pressurised gas/air/radiant; [d]Self-harm missing for n=21; [e]Body area missing for n= 78; [f]Face involved missing for n= 78; [g]Blood culture missing for n= 18; [h]Operative management missing for n=3

6.5 PREDICTORS OF LOS

Table 14 summarises factors associated with an increased LOS, these included: age, CCI, injury intent, %TBSA, an associated inhalation injury, case volume, a positive blood culture and operative management. On multivariate analysis, significant associations persisted for increased age, %TBSA, CCI, an associated inhalation injury and self-harm injuries (Table 15).

Table 14 LOS linear regression (univariate analysis)

Factor	Ratio of geometric means (95% CI)	P-value
Age	1.01 (1.00, 1.02)	<0.01
Gender		
Male (reference)	1.00	
Female	1.24 (0.98, 1.57)	0.08
Charlson Co-morbidity Index[a]		
0 (reference)	1.00	
1	1.52 (1.19, 1.93)	<0.01
≥2	2.24 (1.67, 3.01)	<0.01
Primary cause of burn injury[b]		
Flame (reference)	1.00	
Other	0.79 (0.60, 1.04)	0.10
Intentional self-harm[c]		
No (reference)	1.00	
Yes	1.58 (1.18, 2.12)	<0.01
%TBSA quartiles		
20-25% (reference)	1.00	
26-30%	1.13 (0.87, 1.45)	0.36
31-49%	1.41 (1.12, 1.80)	<0.01
>50%	2.04 (1.51, 2.75)	<0.01
Inhalation injury		
No (reference)	1.00	
Yes	1.65 (1.35, 2.02)	<0.01
Body area[d]		
Above waist only (reference)	1.00	
Above and below waist	1.11 (0.85, 1.44)	0.45
Below waist only	1.05 (0.37, 2.97)	0.93
Face involved[e]		
No (reference)	1.00	
Yes	1.10 (0.86, 1.40)	0.45
Case Volume		
≥100 (reference)	1.00	
<100	0.75 (0.62, 0.91)	<0.01
Blood Cultures[f]		
None taken (reference)	1.00	
Positive	5.55 (4.36, 7.08)	<0.01
Negative	2.79 (2.29, 3.39)	<0.01
Operative management[g]		
No (reference)	1.00	
Yes	2.84 (2.01, 4.02)	<0.01
HITH[h]		
No (reference)	1.00	
Yes	0.72 (0.49, 1.08)	0.11

All deceased patients excluded; [a]CCI data missing for n=7; [b]Primary cause data missing for n=1; [c]Self-harm data missing for n=21; [d]Body area data missing for n= 78; [e]Face involvement data missing for n= 78; [f]Blood culture data missing for n= 18; [g]Operative management data missing for n=3; [h]HITH data missing for n=1

For every additional year in age, there was a 1% increase in LOS, after adjusting for other key predictors of LOS (Table 15). The LOS was 40% higher in those with an inhalation injury compared to those without, and was also 80% greater in those with a CCI of two or greater compared with this with a CCI of 0, after adjusting for other key predictors of LOS (Table 15). Intentional self-harm patients had an increased LOS of 47% when compared with those without such injuries, after adjusting for confounders (Table 15).

Table 15 LOS linear regression (multivariate analysis)

Factor	Ratio of geometric means (95% CI)	P-value
Age	1.01 (1.00, 1.01)	0.02
Gender		
Male (reference)	1.00	
Female	1.14 (0.91, 1.42)	0.26
Inhalation injury		
No (reference)	1.00	
Yes	1.40 (1.15, 1.71)	<0.01
%TBSA quartiles		
20-25% (reference)	1.00	
26-30%	1.07 (0.84, 1.35)	0.60
31-49%	1.31 (1.04, 1.66)	0.02
>50%	1.74 (1.31, 2.32)	<0.01
Charlson Co-morbidity Index[a]		
0 (reference)	1.00	
1	1.33 (1.04, 1.70)	0.02
≥2	1.80 (1.35, 2.41)	<0.01
Intentional self-harm[b]		
No (reference)	1.00	
Yes	1.47 (1.12, 1.94)	<0.01
HITH[c]		
No (reference)	1.00	
Yes	0.89 (0.61, 1.30)	0.53

All deceased patients excluded; [a]Charlson Co-morbidity Index data missing for n=7; [b]Intentional self-harm data missing for n=21; [c]HITH data missing for n= 1

6.6 PROFILE OF PATIENTS BY DISCHARGE DESTINATION

Dispositions included discharge to a place of residence, inpatient rehabilitation, transfer to another hospital, and hospital in the home (HITH). All in-hospital deaths were excluded. Table 16 summarises demographic data with regards to discharge destination. Patients discharged to a place of residence or to HITH had similar characteristics and tended to be younger, have less severe burns, lower rates of self-inflicted injury, lower LOS and lower rates of positive blood cultures than those discharged elsewhere (Table 16). The majority of patients discharged to inpatient rehabilitation were older, had more co-morbidities, higher rates of self-harm, greater %TBSA burns and more associated inhalation injuries (Table 16). They also had higher LOS and higher rates of positive blood cultures. Similar characteristics were also seen in patients discharged to another hospital, with these patients tending to be older and have higher %TBSA, LOS, positive blood culture rate and higher rates of self-injury (Table 16). Patients generally underwent at least one operative procedure regardless of final discharge destination.

Table 16 Patient demographics based on disposition at time of discharge

Characteristics	Home N= 258	Inpatient rehab N= 64	Other hospital N= 63	HITH N= 26	P-value
Age					
Median (IQR)- years	32 (18-78)	49 (18-84)	42 (18-84)	34 (19-83)	<0.01
Range- years	18-80	18-84	18-84	19-83	
Gender					
Male	204 (79.1%)	46 (71.9%)	49 (77.8%)	24 (92.3%)	0.20
Female	54 (20.9%)	18 (28.1%)	14 (22.2%)	2 (7.7%)	
Charlson Co-morbidity Index[a]					
0	198 (78.0%)	22 (34.4%)	41 (68.3%)	20 (76.9%)	<0.01
≥1	56 (22.0%)	42 (65.7%)	19 (31.7%)	6 (23.1%)	
Primary cause of burn injury[b]					
Flame	222 (86.4%)	53 (82.8%)	53 (84.1%)	22 (84.6%)	0.89
Other specified cause[c]	35 (13.6%)	11 (17.2%)	10 (15.9%)	4 (15.6%)	
Intentional self-harm[d]					
Yes	23 (9.2%)	12 (19.7%)	15 (24.2%)	0	<0.01
No	227 (90.8%)	49 (80.3%)	47 (75.8%)	24 (100.0%)	
%TBSA					
20-25%	102 (39.5%)	9 (14.1%)	16 (25.4%)	9 (34.6%)	<0.01
26-30%	62 (24.0%)	13 (20.3%)	12 (19.1%)	14 (53.9%)	
>30	94 (36.4%)	42 (65.6%)	35 (55.6%)	3 (11.6%)	
Associated inhalation injury					
Yes	75 (29.1%)	35 (54.7%)	19 (30.2%)	6 (23.1%)	<0.01
No	183 (70.9%)	29 (45.3%)	44 (69.8%)	20 (76.9%)	
Body area[e]					
Above or below waist	53 (24.3%)	7 (12.7%)	16 (28.1%)	6 (27.3%)	0.21
Above and below waist	165 (75.7%)	48 (87.3%)	41 (71.9%)	16 (72.7%)	
Face involved[f]					
Yes	155 (71.1%)	42 (76.4%)	46 (80.7%)	13 (59.1%)	0.21
No	63 (28.9%)	13 (23.6%)	11 (19.3%)	9 (40.9%)	
Hospital volume					
<100	160 (62.0%)	26 (40.6%)	48 (76.2%)	2 (7.77%)	<0.01
≥100	98 (38.0%)	38 (59.4%)	15 (23.8%)	24 (92.3%)	
Length of stay					
0-40 days	208 (80.6%)	12 (18.8%)	41 (65.1%)	23 (88.5%)	<0.01
>40 days	50 (19.4%)	52 (81.3%)	22 (34.9%)	3 (11.5%)	
Blood cultures[g]					
Positive	29 (11.6%)	29 (46.0%)	20 (33.3%)	3 (11.5%)	<0.01
Negative	150 (59.8%)	32 (50.8%)	23 (38.3%)	15 (57.7%)	
Non taken	72 (28.7%)	2 (3.2%)	17 (28.3%)	8 (30.8%)	
Operative management[h]					
Yes	232 (90.3%)	63 (98.4%)	58 (93.5%)	24 (92.3%)	0.18
No	25 (9.7%)	1 (1.6%)	4 (6.5%)	2 (7.7%)	

All deceased patients excluded [a]Charlson Co-morbidity Index data missing for n=7; [b]Primary cause of burn injury data missing for n=1; [c]Contact, chemical, friction, electrical, pressurised gas/air (non-flame), radiant heat; [d]Intentional self-harm data missing for n=21; [e]Body area data missing for n= 78; [f]Face involvement data missing for n= 78; [g]Blood culture data missing for n= 18; [h]Operative management data missing for n=3

6.7 PREDICTORS OF DISCHARGE DESTINATION

Table 17 summarises factors associated with discharge destination based on the univariate multinomial regression analyses. Older patients had significantly higher rates of discharge to inpatient rehabilitation or another hospital than home. The same pattern was also seen with %TBSA, patients who intentionally self-harmed and those with a positive blood culture. A higher CCI was significantly associated with being discharged to inpatient rehabilitation or another hospital, as was the presence of an associated inhalation injury.

Both increased age and %TBSA persisted as a factor associated with discharge to inpatient rehabilitation or another hospital as opposed to a place of residence, after adjusting for possible confounders (Table 18). Patients with higher a CCI and positive blood cultures had higher rates of discharge to inpatient rehabilitation than home, after adjusting for possible confounders. Patients who intentionally self-harmed demonstrated greater adjusted odds of being discharged to another hospital when compared to patients discharged home. As there were no patients with self-harm injuries discharged to HITH, a relative risk ratio could not be calculated for this group.

