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# Epidemiology of burns

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## PROMOTIECOMMISSIE

| | |
|---|---|
| Promotor: | prof. dr. R.S. Breederveld |
| Co-promotores: | dr. H. Boxma<br>dr. M.E. van Baar |
| Overige leden: | prof. dr. E.J. Kuijper<br>prof. dr. P. Patka<br>prof. dr. E. Middelkoop |

*Aan mijn ouders,*
*Ter nagedachtenis*

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# PART ONE

## Epidemiology

# Chapter 1

## Introduction and Outline of the Thesis

## 1. HISTORY OF CENTRALIZED BURN CARE IN THE NETHERLANDS

Since ancient times, burn injuries have been documented as a category of wounds with a protracted course of illness, life-long sequelae and an often fatal outcome.
Major improvements in treating burn patients were obtained with the introduction of topical treatment with Tannine by Davidson in 1925 [1], insights into shock therapy and the availability of antibiotics in the Second World War period and in the late sixties of the last century, when silver products as topical therapy were introduced by Fox [2]. Later, new operative techniques such as mesh grafting, introduced by Tanner and Vandeput, [3] and early excision by Janzekovic [4] became available [5,6].
During this period, doctors also became aware that specific knowledge and skills, a multidisciplinary approach and special architectural provisions for isolation and climate control were required to treat patients with burns, eventually leading to the awareness that these patients should be treated in specialized centres.
In the Netherlands at that time, concentrations of patients with burns were particularly influenced by special local situations.
In the sixties professor R. P. Hermans, a surgeon at the Red Cross Hospital in Beverwijk, during a period of minimal safety legislation in the industry, was frequently confronted with patients with burn injuries from the nearby steel factory.
Because of the lacking knowledge and the nearly nonexistent interest from the regional universities, this group of patients who required intensive treatment, long hospital stays and extreme hygienic measures could not be referred. For this reason, Hermans focused on caring for burn patients in his own hospital and he became the pioneer of specialized burn care in the Netherlands [7].
In Rotterdam, the situation was nearly the same. In the former Zuiderziekenhuis, at the time the nearest hospital in a region with a large petrochemical industry, professor P.J. Kooreman frequently received patients with extensive burn injuries; this hospital also did not have the possibility of referring these patients to a tertiary care centre because the medical faculty in Rotterdam did not exist until 1966.
This is why Kooreman initiated special care and research for burn patients in the Department of Surgery of the Zuiderziekenhuis.
Lack of interest by the local university also played a role when plastic surgeon professor A. J. C. Huffstadt attempted to establish a burn care facility in Groningen, in the northern part of the country. He then concentrated burn patient care in the former Roman Catholic Hospital, which wanted to create a spearhead of care.
These local situations eventually led to the creation of 3 burn centres in non-university hospitals.

The burn centre of the Red Cross Hospital in Beverwijk, based on the model of the Shriners Burn Institute at Massachusetts General Hospital, which focused primarily on a multidisciplinary team approach and infection control, officially opened in 1974 (Hermans, Spijker).
In that same year, patients in the Rotterdam Zuiderziekenhuis were treated in 2 laminar-flow units in surgical intensive care (Figure 1) and in separate wings of the surgical and pediatric wards.
A new state-of-the-art, stand-alone, 20-bed burn centre in the Zuiderziekenhuis (later renamed Maasstad Hospital) was opened in 1986 (Boxma, Dokter) (Figures 2 and 3).
In Groningen, the Burn Centre of the Roman Catholic Hospital was officially opened in 1979 (Klasen, Sauer).
The ultimate goal of centralized burn care was to improve care quality by concentrating on this specific group of patients with specific emergency management challenges, diagnostics and treatment. As a direct consequence, this also included the need to improve care through research and education.
However, in the Netherlands, only university hospitals receive government funding for these purposes. Therefore, to enable grants for scientific research, Hermans and Huffstadt in 1971 founded the Dutch Burns Foundation for fundraising through donations, legacies and a national collection.
The foundation's original objective was to support research concerning burn treatment, which was later extended to promoting fire and burn prevention through public information in order to promote quality of care and quality of life for patients with burns; it also expanded into operating a national skin bank, which was later the European Skin Bank (1995).
In 1988, the foundation installed a research department with 4 divisions: pathophysiology in Groningen, wound healing in Beverwijk, epidemiology in Rotterdam and psychological care, directed from Groningen actually implemented at all locations.
This construction led to a significant boost in clinical and experimental studies, leading to papers, publications and theses, following early Dutch theses on burns by A.J. Sneep [8], J. R. Borggreve [9], R. P. Hermans [10] and R. J. A. Goris [11].
To promote mutual contact, publications, and the organization of meetings and symposia, as well as maintaining contacts with related (inter-)national associations, burn care professionals in 1974 founded the Dutch Burns Club, changing its name in 1997 to the Dutch Society for Burn Care (Nederlandse Vereniging voor Brandwonden Zorg, NVBZ).
Reconsidering the framework for Dutch Burns Foundation research grants, Maljers in 2000 [12] concluded that there was a non-transparent and complex structure of consultation, no common vision on scientific research, split efforts and a vulnerable research department.
In a memo concerning adapting the structure of the Dutch Burns Foundation, van de Poll in 2002 [13] advised the foundation to return to its core business (fundraising, prevention, skin

bank) and to link the burn centres in one structure, including the research department and with appropriate funding. Furthermore, an appraisal of projects by an external independent scientific advisory board (Wetenschappelijke Advies Raad, WAR) was recommended to replace the Medical Advisory College (MAC) that had existed since 1974 and consisted of burn centre professionals.

In line with this development, the Dutch Council for Healthcare Research (Raad voor Gezondheids Onderzoek, RGO), which advises ministers of public health, education, science, and economic affairs about priorities and infrastructure in healthcare research, chaired by professor D. J. Gouma, published its advisory on research in trauma care [14].

It was concluded that the trauma research infrastructure in the Netherlands was not particularly well developed, with a relatively small number of researchers, isolated and mostly short-term projects, multidisciplinary research being performed only exceptionally and the lack of a nationwide uniform registration system.

The council recommended creating a Centre of Knowledge in Traumatology and set priorities for research themes. Because burn care is a special dimension in the care of trauma victims and because the majority of research in this field had been performed by the burn centres, the centres were explicitly instructed to contribute to the functioning of the Centre of Knowledge in Traumatology.

The council also recommended a nationwide registration and information system that confirmed to international standards and that would include background information about accidents (aiming at prevention), data on (pre-)clinical care, information concerning research and long-term sequels; in these ways, the system would enable monitoring and evaluating the nature, quality and efficiency of care.

As a result, the Association of Dutch Burn Centres (ADBC; Vereniging Samenwerkende Brandwondencentra Nederland, VSBN) was founded in 2003 to improve the treatment of burn victims in every aspect, expand the knowledge about burn care and patients, improve the quality of research on burns and implement results from preclinical research in the clinic ("from bench to bedside").

The ADBC research program, directed by Professor E. Middelkoop, was divided into preclinical, clinical, and psychological research and epidemiology and registration.

## 2. RATIONALE OF REGISTRATION

The rationale for a burn-specific registration is determined by different causes of burns (scalds, flame, chemical, electrical), the fact that many factors influence trauma severity (total body surface area burned, age, depth, localization, co-morbidity) and burn-specific pathophysiology in time (shock, infection, hypermetabolism).

When the new Rotterdam Burn Centre was opened in 1986 and conformed to the advice of the Dutch Council for Healthcare Research, stressing the importance of registration as a quality control system and a standard for care outcomes, methods of registration in the Rotterdam Burn Centre were reconsidered.

At that time, there was no uniformity of registration in the three Dutch burn centres. In fact, the Rotterdam centre had to work with 6 separate registration systems: the local hospital administration registration, a burn centre based clinical dataset, a registration of the hospital Department of Bacteriology, datasets from the Dutch Burns Foundation and the National Hospital Discharge Register (Landelijke Medische Registratie, LMR), and a registry from the Consumer Safety Foundation (Stichting Consument en Veiligheid, SCV).

Many of the existing registration systems did not meet the burn centres' requirements. The LMR was insufficient for describing the extent and severity of burn injuries, and scoring systems such as the Major Trauma Outcome Score (MTOS) included too few burn patients to validate changes in burn survival. The frequently used Baux score also provided only limited data for exactly predicting survival chances in a great variety of burn injuries.

Because of the lack of uniformity in registration, the author of this thesis together with H. Boxma started a comprehensive registration system for the Rotterdam Burn Centre in 1986 that showed an annual growth up to 6308 patients until January 2016 (Figure 4).

Since its beginning, this dataset has been a source of many studies, presentations and publications on specific topics, for example burns in the elderly, inhalation injuries and the repatriation of burn victims.

The epidemiology and registration division of the ADBC in Rotterdam began efforts to develop a uniform nationwide burn-specific registration, the Dutch Burns Information System (DBIS; Nederlands Brandwonden Informatie System, NBIS). The DBIS was supposed to use relevant WHO classifications to collect patient data, information about etiology (International Classification of External Causes of Injury, ICECI), injury diagnoses (International Classification of Diseases, ICD-10), treatment (International Classification of Procedures in Medicine, ICPM), wound healing (with digital photography), complications and outcomes in terms of morbidity and survival.

The future perspective should entail registering separate dimensions of care such as bacteriological and psychosocial data and more treatment and outcome parameters (International Classification of Functioning, Disability and Health, ICF), eventually aiming at developing an international burn information system.

Using Internet facilities for data transport within the DBIS digital certificates and biometrical verification with fingerprint recognition, encryption and decryption via the keys of a digital notary as a trusted third party and firewalls were used to secure reliable input and output. Via biometric verification, data could be extracted for ad hoc analyses, standard reports such as morbidity and mortality figures, and multidisciplinary meetings. In the future, websites

could be filled with validated data for non-burn centre hospitals as a reference base for treatment and referral criteria to burn centres. Citizens would be able to obtain information about burn wounds, first aid and prevention.
Developing this system, however, was extremely time consuming, and it posed a significant financial burden for the burn community. Combined with problems concerning privacy legislation and safety procedures, the project eventually had to be abandoned.
The most relevant development was merging the historical databases of the 3 burn centres in 2008 and the Dutch Burn Repository (DBR) R3 registration system, which became operational in 2009 and which contains information on all patients who were admitted to the 3 Dutch burn centres, including etiology, treatment and outcomes.
This database is adapted and expanded in close consultation with its users and updated with developments in burn care, creating possibilities for comparison with international databases.

## 3. AIM AND CONTENTS OF THIS THESIS

This thesis aims to acquire knowledge on the epidemiology, treatment and outcomes of specialized burn care in the Netherlands and is based on data from the Rotterdam Burn centre since 1986, historical databases from the burn centres in Groningen and Beverwijk and the common Dutch Burn Repository R3 since 2009.
**Part One** includes 2 studies on epidemiology.
**Chapter 2** analyses the population of patients with burns in the Netherlands, with special reference to patients who were admitted to one of the 3 Dutch burn centres.
It is based on the historical databases of the burn centres and the Dutch Burn Repository R3 dataset from 1995 through 2011 and it also includes data derived from the National Hospital Discharge Register.
The relatively high number of children who have sustained burn injuries in the Netherlands is the subject of the epidemiological study in **Chapter 3**, in which 2 age groups, 0-4 years and 5-17 years, are compared in the 2 time periods 1995-1999 and 2000-2007. The chapter describes referral patterns and admission rates in Dutch burn centres for younger patients with less severe burns.
**Part Two** addresses 2 different aspects of managing patients with burns.
A relatively high percentage of burn centre admissions concerns younger children, who are most frequently injured by scalds. Treatment options are addressed in **Chapter 4**, comparing topical therapy versus modern wound dressings in children from 0-4 years with scald burns on up to 10% of total body surface area (TBSA) who were admitted to the Rotterdam Burn Centre between 1987 and 2010.

Facilitated by the defective skin barrier and the patient's innate immune response, infections remain one of the major complications in the period following severe burns.

**Chapter 5** discusses the rationale for taking bacteriological cultures on admission. The objective was to assess the frequency of colonization with potentially pathogenic microorganisms on admission and identify the bacteria involved and their potential roles in later septic complications in a large cohort of patients over a 24-year period.

For this study, data from the Rotterdam Burn Centre were merged with data from the Department of Bacteriology of the Maasstad Hospital.

Prognosis and outcomes are evaluated in **Part Three**.

Infectious complications and sepsis in later phases are closely related to mortality in patients with burns. Chances of survival in earlier stages can be determined by scoring systems such as the Baux score. **Chapter 6** is a validation study of the revised Baux score, which, combined with TBSA burned, age and inhalation injury, is recognized as an important contributor to mortality. Data were analyzed for all 4389 patients with acute burn injury who were admitted to the Rotterdam Burn Centre in the period 1987–2009.

Mortality is an important outcome parameter of burn injuries.

**Chapter 7** focuses on mortality and causes of death at the Rotterdam Burn Centre between 1996 and 2006 and compares these data with the National Burn Repository, a large American database of over 70 burn centres at the time of the study.

**Chapter 8** studies early and late mortality in the Burn Centres of Rotterdam and Beverwijk during the period 2006-2011.

Summaries and conclusions in English and Dutch are presented in **Chapter 9**, followed by an addendum with acknowledgements in Dutch, a bibliography and the authors' curriculum vitae.

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**Figure 1:** Surgical Intensive Care with 2 Laminar Flow Units of the Burn Centre Zuiderziekenhuis Rotterdam 1976

**Figure 2:** Burn Centre Zuiderziekenhuis Rotterdam 1986

**Figure 3:** Intensive Care Burn Centre Zuiderziekenhuis Rotterdam

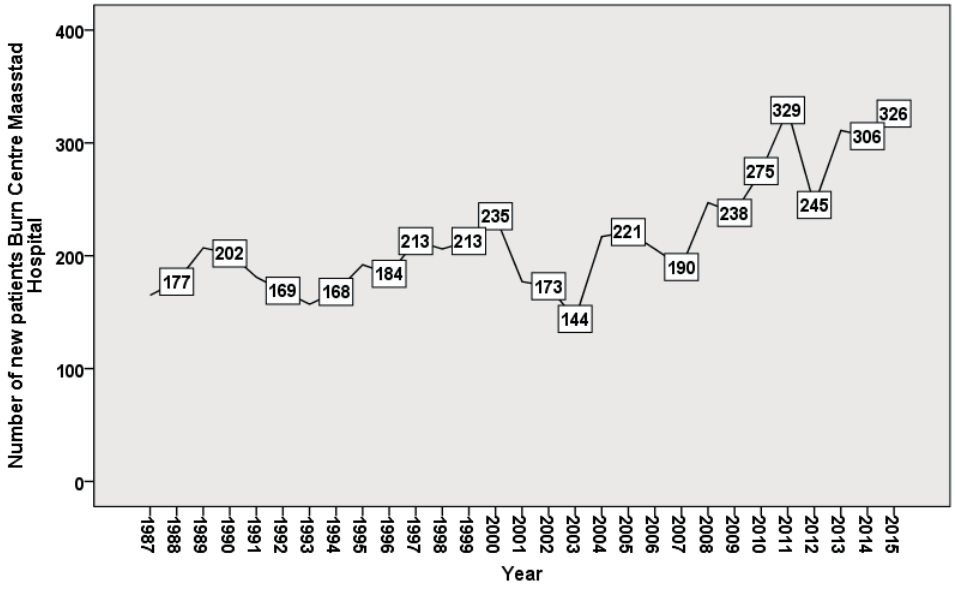


**Figure 4:** Growing number of admissions in the Rotterdam Burn Centre over the last decade

# Chapter 2

# Epidemiology and trends in severe burns in the Netherlands

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Burns. 2014 Nov;40(7):1406-14.

## ABSTRACT

***Introduction:*** The aim of this study was to characterize the epidemiology of severe burns in the Netherlands, including trends in burn centre admissions, non-burn centre admissions and differences by age.

***Methods:*** Patients with burn-related primary admission in a Dutch centre from 1995 to 2011were included. Nationwide prospectively collected data were used from three separate historical databases and the uniform Dutch Burn Repository R3 (2009 onwards). General hospital data were derived from the National Hospital Discharge Register. Age and gender-adjusted rates were calculated by direct standardization, using the 2005 population as the reference standard.

***Results:*** The annual number of admitted patients increased from 430 in 1995 to 747 in 2011, incidence rates increased from 2.72 to 4.66 per 100,000. Incidence rates were high in young children, aged 0–4 years and doubled from 10.26 to 22.96 per 100,000. Incidence rates in personsfrom 5 up to 59 increased as well, in older adults (60 years and older) admission rates were stable. Overall burn centre mortality rate was 4.1%, and significantly decreased over time.
There was a trend towards admissions of less extensive burns, median total burned surface area (TBSA) decreased from 8% to 4%. Length of stay and length of stay per percent TBSA decreased over time as well.