Table 17 Multinomial logistic regression based on disposition (individual factors)

Factor	Rehabilitation or other hospital vs. home N= 127	HITH vs. home N= 26
	Relative Risk Ratio (95% CI; P-value)	
Age	1.04 (1.03, 1.06; p<0.01)	1.01 (0.98, 1.04; p=0.45)
Gender		
Male (reference)	1.00	1.00
Female	1.27 (0.77, 2.10; p=0.35)	0.31 (0.07, 1.37; p=0.12)
Charlson Co-morbidity Index[a]		
0 (reference)	1.00	1.00
1	2.58 (1.49, 4.46; p<0.01)	1.27 (0.45, 3.59; p=0.65)
≥2	5.36 (2.76, 10.40; p<0.01)	0.58 (0.07, 4.61; p=0.61)
Primary cause of burn injury[b]		
Flame (reference)	1.00	1.00
Other	1.26 (0.70, 2.26; p=0.45)	1.15 (0.38, 3.55; p=0.80)
Intentional self-harm[c]		
No (reference)	1.00	1.00
Yes	2.78 (1.52, 5.09; p<0.01)	*
%TBSA quartiles		
20-25% (reference)	1.00	1.00
26-30%	1.65 (0.87, 3.11; p=0.13)	2.56 (1.05, 6.26; p=0.04)
31-49%	2.41 (1.35, 4.31; p<0.01)	0.32 (0.07, 1.52; p=0.15)
>50%	6.21 (3.13, 12.31; p<0.01)	0.49 (0.06, 4.08; p=0.51)
Inhalation injury		
No (reference)	1.00	1.00
Yes	1.80 (1.16, 2.81; p<0.01)	0.73 (0.28, 1.89; p=0.52)
Body area[d]		
Above waist only (reference)	1.00	1.00
Above and below waist	1.15 (0.66, 2.01; p=0.63)	0.79 (0.29, 2.13; p=0.65)
Below waist only	*	*
Face involved[e]		
No (reference)	1.00	1.00
Yes	1.49 (0.87, 2.55; p=0.15)	0.59 (0.24, 1.44; p=0.25)
Case Volume		
≥100 (reference)	1.00	1.00
<100	0.86 (0.55, 1.32; p=0.48)	0.05 (0.01, 0.22; p<0.01)
Blood Cultures[f]		
None taken (reference)	1.00	1.00
Positive	6.40 (3.23, 12.68; P<0.01)	0.93 (0.23, 3.76; p=0.92)
Negative	1.39 (0.77, 2.51; 0.28)	0.90 (0.36, 2.22; p=0.82)
Operative management[g]		
No (reference)	1.00	1.00
Yes	2.61 (0.97, 6.98; p=0.06)	1.29 (0.29, 5.80; p=0.74)

Reference category is Residence (n=258); Deceased patients excluded; *Not enough cases; [a]CCI missing for n=7; [b]Primary cause missing for n=1; [c]Self-harm missing for n=21; [d]Body area missing for n= 78; [e]Face involved missing for n= 78; [f]Blood culture missing for n= 18; [g]Operative management missing for n=3

Table 18 Multinomial logistic regression based on disposition (Adjusted analysis)

Factor	Rehabilitation or other hospital vs. home N= 127	HITH vs. home N= 26
	Relative Risk Ratio (95% CI)	
Age	1.05 (1.03, 1.06; p<0.01)	1.01 (0.98, 1.04; p=0.65)
Gender		
Male (reference)	1.00	1.00
Female	1.37 (0.76, 2.49; p=0.30)	*
Inhalation injury		
No (reference)	1.00	1.00
Yes	0.94 (0.54, 1.64; 0.83)	1.01 (0.36, 2.83; p=1.00)
%TBSA quartiles		
20-25% (reference)	1.00	1.00
26-30%	1.56 (0.75, 3.27; p=0.23)	2.77 (1.06, 7.27; p=0.04)
31-49%	2.65 (1.33, 5.28; p<0.01)	0.37 (0.08, 1.83; p=0.22)
>50%	10.11 (4.42, 23.08; p<0.01)	0.61 (0.07, 5.41; p=0.66)
Charlson Co-morbidity Index[a]		
0 (reference)	1.00	1.00
1	1.89 (1.00, 3.57; p=0.05)	1.34 (0.43, 4.24; p=0.62)
≥2	4.11 (1.92, 8.77; p<0.01)	0.59 (0.07, 5.04; p=0.63)
Intentional self-harm[b]		
No (reference)	1.00	1.00
Yes	2.92 (1.44, 5.90; p<0.01)	*

The reference category for outcome is Residence (N=258); All deceased patients excluded;*Not enough cases
[a]Charlson Co-morbidity Index data missing for n=7; [b]Intentional self-harm data missing for n=21

7 COMPARISON OF BURN SERVICES

There were six sites across five Australian states and New Zealand with case volumes over 50 for the study period and detailed analysis was carried out to investigate cases treated within these centres.

7.1 PROFILE OF PATIENTS AND BURN INJURY EVENT BY BURN SERVICE

Demographic data for these sites are summarised in Table 19. The median age ranged from 31 (Hospital C) to 42 (Hospital B) years. The proportion of patients aged over 55 was lower at Hospital C (10%). This was compared to rates of 16% to 30% across all other sites. Males predominated at all sites (70-79%) (Table 19).

The %TBSA involved was consistent across hospitals A, B, C, D and F, however hospital E significantly differed from all others with a lower proportion of burns greater than or equal to 50% TBSA (12%) than other sites (22-33%) (Table 19). Hospitals C and D had the highest rate of burns involving ≥50% TBSA.

Table 19 Patient demographics based on treating hospital

Characteristics	Hospital A N= 109	Hospital B N= 105	Hospital C N= 63	Hospital D N= 62	Hospital E N= 57	Hospital F N= 53	P-value
Age							
Median (IQR)- years	37 (27-53)	42 (29-56)	31 (22-45)	39 (28-50)	32 (25-45)	40 (27-57)	0.06
Range- years	18-97	18-85	18-93	18-86	18-86	18-77	
Gender							
Male	81 (74.3%)	80 (76.2%)	44 (69.8%)	46 (74.2%)	44 (77.2%)	42 (79.3%)	0.89
Female	28 (25.7%)	25 (23.8%)	19 (30.2%)	16 (25.8%)	13 (22.8%)	11 (20.8%)	
Admission source- Number (%)							
Ambulance from injury scene	10 (9.2%)	61 (58.1%)	19 (30.2%)	19 (30.7%)	30 (52.6%)	18 (34.0%)	<0.01
Inter-hospital transfer	96 (88.1%)	39 (37.1%)	35 (55.6%)	43 (69.4%)	26 (45.6%)	28 (52.8%)	
Other	3 (2.8%)	5 (4.8%)	9 (14.3%)	0	1 (1.8%)	7 (13.2%)	
%TBSA quartiles							
20-25%	28 (25.7%)	27 (25.7%)	18 (28.6%)	15 (24.2%)	23 (40.6%)	10 (18.9%)	0.03
26-30%	23 (21.1%)	32 (30.5%)	7 (11.1%)	11 (17.7%)	11 (19.3%)	9 (17.0%)	
31-49%	34 (31.2%)	19 (18.1%)	17 (27.0%)	17 (27.4%)	16 (28.1%)	20 (37.7%)	
≥50%	24 (22.0%)	27 (25.7%)	21 (33.3%)	19 (30.7%)	7 (12.3%)	14 (26.4%)	

A combination of both partial thickness and full thickness burn types predominated across all sites for all %TBSA (Figure 11). Hospital E had the highest rate of deep partial/full thickness burns, which included 43% of patients with an area of deep partial or full thickness burn and hospital B the lowest rate of deep partial/full thickness burns (6.3%) (Figure 11). Rates of superficial partial thickness burn were generally steady across sites A, C, D and E (27-29%), with site F having the lowest proportion of this type of burn (10%) (Figure 11).

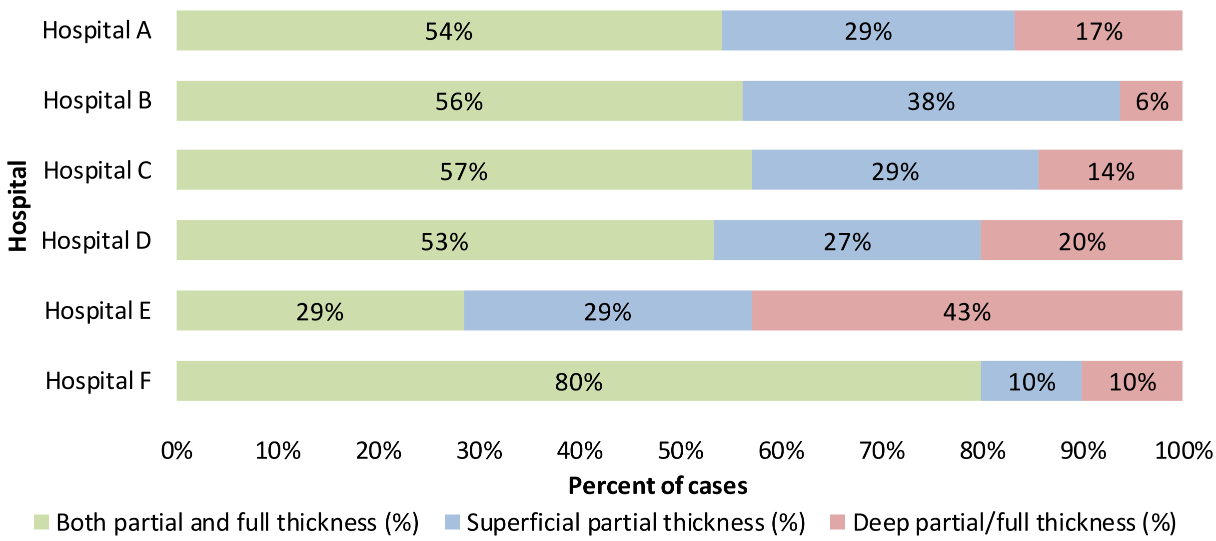


Figure 11 Burn injury depth based on treating hospital

Flame burns were predominant at all sites (Table 20). Similarly, burns tended to mostly occur within the home across most sites (49%-68%). Hospital D had the highest proportion of patients presenting with injuries sustained in a street or trade/service area (24%). Hospitals A and B both had higher rates of patients with an associated inhalation injury (47.6% and 50.5% respectively). Approximately half of the patients admitted to hospitals E and F had injuries where alcohol/drugs may have also been involved, this was higher when compared to other sites where rates ranged from 12% to 28%.

Table 20 Place, action and primary cause that resulted in severe burn injury based on treating hospital

Place, activity and primary cause that resulted in severe burn injury	Hospital A N= 109	Hospital B N= 105	Hospital C N= 63	Hospital D N= 62	Hospital E N= 57	Hospital F N= 53	P-value
Place of burn injury							
Home	68 (64.2%)	48 (48.5%)	38 (67.9%)	39 (62.9%)	28 (51.9%)	27 (52.9%)	<0.01
Street, trade or service area	11 (10.4%)	11 (11.1%)	5 (8.9%)	15 (24.2%)	5 (9.3%)	6 (11.8%)	
Farm, industrial or construction site	14 (13.2%)	14 (14.1%)	0	5 (8.1%)	6 (11.1%)	4 (7.8%)	
Other specified place[a]	13 (12.3%)	26 (26.3%)	13 (23.2%)	3 (4.8%)	15 (27.8%)	14 (27.5%)	
Action when burn injury occurred							
Intentional self-harm	21 (19.6%)	22 (23.2%)	17 (28.8%)	7 (11.5%)	5 (8.9%)	8 (15.1%)	0.03
Leisure activity[b]	28 (26.2%)	33 (34.7%)	19 (32.2%)	20 (32.8%)	19 (33.9%)	14 (26.4%)	
Working[c]	24 (22.4%)	27 (28.4%)	8 (13.6%)	19 (31.2%)	11 (19.6%)	14 (26.4%)	
Other specified activities[d]	34 (31.8%)	13 (13.7%)	15 (25.4%)	15 (24.6%)	21 (37.5%)	17 (32.1%)	
Primary cause of burn injury							
Flame	88 (81.5%)	92 (87.6%)	56 (89.0%)	57 (91.9%)	56 (98.3%)	40 (75.5%)	<0.01
Other specified cause[e]	20 (18.6%)	13 (12.4%)	7 (11.2%)	5 (8.1%)	1 (1.8%)	13 (24.6%)	
Associated inhalation injury							
Yes	55 (50.5%)	50 (47.6%)	16 (25.4%)	31 (50.0%)	16 (28.1%)	17 (32.1%)	<0.01
No	54 (50.5%)	55 (52.4%)	47 (74.6%)	31 (50.0%)	41 (71.9%)	36 (67.9%)	
Alcohol/drugs involved							
Alcohol and/or drugs	12 (12.0%)	17 (19.1%)	14 (27.5%)	10 (19.2%)	26 (48.2%)	15 (51.7%)	<0.01
No alcohol or drugs	88 (88.0%)	72 (80.9%)	37 (72.6%)	42 (80.8%)	28 (51.9%)	14 (48.3%)	

[a]Other specified places include: Residential other than patients home (e.g. friends home), school or public administrative area, sports area or other place of recreation; [b]Leisure activities include hobbies, sports, preparing food/cooking, gardening and other activities with an entertainment element such as going to a cinema, party or dance club; [c]Working includes working for income and household/vehicle maintenance; [d]Other specified activities include: Cleaning, near person preparing food/drink, driving, bathing, sleeping or suspected illegal activity; [e]Other specified causes include: Scald, contact, chemical, friction, electrical, pressurised gas/air (non-flame), radiant heat

Number of missing cases:

Place of burn injury: 3 (Hospital A); 6 (Hospital B); 7 (Hospital C); 3 (Hospital E); 2 (Hospital F)

Activity when burn injury occurred: 2 (Hospital A); 10 (Hospital B); 4 (Hospital C); 1 (Hospital D); 1 (Hospital E)

Primary cause of burn injury: 1 (Hospital A)

7.2 CARE CHARACTERISTICS

Both Hospitals C and E had higher rates of operative treatment for patients than other sites, with 95% of patients from both sites undergoing an operative procedure (Figure 12). The rate of operative management across all other sites ranged from 74% to 85%, which showed no significant variation after the exclusion of hospitals C and E (p-value= 0.28).

The median length of stay was similar between sites ranging from 22 to 28 days (Table 21). The median time to admission from injury was lowest at Hospital B (3 hours). Both Hospitals A and C showed higher times to admission (7 and 10 hours respectively). Time to graft surgery tended to reflect time to admission, with Hospital B having the lowest (median time of 91 hours) and Hospital C the highest (166 hours).

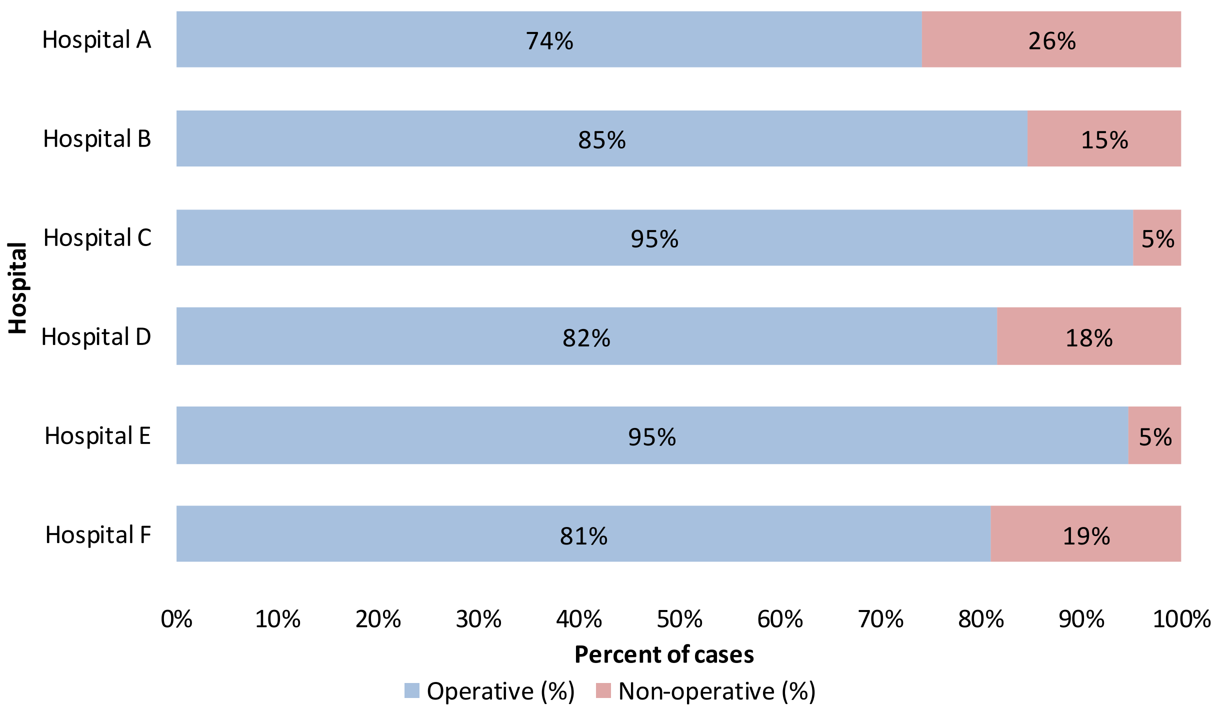


Figure 12 Operative vs. non-operative management based on treating hospital

Table 21 Care characteristics based on treating hospital

Characteristics	Hospital A N= 109	Hospital B N= 105	Hospital C N= 63	Hospital D N= 62	Hospital E N= 57	Hospital F N= 53	P-value
Length of stay							
Median (IQR)- years	27.0 (14-44)	25.6 (12-43)	25.8 (13-45)	27.7 (15-47)	23.0 (18-51)	21.6 (10-38)	0.79
Range- days	0.2-154.7	0.2-166.8	0.2-114.8	0.1-185.4	2.2-139.0	0.1-237.5	
Length of stay quartiles							
0-20 days	41 (37.6%)	42 (40.0%)	26 (41.3%)	23 (37.7%)	26 (45.6%)	25 (47.2%)	0.85
21-40 days	36 (33.0%)	35 (33.3%)	19 (30.2%)	17 (27.9%)	12 (21.1%)	16 (30.2%)	
≥41 days	32 (29.4%)	28 (26.7%)	18 (28.6%)	21 (34.4%)	19 (33.3%)	12 (22.6%)	
Time frame (Hours)- Median (IQR)							
Injury to admission	7.1 (5-9)	2.5 (1.3, 4.5)	9.8 (2-43)	4.8 (3-7)	4.3 (2-8)	4.1 (2-9)	<0.01
Injury to burns team assessment	9.0 (6-15)	5.5 (3.3, 10.4)	19.9 (11-75)	5.1 (3-7)	6.3 (2-9)	8.3 (4-25)	<0.01
Admission to surgeon assessment	7.2 (5-29)	9.6 (4.8, 21.6)	12 (5-19)	31.2 (2-58)	7.2 (2-17)	7.2 (2-10)	0.41
Admission to graft surgery	100.8 (48-158)	91.2 (22-166)	165.6 (120-334)	88.8 (46-161)	127.2 (70-228)	130.8 (60-218)	<0.01

Number of missing cases:

Injury to admission: 8 (Hospital A); 28 (Hospital B); 12 (Hospital C); 17 (Hospital D); 20 (Hospital E); 25 (Hospital F)

Injury to burns team assessment: 37 (Hospital B); 2 (Hospital C); 12 (Hospital D); 1 (Hospital E); 5 (Hospital F)

Admission to surgeon assessment: 58 (Hospital A); 26 (Hospital B); 38 (Hospital C); 59 (Hospital D); 46 (Hospital E); 32 (Hospital F)

Admission to graft surgery: 52 (Hospital A); 48 (Hospital B); 22 (Hospital C); 28 (Hospital D); 6 (Hospital E); 25 (Hospital F)

Hospital E was the only site to routinely use skin cell products (i.e. CEA) for burn wound grafting (Figure 13). Hospitals C and D were the only other sites to use CEA. The most common unique operative procedure across all sites for all burn severities was debridement and autologous grafting (Figure 13). Integra was mostly used in higher %TBSA burns. Hospitals F and E used the product in 25% and 15% of burn injuries of 50% TBSA or greater, respectively. Hospital A was the only burn service not to use Integra and hospitals C and E were the only services to use Biobrane, which was mainly used to treat lower %TBSA burns (Figure 13). Positive blood culture rates were highest amongst Hospitals C and E, where 43% and 40% of cultures taken were positive, respectively (Table 22). This compared with positive rates of 20% to 32% across all other sites. Almost every patient admitted to hospital D had a blood culture taken (98%), with less than a quarter yielding a positive result (Table 22).

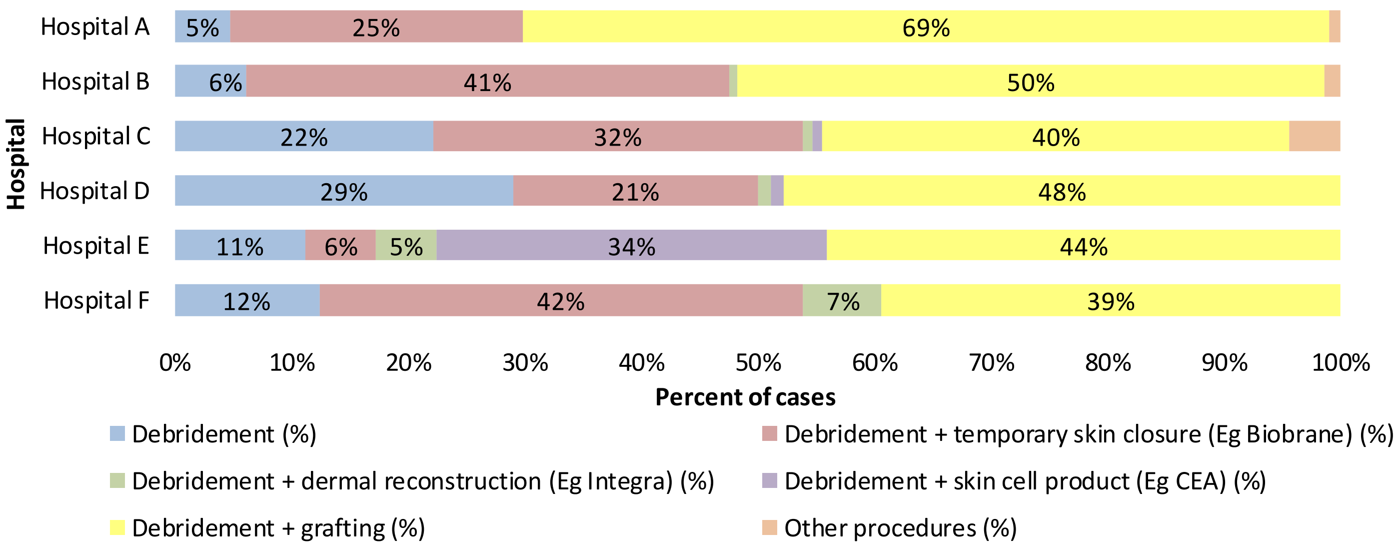


Figure 13 Procedure undertaken based on treating hospital

Table 22 Blood cultures based on treating hospital

Culture status	Hospital A N= 109	Hospital B N= 105	Hospital C N= 63	Hospital D N= 62	Hospital E N= 57	Hospital F N= 53	P-value
Culture taken							
Yes	90 (82.6%)	72 (68.6%)	44 (78.6%)	51 (98.1%)	25 (43.9%)	37 (69.8%)	<0.01
No	19 (17.4%)	33 (31.4%)	12 (21.4%)	<5	32 (56.1%)	16 (30.2%)	
Culture positive							
Yes	23 (25.6%)	20 (27.8%)	19 (43.2%)	10 (19.6%)	10 (40.0%)	12 (32.4%)	0.13
No	67 (74.4%)	52 (72.2%)	25 (56.8%)	41 (80.4%)	15 (60.0%)	25 (67.6%)	