***Conclusions:*** Data on 9031 patients admitted in a 17-year period showed an increasing incidence rate of burn-related burn centre admissions, with a decreasing TBSA and decreasing in-burn centre mortality.
These data are important for prevention and establishment of required burn care capacity.

## 1. INTRODUCTION

The epidemiology of burns has been described in multiple publications, traditionally based on data from one burn centre.

In the past decade, publications have become available describing the epidemiology of burns in a series of burn centres from one country, for instance from Germany [1] or the USA [2]. In addition, nationwide data were published on burnrelated Emergency Department (ED) treatments from North

Carolina, USA [3] and hospital admissions from Norway [4], Sweden [5], China [6]. In some publications several health care settings are included, for instance emergency department presentations, hospital admissions and injury mortality in a paper on data from Victoria, Australia [7].

Nationwide data on burn centre admissions are scarce, because of the necessary participation of all burn centres in one data repository. In the Netherlands, a uniform nationwide burn centre registration was established in 2009, including the three burn centres, with 100% coverage of admitted burn centre patients. The Dutch Burn Repository R3 was combined with the historical databases from each burn centre to investigate the epidemiology of burns in the past decades.

Up to now, a few mostly outdated publications presented incidence rates, on medically treated burns including Dutch burn centres [8] and on burn-related ED treatments and hospital treatments [9]. Recent publications addressed the epidemiology of specific risk groups, i.e. children [10] and patients with facial burns [11]. A recent complete overview however, including nationwide incidence rates on burn centre admissions and trends, is still lacking.

Recently, Brusselaers et al. [12] and Peck [13] reviewed the epidemiology of burns in Europe and worldwide. Both reviewers conclude there is a decline in burn incidence and in burn severity in high-income countries. In low and middle income countries mixed trends are described [14].

In the Netherlands, criteria for referral to a burn centre were introduced in 1980 [15], but were used as an advise [10]. In 1998 the course Emergency Management of Severe Burns (EMSB) was introduced, with new referral criteria [16]. These criteria were more compulsory and nowadays well adopted in the Netherlands [10]. All children with burns over 5% and adults with burns over 10% TBSA are advised to be referred Additional referral criteria are largely similar to the ABA referral criteria (see Table 1).

The aim of this study is to characterize the epidemiology of severe burns in the Netherlands, including trends in burn centre admissions, non-burn centre admissions and differences by age.

First, trends are described in number of burn centre admissions, burn size, length of stay, time to first surgery and mortality. Trends in burn centre admissions will be compared to burn-related primary hospital admissions in non-specialized burn care hospitals. Next, differences in severe burns by age are described.

**Table 1.** Criteria for referral to a Dutch burn centre.

| |
|---|
| **Period 1980–1999 [15]** |
| • Burns greater than 25% TBSA in adults or deep burns over 10%TBSA<br>• Burns greater than 10% TBSA in children and elderly, irrespectively the depth<br>Minor burns associated with another injury or pre-existent disease that may increase the risk for complications |
| **Period 1998 onwards: EMBS Criteria for referral to a Dutch Burn Centre [16]** |
| • Burns greater than 10% Total Body Surface Area (TBSA) in adults.<br>• Burns greater than 5% TBSA in children.<br>• Burns of special areas–face, hands, feet, perineum, genitalia and major joints.<br>• Full thickness burns greater than 5% TBSA.<br>• Electrical burns.<br>• Chemical burns.<br>• Burns with associated inhalation injury.<br>• Circumferential burns of the limbs or chest.<br>• Burns at the extremes of age – children and the elderly.<br>• Burn in patients with pre-existing medical disorders which could complicate management and prolong recovery or effect mortality.<br>• Any burn patient with associated trauma. |

## 2. METHODS

### 2.1. Patients and setting specialized burn care

All patients with a burn-related primary (i.e. first) admission in a burn centre in the Netherlands from 1 January 1995 to 31 December 2011 were included. In the Netherlands (population 2011: 16.75 million, area 41,528 $km^2$), three burn centres deliver specialized burn care (Red Cross Hospital Beverwijk, Martini Hospital Groningen and Maasstad Hospital Rotterdam) with a total of 65 beds, including 11 ICU beds. In 1995 42 beds, and from 2001 onwards a total of 60 beds was available.

To compare trends in specialized burn care to trends in non-specialized burn care, data on burn related admissions in general hospitals in this study period were derived from the National Hospital Discharge Register (NHDR).

## 2.2. Data collection

Data on specialized burn care were prospectively collected in separate databases, by burn care professionals in each Dutch burn centre from 1995 to 2008. From 2009 onwards the uniform Dutch Burn Repository R3 is used in all three burn centres.

The Dutch Burn Repository R3 is an extensive database including data on all admitted patients in specialized burn care, including patients for reconstructive surgery after burns. The database is filled by dedicated burn care professionals, and quality monitoring by a coordinator and improvement is formally organized. The Dutch Burn Repository is supported by the participating hospitals, the Association of Dutch Burn Centres (ADBC) and the Dutch Burns Foundation.

The historical databases of each burn centre were combined, after permission of relevant representatives from the three burn centres. Next, the historical database was merged with the Dutch Burn Repository into one nation-wide database including 17 years of specialized burn care with data on numbers and characteristics of patient (age, gender) injury (aetiology, referral, the total body surface area (TBSA), inhalation injury (based on clinical diagnosis), treatment (surgery, mechanical ventilation), and outcome (length of stay and mortality).

Data collection and use of the Dutch Burn Repository R3 and its predecessors were conducted with approval of participating hospitals and the relevant medical ethical committees.

Information on burn related admissions in non-specialized burn care was derived from the National Hospital Discharge Register (NHDR). All primary burn related admissions were extracted, using the International Classification of Diseases (ICD-9) codes 940–949 from 131 Dutch hospital locations with 105 ED's in 2011. A selection was made of all primary burn related hospital admissions in non-specialized burn care excluding primary admissions in specialized burn care, to compare with the admission numbers in specialized burn care. Data from NHDR were not directly accessible and therefore information by 5 age groups, but no digital data, was obtained on demand from the Consumer Safety Institute, Amsterdam, the Netherlands.

## 2.3. Statistical analyses

Incidence density rates, the number of burn-related admissions in a Dutch burn centre in an age category in one year, divided by the total number of persons at risk in this age category in the Netherlands in the same year, were calculated. The denominator data refer to the population at July 1st of a specific year, using the mean of the population at January 1st that year and the population at January 1st of the following year. Incidence rates were calculated, using population data from Statistics Netherlands [17].

Subsequently, using direct standardization, age- and gender-adjusted rates were calculated to control for changes in the Dutch population related to age and gender. Data were categorized into 10 age/sex groups. Weighting the age- and gender-specific rates with the 2005 Dutch population, age- and gender-adjusted burn incidence rates per 100,000 persons years were obtained.
No gender specific NHDR data were available; thus comparison of admission rates between burn centre hospitals and general hospitals were based on age-standardized data (instead of age, gender standardized data). 95% Confidence intervals (95%CI) were calculated using Byar's method [18].
The incidence rate ratio (IRR) for male/female incidences and 95%CI were calculated using Poisson regression model, adjusted for age and admission year. To identify trends in incidence rates, Joinpoint regression model and permutation tests were performed, expressed in annual percentage of change and 95%CI [19]. Length of stay was calculated by the difference in days between admission and discharge (i.e. overnight stay). Kruskal–Wallis test was performed to test for trends in length of stay, TBSA and length of stay per % TBSA. Analysis of variance was performed to test for trends in time to first surgery. Differences between age groups were tested by $x^2$ test (aetiology, place of occurrence, TBSA, ICU stay (yes/no), surgery (yes/no) mortality and mode of discharge), Kruskal–Wallis test (median length of stay) and analysis of variance (time to first surgery).
Analyses were performed using Joinpoint Regression Programme, Version 3.5 [20] Joint point (regression and permutation test) and standard statistical programmes (SPSS v 19, PASW statistics 18 and Excel).

## 3. RESULTS

### 3.1. Trends in burn centre admissions

A total of 9031 patients had a burn-related primary admission in a Dutch burn centre in the Netherlands from 1995 to 2011. The mean annual number of admitted patients was 531 and increased from 430 in 1995 to 747 in 2011. The standardized incidence rates increased from 2.72 to 4.66 cases per 100,000 population (see Fig.1), with an annual increase of 2.7% (95%CI 1.9; 3.4).
Overall, males outnumbered the females in burn centre admissions (65.0% versus 35.0%), the standardized IRR was 1.86 (95%CI 1.74; 1.99). In men, standardized incidence rates increased from 3.36 to 6.13 per 100,000 men in 2011, with an annual increase of 3.3% (95%CI 2.4–4.1). In women, incidence rates increased from 2.10 to 3.22 per 100,000 women in 2011. Trend analysis indicated a change in trend in 2008 ($p < 0.05$).

A stable incidence rate for women was found up to 2008 (annual percentage of change 0.3; 95%CI -0.7; 13); from 2008 onwards an annual increase was observed (annual percentage of change 13.4; 95%CI -3.0; 24.9).
The incidence rates of severe burns were strongly correlated to age groups. Infants and children <5 years of age were the most frequently admitted age category in our centres. The incidence rate was 15.31 per 100,000 children in young children (0–4), compared to incidence rates between 2.00 (age 60 years and over) and 2.89 (20–39 years) per 100,000 in other age categories (see Fig.2)

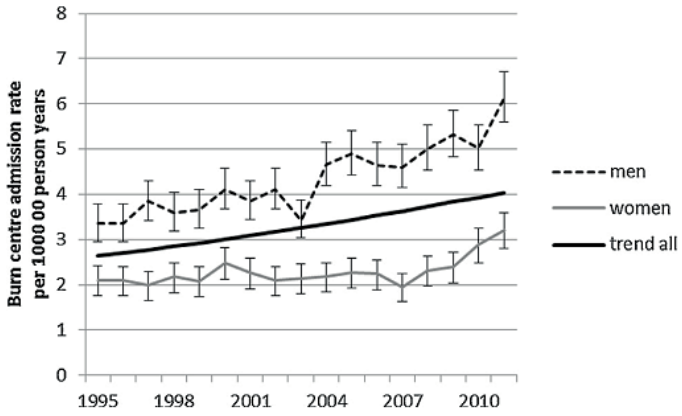


**Fig. 1 – Trends in burn centre admissions, by gender (standardized incidence rates).**

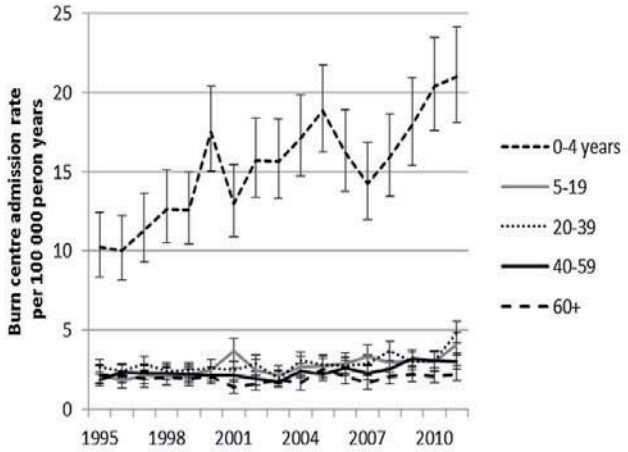


**Fig. 2 – Trends in burn centre admissions, by age (standardized incidence rates).**

Incidence rates in young children doubled in the study period, from to 10.26 in 1995 to 20.96 per 100,000 in 2011; with an average annual increase of 3.9% (95%CI 2.61; 5.2). Incidence rates in persons up to 59 increased as well, from 2.19 to 4.09 per 100,000 per year in children aged 5–19 (annual percentage of change 3.5%; 95%CI 1.9; 5.0) in young adults (20–39) from 2.69 to 4.85 per 100,000 per year (annual percentage of change 2.5%; 95%CI 0.8; 4.1) and in middle aged adults from 1.88 to 3.01(annual percentage of change 2.2%; 95%CI 0.9; 3.6). In older adults no change was observed (annual percentage of change 0.4; 95%CI - 1.2; 2.0).

## 3.2. Trends in burn-related hospital admissions

The total number of acute burn-related hospital admissions in the Netherlands varied between 1080 and 1340 admission a year. This included data from both general hospitals as well as specialized burn care. A peak was observed in 2001, after the Volendam fire disaster [21] (see Fig.3).

Overall burn related admission rates showed a mixed trend: after a significant downward trend up to 2008 (annual percentage of change -1.0; 95%CI -2.0; -0.1), a trend upwards was observed up to an incidence of 8.50 primary admissions per 100,000 persons years in 2011(annual percentage of change 7.3; 95%CI 2.2; 17.7).

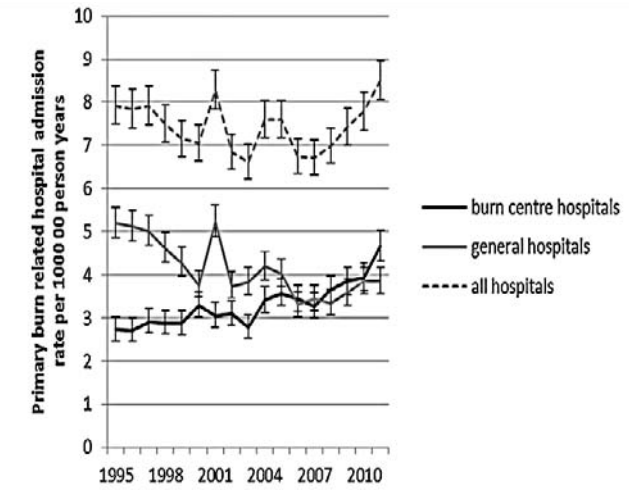


**Fig. 3 – Trends in burn-related primary hospital admissions in specialized burn care versus general hospitals (standardized incidence rates).**

However, trend analyses for specialize burn care versus general hospitals showed uniform trends: a decrease in non-specialized burn care and an increase in specialized burn care admissions (annual percent of change -2.3; 95%CI -3.4; -1.3 and 2.7; 95%CI 1.9; 3.4, respectively (Fig.3). The proportion of burn-related hospital admissions in specialized burn care increased from 34% in 1995 to 55% in 2011.

### 3.3. Trends in burn centre aetiology

The most prevalent causes of burns in recent burn centre admissions were both scalds and flames; after a dominance of flame burns in the1990s (Fig.4). Fat burns were the third major aetiology in the past five years, accounting for 6.7% of the admissions in the past five years. Admission rates of scalds increased 4.9% annually (95%CI 3.5; 6.3); flame burns were stable (annual percent of change 0.8; 95%CI -0.4; 1.9). Admission rates of burns by hot fat/oil and chemical burns increased over time, to 6.7 and 4.1% of the admissions in the past five years with estimated annual increases of 5.3% (95%CI 2.8; -7.8) and 14.0% (95%CI 8.6; 19.7). Admission rates of contact burns were small and stable up to 2006, afterwards rose to a 5.3% of the admissions in the past five years, with an estimated annual increase of 24.7% (95% CI 7.2; 45.2).

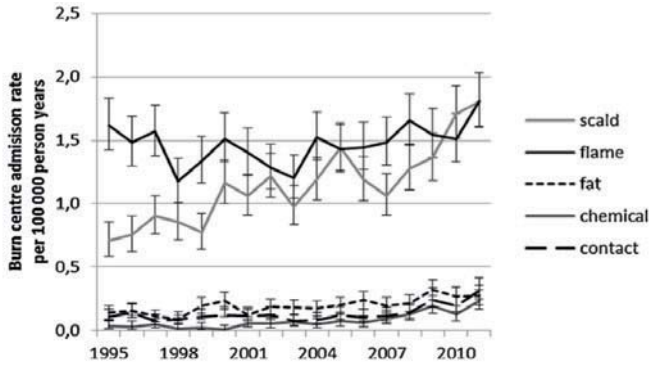


**Fig. 4 – Trends in burn centre admissions, by aetiology (standardized incidence rates).**

### 3.4. Trends in burn centre burn severity

Overall burn severity in admitted patients, as assessed by percentage TBSA, reduced over time; the median TBSA in admitted patients decreased from 8 to 4%.
Incidence rates of burns <10% TBSA increased, from 1.46 to 3.62 per 100,000 per year, with an annual increase of 5.1% (95%CI 4.2; 6.0) (Fig.5). In the past 5 years 80.0% of the patients

had a TBSA <10%. Incidence rate of moderate (TBSA ≥10%, <20%) and severe burns (TBSA ≥20%) reduced over time (annual percent of change -3.0; 95%CI -4.3; -1.80 and -3.5; 95%CI -4.6; -2.3, respectively), but seemed to stabilize in recent years.