Number of missing cases:
Blood cultures taken: 17

There were no significant differences between burn services in terms of mortality (P-value= 0.47) (Figure 14). Mortality rates were lowest amongst Hospital E patients (13%) and half of these in-hospital deaths were unexpected. Just over a quarter of patients were discharged to home by Hospital B (28%). However, nearly half of Hospital B patients were discharged to either inpatient rehabilitation (24%) or HITH (24%). Hospital E was the only other centre to use HITH (4%), though the majority of patients were discharged back to a place of residence (79%).

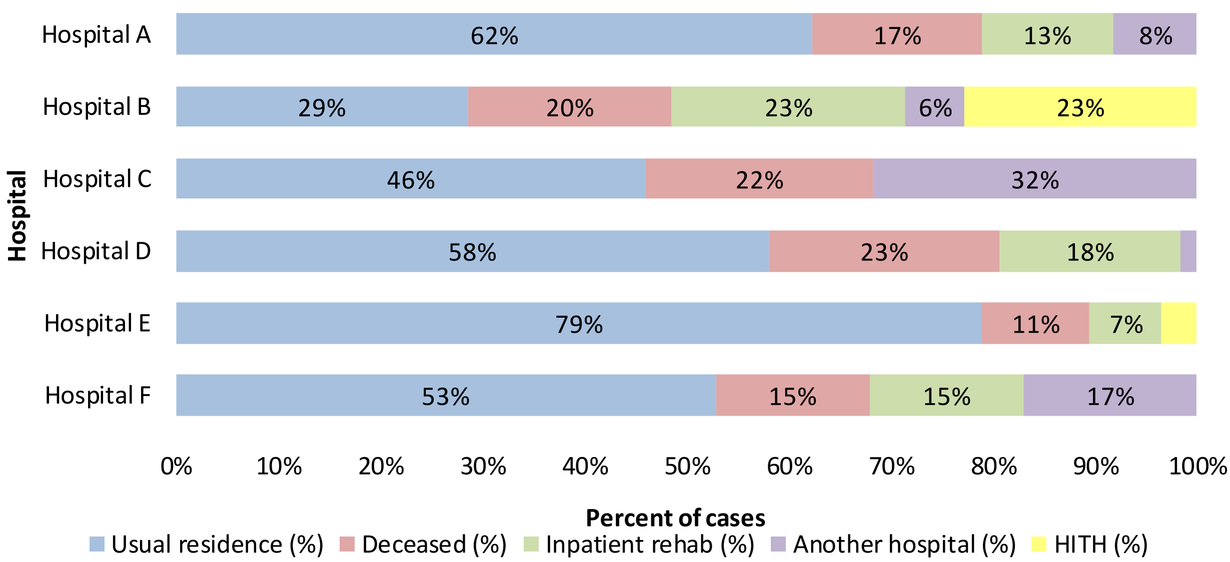


Figure 14 Disposition based on treating hospital

8 DISCUSSION

This chapter discusses the major findings of the descriptive epidemiology of severe burns (≥20% TBSA) in adults presenting to burn services contributing to the burns registry of Australia and New Zealand. The implications of these findings, and others relating to surgical management, mortality, LOS, discharge destination and burn service comparisons are also presented in this chapter.

8.1 KEY FINDINGS

As discussed previously there was a lack of published data describing the epidemiology of severe burn injuries in adults. Whilst some data was available, it was in the form of small regional based studies or subset analysis from review papers. Novel data presented in this thesis included a detailed description of the epidemiology of adult severe burn injuries in Australia and New Zealand, significant independent risk factors for death, LOS and factors associated with different discharge destinations.

8.2 THE EPIDEMIOLOGY OF ADULT PATIENTS WITH SEVERE BURNS IN AUSTRALIA AND NEW ZEALAND

There was a predominance of flame type injuries in the home, primarily affecting males aged between 18-55. In total 84 patients died corresponding to a mortality rate of 17% for the total population. The median length of stay for severe burns in Australian and New Zealand adults was 24 days with home representing the most common discharge destination (over 50% of cases).

No studies based on Australian or New Zealand adult populations have specifically investigated the epidemiology of severe burn injuries. Previous investigations were limited to regional based studies in New South Wales, Queensland and Victoria [1, 11-13]. The results of this thesis describe the epidemiology of severe burn injuries in adults on a scale and level of detail that such regional studies are not able to do. This study demonstrated that severe burn injuries in adults were relatively uncommon, accounting for 496 of the 10224 (4.9%) cases enrolled in BRANZ up until June 2013. The proportion of burn injury patients with severe injuries admitted to regional burn centres in a number of different studies ranged from 8% to 31% [23, 29, 33, 42]. These figures were higher than those found in this thesis. Both the NBR in the USA and a single centre study involving 1,063 cases from Hong Kong quoted severe burn injury proportions of 8% [29, 33]. The NBR and BRANZ were comparable in terms of patient demographics, burn injury characteristics and human development index (HDI) [31, 166].

These differences in burn severity admission numbers have also been noted in previous BRANZ reports [31]. It is possible that in the USA, a higher proportion of burn injuries were managed at non-burns unit hospitals, as compared to Australia and New Zealand where there was a greater compliance with admission guidelines [31]. It is also possible that in Australia and New Zealand a greater proportion of patients were admitted to dedicated burn services with less severe injuries that could have been managed elsewhere [31]. This may have also accounted for the lower proportion of admitted patients with severe injuries when compared with the cohort from Hong Kong [33]. The highest proportions were seen in a Brazilian (31%) and North Eastern Chinese (20%) cohort of patients [23, 42]. These dramatically higher proportions of severe burn injuries amongst adults were likely the result of a combination of factors, including higher rates of work-related flame injuries and inadequate safety equipment [23, 42]. In the Brazilian study by De-Souza et al, it was noted that there were high numbers of suicide attempts by adult women from low socioeconomic backgrounds and poor living conditions which may have contributed to the higher number of severe burn injuries reported [42].

Severe burn injuries in BRANZ patients predominantly occurred in males aged 18-55. Data from other Australian and international studies investigating high income countries was consistent with a male predominance in adults, regardless of burn size [18, 21, 25, 31, 48]. This pattern was not consistent though, with a number of LMICs in South Asia demonstrating a higher proportion of female patients, particularly amongst adolescent and older women who sustain burn injuries in the kitchen [22]. A review of all burn injuries in LMICs by Forjuoh found amongst adults the number of burns was relatively low until the ages of 30-39 [43]. For patients in this thesis there was a consistent step-wise decrease in injury frequency from decade to decade.

Flame type burn injuries (86% of total) in the home (58% of total) constituted the majority of cases presenting to Australian and New Zealand burn units with scald burns most prevalent in elderly patients accounting for 32% of severe burns in those aged ≥75 years of age. This was consistent with other higher income countries [12, 18, 21, 22, 29-31]. In LMICs work-place injuries were more frequent than those seen in the BRANZ (14% of severe burns in this thesis) [24, 32]. Amongst adults with burns of all sizes in LMICs Forjuoh found most occurring within the home, outdoors and work places in roughly equal proportions [43]. For burns greater than or equal to 20%TBSA Forjuoh noted a predominance of flame type injuries in LMICs [43]. Data from the international Burn Injury Database (iBID) for England and Wales demonstrated a predominance of flame type burns in adult males aged 16-64 (27%) compared with scald burns (17%) [30]. This changed to 23% and 36% for flame and scald injuries, respectively, for women of the same age group (though this did include burns of <20% TBSA).

Patients did not significantly differ in terms of age and gender from site to site, and this was not surprising given most burn centres included in this thesis were located within major urban centres. However, there were significant variations in terms of place of burn injury, action when the injury occurred, primary cause of burn, an associated inhalation injury and the involvement of drugs and/or alcohol. Though these proportions were sporadic in nature, and differences generally weren't correlated with burn service size or patient volume suggesting other underlying factors that may have been regionally specific. Another possibility may have been that better recording practices were observed at certain sites, accounting for the variations between burn services.

A significant difference in terms of %TBSA was observed between burn services, and this was identified as relating to hospital E which had a significantly lower proportion of burns of 50% TBSA or greater, and higher proportion of burns less than or equal to 25% TBSA (Table 19). When Hospital E was excluded from comparative analysis, no significant differences were observed between sites in terms of %TBSA, despite differing case volumes. There was a general pattern towards increasing hospital volume and higher %TBSA. This was in keeping with results from the NBR, where %TBSA did not significantly differ between low volume (<100 initial admissions per year), medium volume (100-300 initial admissions per year) or high volume (>300 initial admissions per year) centres [29]. The difference observed between hospital E and all other sites may represent a systematic bias, where burn size is assessed, recorded or coded differently to other sites, or it may be related to regional differences.

Despite having the lowest proportion of 50% TBSA or greater burns of all included burn services, hospital E had by far the largest proportion of patients with an area of deep partial/full thickness burn (43%). The closest other service was hospital D with 20% (Figure 11). Again it was not clear if site specific assessment or coding practices differed at this site, or if these differences were the result of regional or demographic based factors.

8.3 THE MANAGEMENT OF ADULT PATIENTS WITH SEVERE BURNS IN AUSTRALIA AND NEW ZEALAND

A wide variety of surgical management options and products are available for the management of burn injury. In this cohort over 85% of patients underwent at least one operative procedure. Data from a 10-year review of the USA's NBR revealed 54% of patients had at least one surgical procedure [167]. This included all ages and burn severities and thus was in keeping with the fact that only more severe injuries were included in this cohort of patients. Comparison of the types of management observed in the BRANZ cohort with other studies is challenging due to the paucity of published studies describing the surgical management of adults with severe burns.

A total of 719 unique procedures were recorded for 420 BRANZ patients who had at least one operation. The most common unique procedure undertaken was debridement and grafting which was performed a total of 341 times (47% of all procedures undertaken). Debridement and autologous skin grafting was the most common procedure across all %TBSA quartiles. The observed rates of autologous skin grafting was consistent with previously reported data for all BRANZ patients. For adults with any severity of burn, debridement and skin grafting accounted for between 47%-69% of procedures [31]. Rates of use of Biobrane and CEA were also similar between the entire BRANZ adult patient population when compared to those with the severe burn cases from BRANZ presented in this thesis. However, the largest discrepancy was seen with the use of Integra, which was used more often in severe burns. For example, 6% of the procedures performed in adults with 50% TBSA burns or greater used Integra. This was compared with no procedures using Integra in burns of 20-25% TBSA in adults. Direct comparisons of surgical management techniques for severe burn injuries in adults were sparse (Table 3). In a meta-analysis of early excision of burns by Ong et al in 2006, only 15 prospective randomised controlled trials investigating early excision and immediate grafting of burns from a search spanning 38 years were found [55]. Of these only six met the papers inclusion criteria [55]. These criteria allowed the inclusion of all ages and burn severity, and sought papers where the intervention was early excision with immediate grafting being compared with patients treated with dressings only followed by delayed grafting after eschar separation. Of these six papers only two specifically investigated adults with severe burn injuries, however they were excluded from the literature review in this thesis as they were published over 25 years ago [55].

In terms of burn service comparisons, both hospitals C and E had significantly higher rates of operative management (95%, respectively) when compared with all other sites (74% to 85%). Whilst hospital E had the lowest proportion of ≥50% TBSA burns, it did have the highest rate of deep partial or full thickness burns, which may have accounted for the increased rate of operative management. Hospital C had a %TBSA profile similar to all other services, as well as similar depth profiles. However, it may have been that patients presenting to hospital C had a higher percent area of deep partial or full thickness burns, which may have accounted for an increased operative load. Another explanation could have been differences in surgical practices at this site.

The surgical procedures used at each site were heterogeneous. Debridement and grafting was used consistently across all sites, in keeping with this being recognised as the gold standard of care [54-58]. The use of CEA skewed the results somewhat, as it was only used routinely at one site (hospital E) which had lower rates of use of Biobrane when compared with all other sites. The diverse use of various surgical management techniques for severe burn wounds across burn services was in keeping with a lack of high quality studies investigating their use in this population. However, differences in management practises amongst different burn services may also be a consequence of differences in patient characteristics between units. It may also be that different units have evolved different treatment practices that are appropriate for their resources and models of care.

Hospital D appeared to take blood cultures routinely, with almost all patients at this burn service (98%) having a culture taken. This was significantly higher than most other burn services (Table 22). Despite this approach, there was no significant increase in positive culture results, in keeping with evidence that suggests blood cultures represent an over-used investigation that should only be performed when clinically indicated [104].

8.4 PREDICTORS OF OUTCOME ADULT PATIENTS WITH SEVERE BURNS IN AUSTRALIA AND NEW ZEALAND

The mortality rate of adults with severe burn injuries admitted to burn services in Australia and New Zealand was 17%. Survivors were younger, female in gender, had fewer co-morbidities, lower rates of intentional self-harm and inhalation injury, lower %TBSA and more often were treated with at least one operative procedure (Table 9). Similar mortality rates have been demonstrated in adults with severe burn injuries in high-income countries such as the USA and regions throughout Europe [18, 29]. For example, in the USA the mortality rate amongst adults with severe burn injuries between 2005 and 2014 was 27%, and down to 19% for those aged between 16 and 60-years [29]. Mortality rates in LMICs with these types of injuries were poorly reported [43]. However higher rates have been described in such patients, with one study from Brazil demonstrating a mortality rate of 33% in adults with severe burn injuries [42].

Older age, intentional self-harm, higher %TBSA and an associated inhalation injury were identified as independent risk factors for death in adults with severe burn injuries (Table 11). Neither flame type burns nor burns involving the face were identified as significant risk factors for death in BRANZ patients. These results were in keeping with previously published literature [18, 25, 48, 101, 119, 120, 123, 124]. The percent of body area affected by full thickness burn was also investigated in this study but not included in the univariate model given the heterogeneous nature of assessment and lower rates of data completeness. Whilst it was identified as a potentially important predictor of mortality, the percent of full thickness burn was thought to be linked to %TBSA; thus only %TBSA was included in this mortality model.

Previously published literature has identified patient co-morbidities as a possible predictor of mortality in burn injuries [5, 133, 134, 136]. However, in this cohort of patients there was a significant association between survival and a *higher* CCI, despite adjusting for possible confounders such as %TBSA and age. Upon further investigation it was found that close to 88% of deaths within 24-hours of admission had a CCI of 0. Thus it may have been that in cases of such early deaths there had been no time to record or collect information on patient co-morbidities, and this association may have been the result of missing data rather than a true relationship. Of patients aged 55 and older discharged within 24-hours, 90% had a CCI of 0. This compared with 38% of patients aged 55 and older who were discharged after 24-hours who had a CCI of 0. This reinforces the proposition that patients discharged within 24-hours may have had a tendency to have incomplete co-morbidity data recorded. Nevertheless, a total of 446 patients had ICD-10 data recorded which equated to a 90% completeness rate. Thus other unknown interactions may have also played a role in the observed result.

Whilst previous studies have identified associations between female gender and higher rates of mortality, no such association was identified in adult BRANZ patients with severe burns [18, 21, 22, 126, 145, 146]. Though the results presented here are in keeping with other studies which also found no association between female gender and mortality [18]. Clear reasons for these discrepancies are yet to be proven, though the fact that this study cohort was based on adults with injuries of 20% TBSA or greater may have played a role.

Subset analysis was carried out on deceased patients to investigate differences between patients who died early (i.e. within 24-hours) and those who died after 24-hours from arrival to the burn service (Table 12). Initially this analysis was carried out comparing patients where treatment was withdrawn (commenced and then stopped) or withheld (palliation on arrival) vs. active treatment leading to unexpected death. Though approximately 27% of deceased patients had no data relating to withdrawal/withholding of active treatment. Thus death within 24-hours of admission was used as a surrogate marker for this variable as most patients where treatment was withheld or withdrawn died within 24-hours of admission. Only one patient (2.9%) deemed an unexpected death died within 24-hours of admission. This was secondary to a condition unrelated to their burn injury. Of note, no significant associations were found between death within 24-hours and age, gender or %TBSA. The importance of %TBSA to prognosis has been well established [101, 119, 121]. One explanation for no observed association between %TBSA and death within 24-hours could have been that the number of patients who died with TBSA burns of <50%TBSA were too low; thus concealing a significant causal relationship. Of deceased patients there were only 23 instances (27%) of burns of <50%TBSA.

Length of stay was shown to be increased by a higher age, inhalation injury, increased %TBSA, higher CCI and self-inflicted injury on multivariate analysis. This was an area not well researched, and available data was often heterogeneous, with many studies failing to specify if they reported on survivors or total populations. Whilst previous studies have identified %TBSA as an important factor in increasing LOS, in particular identifying average LOS/%TBSA, there was little data assessing other factors in adults with severe burns [28, 102, 103]. In BRANZ patients, the median LOS roughly correlated with %TBSA for burns up to 50% TBSA, as demonstrated in Table 13, which was in keeping with other published data [28, 102, 103]. No previous studies were identified that specifically investigated or modelled predictors of discharge destination. On multivariate analysis older age, increased %TBSA, higher CCI and intentional self-harm were associated with discharge to either rehab or another hospital when compared to discharge to a place of residence. These results were in keeping with more severe injuries, or patients with lower physiological reserve, requiring extended rehabilitation, hospital care and treatment times.

There was a significant association between death and no blood cultures taken on univariate analysis (Table 10). This was because many patients (87%) who died within 24-hours had no blood cultures taken. Thus the significant association between risk of death and no blood cultures being taken was a spurious result and excluded from multivariate analysis. There was also a significant association between operative management and survival, which would be expected (Table 10). However, patients with injuries deemed un-survivable and where treatment was withheld would not have been offered an operative procedure. Thus in this patient population the association between receiving at least one operative procedure and survival was causally related to burn severity rather than an accurate assessment of the impact of operative management on survival. For this reason, it was excluded from multivariate analysis. All other variables identified as being associated with mortality on univariate analysis were included in the multivariate model (Table 11).

Comparison of individual burn services showed that both Hospitals B and F reported zero unexpected deaths, which may have reflected differences in data coding at different burn services, as this would be unexpected in a population of severe burn injury admissions over a three-year period. Despite differences in case volume, severity, burn injury characteristics and management amongst some services there was no significant difference in terms of mortality rate (P-value= 0.47) amongst included hospitals. It may have been that the lack of significance was related to lower case numbers which may change as more data accumulates. Nevertheless, this was in contrast to data from the NBR which demonstrated a significant difference in mortality rates amongst included USA burn services [29]. Differences between sites in terms of discharge destination for survivors was significant, with some sites more often utilising transfer to other hospitals or inpatient rehabilitation services than other services. This was likely due to local practices and some burn services having larger geographical catchment areas, and thus transferring patients closer to home rather than discharging immediately from their service.

8.5 STRENGTHS AND LIMITATIONS

The use of prospectively collected data from the Burns Registry of Australia and New Zealand provides a number of advantages. Firstly, it provided data from a wide-range of geographical locations and was far more inclusive of patients when compared to local single-centre derived cohorts. This enabled greater patient capture and more reliable data.

Secondly, quality assurances for data collection were in place to ensure more accurate collection and recording of information. Such quality assurances included the BRANZ steering committee, a formalised governance structure with support from ANZBA and local burn services, appropriate ethics approvals for all sites involved, dedicated data collectors with formal training, regular reviews of dataset definitions, validity and database functionality checks and regular reporting of results in the form an annual BRANZ report [10]. Many of these formalised quality checks are unique to registries, which helped to ensure the data presented in this thesis was accurate, reliable and adequately captured a large sample of the adult Australian and New Zealand population affected by severe burns.

Thirdly, this thesis represents that largest epidemiological review of adult severe burns in Australia and New Zealand. It is also one of few dedicated reports investigating this type of injury. Whilst there were a multitude of regional based epidemiological reports investigating burn injuries, there were few published multicentre studies and none that could be found specifically describing severe burn injuries in adults.

Whilst the BRANZ provided a robust method of review for this thesis, there were a number of limitations. Being a relatively new registry data for this thesis was taken from 2009-13 and included a total of 496 patients from a pool of over 10224 cases in the BRANZ. This was much lower than the numbers seen in comparable registries from the USA's NBR (203,422 cases from 2005-14) and the iBID from England and Wales (81,181 cases from 2003-11) [29, 30]. The smaller patient population was compounded by the fact that data from one centre in North

Eastern Australia (the Royal Brisbane Hospital) was not included in this thesis as ethics approval for this site was not obtained until 2015. This meant a lack of data from burns patients in the Australian state of Queensland, which has a total population of over 4.8 million people [168]. In addition to this, the shorter time period of operation of the BRANZ has meant temporal comparisons and assessment of trends in burn injuries, care and outcomes was not yet possible and thus could not be performed in this thesis.