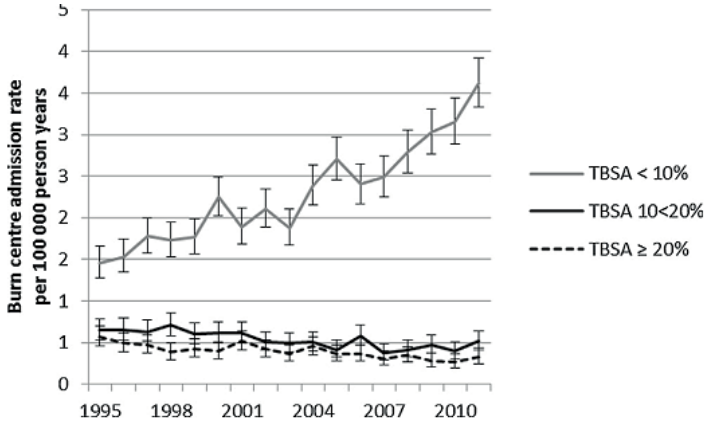


**Fig. 5 – Trends in burn centre admissions, by TBSA (standardized incidence rates).**

## 3.5. Trends in burn centre treatment

The median length of stay decreased over time from 15 days in 1995 to 5 days in 2011 ($p < 0.001$). Both overall and in all specific age groups. The mean length of stay decreased from 23 to 11 days. The median length of stay per percent TBSA did change as well, from 1.7 days in 1995 to 1.0 day in 2011 (Kruskall–Wallis test, $p < 0.001$).

The mean time to first surgery was 14.7 days post burn (SD10.0). No trend was observed (ANOVA, $p = .427$).

## 3.6. Trends in burn centre mortality

Mortality rate in admitted patients was 4.1% (n = 371). The majority of the patients died after flame burns (85.8%) (Fig.6). This applied to all age categories except the young children (not shown). In these children mortality occurred both after scalds (n = 4) and flame burns (n = 4). Standardized mortality rates significantly decreased over time, in the total population with an annual percentage of change of -4.1% (95%CI -6.2; -2.0) (Fig.6) and in men and women separately (annual percentage of change -5.0%, 95% CI -7.9; -2.2 and -2.9(95%CI -5.8; -0.0).

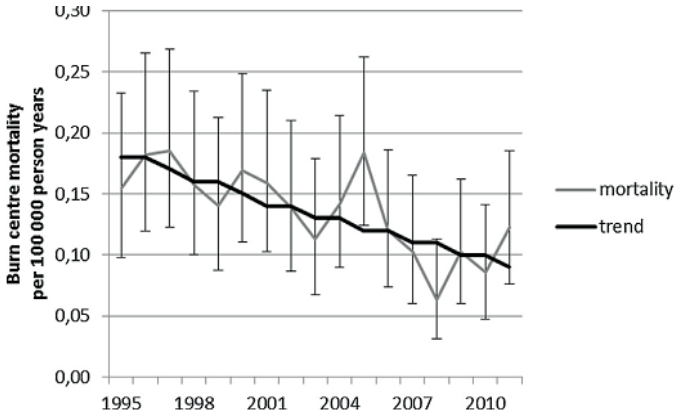


**Fig. 6 – Trend in burn centre mortality (standardized mortality rates).**

Standardized mortality rates in elderly patients (60+) significantly decreased over time, (annual percent of change -6.3% (95%CI -9.5; -3.0); but not in patients aged 40–59 (annual percentage of change -2.2%, 95%CI -6.4; 2.1). younger age categories were not analyzed because of small numbers of deceased patients.
Known risk factors for mortality: age, TBSA and inhalation injury remained stable over time. The overall mean Baux score of the deceased patients (age + TBSA) was 102 (SD 28) and the mean Revised Baux Score (RBS = age + TBSA + inhalation injury x 17) was 106 (SD 29).
Mortality often occurred in the first days after admission: 40.7% (n = 151) of the deceased patients died on the day of admission or the next day. This included patients receiving only palliative care because of the severity of the burn. The median LOS in deceased patients was 4 days.

## 3.7. Epidemiology of burn centre admissions by age

Important overall causes of burns resulting in a burn centre admission were flames (46.3%) and scald (35.7%). Scald was the predominant cause of burns in young children admitted to the burn centres (Table 2). In all other ages, flames were the most important cause for burn centre admission (>59.9%). Chemical burns were seen in the working-age population (4.3% in young adults, 4.6% in middle aged adults), contact burns were most prevalent in the elderly (8.5%).
The majority of accidents occurred in the house, especially in young children and in elderly. In children and adolescents (5–19) burns also occurred relatively often in the direct neighbourhood of the house (18.6%). In the working-age population almost one in five admissions was the result of an accident at work or in a business area.

Most young children were admitted with small burns (TBSA <10%, 81.8%). Severe burns (TBSA ≥20%) were rare in young children (3.3%), compared to adults and elderly (>11.9%) (see Table 2).

**Table 2 – Burn characteristics of burn centre admissions, by age: 1995–2011 (*n* = 9031).**

| | Patients | | TBSA | | Aetiology | | Site of occurrence | | |
|---|---|---|---|---|---|---|---|---|---|
| | Total | Annual | <10% | ≥20% | Scalds | Flame | In house | Around house | Business (area) |
| | *n* | *n* | *n* = 2028 (%) | *n* = 81 (%) | *n* = 3111 (%) | *n* = 4035 (%) | *n* = 4478 (%) | *n* = 1357 (%) | *n* = 707 (%) |
| *Age (yr)* | | | | | | | | | |
| 0–4 | 2534 | 149 | 81.8 | 3.3 | 84.5 | 5.4 | 76.5 | 14.9 | 0.4 |
| 5–19 | 1356 | 80 | 73.6 | 11.9 | 23.8 | 59.9 | 41.9 | 23.4 | 2.7 |
| 20–39 | 2220 | 131 | 65.2 | 16.4 | 12.3 | 64.0 | 38.1 | 16.0 | 18.6 |
| 40–59 | 1855 | 109 | 65.7 | 16.8 | 14.2 | 63.8 | 44.8 | 15.1 | 17.0 |
| 60+ | 1065 | 63 | 62.9 | 18.5 | 19.5 | 60.2 | 65.8 | 15.0 | 2.0 |
| All ages | 9031 | 531 | 70.9 | 12.4 | 35.7 | 46.3 | 54.5 | 16.5 | 8.6 |

*Missing values*: age (*n* = 1), aetiology (*n* = 319), site of occurrence (*n* = 815), burn size (*n* = 186). *p*-Value aetiology, site of occurrence, TBSA: <0.001.

Some seasonal variation in admission rates was detected ($p < 0.001$). Admission rates were highest in summer months and around the end of the year festivities (data not shown).
Length of stay increased by age, as did the prevalence of surgery. Intensive care was highly prevalent in the young age groups, up to 39.3% in young children (0–4), often comprising the monitoring of IV fluids resuscitation. The timing of surgery did not differ between age groups, with a mean of 14.7 days after the accident (SD 10.0, see Table 3).
Survival was strongly related to the age of the patient and was lowest in patients of 60 years

**Table 3 – Treatment characteristics in burn centre admissions, by age: 1995–2011.**

| Age (yr) | Patients | Length of stay, days | | Intensive care | Surgery | Timing of surgery, days post burn | |
|---|---|---|---|---|---|---|---|
| | *n* | Median | Mean (SD) | (%) | (%) | *n* | Mean (SD) |
| 0–4 | 2534 | 6.0 | 9.6 (10.8) | 39.3 | 27.6 | 582 | 13.9 (7.3) |
| 5–19 | 1356 | 8.0 | 15.8 (22.6) | 35.5 | 46.9 | 530 | 15.3 (10.4) |
| 20–39 | 2220 | 9.0 | 17.4 (26.5) | 14.3 | 45.4 | 843 | 14.8 (10.1) |
| 40–59 | 1855 | 12.0 | 20.1 (25.3) | 15.4 | 56.5 | 868 | 14.8 (10.7) |
| 60+ | 1065 | 17.0 | 23.8 (25.3) | 19.2 | 60.7 | 557 | 14.6 (10.9) |
| All ages | 9031 | 9.0 | 16.3 (22.6) | 25.3 | 44.7 | 3380 | 14.7 (10.0) |

*Missing values*: LOS (*n* = 18), IC (*n* = 195), surgery y/n (*n* = 3), timing of surgery (*n* = 655 of 4035 patients with surgery). *p*-Value LOS, IC, surgery $p < 0.001$ timing of surgery $p = 0.21$.

and over. Most patients were discharged home. With increasing age patients were more frequently discharged to other hospitals and nursing homes. A small proportion of patients was discharged to centres for mental health care and rehabilitation centres (see Table 4).

**Table 4 – Mortality and discharge in burn centre admissions, by age: 1995–2011.**

| Age (yr) | Patients | Mortality | Mode of discharge | | | | |
|---|---|---|---|---|---|---|---|
| | *n* | *n* = 371 (%) | Home *n* = 7247 (%) | Hospital *n* = 249 (%) | Nursing home *n* = 133 (%) | Rehabilitation *n* = 101 (%) | Mental health care *n* = 180 (%) |
| 0–4 | 2534 | 0.3 | 97.8 | 1.5 | 0.0 | 0.1 | 0.0 |
| 5–19 | 1356 | 0.7 | 95.3 | 1.4 | 0.0 | 1.6 | 0.4 |
| 20–39 | 2220 | 2.9 | 87.0 | 3.0 | 0.2 | 1.7 | 3.6 |
| 40–59 | 1855 | 4.7 | 80.4 | 4.4 | 1.5 | 2.1 | 4.6 |
| 60+ | 1065 | 18.8 | 58.5 | 6.1 | 10.5 | 0.8 | 2.1 |
| All ages | 9031 | 4.1 | 86.6 | 3.0 | 1.6 | 1.2 | 2.2 |

*Missing value*: mode of discharge (*n* = 662). *p*-Value mortality, mode of discharge: <0.001.

## 4. DISCUSSION

This study characterized the epidemiology and trends of severe burns in the Netherlands, over a 17-year time period. The Dutch Burn Repository and its predecessors were used to create a nationwide dataset comprising all burn centre admissions in our country. Data on 9031 patients admitted in the study period showed an increasing incidence rate of burn-related burn centre admissions, with a decreasing TBSA and decreasing in-burn centre mortality. Data on burn related general hospital admissions showed a decreased incidence rate in non-specialized burn care. In specialized burn care, type of burn, treatment and outcome characteristics varied with specific age categories.

Incidence rates of burn centre admissions increased over time from 2.9 in 1995 to 4.6 per 100,000 person years in 2011. The 1995 data are similar to the incidence rate of 2.9, based on early data from the three Dutch burn centres [8]. International incidence rates of burn centre admissions are hardly reported. Al Shaqsi etal. reported higher burn unit incidence rates, with 7.05 patients per 100,000 in the national burn unit of Oman [22]. Most incidence rates on burns reflect overall hospital admission rates, derived from national hospital discharge registers. Our study showed an incidence rate of primary admissions of 8.5 per 100,000 inhabitants in 2011. This number varies in Europe between 2 and 29 per 100,000 inhabitants [12], in Australia 36 per 100,000 has been reported [23]. In the Netherlands, an overall hospital admission rate, including readmissions of 11 burn related admissions per 100,000 inhabitants was observed in 2010 [24].

Burn centre admissions rates increased over time. These increasing incidences were based on increases in the younger age categories (up to 39 years of age), especially in the youngest children. However, overall burn related hospitals admissions rates (including burn centre admissions) seem to be stable in the Netherlands over the past decade [24].

In a systematic review a declining incidence rate of severe burns needing hospitalization

was described [12]. Several studies reported declining burn-related hospital admission rates, both in low and middle-income countries [14], as well as in high-income countries [25].

Vloemans et al. analyzed the Dutch paediatric burn centre admissions in 1995–2007 and suggested a changing referral pattern in paediatric burns in the Netherlands. The proportion of children admitted to specialized burn centres, rather than general hospitals, increased over time from about 30% in 1995 to almost 50% in 2007 [10]. As shown in our data, this trend continued and applied to most age categories.

The reduction in length of stay over time is in line with described trends in burn care in developed countries [5,23,26,27] and can be explained by the higher admission rates of smaller burns, the use of new treatment techniques [28] and the expanding outpatient facilities in Dutch burn care.

It can be concluded that more and more burn patients are referred to specialized burn care, for assessment and/or treatment. This is in line with the guidelines for the Emergency Management of Severe Burns (EMSB), introduced in the Netherlands in 1998 [10,16]. Referral was now advised in children with 5% TBSA or more (instead of 10% before) and also in case of chemical and contact burns. In addition, there is a trend towards further specialization of health care in general in our country, also because of limited travel distances. The trend towards a growing specialized burn care has been described in other countries as well [29,30]. Vercruysse (USA) et al. suggest that many patients are transferred towards tertiary care facilities because of a lack of basic skills in the assessment and care of burn wounds at community and rural hospitals.

Burn centre mortality rates declined over time. This decline cannot be explained by the lower injury severity of admitted patients; Baux scores were stable over time. Thus, the lower mortality rate is probably the result of improved burn care, including improved resuscitation protocols and intensive

care. Peck described a decline across the world in mortality due to fire and flames [13]. Declines in burn related mortality have been described in several hospital based studies [5,31] and burn centre based studies [26], but not in all studies [1]. Burn centre mortality is only a small part of burn related mortality. In the Netherlands, approximately 75 persons die of burns annually, according to data from fire department statistics [32] and mortality statistics. These patients generally die at the scene of the accident or before they reach specialized burn care.

A seasonal variation was also described by others: studies from several countries in North America, Europe and Asia [3,33–36] describe a peak in summer months. We noticed an additional peak in the winter months December and January, possibly related to the end of year festivities including fireworks and the more frequent use of fireplaces and highly flammable fuels in table cookers.

Patient profiles in burn care were strongly correlated to age groups. For instance, in young children scalds were most prevalent, frequently caused by an accident in house, which resulted in relatively small burns. Extensive burns, over 20% TBSA, were hardly prevalent in young children. Older patients most often suffered from flame burns, after accidents in the house (40%) or at work (18%), which generally resulted in burns of max. 10% TBSA (>60%) but sometimes also in extensive burns (16–19% of the elderly patients). Similar findings are reported by other burn centres in Europe or North America. Future in-depth studies on the epidemiology of specific age groups are planned to reveal detailed information for prevention and quality control.

Mean time to surgery in the Netherlands was 15 days post burn in the past decades, no significant trend was observed. This reflects the current treatment strategy in Dutch burn centres; mixed partial to full thickness wounds are conservatively treated for 10–14 days, followed by excision and split skin auto grafting of the remaining non healed areas [37]. The optimal timing of excision and grafting is subject of ongoing debate [38]. In a recent meta-analysis early excision ranged from <24 h to <144 h post burn [39]. This review of six randomized, controlled trials compared early excision of burns with wound dressing and grafting after eschar separation and found a trend towards a reduction in mortality with early excision and a significant reduction in the length of hospitalization. However, in patients who underwent early excision, blood-transfusion was increased. There was no consistent evidence of reduced sepsis or a better cosmetic or functional outcome with early excision. In the near future a Cochrane review will address this topic [40].

The merit of our Dutch Burn Repository is in the nationwide character and the 100% coverage of burn centre patients. In other countries with larger numbers of burn centres, like the UK, Australia and New Zealand, similar burn centre based registrations have been developed, including data on all patients, outcome and quality of care, but nationwide participation is not always reached [41]. In the USA, the National Burn Repository (NBR) covers 91 of 123 US burn centres, plus 5 centres from Canada and Sweden. In the NBR, burn centre deliver data from convenience samples of patients, not necessary all patients [27].

Some shortcomings of our study have to be mentioned. Data are lacking on outpatient treatments. Data on these outpatient activities of burn centres would add to our knowledge on the whole spectrum of specialized burn care. We aim to include these data into the Dutch Burn Repository R3 in the near future. Next, specific patient characteristics (e.g. comorbidity, socio-economic status) cannot be discussed, since these variables were absent in the historical databases. However, with the uniform database from 2009 onwards several problems are overcome and more detailed information is available. As a result we can direct prevention, monitor quality of care and facilitate scientific research. Finally, we did not have the digital NHDR data, and thus only limited analyses could be done on the overall burn related admissions in the Netherlands. A frequent problem in these data sets is the

double counting of patients with an admission in the first hospital and in the subsequent burn centre. This problem will apply to the Dutch data, but only to a small minority. The majority of our patients are first seen on EDs of general hospitals. However, they are transferred immediately to a burn centre for admission and further treatment because of the short distances to specialized burn care in our country. Thus the delivered data was of good quality and sufficient to compare trends in specialized burn care to trends in non-specialized burn care.

In conclusion, this study gives a unique overview of specialized Dutch burn care in the past 17 years. Data on 9031 patients show a shift in burn centre utilization, with increasing incidence rates of burn-related burn centre admissions, a decreasing incidence rate of burn related admissions in general hospitals, a decreasing burn severity in burn centres and decreasing in-burn centre mortality rates. Patients with burns needing hospital admission are more and more referred to specialized burn care, rather than general hospitals. These data are important for prevention and adequate establishment of the burn care facilities capacity.

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## Conflict of interest statement

The authors declare that they have no conflict of interest.

## Acknowledgements

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## Appendix A

The 'Dutch Burn Repository Group' consists of:

- Burn Centre Beverwijk: EC Kuijper, FRH Tempelman, AFPM
- Vloemans, PPM van Zuijlen.
- Burn Centre Rotterdam: A van Es, H Hofland, J Dokter.
- Burn Centre Groningen: J Eshuis, J Hiddingh, S ScholtenJaegers.
- Association of Dutch Burn Centres: ME van Baar, E Middelkoop, MK Nieuwenhuis, A Novin, M Novin.

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# Chapter 3

# Epidemiology of children admitted to the Dutch burn centres. Changes in referral influence admittance rates in burn centres

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## ABSTRACT

***Background:*** In the Beverwijk Burn Centre a remarkable rise has been noted in the number of paediatric admissions since 2000. To investigate if this is a national trend and, if so, what may have caused it, a retrospective epidemiological study has been undertaken.

***Materials and methods:*** The databases of the three Dutch burn centres were combined. Data on the population at risk for admission in a burn centre and data on burns related hospital admissions were added. Two age groups, 0–4 years and 5–17 years and two time periods, 1995–1999 and 2000–2007, were compared.

***Results:*** The mean number of paediatric admissions in the Dutch burn centres per year increased by 44.0% and 44.3% for the younger children (0–4 years) and the older children (5–17 years), respectively, whereas the number of paediatric burn admissions in other hospitals in the Netherlands decreased. The percentage of children that was referred from other hospitals increased in both age groups, and for the younger children this was significant.

***Conclusion:*** There has been a shift in paediatric burn care towards a greater volume of admissions in specialized burn care of especially young children with less severe burns. A possible explanation for the increased number of referred children may be the introduction of the EMSB course in 1998, since EMSB guidelines dictate stricter and generally accepted referral criteria.

## 1. INTRODUCTION

Epidemiological data on burns are published frequently. The majority of publications concern epidemiological data on burns in a specific country, a regional area or a group of patients. The results are used to achieve understanding of the aetiology of burns and subsequently establish effective prevention campaigns [1–3] with the ultimate goal of reducing the number of severe burns. Other studies concern patients admitted to a single burn centre or burn unit. Besides determining the targets for future prevention campaigns, the goal of these studies is to gain insight in the numbers of admitted patients, aetiology, duration of admission and mortality or for purposes of treatment evaluation, quality and capacity control [4–13]. Some of these studies concern a prolonged time span and attempt to elucidate changing number of patients referred to a burns centre, patterns in aetiology, and mortality [9].

In the Netherlands (population 2011 16.75 million, area 41,528 km$^2$), the registration of burn patients began with the establishment of the first of three burns centres in 1974. The burn centres were housed non-university hospitals, located in the northeast, Groningen, in the midwest, Beverwijk and in the southwest of the Netherlands, Rotterdam (Fig. 1).


**Fig. 1 – Location of burn centres in the Netherlands.**

Except for a recent publication on mortality and causes of death in a Dutch burns centre [6], epidemiological studies of patients admitted to the Dutch burn centres have not yet been published.

In the Beverwijk Burn Centre a preliminary analysis on the number of admitted children showed a marked rise in paediatric admissions from 2000 onwards. We wanted to identify if this increase in admissions represented a national trend and investigate the potential causes. Possible explanations for the rise in admissions included an increase in the number of children in the Dutch population and an increase in the incidence of burns in children in the Netherlands, or a change in the referral pattern. A plausible cause for an increase of referrals would be the introduction of the Emergency Management of Severe Burns course (EMSB) in 1998 [14]. The referral criteria of the EMSB (Table 1) are more strict and binding than the formerly applied directives of the Dutch burn centres (Table 2) [15,16]. The doctrine of EMSB and similar courses like Advanced Trauma Life Support (ATLS) has become the precept in most Dutch casualty departments and stricter adherence might have contributed to a difference in the referral pattern.

**Table 1 – EMBS Criteria for referral to a Dutch Burn Centre [16].**

- Burns greater than 10% Total Body Surface Area (TBSA) in adults.
- Burns greater than 5% TBSA in children.
- Burns of special areas – face, hands, feet, perineum, genitalia and major joints.
- Full thickness burns greater than 5% TBSA.
- Electrical burns.
- Chemical burns.
- Burns with associated inhalation injury.
- Circumferential burns of the limbs or chest.
- Burns at the extremes of age – children and the elderly.
- Burns in patients with pre-existing medical disorders which could complicate management and prolong recovery or effect mortality.
- Any burn patient with associated trauma.

**Table 2 – Formerly applied criteria for referral to a Burn Centre [15].**

- Burns greater than 25% TBSA in adults or deep burns over 10%TBSA
- Burns greater than 10% TBSA in children and elderly, irrespectively the depth
- Minor burns associated with another injury or pre-existent disease that may increase the risk for complications

To investigate these hypotheses, further analysis was necessary of the data from the Beverwijk burn centre, the data from the other Dutch burn centres and of the data on burn injury related admissions to the other Dutch hospitals, particularly also in view of the consequences that the results of these analyses might have for the allocation of paediatric

burn designated beds in the Dutch burn centres.
Because all three burns centres had data sets on admitted patients as going back to 1995, two time periods were compared; 1995–1999 and 2000–2007. In this retrospective study the results of these separate registrations were combined and analysed, focussing on children with burns.
The aim of this study was to describe the epidemiology of paediatric patients admitted to Dutch burn centres in order to elucidate potential changes in the number of patients injured, referral patterns and characteristics of patients, as well as burns and treatment related characteristics.



## 2. MATERIALS AND METHODS

### 2.1. Population

All children up to 18 years of age, with a primary admission to one of the three Dutch burn centres in the period 1995–2007 were included in this study.
We focused on differences between two periods and between young children (aged 0–4 years) and older children (aged 5–17 years). As young children have other activities and therefore often a different aetiology for their injuries compared to older children, the partition was made at 4 years old [1,13]. According to the Dutch law children reach adults status at the age of 18; therefore the upper age limit was set at 17 years.
In the analysis, two time periods were reviewed, 1995–1999 and 2000–2007. As a reference group, data on the incidence of primary burn centre admissions of adults (18 years and over) were included.

### 2.2. Data collection

Data on the patient (age, gender), the burns (site of the accident, aetiology, referral, the total body surface area (TBSA), the depth of the burn), and treatment related characteristics (need for surgical intervention, ventilation, length of stay and mortality) were derived from historical registrations of the three Dutch
burn centres. After permission of relevant representatives from the respective hospitals the anonymous data were combined into one dataset and this dataset was checked for inconsistencies and missing data. These data were then corrected based on patients' files, discharge records and operation reports. Data analysis was performed on the corrected database. To interpret the number of admissions in the Burn centres, proportions and incidence density rates were calculated as follows: the proportion of paediatric burn related hospital admissions in specialized burn centres was calculated by the number of the paediatric burn related hospital admissions in specialized burn centres in one year, divided by the total number of paediatric burn related hospital admissions in all hospitals in the Netherlands in the same year. Data on burns related admissions in all Dutch hospital were derived from the National Hospital Discharge Register (NHDR) and from the Consumer

Safety Institute (CSI) [17]. All primary burn related admissions were extracted, using the International Classification of Diseases (ICD-9) codes 940–949. A distinction was made between burns related hospital admissions in hospitals with a burn centre versus general hospitals.
Incidence density rates were calculated as the number of admissions in a Dutch burn centre in a specific age category in one year, divided by the total number of persons at risk in this age category in the Netherlands in the same year. The denominator data refer to the population on July 1st of a specific year, using the mean of the population at January 1st that year and the population at January 1st of the following year. Data on the population at risk for admission in a Dutch burn centre, being the total number of children aged 0–17 residing in the Netherlands, were derived from the population's statistics available on StatLine, Statistics Netherlands [18]. In the study periods the mean population was 15.98 million, with a share of 6.2% young children (0–4 years) and 15.8% of children aged 5–17.

### 2.3. Statistical analysis

Change in admissions were analysed by the Chi square test for trend. Differences between time periods and age groups were analysed with logistic regression, calculating odds ratios (OR) and their corresponding 95% confidence intervals (C.I.). Differences in median TBSA, length of stay and length of stay per %TBSA were analysed using Mann–Whitney U. To assess risk profiles for a burn centre admission in children 5 years and older, we used backward multiple logistic regression. Data were analysed in SPSS 1 software version 17 and 18 (PASW Statistics).

## 3. RESULTS

### 3.1 Incidence of paediatric burn centre admissions

From the first period (1995–1999) to the second period (2000–2007) the mean number of admission in the Dutch burn centres per year increased from 113 to 163 for the younger children and from 50 to 71 for the older children, representing an increase of 44.0 and 44.3%, respectively. In patients over 18
years old the annual mean number of admissions increased from 290 to 303, a rise of 4.3%. The proportion of children admitted to specialized burn centres, rather than to general hospitals, increased over time from approximately 30% in 1995 to almost 50% in 2007 in both age groups ( $p < 0.001$). In the 0–4 years age group, almost 50% of all burn admissions in the Netherlands was to a specialized burn care setting (Fig. 2).
The incidence of burn centre admissions per 100,000 population in the period 1995–2007 is represented in Fig. 3. For the 5–17 years age group and the adults the incidence was about the same. However, it can be noted that the relative risk for a small child (0–4 years) to be admitted to a burn centre was up to five times higher than for an older child (5–17 years) and an adult (Fig. 3).

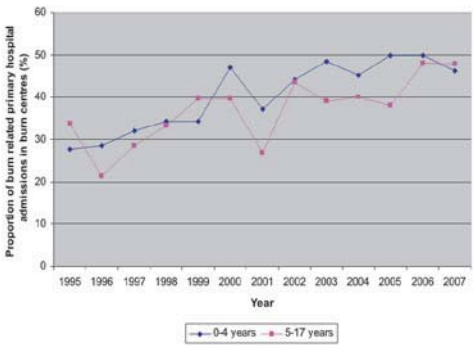


**Fig. 2 – Proportion of paediatric burn related hospital admissions in specialized burn centres, over time.**

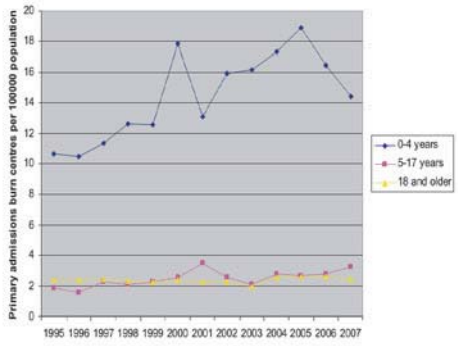


**Fig. 3 – Incidence of paediatric burn centre admissions in the Netherlands, by age category.**

## 3.2. Patient and burns related characteristics

In the time period of 2000–2007, significantly fewer accidents occurred in and around the house (Table 3). Also, the referral pattern for the younger children changed significantly. In 62.9% children were referred by another hospital, this increased to 68.8% in the second time period. In the older children the increase in referrals from another hospital was not significant (Table 3).

In both age groups more boys than girls were admitted and this ratio did not change in the two time periods. In children aged 0–4 years, burn size decreased significantly over time and the percentage of these children diagnosed with full thickness burns was also reduced. In the age group of children aged 5–17 years, fewer children with burns over 10% were admitted (Table 3).

The TBSA in young children decreased from 7% TBSA (IQR: 4–11) to 5% (IQR = 3–8) ( $p < 0.01$); the mean burn size decreased from 8.7% (SD 7.6) to 6.4% (SD 6.2) ( $p < 0.01$). In children aged 5 years and over, median burn size was stable with 6% in period 1 (IQR 3–13), and 5% in period 2 (IQR 3–10) ( $p = 0.05$). The mean burn size was 9.4% (SD 10.0) and 9.5% (SD 13.4) ( $p = 0.86$).

**Table 3 – Patient and burn related characteristics of young and older children admitted to Dutch burn centres, by study period.**

| | 0–4 years | | | | 5–17 years | | | |
|---|---|---|---|---|---|---|---|---|
| | 1995–1999 N = 563 % | 2000–2007 N = 1300 % | OR | (95%C.I.) | 1995–1999 N = 248 % | 2000–2007 N = 571 % | OR | (95%C.I.) |
| Gender | | | | | | | | |
| Boy | 57.9 | 61.3 | 1.0 | | 70.2 | 70.9 | 1.0 | |
| Girl | 42.1 | 38.7 | 0.9 | (0.7;1.1) | 29.8 | 29.1 | 1.0 | (0.7;1.3) |
| Site of accident | | | | | | | | |
| In, around the house | 93.5 | 89.2 | 0.6 | (0.4;0.9) | 71.6 | 64.7 | 0.7 | (0.5;1.0) |
| Other | 6.5 | 10.8 | 1.0 | | 28.4 | 35.3 | 1.0 | |
| Aetiology | | | | | | | | |
| Scald | 81.4 | 85.5 | 1.0 | (0.4;2.3) | 23.4 | 22.4 | 0.8 | (0.3;1.8) |
| Fat | 7.2 | 3.7 | 0.5 | (0.2;1.2) | 13.0 | 7.6 | 0.5 | (0.2;1.2) |
| Flame | 7.4 | 6.1 | 0.8 | (0.3;2.0) | 57.6 | 62.9 | 0.9 | (0.4;2.0) |
| Contact | 2.5 | 3.1 | 1.2 | (0.4;3.5) | 2.2 | 2.4 | 0.9 | (0.3;3.2) |
| Other | 1.5 | 1.6 | 1.0 | | 3.9 | 4.7 | 1.0 | |
| Referral | | | | | | | | |
| Hospital | 62.9 | 68.8 | 1.3 | (1.1;1.6) | 56.0 | 63.3 | 1.4 | (1.0;1.9) |
| Self referral, GP, AED | 37.1 | 31.2 | 1.0 | | 44.0 | 36.7 | 1.0 | |
| TBSA burned | | | | | | | | |
| 0–5% | 41.0 | 56.1 | 1.0 | | 47.4 | 55.4 | 1.0 | |
| >5–10% | 32.3 | 30.5 | 0.7 | (0.5;0.9) | 20.2 | 20.2 | 0.9 | (0.6;1.3) |
| >10% | 26.6 | 13.5 | 0.4 | (0.3;0.5) | 32.4 | 24.4 | 0.6 | (0.5;0.9) |
| Median (IQR) | 7 (4–11) | 5 (3–8) | n.a. | n.a. | 6 (3–13) | 5 (3–10) | n.a. | n.a. |
| Full thickness burns | | | | | | | | |
| No | 46.2 | 61.1 | 1.0 | | 34.7 | 39.2 | 1.0 | |
| Yes | 53.8 | 38.9 | 0.5 | (0.4;0.7) | 65.3 | 60.8 | 0.8 | (0.6;1.1) |

IQR = interquartile range, 25th–75th percentile, n.a. = not applicable.
Missing values 0–4 years period 1, period 2: site of accident $n = 53$, $n = 64$; aetiology $n = 35$, $n = 24$; referral $n = 38$, $n = 180$.
Missing values 5–17 years period 1, period 2: site of accident $n = 37$, $n = 42$; aetiology $n = 17$, $n = 18$; referral $n = 23$, $n = 56$.

**Table 4 – Treatment related characteristics of young and older children admitted to Dutch burn centres, by study period.**

| | 0–4 years | | | | 5–17 years | | | |
|---|---|---|---|---|---|---|---|---|
| | 1995–1999 N = 563 % | 2000–2007 N = 1300 % | OR | (95%C.I.) | 1995–1999 N = 248 % | 2000–2007 N = 571 % | OR | (95%C.I.) |
| Surgery | | | | | | | | |
| No | 61.6 | 73.4 | 1 | | 47.2 | 52.0 | 1 | |
| Yes | 38.4 | 26.6 | 0.6 | (0.5;0.7) | 52.8 | 48.0 | 0.8 | (0.6;1.1) |
| Ventilation | | | | | | | | |
| No | 98.8 | 97.6 | 1.0 | | 94.8 | 91.4 | 1.0 | |
| Yes | 1.2 | 2.4 | 2.1 | (0.9;5.2) | 5.2 | 8.6 | 1.7 | (0.9;3.2) |
| Length of stay | | | | | | | | |
| 1–6 days | 31.3 | 48.1 | 1.0 | | 33.2 | 36.8 | 1.0 | |
| 7–13 days | 24.0 | 21.4 | 0.6 | (0.4;0.8) | 15.4 | 17.5 | 1.0 | (0.7;1.6) |
| 14 days and more | 44.8 | 30.5 | 0.4 | (0.4;0.6) | 51.4 | 45.7 | 0.8 | (0.6;1.1) |
| Median (IQR) | 11 (5–22) | 7 (3–16) | n.a. | n.a. | 14 (4–26) | 10 (3–23) | n.a. | n.a. |
| LOS per %TBSA, median (IQR)* | 1.5 (1.0–2.5) | 1.4 (0.8–2.4) | n.a. | n.a. | 2.0 (1.1–3.5) | 2.0 (1.0–3.4) | n.a. | n.a. |
| Deceased | | | | | | | | |
| No | 99.8 | 99.4 | 1.0 | | 99.2 | 98.9 | 1.0 | |
| Yes | 0.2 | 0.6 | 3.5 | (0.4;27.9) | 0.8 | 1.1 | 1.3 | (0.3;6.5) |

IQR = interquartile range, 25th–75th percentile, n.a. = not applicable.