Whilst there were a number of processes in place to ensure high levels of completeness and accuracy for entered data, there were a number of variables that depended on subjective assessment and may have differed in interpretation from site to site. For example, the assessment of %TBSA, depth and body areas involved were assessed clinically by burn clinicians, and thus may be subject to misclassification given the subjective nature of assessment. This effect was minimized by having a standardised protocol for %TBSA assessment (i.e. the 'rule of 9's) and clearly defined body areas and depth guidelines [31]. Assessing burn depth was more complex and resulted in a lower than average rate of completion (entered for 69% of cases). This was because there were a number of different nomenclatures in use, and assessment can be difficult in large complex burn injuries. However a standardised approach to assess, record and input burn depth was used within the BRANZ to maximise the accuracy of burn depth recordings [29, 31]. Caution must also be taken when interpreting some results where variables with low numbers were included, for example predictors of disposition.

In Australia and New Zealand, and thus the BRANZ, all depths were recorded as either superficial dermal, mid dermal, deep dermal or full thickness [31]. As described in the methods, these results were then presented in this thesis in the form of superficial partial thickness (superficial dermal and mid dermal) or deep partial/full thickness for the sake of simplicity [31]. However, in the USA for example, the traditional nomenclature of first, second and third degree burns was used, making direct comparisons difficult [29]. Inhalation injury also represented a difficult factor to assess as no formalised definition exists [31]. Thus the presence of an associated inhalation injury may have been assessed differently across BRANZ sites. Patients were designated as having an inhalation injury if it was documented in the patient history, however site specific definitions differed and were based on varying combinations of a history of smoke exposure, clinical presentation and diagnostic investigations [31].

8.6 SUMMARY AND RECOMMENDATIONS FOR FUTURE RESEARCH

This thesis has described in detail the epidemiology of severe burn injury in adults in Australia and New Zealand. This has added to the body of literature published from regions elsewhere whilst also providing a comprehensive description of the epidemiology of a serious cause of mortality and morbidity locally, which has not been done before. There still remains a lack of data from middle-low income countries and future epidemiological studies and/or dedicated registries are needed to further investigate burn injury populations in these areas.

Important issues raised by this thesis included a lack of clarity with regards to the reporting of severe burn injury incidence, and different admission and transfer practices that may influence relative %TBSA and reported mortality rates. From a public health perspective population based data about incidence and outcomes is important, but most reports are from hospitals that, for example, may only admit patients for treatment if they are thought to have a reasonable chance of survival. Many of these reports may be relatively opaque in terms of which patients get admitted and the lack of a standardized approach to reporting makes it very difficult to compare outcomes. This thesis also included data on the surgical management of severe burn injuries in adults, however more data is required.

Thus it is recommended that reports should always provide data on variables such as %TBSA and age to enable subgroup analysis, that definitions of children, adults and elderly be standardized and that agreements on relevant ways to report incidence, inhalation injury and burn depth and clarity as to what cases are captured also be standardised. In addition, higher quality comparative studies are required to better investigate the treatment of severe burn injuries, given the paucity of data in this area. Finally, some of the differences identified in this thesis between burn services in terms of burn severity, management regimens and discharge practices highlight the need to ensure coding and documentation practices amongst reporting sites is homogeneous.

This thesis sets the foundations for further research from the BRANZ which may include further research into management, particularly with regards to newer treatment modalities such as CEA and other biological skin replacement products. Other potential research areas include outcomes based on different management techniques and temporal studies in the future to assess for changes in terms of demographics, management and outcomes since the implementation of BRANZ.

9 REFERENCES

1. Wasiak, J., et al., *The epidemiology of burn injuries in an Australian setting, 2000-2006.* Burns, 2009. **35**(8): p. 1124-32.
2. Greenwood, J.E., R. Tee, and W.L. Jackson, *Increasing numbers of admissions to the adult burns service at the Royal Adelaide Hospital 2001-2004.* ANZ J Surg, 2007. **77**(5): p. 358-63.
3. Watterson, D., et al., *Level of agreement between coding sources of percentage total body surface area burnt (%TBSA).* HIM J, 2011. **40**(1): p. 21-4.
4. Jeschke, M.G., et al., *Burn size determines the inflammatory and hypermetabolic response.* Crit Care, 2007. **11**(4): p. R90.
5. Germann, G., et al., *The impact of risk factors and pre-existing conditions on the mortality of burn patients and the precision of predictive admission-scoring systems.* Burns, 1997. **23**(3): p. 195-203.
6. Turner, D.G., et al., *The revised burn diagram and its effect on diagnosis-related group coding.* J Burn Care Rehabil, 1996. **17**(2): p. 169-74.
7. Wallis, K.L., et al., *Surviving "Payment by Results": a simple method of improving clinical coding in burn specialised services in the United Kingdom.* Burns, 2009. **35**(2): p. 232-6.
8. Cleland, H., et al., *Clinical application and viability of cryopreserved cadaveric skin allografts in severe burn: a retrospective analysis.* Burns, 2014. **40**(1): p. 61-6.
9. Cleland, H., *Burn care in Australia.* ANZ J Surg, 2006. **76**(9): p. 768.
10. Watterson, D., et al., *Developing the first Bi-National clinical quality registry for burns--lessons learned so far.* Burns, 2012. **38**(1): p. 52-60.
11. Pegg, S.P., *Burn epidemiology in the Brisbane and Queensland area.* Burns, 2005. **31 Suppl 1**: p. S27-31.
12. Duggan, D. and S. Quine, *Burn injuries and characteristics of burn patients in New South Wales, Australia.* Burns, 1995. **21**(2): p. 83-9.
13. Goltsman, D., et al., *Geospatial and epidemiological analysis of severe burns in New South Wales by residential postcodes.* Burns, 2014. **40**(4): p. 670-82.
14. Watterson, D., et al., *Developing clinical quality indicators for a Bi-National Burn Registry.* Burns, 2011. **37**(8): p. 1296-308.
15. Peck, M.D., *Epidemiology of burns throughout the world. Part I: Distribution and risk factors.* Burns, 2011. **37**(7): p. 1087-1100.
16. *WHO | Burns*. 2015 [cited 2015 29/11/2015]; Available from: http://www.who.int/violence_injury_prevention/other_injury/burns/en/.
17. Blais, M., et al., *Concise review: tissue-engineered skin and nerve regeneration in burn treatment.* Stem Cells Transl Med, 2013. **2**(7): p. 545-51.
18. Brusselaers, N., et al., *Severe burn injury in Europe: a systematic review of the incidence, etiology, morbidity, and mortality.* Crit Care, 2010. **14**(5): p. R188.
19. *ISBI*. 2015 [cited 2015 29/11/2015]; Available from: http://www.worldburn.org.
20. Albornoz, C., et al., *Analysis of the burns profile and the admission rate of severely burned adult patient to the National Burn Center of Chile after the 2010 earthquake.* Burns, 2011. **37**(4): p. 678-81.
21. Othman, N. and D. Kendrick, *Epidemiology of burn injuries in the East Mediterranean Region: a systematic review.* BMC public health, 2010. **10**: p. 83.
22. Golshan, A., C. Patel, and A.A. Hyder, *A systematic review of the epidemiology of unintentional burn injuries in South Asia.* J Public Health (Oxf), 2013. **35**(3): p. 384-96.
23. Jie, X. and C.B. Ren, *Burn injuries in the Dong Bei area of China: a study of 12,606 cases.* Burns, 1992. **18**(3): p. 228-32.
24. Forjuoh, S.N., *Burns in low- and middle-income countries: A review of available literature on descriptive epidemiology, risk factors, treatment, and prevention.* Burns, 2006. **32**(5): p. 529-537.

25. Stylianou, N., I. Buchan, and K.W. Dunn, *A model of British in-hospital mortality among burns patients.* Burns, 2014. **40**(7): p. 1316-21.
26. Dokter, J., et al., *Epidemiology and trends in severe burns in the Netherlands.* Burns, 2014. **40**(7): p. 1406-14.
27. Harats, M., et al., *Burns in Israel, comparative study: Demographic, etiologic and clinical trends 1997-2003 vs. 2004-2010.* Burns, 2015.
28. den Hollander, D., et al., *Epidemiology and referral patterns of burns admitted to the Burns Centre at Inkosi Albert Luthuli Central Hospital, Durban.* Burns, 2014. **40**(6): p. 1201-8.
29. *National Burn Repository: Report of Data from 2005-2014.* American Burn Association, 2015.
30. Stylianou, N., I. Buchan, and K.W. Dunn, *A review of the international Burn Injury Database (iBID) for England and Wales: descriptive analysis of burn injuries 2003-2011.* BMJ Open, 2015. **5**(2): p. e006184.
31. *Burns Registry of Australia and New Zealand Annual report 2009-2013.* Australia and New Zealand Burns Association, 2014.
32. Nthumba, P.M., *Burns in sub-Saharan Africa: A review.* Burns, 2015.
33. Ho, W.S. and S.Y. Ying, *An epidemiological study of 1063 hospitalized burn patients in a tertiary burns centre in Hong Kong.* Burns, 2001. **27**(2): p. 119-23.
34. Tang, K., et al., *Characteristics of burn patients at a major burn center in Shanghai.* Burns, 2006. **32**(8): p. 1037-43.
35. Kobayashi, K., et al., *Epidemiological and outcome characteristics of major burns in Tokyo.* Burns, 2005. **31 Suppl 1**: p. S3-S11.
36. Nakae, H. and H. Wada, *Characteristics of burn patients transported by ambulance to treatment facilities in Akita Prefecture, Japan.* Burns, 2002. **28**(1): p. 73-9.
37. Chen, S.H., et al., *Epidemiology of burns in Taiwan: a nationwide report including inpatients and outpatients.* Burns, 2014. **40**(7): p. 1397-405.
38. Song, C. and A. Chua, *Epidemiology of burn injuries in Singapore from 1997 to 2003.* Burns, 2005. **31 Suppl 1**: p. S18-26.
39. Seo, D.K., et al., *Epidemiological trends and risk factors in major burns patients in South Korea: a 10-year experience.* Burns, 2015. **41**(1): p. 181-7.
40. Franco, M.A., et al., *Epidemiological and clinical profile of burn victims Hospital Universitario San Vicente de Paul, Medellin, 1994-2004.* Burns, 2006. **32**(8): p. 1044-51.
41. Ortiz-Prado, E., L. Armijos, and A.L. Iturralde, *A population-based study of the epidemiology of acute adult burns in Ecuador from 2005 to 2014.* Burns, 2015. **41**(3): p. 582-9.
42. De-Souza, D.A., W.G. Marchesan, and L.J. Greene, *Epidemiological data and mortality rate of patients hospitalized with burns in Brazil.* Burns, 1998. **24**(5): p. 433-8.
43. Forjuoh, S.N., *Burns in low- and middle-income countries: a review of available literature on descriptive epidemiology, risk factors, treatment, and prevention.* Burns, 2006. **32**(5): p. 529-37.
44. Garner, W.L. and M. Reiss, *Burn care in Los Angeles, California: LAC+USC experience 1994-2004.* Burns, 2005. **31 Suppl 1**: p. S32-5.
45. Ahuja, R.B., J.K. Dash, and P. Shrivastava, *A comparative analysis of liquefied petroleum gas (LPG) and kerosene related burns.* Burns, 2011. **37**(8): p. 1403-10.
46. Dongo, A.E., et al., *A five-year review of burn injuries in Irrua.* BMC Health Serv Res, 2007. **7**: p. 171.
47. Agbenorku, P., et al., *Burn disasters in the middle belt of Ghana from 2007 to 2008 and their consequences.* Burns, 2010. **36**(8): p. 1309-15.
48. Stylianou, N., et al., *Mortality risk prediction in burn injury: Comparison of logistic regression with machine learning approaches.* Burns, 2015. **41**(5): p. 925-34.
49. Pham, C., et al., *Bioengineered skin substitutes for the management of burns: a systematic review.* Burns, 2007. **33**(8): p. 946-57.