* Mann–Whitney *U* test difference between periods: 0–4 year, $p = 0.01$; 5–17 years, $p = 0.60$.

### 3.3. Treatment

In Table 4 the treatment related characteristics of children admitted to Dutch Burn centres by age group are summarized. The number of children that required surgery was significantly reduced for the younger children in time period 2000–2007. For the older children the requirement for surgery was also reduced, however this difference was not statistically significant. In both age groups the percentage of children that was ventilated has increased, but this did not reach a level of statistical significance. For children aged 0–4 years, the percentage of children that required a hospital stay of 7 days or more was significantly reduced. In addition, median length of stay and length of stay per % TBSA decreased as well. For the older children the change in length of stay was not statistically significant.
In the two age groups and time periods mortality did not change.

### 3.4. Risk profile

We used a multivariate analysis to extract a risk profile for a burn centre admission in children 5 years and older. Admissions of older children and adolescents are predominantly the result of an accident not being in and around the house (odds ratio = 0.4). The type of injury is primarily a flame burn (OR = 4.9) and not a scald (OR = 0.2).

## 4. DISCUSSION

The aim of this study was to describe the epidemiology of paediatric patients admitted to Dutch burn centres in order to elucidate potential changes. Initially this study was a monocentre analysis performed in 2005 with equal time periods
1995–1999 and 2000–2005. To present a nationwide analysis, data from the other two burn centres were included and recent data from the years 2006 and 2007 were added. However, as there were to many missing data before 1995, the years 1993 and 1994 could not be included.
Our assumption that after the year 2000 the number of admitted children in the Dutch burns centres has increased is confirmed by this study. The mean annual number of paediatric burn centre admissions increased by 44%, while
in the adult group the increase was only 4.3%. The proportion of paediatric burn related hospital admissions in specialized burn centres also showed an increase, as did the incidence rate (per 100,000 population). This means there is a shift in
paediatric burn care towards a greater volume of admissions in specialized burn centres [17,18].
The peak in admissions of children of 5–17 years in 2001 (Fig. 3) is caused by the high number of burn victims from the Volendam disaster on January 1, 2001 [19]. In this year the

incidence of paediatric burn centre admissions shows a decrease for the children between 0 and 4 years of age, which can be explained by a shortage of capacity in the burn centres for an extended time, because the older children occupied most paediatric beds. Similarly, the proportion of burn related primary hospital admissions in burn centres (Fig. 2) decreased during that year as a relatively high number of burn victims was admitted to non-specialized hospitals, since the burn centres were fully occupied and had no admission capacity. Comparison of our paediatric incidence to literature data is hampered by a lack of studies with clear catchment populations and differentiation in age categories, as described earlie by Burd and Yuen [20]. Three state wide studies from Australia, Canada en the USA presented incidence data of hospitalized paediatric burn patients varying between 29.7 and 76.1 admissions per 100,000 population in young children (0–4 years) and 8–115.7 per 100,000 in older children (10–14 years) [21–23]. Our data correspond tot the lower limits of these incidence data, given the fact that the burn centres treat a proportion of up to 50% of all hospitalized paediatric burn patients in the Netherlands. Incidence data of specialized burn care paediatric patients are hardly available. Sharma et al., in a single burn centre study reported an overall incidence of paediatric burn centre admissions in Kuwait of 17.5/100,000 in children aged 0–14 and 34/100,000 in young children, aged 0–4 [24]. These data are based on a single burn centre, representing 93% of all burn related hospital admissions.

Children with burns requiring a hospital admission are more often referred to specialized burn centres than to general hospitals. As a result, more children with smaller and more superficial burns are seen in our burn centres. This change in burn size has been described earlier for American burn centre admissions [25].

In our study, the cause of injury shows patterns similar to those described in the literature. In young children (0–4 years) scalding is by far the most important cause of the burns, followed by flame burns and burns by hot fat or oil. In older children (5–17 years) flame burns are the most common, followed by scalding and hot fat or oil. The aetiology has not changed over time. However, significantly less young children sustained a burn in and around the house. The number of children referred from another hospital has statistically significantly increased in young children, but in older children the increase in referrals was not significant. In young children, burn size decreased considerably over time and fewer full thickness burns were diagnosed. In the older children, overall burn size remained the same, but fewer burns >10% TBSA were seen. It may be concluded that hospitals refer more children with smaller and less deep burns in the time period 2000–2007 compared to the time period 1995–1999.

The possible role of the introduction of the EMSB course was not suspected at the time of the first analysis. Although the EMSB was introduced in the Netherlands in 1998, the awareness of the stricter referral criteria became known only a couple of years later.

An explanation for the increased referral of children may be an alteration in nationally

accepted protocols on referral of burn victims. The organisation of burn care in the Netherlands started in 1970 with the start of the Dutch Burns Foundation (DBF). Prevention of burns, informing the public, carrying out scientific research in the field of burn treatment and management of the skin bank were the main goals of the DBF. In 1974 the first Dutch burn centre was established in Beverwijk, followed by burns centres in Groningen and Rotterdam in later years. Standard referral criteria for all three centres were established and published in 1980 [15] and these criteria (Table 2) were sent to all Dutch hospitals. They only served as guidance for physicians in the Netherlands who rendered the first treatment to burn victims and following these guidelines was non-mandatory. With the introduction of Advanced Trauma Life Support, ATLS, the emergency treatment of multitrauma patients in all Dutch hospitals was standardized through set protocols. In 1998 the course on Emergency Management of Severe Burns (EMSB) was introduced in the Netherlands. In this course, focussed on the emergency management of burn patients, the principles of initial treatment of trauma patients were similar as in the ATLS protocol. The guidelines for referral of burn patients were tightened and became compulsory for the physicians in the emergency wards. With regard to children, the "old" recommendations advised to refer children with burns over 10% TBSA, whereas the new EMSB referral criteria advise to refer children with burns exceeding 5%. The referral criteria are well adopted in the Netherlands. An additional factor also may have contributed to the increased referral of children with burns. After the Volendam disaster, burn care for children received a great deal of publicity and this exerted pressure to doctors to refer children to burn centres. Although the mean and median TBSA of small children with burns were reduced in time, the majority of patients is referred appropriately, according to the referral criteria [26]. Therefore the admittance of these patients to a specialized centre is justified and indicated. In addition, Dutch burn centres have enough capacity for children with small burns. Lack of capacity exists mainly when there is an excessive request for referral of patients with major burns, requiring Intensive Care treatment. Moreover non-burn hospitals lack a dedicated team of nurses and paramedics trained in the treatment as well as specialized aftercare of children with burns.

As can be expected from the changed patient and burn related characteristics, the treatment related characteristics have also changed in the second time period. As the burns of the referred children aged 0–4 years were smaller and less deep, the number of operations and the length of stay have decreased.

Remarkably, it seems that more children were artificially ventilated during their admission, although the numbers are small. Many of them were ventilated before being transferred to the burn centre. This is in line with the findings of Mackie et al., who recently described a mixed population of adults and children admitted in a Dutch burn centre [27].

Prior to this study, we had no indications of whether the introduction of the stricter EMSB referral criteria had any impact on our admission rates. Until now, it had not been studied if

these stricter referral guidelines did result in more admissions. Knowledge of changes in the pattern of referral is important to guarantee sufficient capacity, especially of the Intensive Care facilities, in the burn centres.
This study also shows the superior value of a national burn registry, compared to single burn centre registries. Only on a national scale, the impact of changed referral criteria can be fully evaluated. In several countries, national registries have been set up. Examples of this type of registry are the National Burn Repository in the United States, the international Burn Injury Database in the United Kingdom, the Bi-National Burns Registry in Australia and New Zealand and the registry in the German speaking countries [27–30].
Since 2004 the three Dutch burns centres closely co-operate in the Association of Dutch Burn Centres (ADBC). One of the purposes of this association is the development of a common burn registration. Data in this paper were derived from a historical database including the three separate registries of the burn centres. In 2009 the Dutch Burn Repository R3 was initiated. With this new registration, trends in burn accidents, patterns of admissions of burn victims and data on mortality will become more easily available. Advice for burn prevention campaigns of the DBF and the CSI can be issued based on these data and the registry also serves as an instrument for quality improvement. Until now only data of admitted patients are included, but in the near future also data of outpatients will be registered as well. With the recent introduction of the electronic patient file (EPF) in the Dutch burn centres, data can be automatically linked to the R3 database. As a result, time-consuming data entry is reduced which increases both data collection and accuracy.

## 5. CONCLUSION

A shift in paediatric burn care towards a greater volume of admissions in specialized burn care has taken place especially with regard to young children with less severe burns. This is probably the result of changes in referral criteria, introduced in the late nineties. As a result, children receive optimal care
by experienced burn care teams.

### Conflict of interest

None.

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# PART TWO

## Management

# Chapter 4

# Reduction in skin grafting after the introduction of hydrofiber dressings in partial thickness burns: A comparison between a hydrofiber and silversulphadiazine

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## ABSTRACT

***Aim/purpose***: The aim of this study was to compare clinical outcome of children with scald burns treated with a hydrofiber dressing (Aquacel®, *Convatec Inc.)* with the former standard of care with silver sulfadiazine (Flammazine®; *Solvay Pharmaceuticals*), considering surgical intervention and length of stay (LOS).

***Methods:*** A retrospective study of all consecutive children from zero to four years with primary scald burns up to 10% admitted to the Burn Centre of the Maasstad Hospital Rotterdam between January 1987 and January 2010 were reviewed. For data collection a prospective computerized database was used. For comparison the study period was divided into two periods representing the period before and after the introduction of the hydrofiber dressing (HFD), respectively 1987–1999 (period 1) and 1999–2010 (period 2).

***Results:*** Over the whole study period 27.3% of 502 patients treated with silver sulfadiazine (Ag-SD) underwent surgery, while before the introduction of HFD 30.5% of 338 Ag-SD treated patients were operated upon. After the introduction of the HFD 20.7% of 164 patients treated with Ag-SD eventually underwent skin grafting, a significant difference with the 11.6% of 302 patients whose wounds were dressed with HFD ( $p < 0.01$).

***Conclusions:*** Compared to silver sulfadiazine treatment a reduced number of surgical interventions was observed in mixed partial thickness scald burns up to 10% TBSA burned in children aged 0–4 years after the introduction of hydrofiber dressings. The mode of treatment with this wound dressing also limited hospital length of stay.

## 1. INTRODUCTION

Silver sulfadiazine (Ag-SD) was introduced in the late sixties and early seventies and is currently worldwide used for the topical treatment of burns. Due to its broad antibacterial spectrum leading to lesser wound infection and sepsis more patients with severe burns could survive [1,2]. In full thickness burns these benefits have been proven and Ag-SD is implemented in many treatment protocols. Different from the treatment of full-thickness burns or burns over a large surface area, where the main goal is to diminish bacterial counts awaiting eventual operative interventions, in fresh non-infected partial thickness burns the focus is directed to the preservation of remaining viable epithelial elements. Especially in scald burns areas of superficial, deep dermal and to a lesser extent subdermal burns are present. In these mixed partial-thickness burn wounds the policy is to wait and see to distinguish between parts that will heal spontaneously and demarcation of larger and deeper areas that require excision and grafting. Meanwhile an environment has to be created where wound healing can emerge from epithelium still present in the wound bed. In the late eighties it became evident that the best suitable environment for wound healing was moist instead of dry [3]. In several studies it was shown that Ag-SD has cytotoxic effects that impair healing of partial thickness burn wounds by inhibition of basal keratinocytes growth [4]. Therefore modern wound dressings that create a moist yet stable environment are used more and more. These include amongst others hydrofiber dressings, for example Aquacel (Aquacel®, Convatec Inc.), achieve this moist and stable environment.

Aquacel® is a primary wound dressing made from sodium carboxymethylcellulose and is produced as a textile fibre presented in the form of a fleece held together by a needle bonding process. The dressing has a large fluid-absorption capacity and interacts with wound exudates to form a soft, hydrophilic, gas-permeable gel providing a micro-environment that facilitates healing. The vertical absorption properties help to maintain the moist area over the wound and reduce the risk of maceration.

In the Burn Centre of the Maasstad Hospital Rotterdam the hydrofiber dressing (HFD) Aquacel® was introduced in 1999, primarily used for scalds of limited surface area.

Before that time also in our centre scalds were mainly treated with Ag-SD (Flammazine®; *Solvay Pharmaceuticals*).

The aim of this study was to compare clinical outcome between children with scald burns treated with HFD (Aquacel®) and the former standard of care with silver sulphadiazine (Flammazine®), considering the surgical intervention, length of stay (LOS) and re-admission in the hospital for treatment of the same burns.

## 2. METHODS

### 2.1 Data collection

In order to obtain a homogeneous population all consecutive children from zero to four years with primary scald burns up to 10% admitted to the Burn Centre of the Maasstad Hospital Rotterdam between January 1987 and January 2010 were reviewed. For data collection a prospective computerized database was used.

### 2.2. Study period and treatment protocols

For comparison the study period was divided into two periods representing the period before and after the introduction of HFD, respectively 1987–1999 (period 1) and 1999–2010 (period 2). In period 1 most scald burns under 10% Total Body Surface Area (TBSA) burned were treated with daily hydrotherapy and change of bandages with Ag-SD.
In period 2 HFD was predominantly applied, as seen in Fig. 1. Depending on the amount of exudate and/or in case of sliding of the dressing an additional layer was applied. After about ten to twelve days HFD were removed to assess the wound and to decide whether skin grafting was necessary.
In period 2 Ag-SD was also applied in a minority of cases, especially in localizations where HFD was less applicable (joints, hand, face).

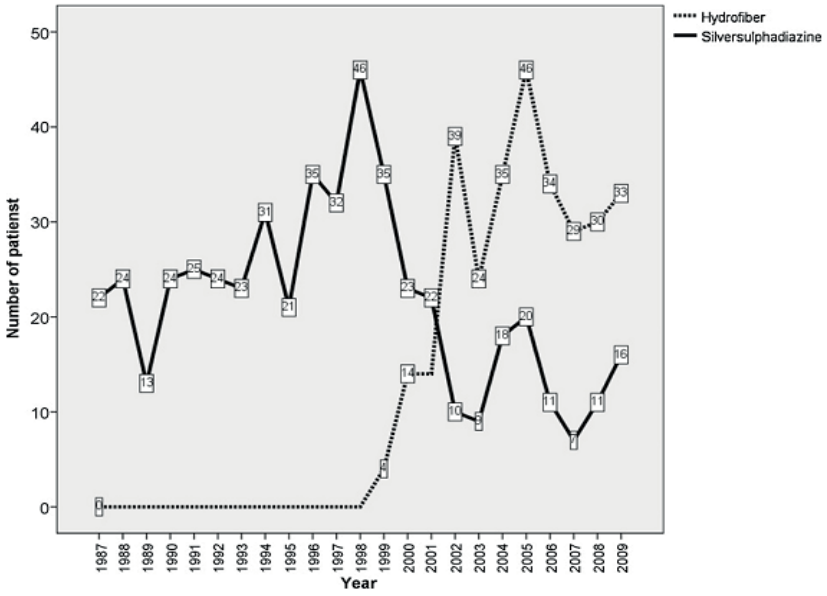


**Fig. 1 – Inclusion of patients treated with Ag-SD and HFD.**

### 2.3. Study endpoints

The primary outcome was the incidence of surgical treatment before and after the introduction of HFD. Surgical treatment was defined as tangential excision and split skin grafting. Secondary endpoints were length of stay and re-admission for treatment of the same burns. The total length of stay was calculated, based on the length of stay during first admission and re-admission(s).

### 2.4. Statistics



Differences in patient demographics and outcome between the three groups (Ag-SD period 1, HFD period 2 and Ag-SD period 2) were tested. Differences in genders, surgical interventions, and re-admissions were analyzed using Chi-square test. Differences in age, TBSA burned and length of stay were analyzed using analysis of variance (ANOVA).
For patients in all groups who underwent surgery Independent Samples Median Test was to determine significance of differences in time between injury and operation.
Statistical significance was declared at the 0.05 level. All statistical analyses were performed using SPSS for Windows, version 15.0.1 (SPSS, Inc., Chicago, IL).

## 3. RESULTS

### 3.1. Demographics

During the study period 5122 patients were admitted to the Burn Centre of Rotterdam, The Netherlands. Of these 401 were hospitalized for secondary reconstructive surgery and 240 were re-admissions, leaving 4481 eligible first admissions: 3314 of them were older than 4 years, 196 children had another etiology than scalds and 167 children with scald burns had a TBSA burned >10%.
Therefore 804 children from 0 to 4 years with primary scald burns up to 10%TBSA were eligible for analysis, 502 were treated with Ag-SD and 302 treated with hydrofiber. The flowchart of the inclusion of patients is shown in Fig. 2.

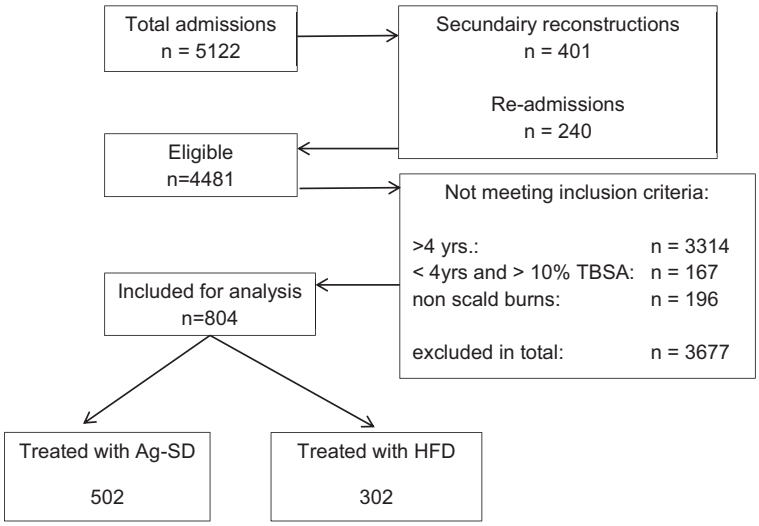


Fig. 2 – Enrolment of 804 patients from January 1987 until January 2010

In period 1, before the introduction of HFD, 338 patients were treated with Ag-SD (Table 1): 202 were boys and 136 girls (ratio of 59.8% vs. 40.2%). In the period after the introduction of HFD 164 patients were treated with Ag-SD. The male–female ratio in this group (55.5% vs. 44.5%) did not differ significantly from the male–female ratio in the first period ( $p = 0.21$). Also there were no differences in male–female ratio between all treated with Ag-SD and HFD treated patients ( $p = 0.43$). Although the difference in mean age of 1.3 years in Ag-SD treated patients vs. 1.1 years in the HFD group is statistically different ( $p < 0.01$), this minor age difference is clinically irrelevant. The mean TBSA burned was also comparable in AgSD and HFD treated patients ( $p = 0.50$)

**Table 1 – Demographics of the three study groups.**

| | Ag-SD before introduction of HFD | Ag-SD after introduction of HFD | AgSD total | HFD | p-Value |
|---|---|---|---|---|---|
| Patients | 338 | 164 | 502 | 302 | |
| Male/female | 202/136 | 91/73 | | | 0.21* |
| | | | 293/209 | 179/123 | 0.43* |
| Mean age (±SD) | 1.3 (±1.04) | 1.3 (±1.09) | | | 0.95** |
| | | | 1.3 (±1.06) | 1.1 | <0.01** |
| Mean TBSA (±SD) | 5.3 (±2.45) | 4.9 (±2.51) | | | 0.06** |
| | | | 5.2 (±2.47) | 5.1 | 0.50** |

SD, standard deviation.
* p-Values using Chi-square.

### 3.2. Primary outcome: need for surgical treatment

Before the introduction of HFD 30.5% of 338 Ag-SD treated patients were operated upon (Table 2). After the introduction of HFD 20.7% of 164 patients treated with Ag-SD eventually underwent skin grafting, a significant reduction over time (p=0.01). Compared to 20.7% operative procedures in the AgSD group after introduction of HFD, a further drop in surgical interventions to 11.6% was observed in patients dressed with HFD (p< 0.01).

**Table 2 – Operative interventions in scalds over time using Ag-SD or HFD.**

| | Ag-SD before introduction of HFD | Ag-SD after introduction of HFD | HFD | *p*-Value |
|---|---|---|---|---|
| Patients | 338 | 164 | 302 | |
| Operations | 103(30.5%) | 34(20.7%) | | 0.01 |
| | | 34(20.7%) | 35(11.6%) | <0.01 |

*p*-Value using Chi-Square.

Further analysis of data reveals that the median interval between time of injury and operation was different in the two Ag-SD groups; 14.0 days for Ag-SD treated patients before the introduction of HFD (range 1–181 days) and 20.5 days (range 10–47 days) for 34 Ag-SD treated patients after the introduction of HFD ( p = 0.02 Independent Samples Median Test). Because of a non-normal distribution of the interval between injury and operation in the 103 operated patients in the Ag-SD group before the introduction of HFD, Independent Samples Median Test was used to determine significance (p=0.02).

### 3.3. Secondary outcome: length of stay and re-admission

Considering length of stay it is relevant to include patients who had to be re-admitted for treatment of the same burn. There was no significant difference in re-admissions of Ag-SD treated patient before and after the introduction of HFD (p=0.43).
In the Ag-SD group 13 children (2.6%) were re-admitted over the total period (Table 3). Eighteen children (6.0%) who were treated with HFD had to be re-admitted to the Burn Centre because further treatment in the outpatient clinic turned out to be impossible after all. Before the introduction of HFD 338 patients treated with Ag-SD had to stay in hospital for 12.4 days (Table 3). In those patients who were treated with Ag-SD in the second period (n = 164), where predominantly HFD was used, length of hospital stay significantly decreased to a mean of 9.7 days (p<0.01). Patients with burns treated with HFD (n = 302) were admitted to hospital for 7.5 days, a further significant decrease in length of stay when compared to Ag-SD treated patients in the same time period (p<0.01).

**Table 3 – Re-admissions of Ag-SD and HFD treated patients and length of stay.**

| | Ag-SD before introduction of HFD | Ag-SD after introduction of HFD | AgSD total | HFD | *p*-Valu |
|---|---|---|---|---|---|
| | 338 | 164 | 502 | 302 | |
| Re-admissions | 8 (2.4%) | 5 (3.0%) | | | 0.42 |
| | | | 13 (2.6%) | 18 (6.0%) | 0.02 |
| Mean LOS (days) (±SD) | 12.4 (±8.55) | 9.7 (±7.60) | | | <0.01 |
| | | 9.7 (±7.60) | | 7.5 (±6.46) | <0.01 |

SD, standard deviation.
* *p*-Values using Chi-Square.
** *p*-Values using ANOVA.

## DISCUSSION

In this study we compared the clinical outcome of the treatment of scald burns up to 10% TBSA in children under 5 years using HFD or Ag-SD between 1987 and 2010. Children treated with HFD had a favourable outcome considering treatment with surgery and length of stay. The prevalence of re-admissions in the HFD group was slightly elevated.

As stated before, wound dressings are indicated in noninfected partial thickness burns to create an optimal environment for outgrowth of remnant epithelium, therefore at the time being the first choice of treatment of this type of injury in our clinic.

However, in some places wound dressings are difficult to apply, for example around fingers in little children, or in localizations like the perineum. In those localizations for example Ag-SD is used for practical reasons and also after the introduction of HFD the use of Ag-SD was not completely abandoned.

Over time a decrease in operative procedures in Ag-SD treated patients before and after the introduction of HFD was observed (30.5 vs. 20.7%; p=0.01).

The question arises if this difference in primary outcome of Ag-SD treated patients in this retrospective study could be based on a selection bias for operative intervention. However, before and after the introduction of HFD operated patients turned out to have the same age (mean 1.6 years) and the same TBSA burned (5.4 vs. 5.7%, Table 4). The decrease of operations in Ag-SD treated patients after the introduction of HFD also refutes a potential bias in terms of selection of deeper scald burns in localizations like hands or perineum, in which case more skin grafting would have been observed.

Further analysis of data reveals that the median interval between time of injury and operation was different in the two Ag-SD groups; 14.0 days for Ag-SD treated patients before the introduction of HFD (range 1–181 days) and 20.5 days (range 10–47 days) for 34 Ag-SD treated patients after the introduction of HFD ( p=0.02 Independent Samples Median Test). Before the introduction of HFD therefore Ag-SD treated patients were operated more frequently and at earlier stage, which could be explained by a more conservative approach

in the period that coincides with the introduction of HFD. Indeed, since the introduction of HFD hospital stay was shortened by earlier discharge to outpatient care. In this outpatient care setting, using HFD, wound inspection is not possible during the time that the adherent wound dressing is in place, i.e. about 10 days and therefore the decision for surgery might be delayed. Observing extensive re-epithelialisation in these partial thickness scald burns after that period we also became more conservative as to (delayed) primary surgery in our Ag-SD treated patients.



**Table 4 – Characteristics of operated patients in the three treatment groups.**

| | Ag-SD before introduction of HFD | Ag-SD after introduction of HFD | HFD | *p*-Val |
|---|---|---|---|---|
| | 103 | 34 | 35 | |
| Median interval injury-operation (days) | 14.0 | 20.5 | | 0.02* |
| | | 20.5 | 17.0 | 0.07* |
| Mean age (±SD) | 1.6 (±1.07) | 1.6 (±1.10) | | 0.98** |
| | | 1.6 (±1.10) | 1.3 (±0.82) | 0.13** |
| Mean TBSA | 5.4 (±2.71) | 5.7 (±2.68) | | 0.66** |
| | | 5.7 (±2.68) | 6.2 (±1.90) | 0.33** |

SD, standard deviation.
* *p*-Values using Independent Samples Median Test.
** *p*-Values using ANOVA.

With the use of HFD only 11.6% of patients underwent skin grafting, a further significant reduction compared to the 20.7% of Ag-SD treated patients who had to be operated in the same period ( $p < 0.01$). The interval between injury and operation for these patient (median 20.5 days) did not differ from the AgSD treated patients after introduction of HFD (median 17.0 days). In conclusion HFD treated patients were operated less frequently but at the same time after injury compared to the Ag-SD group in period 2.

The same trend in time in reducing the number of surgical interventions is also reflected in the length of stay. Before the use of HFD Ag-SD treated patients were admitted to hospital 12.4 days on average; after the introduction of HFD admission time of these patients was reduced significantly to 9.7 days ($p<0.01$). Ag SD requires daily wound care, reason for clinical treatment of these patients. Explanation for a shorter admission time is a change in policy where Ag-SD in advanced wound healing at some point is replaced by paraffin impregnated gauzes, which need to be changed less frequently, allowing for outpatient treatment.

A further significant reduction in hospital stay to 7.5 days was obtained with the use of HFD ( $p < 0.01$). In the first days of hospital stay daily inspection is performed to see if the HFD is saturated or shifted, in which cases new or extra HFD is applied. The clinical or social circumstances permitting, the patients then continued outpatient treatment. Compared to data in the literature this length of stay is longer than the 3.8 days published by Paddock, who in his study of partial thickness burns in children comparing HFD-Ag with Ag-SD also

found a reduction in hospital length of stay in favour of the HFD-Ag treated patients [7].
At present, obtaining more experience with HFD applications, also in our Burn Centre admission times decrease to a few days, sending home those children who eat and drink well and have no fever.
Although there are relatively more re-admissions in the HFD treated patients HFD 6.0% vs. 2.6% for Ag-SD: $p = 0.02$), we found no difference in the percentage of patients re-admitted for skin grafting (HFD 12/18 = 66.7%, Ag-SD 9/13 = 69.2%: $p = 0.60$). This leaves 6 HFD treated patients and 4 Ag-SD treated patients to be re-admitted for other reasons, e.g. because of clinical conditions like fever or social circumstances.
In the studies by Caruso et al. it was shown that the use of silver impregnated hydrofibers (HFD-Ag) was associated with less pain and anxiety during dressing changes, less burning and stinging during wear, fewer dressing changes, less nursing time, and fewer procedural medications compared with Ag-SD [5,6]. In this prospective randomized study HFD Ag was used with less patients (42 in each group) compared to our study; it was also shown that a greater rate of reepithelialisation was achieved with the use of HFD-Ag in comparison with Ag-SD. In the Cochrane review by Wasiak et al. [8] it is stated that the use of Ag-SD as a comparator on burn wounds for the full duration of treatment needs to be reconsidered, as a number of studies showed delays in time to wound healing and increased number of dressing applications in patients treated with Ag-SD dressings.

## 5. CONCLUSIONS

Compared to silver sulphadiazine treatment a reduced need for surgical interventions was observed in mixed partial thickness scald burns up to 10% TBSA burned in children aged 0–4 years after the introduction of hydrofiber dressings. The mode of treatment with this wound dressing also limited hospital length of stay.

### Conflict of interest statement

We declare that there is no conflict of interest including any financial, personal or other relationship.

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# Chapter 5

# Bacteriological cultures on admission of the burn patient: To do or not to do, that's the question

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## ABSTRACT

***Introduction:*** In many burn centers, routine bacteriological swabs are taken from the nose, throat, perineum, and the burn wound on admission, to check for the presence of microorganisms that require specific measures in terms of isolation or initial treatment. According to the Dutch policy of "search and destroy," for example, patients infected by multiresistant bacteria have to be strictly isolated, and patients colonized with *β-haemolytic Streptococcus pyogenes* must receive antibiotic therapy to prevent failed primary closure or loss of skin grafts. In this respect, the role of bacteria cultured on admission in later infectious complications is investigated. The aim of this study is to assess systematic initial bacteriological surveillance, based on an extensive Dutch data collection.

***Materials and methods*:** A total of 3271 patients primarily admitted to the Rotterdam Burn Centre between January 1987 and August 2010 with complete bacteriological swabs from nose, throat, perineum, and the burn wounds were included. For this study, microbiological surveillance was aimed at identifying resistant microorganisms such as methicillin-resistant *Staphylococcus aureus (MRSA)*, multiresistant *Acinetobacter*, and multiresistant *Pseudomonas*, as well as Lancefield A β-hemolytic streptococci (HSA), in any surveillance culture.
The cultures were labelled as "normal flora or non-suspicious" in the case of no growth or a typical low level of bacterial colonization in the nose, throat, and perineum and no overgrowth of one type of microorganism.
Further, the blood cultures of 195 patients (6.0%) who became septic in a later phase were compared with cultures taken on admission to identify the role of the initially present microorganisms. Statistical analysis was performed using SPSS 20.0.

***Results:*** Almost 61% of the wound cultures are "non-suspicious" on admission. MRSA was cultured in 0.4% (14/3271) on admission; 12 out of these 14 patients (85.7%) were repatriated. Overall, 9.3% (12/129) of the repatriated patients were colonized with *MRSA*. Multiresistant *Acinetobacter* or *Pseudomonas* was detected in 0.3% (11/3271 and 10/3271, respectively). In total, 18 of the 129 repatriated patients (14%) had one or more resistant bacteria in cultures taken within the first 24 h after admission in our burn center. On admission, *S. pyogenes* was found in 3.6% of patients (117/3271), predominantly in children up to 10 years of age (81/1065 = 7.6%).

***Conclusions:*** Resistant bacteria or microorganisms that impede wound healing and cause major infections are found only in few bacteriological specimens obtained on admission of patients with burn wounds. However, the consequences in terms of isolation and therapy are of great importance, justifying the rationale of a systematic bacteriological surveillance on admission.

Patients who have been hospitalized for several days in a hospital abroad and are repatriated show more colonization at admission in our burn center. The microorganisms identified are not only (multi)resistant bacteria, showing that a hospital environment can quickly become a source of contamination. These patients require special attention for resistant bacteria. HSA contamination is observed more frequently in younger children. Bacteria present at admission do not seem to play a predominant role in predicting later sepsis.

## 1. INTRODUCTION



Infections remain one of the major complications after severe burns. They are facilitated by the suppressed innate immune response of the patient and the skin barrier defect, covered with debris and necrotic tissue [1,2]. The human body is host to a number of microbes occurring in various forms of host–microbe associations, such as commensals, mutualists, pathogens, and opportunistic symbionts [3]. Potentially pathogenic microorganisms can be present on the skin as commensal flora, or they may be transferred acutely (e.g., by cooling with contaminated water) or during hospitalization (hospital acquired). The amount and type of microorganisms on and in the burned tissue do influence wound healing, the frequency of invasive infections, and the clinical characteristics of such infections [4]. Therefore, knowledge of the colonization status at any time is important in the treatment of burn patients [4].

For this reason, as in other intensive care units, most burn centers (BCs) use routine surveillance, based on cultures taken on admission and routinely afterwards (e.g., weekly) [2,4]. Apart from the burn wounds, the body sites cultured most often are the nose, throat, and perineum [2,5,6]. Positive surveillance cultures may lead to more infection prevention measures, for example, methicillin-resistant *Staphylococcus aureus (MRSA)*, which can guide antimicrobial therapy and may identify and control outbreaks (source determination) [7–11]. Surprisingly, little is known about the initial colonization status of burn patients at admission, as most studies have included few patients or only studied specific microorganisms (e.g., Pseudomonas spp.) [20,21]. It might be assumed that deep burn wounds are initially sterile, as they are exposed to the heat source. But is this still the case when the patient arrives in the BC a few hours later? Therefore, the objective of this study was to assess the frequency of colonization on admission, and to identify the microorganisms involved and their potential role in later septic complications in a large cohort of burn patients over a 24-year time period.