50. Jones, I., L. Currie, and R. Martin, *A guide to biological skin substitutes.* Br J Plast Surg, 2002. **55**(3): p. 185-93.
51. Hansen, S.L., et al., *Using skin replacement products to treat burns and wounds.* Adv Skin Wound Care, 2001. **14**(1): p. 37-44; quiz 45-6.
52. Jackson, D., et al., *Primary excision and grafting of large burns.* Ann Surg, 1960. **152**: p. 167-89.
53. Janzekovic, Z., *A new concept in the early excision and immediate grafting of burns.* J Trauma, 1970. **10**(12): p. 1103-8.
54. Engrav, L.H., et al., *Early excision and grafting vs. nonoperative treatment of burns of indeterminant depth: a randomized prospective study.* J Trauma, 1983. **23**(11): p. 1001-4.
55. Ong, Y.S., M. Samuel, and C. Song, *Meta-analysis of early excision of burns.* Burns, 2006. **32**(2): p. 145-50.
56. Burke, J.F., C.C. Bondoc, and W.C. Quinby, *Primary burn excision and immediate grafting: a method shortening illness.* J Trauma, 1974. **14**(5): p. 389-95.
57. Alexander, J.W., et al., *Treatment of severe burns with widely meshed skin autograft and meshed skin allograft overlay.* J Trauma, 1981. **21**(6): p. 433-8.
58. Cryer, H.G., et al., *Effects of early tangential excision and grafting on survival after burn injury.* Surg Gynecol Obstet, 1991. **173**(6): p. 449-53.
59. Herndon, D.N., et al., *A comparison of conservative versus early excision. Therapies in severely burned patients.* Ann Surg, 1989. **209**(5): p. 547-52; discussion 552-3.
60. Desai, M.H., R.L. Rutan, and D.N. Herndon, *Conservative treatment of scald burns is superior to early excision.* J Burn Care Rehabil, 1991. **12**(5): p. 482-4.
61. Subrahmanyam, M., *Early tangential excision and skin grafting of moderate burns is superior to honey dressing: a prospective randomised trial.* Burns, 1999. **25**(8): p. 729-31.
62. Hosseini, S.N., et al., *A biological dressing versus 'conventional' treatment in patients with massive burns: a clinical trial.* Ulus Travma Acil Cerrahi Derg, 2009. **15**(2): p. 135-40.
63. Sun, T., et al., *Transplantation of microskin autografts with overlaid selectively decellularized split-thickness porcine skin in the repair of deep burn wounds.* J Burn Care Res, 2011. **32**(3): p. e67-73.
64. Chen, X., et al., *Application of acellular dermal xenografts in full-thickness skin burns.* Exp Ther Med, 2013. **6**(1): p. 194-198.
65. Xiao, H., et al., *A new method of microskin autografting with a Vaseline-based moisture dressing on granulation tissue.* Burns, 2014. **40**(2): p. 337-46.
66. See, P., et al., *Our Clinical Experience using Cryopreserved Cadaveric Allograft for the Management of Severe Burns.* Cell and Tissue Banking, 2001. **2**(2): p. 113-117.
67. Webster, J.P., *Refrigerated Skin Grafts.* Ann Surg, 1944. **120**(4): p. 431-48.
68. Matthews, D.N., *STORAGE OF SKIN FOR AUTOGENOUS GRAFTS.* The Lancet. **245**(6356): p. 775-778.
69. Cochrane, T., *The low temperature storage of skin: a preliminary report.* Br J Plast Surg, 1968. **21**(2): p. 118-25.
70. Richters, C.D., et al., *Morphology of glycerol-preserved human cadaver skin.* Burns, 1996. **22**(2): p. 113-6.
71. Kumar, R.J., et al., *Treatment of partial-thickness burns: a prospective, randomized trial using Transcyte.* ANZ J Surg, 2004. **74**(8): p. 622-6.
72. Gerding, R.L., et al., *Outpatient management of partial-thickness burns: Biobrane versus 1% silver sulfadiazine.* Ann Emerg Med, 1990. **19**(2): p. 121-4.
73. Noordenbos, J., C. Dore, and J.F. Hansbrough, *Safety and efficacy of TransCyte for the treatment of partial-thickness burns.* J Burn Care Rehabil, 1999. **20**(4): p. 275-81.
74. Hansbrough, J.F., et al., *Clinical trials of a biosynthetic temporary skin replacement, Dermagraft-Transitional Covering, compared with cryopreserved human cadaver skin for temporary coverage of excised burn wounds.* J Burn Care Rehabil, 1997. **18**(1 Pt 1): p. 43-51.

75. Purdue, G.F., et al., *A multicenter clinical trial of a biosynthetic skin replacement, Dermagraft-TC, compared with cryopreserved human cadaver skin for temporary coverage of excised burn wounds.* J Burn Care Rehabil, 1997. **18**(1 Pt 1): p. 52-7.
76. Spielvogel, R.L., *A histological study of Dermagraft-TC in patients' burn wounds.* J Burn Care Rehabil, 1997. **18**(1 Pt 2): p. S16-8.
77. Heimbach, D., et al., *Artificial dermis for major burns. A multi-center randomized clinical trial.* Ann Surg, 1988. **208**(3): p. 313-20.
78. Peck, M.D., et al., *A trial of the effectiveness of artificial dermis in the treatment of patients with burns greater than 45% total body surface area.* J Trauma, 2002. **52**(5): p. 971-8.
79. Waymack, P., R.G. Duff, and M. Sabolinski, *The effect of a tissue engineered bilayered living skin analog, over meshed split-thickness autografts on the healing of excised burn wounds. The Apligraf Burn Study Group.* Burns, 2000. **26**(7): p. 609-19.
80. Boyce, S.T., et al., *Comparative assessment of cultured skin substitutes and native skin autograft for treatment of full-thickness burns.* Ann Surg, 1995. **222**(6): p. 743-52.
81. Madden, M.R., et al., *The epidemiology and prevention of burn injuries to firefighters.* Journal of Burn Care & Rehabilitation, 1995. **16**(4): p. 461-5.
82. Duinslaeger, L.A., et al., *Cultured allogeneic keratinocyte sheets accelerate healing compared to Op-site treatment of donor sites in burns.* J Burn Care Rehabil, 1997. **18**(6): p. 545-51.
83. Barret, J.P., et al., *Biobrane versus 1% silver sulfadiazine in second-degree pediatric burns.* Plast Reconstr Surg, 2000. **105**(1): p. 62-5.
84. Lal, S., et al., *Biobrane improves wound healing in burned children without increased risk of infection.* Shock, 2000. **14**(3): p. 314-8; discussion 318-9.
85. Cassidy, C., et al., *Biobrane versus duoderm for the treatment of intermediate thickness burns in children: a prospective, randomized trial.* Burns, 2005. **31**(7): p. 890-3.
86. Demling, R.H. and L. DeSanti, *Management of partial thickness facial burns (comparison of topical antibiotics and bio-engineered skin substitutes).* Burns, 1999. **25**(3): p. 256-61.
87. Still, J., et al., *The use of a collagen sponge/living cell composite material to treat donor sites in burn patients.* Burns, 2003. **29**(8): p. 837-41.
88. Fratianne, R., et al., *Keratinocyte allografts accelerate healing of split-thickness donor sites: applications for improved treatment of burns.* J Burn Care Rehabil, 1993. **14**(2 Pt 1): p. 148-54.
89. Purdue, G.F., et al., *Biosynthetic skin substitute versus frozen human cadaver allograft for temporary coverage of excised burn wounds.* J Trauma, 1987. **27**(2): p. 155-7.
90. Wood, F.M., M.L. Kolybaba, and P. Allen, *The use of cultured epithelial autograft in the treatment of major burn injuries: a critical review of the literature.* Burns, 2006. **32**(4): p. 395-401.
91. Stark, G.B., et al., *Cultured autologous keratinocytes suspended in fibrin glue (KFGS) with allogenic overgraft for definitive burn wound coverage.* European Journal of Plastic Surgery, 1995. **18**(6): p. 267-271.
92. Boyce, S.T., et al., *Cultured skin substitutes reduce donor skin harvesting for closure of excised, full-thickness burns.* Ann Surg, 2002. **235**(2): p. 269-79.
93. Ryan, C.M., et al., *Use of Integra artificial skin is associated with decreased length of stay for severely injured adult burn survivors.* J Burn Care Rehabil, 2002. **23**(5): p. 311-7.
94. Munster, A.M., S.H. Weiner, and R.J. Spence, *Cultured epidermis for the coverage of massive burn wounds. A single center experience.* Ann Surg, 1990. **211**(6): p. 676-9; discussion 679-80.
95. Zhang, M.L., et al., *Microskin grafting in the treatment of extensive burns: a preliminary report.* J Trauma, 1988. **28**(6): p. 804-7.
96. Ayaz, M., *Comment on "A new method of microskin autografting with a Vaseline-based moisture dressing on granulation tissue".* Burns, 2015. **41**(3): p. 643-5.

97. Livesey, S.A., et al., *Transplanted acellular allograft dermal matrix. Potential as a template for the reconstruction of viable dermis.* Transplantation, 1995. **60**(1): p. 1-9.
98. Zhang, M.L., et al., *Microskin grafting. I. Animal experiments.* Burns Incl Therm Inj, 1986. **12**(8): p. 540-3.
99. *Outcome measures for adult and paediatric services*. 2012, British burn association.
100. Wasiak, J., et al., *Measuring common outcome measures and their concepts using the International Classification of Functioning, Disability and Health (ICF) in adults with burn injury: a systematic review.* Burns, 2011. **37**(6): p. 913-24.
101. Hussain, A., F. Choukairi, and K. Dunn, *Predicting survival in thermal injury: a systematic review of methodology of composite prediction models.* Burns, 2013. **39**(5): p. 835-50.
102. Johnson, C.C., et al., *The effect of a physician education program on hospital length of stay and total patient charges.* J S C Med Assoc, 1993. **89**(6): p. 293-301.
103. Johnson, L.S., et al., *Hospital length of stay--does 1% TBSA really equal 1 day?* J Burn Care Res, 2011. **32**(1): p. 13-9.
104. Keen, A., et al., *Effective limitation of blood culture use in the burn unit.* J Burn Care Rehabil, 2002. **23**(3): p. 183-9.
105. Mason, A.D., Jr., A.T. McManus, and B.A. Pruitt, Jr., *Association of burn mortality and bacteremia. A 25-year review.* Arch Surg, 1986. **121**(9): p. 1027-31.
106. Bharadwaj, R., B.N. Joshi, and S.A. Phadke, *Assessment of burn wound sepsis by swab, full thickness biopsy culture and blood culture--a comparative study.* Burns Incl Therm Inj, 1983. **10**(2): p. 124-6.
107. Keen, E.F., 3rd, et al., *Incidence and bacteriology of burn infections at a military burn center.* Burns, 2010. **36**(4): p. 461-8.
108. Willebrand, M., et al., *Long-term assessment of personality after burn trauma in adults.* J Nerv Ment Dis, 2002. **190**(1): p. 53-6.
109. Hirschfeld, R.M., et al., *Assessing personality: effects of the depressive state on trait measurement.* Am J Psychiatry, 1983. **140**(6): p. 695-9.
110. Fauerbach, J.A., et al., *Personality predictors of injury-related posttraumatic stress disorder.* J Nerv Ment Dis, 2000. **188**(8): p. 510-7.
111. Pavoni, V., et al., *Outcome predictors and quality of life of severe burn patients admitted to intensive care unit.* Scand J Trauma Resusc Emerg Med, 2010. **18**: p. 24.
112. Patterson, D.R., et al., *Psychological effects of severe burn injuries.* Psychol Bull, 1993. **113**(2): p. 362-78.
113. EuroQol, G., *EuroQol--a new facility for the measurement of health-related quality of life.* Health Policy, 1990. **16**(3): p. 199-208.
114. Anzarut, A., et al., *Quality-of-life and outcome predictors following massive burn injury.* Plast Reconstr Surg, 2005. **116**(3): p. 791-7.
115. Saffle, J.R., et al., *Return to work as a measure of outcome in adults hospitalized for acute burn treatment.* J Burn Care Rehabil, 1996. **17**(4): p. 353-61.
116. Fauerbach, J.A., et al., *Burden of burn: a norm-based inquiry into the influence of burn size and distress on recovery of physical and psychosocial function.* J Burn Care Rehabil, 2005. **26**(1): p. 21-32.
117. Dyster-Aas, J., M. Kildal, and M. Willebrand, *Return to work and health-related quality of life after burn injury.* J Rehabil Med, 2007. **39**(1): p. 49-55.
118. Moons, K.G., et al., *Prognosis and prognostic research: what, why, and how?* BMJ, 2009. **338**: p. b375.
119. Ryan, C.M., et al., *Objective estimates of the probability of death from burn injuries.* N Engl J Med, 1998. **338**(6): p. 362-6.
120. Osler, T., L.G. Glance, and D.W. Hosmer, *Simplified estimates of the probability of death after burn injuries: extending and updating the baux score.* J Trauma, 2010. **68**(3): p. 690-7.

121. Tobiasen, J., J.M. Hiebert, and R.F. Edlich, *The abbreviated burn severity index.* Ann Emerg Med, 1982. **11**(5): p. 260-2.
122. Brusselaers, N., et al., *Outcome and changes over time in survival following severe burns from 1985 to 2004.* Intensive Care Med, 2005. **31**(12): p. 1648-53.
123. Taylor, S.L., et al., *Predicting mortality from burns: the need for age-group specific models.* Burns, 2014. **40**(6): p. 1106-15.
124. Smith, D.L., et al., *Effect of inhalation injury, burn size, and age on mortality: a study of 1447 consecutive burn patients.* J Trauma, 1994. **37**(4): p. 655-9.
125. Tredget, E.E., et al., *The role of inhalation injury in burn trauma. A Canadian experience.* Ann Surg, 1990. **212**(6): p. 720-7.
126. O'Keefe, G.E., J.L. Hunt, and G.F. Purdue, *An evaluation of risk factors for mortality after burn trauma and the identification of gender-dependent differences in outcomes.* J Am Coll Surg, 2001. **192**(2): p. 153-60.
127. Galeiras, R., et al., *A model for predicting mortality among critically ill burn victims.* Burns, 2009. **35**(2): p. 201-9.
128. Moore, E.C., et al., *The Burns Evaluation and Mortality Study (BEAMS): predicting deaths in Australian and New Zealand burn patients admitted to intensive care with burns.* J Trauma Acute Care Surg, 2013. **75**(2): p. 298-303.
129. Knaus, W.A., et al., *APACHE II: a severity of disease classification system.* Crit Care Med, 1985. **13**(10): p. 818-29.
130. Tanaka, Y., M. Shimizu, and H. Hirabayashi, *Acute physiology, age, and chronic health evaluation (APACHE) III score is an alternative efficient predictor of mortality in burn patients.* Burns, 2007. **33**(3): p. 316-20.
131. McNamee, J.J., et al., *Mortality prediction and outcomes among burns patients from Australian and New Zealand intensive care units.* Crit Care Resusc, 2010. **12**(3): p. 196-201.
132. Sheppard, N.N., et al., *Prognostic scoring systems in burns: a review.* Burns, 2011. **37**(8): p. 1288-95.
133. Apesos, J., B.K. Dawson, and E.J. Law, *Comparative statistical methods in the analysis of burn victims.* Burns, 1980. **6**(3): p. 181-189.
134. Brezel, B.S., J.M. Kassenbrock, and J.M. Stein, *Burns in substance abusers and in neurologically and mentally impaired patients.* J Burn Care Rehabil, 1988. **9**(2): p. 169-71.
135. Kelley, D. and J.B. Lynch, *Burns in alcohol and drug users result in longer treatment times with more complications.* J Burn Care Rehabil, 1992. **13**(2 Pt 1): p. 218-20.
136. Gauthier, S., T. Reisch, and C. Bartsch, *Self-burning - a rare suicide method in Switzerland and other industrialised nations - a review.* Burns, 2014. **40**(8): p. 1720-6.
137. Thombs, B.D. and M.G. Bresnick, *Mortality risk and length of stay associated with self-inflicted burn injury: evidence from a national sample of 30,382 adult patients.* Crit Care Med, 2008. **36**(1): p. 118-25.
138. Nakae, H., et al., *Characteristics of self-immolation attempts in Akita Prefecture, Japan.* Burns, 2003. **29**(7): p. 691-6.
139. Rashid, A. and J.P. Gowar, *A review of the trends of self-inflicted burns.* Burns, 2004. **30**(6): p. 573-6.
140. Duarte, D.W., C.R. Neumann, and E.S. Weber, *Intentional injuries and patient survival of burns: a 10-year retrospective cohort in southern Brazil.* Burns, 2015. **41**(2): p. 271-8.
141. Mackay, N. and C. Barrowclough, *Accident and emergency staff's perceptions of deliberate self-harm: attributions, emotions and willingness to help.* Br J Clin Psychol, 2005. **44**(Pt 2): p. 255-67.
142. McAllister, M., et al., *Nurses' attitudes towards clients who self-harm.* J Adv Nurs, 2002. **40**(5): p. 578-86.
143. Varley, J., et al., *Self harm is an independent predictor of mortality in trauma and burns patients admitted to ICU.* Injury, 2012. **43**(9): p. 1562-5.

144. Forster, N.A., et al., *Attempted suicide by self-immolation is a powerful predictive variable for survival of burn injuries.* J Burn Care Res, 2012. **33**(5): p. 642-8.
145. Kerby, J.D., et al., *Sex differences in mortality after burn injury: results of analysis of the National Burn Repository of the American Burn Association.* J Burn Care Res, 2006. **27**(4): p. 452-6.
146. McGwin, G., Jr., et al., *Gender differences in mortality following burn injury.* Shock, 2002. **18**(4): p. 311-5.
147. Moore, E.C., et al., *Women are more than twice as likely to die from burns as men in Australia and New Zealand: an unexpected finding of the Burns Evaluation And Mortality (BEAM) Study.* J Crit Care, 2014. **29**(4): p. 594-8.
148. Cochran, A., et al., *The relationship of serum lactate and base deficit in burn patients to mortality.* J Burn Care Res, 2007. **28**(2): p. 231-40.
149. Tahir, S., et al., *Prediction of mortality after major burn: physiological versus biochemical measures.* Wounds, 2009. **21**(7): p. 177-82.
150. Rees, J.M. and A.R. Dimick, *Measuring quality in burn treatment requires a burn registry.* J Burn Care Rehabil, 1988. **9**(2): p. 220-1.
151. Light, T.D., et al., *The effect of burn center and burn center volume on the mortality of burned adults--an analysis of the data in the National Burn Repository.* J Burn Care Res, 2009. **30**(5): p. 776-82.
152. McCrum, M.L., et al., *Beyond volume: does hospital complexity matter?: an analysis of inpatient surgical mortality in the United States.* Med Care, 2014. **52**(3): p. 235-42.
153. Pacella, S.J., et al., *Hospital volume outcome and discharge disposition of burn patients.* Plast Reconstr Surg, 2006. **117**(4): p. 1296-305; discussion 1306-7.
154. Forster, N.A., et al., *30 years later--does the ABSI need revision?* Burns, 2011. **37**(6): p. 958-63.
155. Williams, D.J. and J.D. Walker, *A nomogram for calculation of the Revised Baux Score.* Burns, 2015. **41**(1): p. 85-90.
156. Wibbenmeyer, L.A., et al., *Predicting survival in an elderly burn patient population.* Burns, 2001. **27**(6): p. 583-90.
157. Bhatia, A.S. and B.N. Mukherjee, *Predicting survival in burned patients.* Burns, 1992. **18**(5): p. 368-72.
158. Belgian Outcome in Burn Injury Study, G., *Development and validation of a model for prediction of mortality in patients with acute burn injury.* Br J Surg, 2009. **96**(1): p. 111-7.
159. ANZBA. *The Australian and New Zealand Burn Association*. 2016 [cited 2016; Available from: http://anzba.org.au/.
160. Stats-NZ. *Statistics New Zealand: Population Clock*. 2016 [cited 2016 23/02/2016]; Available from: http://www.stats.govt.nz.
161. ABS. *The Australian Bureau of Statistics: Population Clock*. 2016 [cited 2016 23/02/2016]; Available from: http://www.abs.gov.au/.
162. Gabbe, B.J., et al., *Comparison of measures of comorbidity for predicting disability 12-months post-injury.* BMC Health Serv Res, 2013. **13**: p. 30.
163. Hettiaratchy, S. and R. Papini, *Initial management of a major burn: II--assessment and resuscitation.* BMJ, 2004. **329**(7457): p. 101-3.
164. Harrell, F.E., *Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis*. 2001: Springer.
165. Hosmer, D.W., S. Lemeshow, and R.X. Sturdivant, *Applied Logistic Regression*. 2013: Wiley.
166. UN. *Human development index (HDI)* 2016; Available from: http://hdr.undp.org/en/content/human-development-index-hdi.
167. Latenser, B.A., et al., *National Burn Repository 2006: a ten-year review.* J Burn Care Res, 2007. **28**(5): p. 635-58.

168. *Queensland population counter* 2016; 06/07/2016:[Available from: http://www.qgso.qld.gov.au/products/reports/pop-growth-qld/qld-pop-counter.php.