## 2. METHODS

### 2.1. Bacteriological survey in our hospital

In the BC of the Maasstad Hospital in Rotterdam, the Netherlands, routine bacteriological swabs are taken from the burn wounds as well as from the nose, throat, and perineum on admission. Other cultures such as blood, urine, and sputum were only taken when clinically indicated on admission. In the case of exceptional microorganisms, necessary measures such as quarantining patients can be taken. When the cultures of these patients reveal Lancefield group A *β-hemolytic streptococci (HSA),* antibiotics are started to prevent failure in primary closure or loss of skin grafts. Furthermore, the Dutch medical system uses a "search-and-destroy" policy with respect to resistant microorganisms, especially for repatriated patients, with a time difference between accident and secondary BC admission. This study focuses on the bacteriological cultures sampled within the first 24 h of BC admission and the follow-up cultures of septic patients.

### 2.2. Study design and population

This retrospective cohort study involved all patients admitted to the Rotterdam Burn Centre (RBC) in the Netherlands between January 1987 and September 2010. Data were gathered by merging a database used for epidemiological purposes and a microbiology database. The standard treatment protocols of the BC are described elsewhere [16].

### 2.3. Routine surveillance

On admission, surveillance cultures were taken from the following four body sites: burn wounds (B), nose (N), throat (T), and perineum (P). The swabs were analyzed in the hospital's microbiological laboratory. Pathogens were identified and
their susceptibility to antimicrobial agents was tested using routine microbiological methods. Cultures were labelled as "normal flora or non-suspicious" in the case of no growth or a typical low level of bacterial colonization in the nose, throat,
and perineum and no overgrowth of one type of microorganism. Based on his or her interpretation, the laboratory technician decided on further analyzing the grown cultures or not. The normal flora for the nose was considered to be *Staphylococcus epidermidis* and diphtheroids. The flora of the nose included *S. epidermidis*, diphtheroids, *Streptococcus viridans* (except for *Streptococcus pneumoniae*), *Neisseria* (except for *Neisseria meningitidis*), whereas that of the perineum included *S. epidermidis* and few Gram-negative bacteria (except for nonfermentatives). Few colonies of *S. epidermidis* or diphtheroids were regarded as the normal flora of burn wounds. Apart from the abovementioned normal flora at various body sites, in the present study, positivity was defined as the presence of the following

potentially pathogenic microorganisms:

- *Staphylococcus aureus* (SA) including *MRSA*
- *S. epidermidis* (coagulase-negative *Staphylococcus (CNS)*)
- *Streptococcus pyogenes*
- *Enterobacte*r species
- Other coliforms (*Escherichia coli, Klebsiella,* etc.)
- *Pseudomonas aeruginosa* (*PsA*)
- *Acinetobacter baumannii*
- Fungi including yeast

A large number of antibiotics were tested and reported. Because of their varying sensitivities , only gentamicin resistance was recorded, but not for the remaining antibiotics (tobramycin, ciprofloxacin, etc.). Furthermore, the known existing microorganism was determined by the once-weekly antibiogram, whereas this was always done with the first isolates.



### 2.4. Relation between bacteria cultured on admission and blood cultures

In septic patients with symptoms such as high fever and hemodynamic instability, blood cultures were performed and compared with the cultures taken on admission.

### 2.5. Statistical analysis and definitions

For analysis, only the data of patients with complete sets of admission cultures (burn wounds, nose, throat, and perineum) were used. Data expression and statistical analyses were performed using SPSS 20.0 (SPSS Inc., Chicago, IL, USA).

The role of routine surveillance cultures on admission to predict pathogens in blood cultures of patients who developed sepsis later was expressed by the following operating characteristics: sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) with respective 95% confidence intervals (CI).

Sensitivity was defined as the proportion of patients with a positive admission culture and also the related positive blood culture (true-positive rate).

Specificity was defined as the proportion of patients with a negative admission culture and also a negative blood culture (true-negative rate).

Microorganisms found either in the surveillance cultures on admission or in the blood cultures were respectively defined as 'false positive' and 'false negative'.

The PPV is the probability of positive blood cultures with the same microorganisms cultured on admission, and the NPV is the probability that both blood cultures and surveillance cultures on admission are negative. Sensitivity, specificity, PPV, and NPV are expressed as percentages.

# 3. RESULTS

## 3.1. Enrolment

In the period from January 1987 until August 2010, 5342 patients were admitted to the RBC. Of these patients, 251 were readmitted for the same burns and 434 for secondary corrections, and 111 patients did not suffer from burns but, for example, were diagnosed with toxic epidermal necrolysis and other non-burn skin defects.
Of the remaining 4546 patients, we were able to match 4219 patients (93%) from the two different databases. Not all cultures (nose, throat, perineum, and wound) were taken from 948 patients within 24 h after admission, leaving 3271 (72%) with complete cultures for analysis (Fig. 1).

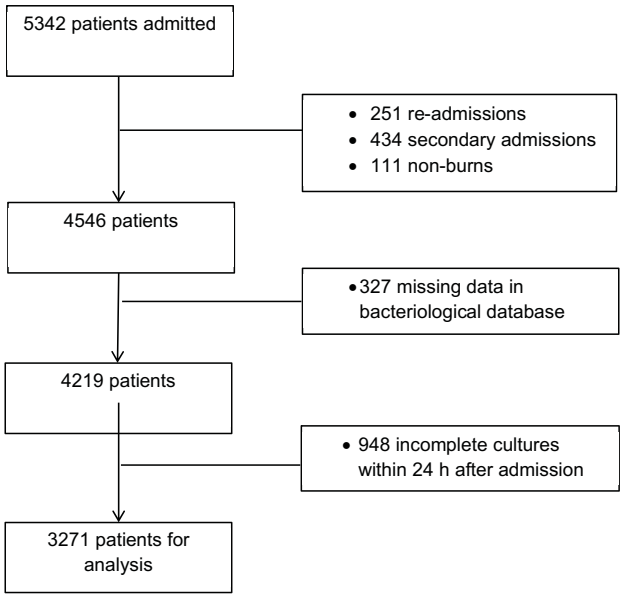


**Figure 1.** Enrollment of the cohort.

## 3.2. Demographics

Most patients were younger men (median age 26.0 years,) with limited burned total body surface area (TBSA) (median 6.0%). The study population included 129 repatriated patients, whose interval between the accident and admission to our BC was on average 6.5 days (0–67). The main characteristics of the analyzed cohort of patients are reported in Table 1.
Values are described as median (interquartile range) and mean (range) or n (%). On average, the repatriated patients are 5 years older and have larger burns.

**Table 1 – Main characteristics of the analyzed cohort of patients ($n = 3271$).**

| | All patients ($n = 3271$) | Patients from NL ($n = 3142$) | Repatriated ($n = 129$) |
|---|---|---|---|
| Age (years) | | | |
| Median (IQR) | 26.0 (3.0–45.0) | 25.0 (3.0–44.0) | 34.0 (12.5–51.5) |
| Mean (range) | 28.1 (0–98) | 27.8 (0–98)* | 32.8 (0–83)* |
| TBSA (%) | | | |
| Median (IQR) | 6.0 (4.0–12.0) | 6.0 (4.0–12.0) | 8.0 (5.0–15.5) |
| Mean (range) | 10.4 (0–85) | 10.2 (0–85)** | 13.9 (1–85)** |
| Male gender (%) | 2221/3271 (67.9) | 2130/3142 (67.8) | 91/129 (70.5%) |
| Repatriated from abroad (%) | 129/3271 (3.9) | 0/3142 (0.0) | 129/129 (100) |

IQR, interquartile range.
* $p < 0.05$.
** $p < 0.001$.

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## 3.3. Microorganisms cultured on admission

The results of the microbiological examination on admission are reported in Table 2.
Here, a distinction is made between the patients admitted directly from the Netherlands and those from abroad. The majority of inventory cultures in the throat and perineum proved to be non-suspicious (75.9/68.2% and 79.1/77.5% respectively). However, the nose (45.2/46.5%) and burn wound (38.6/51.9.2%) were frequently colonized.
Positive cultures included a wide range of Gram-positive and Gram-negative microorganisms, predominantly SA (40.4/48.8%) and streptococci (29.8/20.2%).

**Table 2 – Microorganisms found on admission.**

| | Nose NL/repat | Throat NL/repat | Perineum NL/repat | Wound NL/repat | Found on admission NL/repat |
|---|---|---|---|---|---|
| Non-suspicious or sterile | 1721/69 (54.8/53.5%) | 2386/88 (75.9/68.2%) | 2485/100 (79.1/77.5%) | 1928/62 (61.4/48.1%)** | |
| *Staphylococcus aureus* (including MRSA) | 743/41 (23.6/31.8%)* | 287/19 (9.1/14.7%)* | 301/17 (9.6/13.2%) | 558/47 (17.8/36.4%)** | 1269/63 (40.4/48.8%) |
| E. coli | 23/1 (0.7/0.8%) | 33/0 (1.0/0.0%) | 31/1 (1.1/0.8%) | 82/1 (2.6/0.8%) | 160/3 (5.1/2.3%) |
| *Enterobacter* | 32/4 (1.0/3.1%) | 27/3 (0.9/2.3%) | 3/1 (0.1/0.8%) | 137/13 (4.4/10.1%)* | 181/17 (5.8/13.2%)* |
| *Serratia, Proteus, Citrobacter* | 59/2 (1.9/1.6%) | 18/3 (0.6/2.3%)* | 7/0 (0.2/0.0%) | 84/10 (2.7/7.8%)** | 149/12 (4.7/9.3%)* |
| *Klebsiella* | 37/1 (1.2/0.8%) | 55/4 (1.8/3.1%) | 6/1 (0.2/0.8%) | 65/7 (2.1/5.4%)* | 144/9 (4.6/7.0%) |
| *Streptococci* (including β-Hemolytic Streptococci) | 258/2 (8.2/1.6%)** | 358/10 (11.4/7.8%) | 323/10 (10.3/7.8%) | 245/7 (7.8/5.4%) | 937/26 (29.8/20.2%)* |
| β-Hemolytic Streptococci | 13/0 (0.4/0.0%) | 78/0 (2.4/0.0%) | 9/0 (0.3/0.0%) | 43/2 (1.4/1.6%) | 115/2 (3.7/1.6%) |
| *Acinetobacter baumanii* | 37/5 (1.2/3.9%)* | 23/4 (0.7/3.1%)* | 5/3 (0.2/2.3%)** | 232/12 (7.4/9.3%) | 265/14 (8.4/10.9%) |
| *Pseudomonas* and other non-fermentatives (exl.*Acinetobacter*) | 50/4 (1.6/3.1%) | 32/5 (1.0/3.9%)* | 32/6 (1.0/4.7%)** | 249/12 (7.9/9.3%) | 319/18 (10.2/14.0%) |
| Yeast and fungi | 19/0 (0.6/0.0%) | 38/6 (1.2/4.7%)** | 3/0 (0.1/0.0%) | 17/2 (0.5/1.6%) | 72/8 (2.3/6.2%)* |

NL = from The Netherlands; repat = repatriated from abroad.
* $p < 0.05$
** $p < 0.01$.

### 3.4. Multiresistant microorganisms on admission in the BC

In 27 of 3271 patients (0.8%), resistant microorganism(s) were cultured within the first 24 h of admission. Three different resistant bacteria were found in two of these patients and two resistant species in four of them (Fig. 2).
MRSA was cultured in 0.4% (14/3271) on admission; 12 of these 14 patients (85.7%) were repatriated from abroad. Overall, 9.3% (12/129) of repatriated patients were colonized with MRSA. Multiresistant Acinetobacter or Pseudomonas was detected in 0.3% (11/3271 and 10/3271, respectively). Overall, in 18 of the 129 (14%) repatriated patients, one or more resistant bacteria were observed in the culture within the first 24 h from admission in our BC. Due to the "search-and-destroy" policy, the incidence of MRSA was low in the Netherlands.

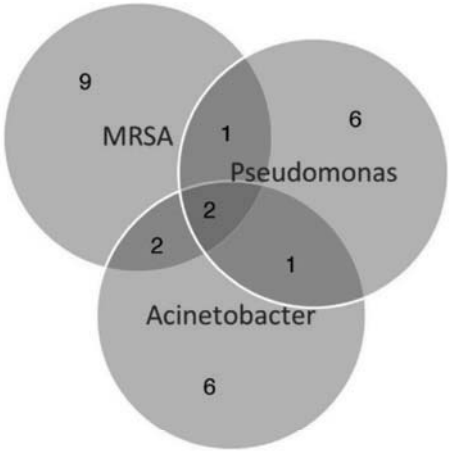


**Fig. 2 – Distribution in 27 patients presenting with resistant microorganisms in the admission cultures.**

### 3.5. HSA on admission

On admission, *S. pyogenes* was found in 3.6% of patients (117/3271), predominantly in children up to 10 years of age (81/1065 = 7.6%; Fig. 3).

### 3.6. Relation between bacteria cultured on admission and in later infectious complications

Six percent (195/3271) of the patients developed infectious complications, and a total of 402 blood cultures were performed. The microorganisms found in these blood cultures are listed in Table 3.


**Fig. 3 – Presence of *Streptococcus pyogenes* (%) in relation to age.**

**Table 3 – Species found in 402 blood cultures of 195 patients with clinical signs of sepsis.**

| | Positive blood cultures |
|---|---|
| *Staphylococcus.epidermidis* (CNS) | 122/195 = 62.6% |
| *Pseudomonas* species and other non-fermentatives species (exl.*Acinetobacter*) | 36/195 = 18.5% |
| *Staphylococcus aureus* including MRSA | 34/195 = 17.4% |
| *Streptococci* | 33/195 = 16.9% |
| *Escherichia coli* | 16/195 = 8.2% |
| *Acinetobacter* species | 16/195 = 8.2% |
| *Klebsiella* species | 13/195 = 6.7% |
| *Enterobacter* species | 11/195 = 5.6% |
| Yeast and fungi | 10/195 = 5.1% |
| *Serratia*, *Proteus*, *Citrobacter* species | 2/195 = 1.0% |

In order to identify the role of microorganisms present on admission and in later septic complications, positive cultures on admission were compared with blood cultures in patients who developed sepsis later.

SA, not detected on admission, was found in blood cultures of 0.9% of patients who developed sepsis later. In patients with SA in initial cultures, 1.2% showed later SA in positive blood cultures, with a non-significant difference (p=0.45). In addition, there was no difference in the percentages of *streptococci* and in Gram-negative enterobacteria such

as *Enterobacter*, *Serratia*, and *Proteus* cultured on admission and in later blood cultures of septic patients.

PsA showed up in 0.9% of later blood cultures of septic patients when negative on admission and in 3.3% when cultured on admission, indicating a significant difference ($p<0.01$). *Klebsiella* (0.3% vs. 2.6% ($p<0.01$)) and *Acinetobacter* (0.4% vs. 1.8%, $p<0.01$) showed a similar trend. However, the PPV and NPV did not differ significantly between the microorganisms involved (Table 4). Therefore, the difference in sensitivity does not seem to be of great clinical importance.

**Table 4 – Value of surveillance cultures on admission to predict these microorganisms later in blood cultures.**

| | Sensitivity | Specificity | Positive predictive value | Negative predictive value |
|---|---|---|---|---|
| *Staphylococcus aureus* | 47.1% (29.8–64.9) | 59.3% (57.6–61.0) | 1.2% (0.7–1.9) | 99.1% (98.5–99.4) |
| *E. coli* | 0% (0–20.8) | 95.0% (94.2–95.7) | 0% (0–2.3) | 99.5% (99.2–99.7) |
| *Enterobacter* | 18.2% (2.8–51.8) | 94.0% (93.1–94.8) | 1.0% (0.2–3.6) | 99.7% (99.4–99.9) |
| *Serratia, Proteus, Citrobacter* | 50% (8.2–91.8) | 90.8% (89.7–91.7) | 0.33% (0.1–1.8) | 99.8% (99.8–99.9) |
| *Streptococci* | 24.2% (11.1–42.3) | 70.5% (68.9–72.1) | 0.8% (0.4–1.6) | 98.9% (98.4–99.3) |
| *Klebsiella* | 30.8% (9.3–61.4) | 95.4% (94.7–96.1) | 2.6% (0.7–6.6) | 99.7% (99.5–99-9) |
| *Acinetobacter* | 31.3% (11.1–58.6) | 91.6% (90.6–92.5) | 1.8% (0.6–4.1) | 99.6% (99.3–99.8) |
| *Pseudomonas* | 30.6% (16.3–48.1) | 89.9% (88.8–90.9) | 3.3% (1.6–5.8) | 99.2% (98.7–99.5) |
| Yeast and Fungi | 30.0% (7.0–65.2) | 97.6% (97.1–98.1) | 3.8% (0.8–10.6) | 99.8% (99.6–99.9) |

Values are presented as percentages and 95% confidence intervals.

## 4. DISCUSSION

Although many BCs perform bacteriological swabs on admission of the patient, what is their value? The aim of the study was to assess the bacteriological cultures on admission and to identify the microorganisms.

In our study population, the patient age and gender reflect the normal distribution of burn patients, and the median TBSA burned is comparable to data from the American Burn Association National Burn Repository.

The data of 327 patients in the bacteriological database (7%) were missing, possibly due to a selection bias. However, we have no reason to assume that they differ from the remaining 93% and a part of the missing data are of patients admitted for day surgery, so the potential for selection bias is very limited.

Many clinicians believe that burns are sterile at admission because of the heat of the skin at the time of the accident. In this study, 61.4% of the burns were found to be non-suspicious on admission. Furthermore, part of it will indeed show no bacterial growth, but, as previously described, the results of the wound cultures also depend on the interpretation of the technician. This can be a subjective bias. After plating the swab and incubating, the

art is to distinguish the clinically relevant colonies from the nonrelevant growth. Notoriously pathogenic microorganisms or a dense growth of a microorganism with respect to the other existing microorganisms is clinically relevant.
On average, the interval between the accident and admission to the BC in repatriated patients was 6.5 days (median 3 days). In these patients, 48.1% of the wound cultures are non-suspicious or sterile, which is significantly different from patients admitted directly from the Netherlands. As seen in Table 2, these wounds are more colonized on admission in terms of *SA* (including *MRSA*), *Enterobacter*, *Serratia*, *Proteus*, *Citrobacter*, and *Klebsiella*. The burn wound is susceptible to microbial colonization from the hospital environment, even if the patient does not use antibiotics. All of the non-suspicious cultures will certainly not be sterile. A culture was further investigated only in cases of a clear overgrowth of one or more bacteria. This implies that nearly 40% of the wounds at admission within 24 h are colonized with one or more potentially pathogenic microorganisms.
Although SA, including MRSA, is a highly common microorganism, MRSA was cultured in only 14 of 3271 patients (0.4%) on admission, explained by the "search-and-destroy" policy in The Netherlands. The chance of detecting resistant bacteria at admission is <1% (27/3271 = 0.8%). In this respect, the necessity of performing several cultures at admission is questionable. However, cultures are clinically relevant in terms of isolation and control of infection. This is especially relevant for patients who are repatriated from abroad, where resistant microorganisms are found nearly 15 times more frequently (18/129 = 14%).

We are of the opinion that the presence of HAS is an indication of antibiotic therapy. This bacterium is found in 3.6% (117/3271) of the patients and nearly twice as much in children (81/1065 = 7.6%). In particular, children with sore throat could be at a risk of developing *S. pyogenes* infection.
Although *PsA* is often hospital acquired, 10.2% of the patients are already colonized with these bacteria at admission. Patients who develop sepsis are generally treated with broad-spectrum antibiotics adjusted on blood cultures. In 122 out of 195 septic patients (62.6%), blood cultures revealed *S.epidermidis* (CNS), predominantly suggesting a central venous catheter-related infection. In recent years, the Netherlands has been confronted with a rise in specific resistant microorganisms, such that the policy of obtaining inventory cultures at admission must be continued.

## 5. CONCLUSION

About 60% of burn wound cultures on admission within 24 h are considered non-suspicious, which indicates that about 40% are colonized with one or more potentially pathogenic microorganisms.

Patients who have been hospitalized for several days abroad show more colonization at admission in our BC of (multi)resistant bacteria, indicating that a hospital environment can quickly become a source of contamination.
Resistant bacteria or microorganisms that impede wound healing and cause major infections are found in <1% of bacteriological specimens obtained on admission of patients with burn wounds. However, consequences in terms of isolation and therapy are highly significant, justifying the rationale of a systematic bacteriological surveillance on admission. This is important especially in patients repatriated from abroad, because 14% of these patients are colonized with resistant microorganisms. The search-and-destroy policy has ensured a low prevalence of MRSA in the population and health facilities of The Netherlands.
HSA are found especially in children up to 10 years of age (7.8%). Bacteria present at admission do not seem to play a predominant role in predicting later sepsis. However, various reasons are attributed to the importance of surveillance, as previously described, which can be applied with great enthusiasm.

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# PART THREE

## Outcome

# Chapter 6

# External validation of the revised Baux score for the prediction of mortality in patients with acute burn injury

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## ABSTRACT

***Background:***
Since the original Baux score was outdated and inhalation injury was recognized as an important contributor to mortality, Osler et al. developed a revised Baux score for the prediction of mortality of burn patients in an American population. The aim of this study was to validate the revised Baux score with data of patients admitted to the Rotterdam Burn Center (RBC) in the Netherlands.

***Methods:***
Prospectively collected data were analyzed for all patients with acute burn injury admitted to the RBC from 1987 to 2009 (n = 4,389), including sex, age, total body surface area involved, inhalation injury, mortality, and premorbid conditions. Logistic regression analysis was used to determine the relationship between mortality and possible contributing variables. The discriminative power of the revised Baux score was assessed by receiver operating characteristics curve analysis.

***Results:***
Overall mortality in our center was 6.5%; mortality in patients with intention to treat was 4.4%. Age, total body surface area, inhalation injury, as well as premorbid circulatory and central nervous system conditions were significant independent predictors of in-hospital mortality. Revised Baux score in the RBC population (area under the curve, 0.96; 95% confidence interval, 0.95Y0.97) performed less specific and sensitive in a selected group of patients with high Baux scores (area under the curve, 0.81; 95% confidence interval, 0.76Y0.84).

***Conclusion:***
The revised Baux score is a simple and accurate model for predicting mortality in patients with acute burn injuries in a burn center setting. (J Trauma Acute Care Surg. 2014;76: 840Y845. Copyright*2014 by Lippincott Williams & Wilkins)

***Level of evidence:***
Prognostic study, level III.



***Key words:***
Burns; mortality; Baux score; revised Baux score; predictors of mortality.

## 1. INTRODUCTION

Traditionally, mortality is the most important outcome measure in patients with acute burn injury.[1] Serge Baux developed a simple score predicting mortality after burn injury[2] In this model, an additional year of age or an additional percentage of body surface area burned each increased the predicted mortality with 1%. Thus, a patient aged 73 years, with a total body surface area (TBS) of 30% has a Baux score of 103. Because of its simple applicability, the original Baux score was widely used. However, nowadays, the original Baux score seems outdated. Since the development of the Baux score in 1961, mortality rates decreased by the establishment of specialized burn centers and by therapeutic improvements including fluid resuscitation, infection prevention, wound care, and use of topical and systemic antibiotics.[3,4] In addition, inhalation injury was recognized as an important contributor to mortality.[5,6]

Following the Baux score, many predictive models have been developed in the past[7,8] also looking at influencing factors other than age and TBS burned. However, since most of these formulas are very complex, their clinical applicability is limited.

Several prediction models for mortality have been developed over time. For instance, the Belgian Outcome in Burn Injury Study Group developed the Belgian Outcome in Burn Injury (BOBI) prediction model. The scoring system is also based on age, TBS burned, and inhalation injury but uses different score points.[9]

Osler et al.[10] developed the revised Baux score, a rather simple and clinical applicable score, including the effect of inhalation injury. The revised Baux score is calculated as the sum of age and TBS burned plus 17 points for inhalation injury; so in case of inhalation injury, the revised Baux score is 17 points higher than the original Baux score. The revised Baux score can be included in a logistic regression model or simply imputed using a nomogram to calculate the predicted mortality.

This model was developed and internally validated using the National Burn Repository (NBR). This database contains

extensive information of burn patients admitted to American burn centers. All prediction models need to be validated to ensure accuracy and guard against potential limitations. The best way to test a prediction model is to validate it in an independent setting or data source, unrelated to the original model development settings (temporal and geographic).[11] The generalizability of the revised Baux score, also known as external validity, has not been tested yet. The aim of our study was to validate the revised Baux score with data of patients with acute burn injuries admitted to the Rotterdam Burn Center (RBC) to offer accurate predictions in subsequent samples of patients.

First, we described the mortality in our population, comparing survivors and nonsurvivors, and the predictive value of the revised Baux score was tested.

Second, we investigated if any contributing factor could possibly play an important role in fine-tuning the scoring system.

## PATIENTS AND METHODS

### Patient Population

All patients with acute burn injury admitted to the RBC from 1987 up to and including 2009 were included. The total population was divided into the subgroups survivors and nonsurvivors. Nonsurvivors included patients admitted with intention to treat (ITT) and patients who received tender loving care (TLC). The decision for TLC was a patient-tailored judgment made by an experienced team of burn specialists on the basis of the important criteria of age, TBS, depth, localization, inhalation injury, and premorbid conditions.

### Study Design

Prospectively collected patient data included age, TBS, sex, inhalation injury, and comorbidity. The diagnosis of inhalation injury was predominantly made on clinical signs and symptoms, especially exposure to smoke or fire, or signs of airway obstruction or the presence of soot in the throat or sputum. In those cases in our opinion, bronchoscopy as a diagnostic tool is not indicated; in case of doubt, bronchoscopy was performed.
Premorbid conditions were roughly divided into circulatory, respiratory, gastrointestinal, urogenital, locomotive, endocrine, and central nervous system (CNS) disorders.

### Statistical Analysis

A comparison was made between survivors and nonsurvivors. All continuous variables were presented as medians with interquartile ranges (p25Yp75); survivors and nonsurvivors were compared using the Mann-Whitney U-test. Categorical variables were calculated as frequencies with percentages, and groups were compared using $X^2$ analyses and Fisher's exact test when applicable.
Univariable logistic regression analysis was used to determine the relationship between mortality and possible contributing factors; odds ratios (ORs) and 95% confidence intervals (CIs) were reported. Factor analysis included patient and injury characteristics. Predicted mortality was computed with a logistic model.[8]
Predictive performance of the revised Baux score was assessed by examining measures of calibration and discrimination. Calibration refers to how close predicted mortality agrees with observed mortality and was tested with the Hosmer-Lemeshow goodness-of-fit statistic. The discriminative power of the revised Baux score refers to the ability to differentiate between patients who died and who survived their burns. This power was

assessed by receiver operating characteristic (ROC) curve analysis, which demonstrates the sensitivity and specificity of the prediction model in a graphic way. The discriminative power is maximal when the area under the curve (AUC) is 1; there is no discriminative power when this area is less than 0.5.

A test was considered significant if the *p* value was smaller than 0.05 (two sided).

Statistical analyses were performed using SPSS for Windows version 15.0 (SPSS Inc., Chicago, IL).

## RESULTS

### Burn Center Mortality

From 1987 to 2009, a total of 4,389 patients with acute burn injury were admitted to the RBC (Table 1).

The median age was 27.0 years (interquartile range [IQR] 4-46), the median TBS was 6% (IQR, 3-12), and 462 patients (10.5%) were diagnosed as having an inhalation injury. The overall mortality rate in our population including 96 patients who received TLC was 6.5%. The mortality of 4,293 patients with ITT was 4.4% (190 of 4,293).

Patients who survived had a significant lower age, TBS, and incidence of inhalation injury in comparison with patients who died .In survivors, the median Bauxscore was 33(IQR, 12-53), and the median revised Baux score was 33.5 (IQR, 12-56). In nonsurvivors, the Baux score was 99 (IQR, 83-115), and the revised Baux score was 108 (IQR, 91-127).

Demographics of nonsurvivors, divided in patients with ITT and patients who received, TLC are shown in Table 2.

**TABLE 1.** Demographics and Comorbidity of RBC Patients for Survivors and Nonsurvivors

| Characteristics | RBC Total | Survivors | Nonsurvivors | *p* |
|---|---|---|---|---|
| No. patients | 4,389 | 4,103 (93.5) | 286 (6.5) | |
| Sex, male | 2,902 (66) | 2,748 (67) | 154 (54) | <0.01 |
| Age, median (IQR), y | 27.0 (4–46) | 25 (3–43) | 62.5 (37.8–79.0) | <0.01 |
| TBS%, median (IQR) | 6 (3–12) | 5 (3–10) | 38 (16–62) | <0.01 |
| Inhalation injury | 462 (10.5) | 296 (7.2) | 166 (58.0) | <0.01 |
| Baux score, median (IQR) | | 33 (12–53) | 99 (83–115) | <0.01 |
| Revised Baux score, median (IQR) | | 33.5 (12–56) | 108 (91–127) | <0.01 |
| Comorbidity | | | | |
| Circulatory | 259 (5.9) | 205 (5.0) | 54 (18.9) | <0.01 |
| Respiratory | 203 (4.6) | 185 (4.5) | 18 (6.3) | 0.11 |
| Gastrointestinal | 177 (4.0) | 146 (3.6) | 31 (10.8) | <0.01 |
| Urogenital | 125 (2.8) | 109 (2.7) | 16 (5.6) | <0.01 |
| Locomotor | 224 (5.1) | 191 (4.7) | 33 (11.5) | <0.01 |
| Endocrine | 155 (3.5) | 120 (2.9) | 35 (12.2) | <0.01 |
| CNS* | 622 (14.5) | 519 (12.6) | 103 (36.0) | <0.01 |

Values are n (%) unless stated otherwise. IQR, 25th to 75th percentile.

Patients in the two groups did not differ in age, but those who received TLC had a significant higher TBS and incidence of inhalation injury, resulting in a significant higher Baux score (120.5 vs. 89) and revised Baux score (134.5 vs. 97.5).

**TABLE 2.** Demographics of Nonsurvivors Divided in Patients With ITT and TLC

| | Nonsurvivors With ITT | Nonsurvivors With TLC | |
|---|---|---|---|
| | n = 190 | n = 96 | *p* |
| Sex, male, n (%) | 110 (58) | 44 (46) | |
| Age, median (IQR) | 61 (38–78) | 71.5 (36.3–83) | 0.09 |
| TBS, median (IQR) | 24.5 (11.8–45.3) | 65 (44–85) | <0.01 |
| Inhalation, n (%) | 86 (45.3) | 80 (83.3) | <0.01 |
| Baux score, median (IQR) | 89 (76–101) | 120.5 (110–137.5) | <0.01 |
| Revised Baux score, median (IQR) | 97.5 (83.8–110) | 134.5 (123.3–153) | <0.01 |

Premorbid conditions were significantly more prevalent in patients who died. This applied to six of seven tracts: circulatory, gastrointestinal, urogenital, locomotor, endocrine, and CNS problems. A large number of patients with CNS problems had psychiatric disorders with more severe burn injuries because of attempted suicide. There was no significant difference in preexisting respiratory disorders between survivors and nonsurvivors (Table 1).

**Predictors of Mortality**

All significant predictors of mortality identified by univariable analysis are shown in Table 3. In this analysis, male sex is more related to mortality (OR, 1.7). Increasing age and more extensive TBS were significant prognostic factors as well as inhalation injury (OR, 17.8).
Premorbid conditions were also significant predictors of mortality. This applied for all seven tracts: circulatory (OR, 4.4), respiratory (OR, 1.4), gastrointestinal (OR, 3.3), urogenital (OR, 2.2), locomotor (OR, 2.7), endocrine (OR, 4.6), and CNS (OR, 3.9).

Correlation between the significant predictors was low (Pearson's <0.20), implying that all factors are additive to one another and independent predictors of outcome.
Significant factors associated with mortality were included in a multivariable logistic regression model. Multivariable analysis showed that age, TBS, inhalation injury and premorbid circulatory, and CNS problems were significant independent predictors associated with mortality. After the effects of age, TBS, inhalation injury, and the circulatory and CNS were taken into account; the other five tracts did not add to the prediction of mortality.

**TABLE 3.** Univariable and Multivariable Logistic Regression Analyses of Factors Related to Mortality

| | Univariable | | Multivariable | |
|---|---|---|---|---|
| **Characteristics** | **OR** | **95% CI** | **OR** | **95% CI** |
| Sex, male | 1.7 | 1.4–2.2 | | |
| Age | | | | |
| Per year | 1.05 | 1.05–1.06 | 1.08 | 1.06–1.09 |
| Per 10 y | 1.67 | 1.58–1.76 | 2.08 | 1.86–2.30 |
| TBS | | | | |
| Per 1% | 1.09 | 1.08–1.10 | 1.10 | 1,09–1.11 |
| Per 5% | 1.56 | 1.50–1.62 | 1.61 | 1.52–1.70 |
| Per 10% | 1.67 | 1.58–1.76 | 2.60 | 2.32–2.90 |
| Inhalation injury | 17.8 | 13.7–23.1 | 3.1 | 2.2–5.0 |
| Comorbidity | | | | |
| Circulatory | 4.4 | 3.2–6.1 | 1.6 | 1.0–2.6 |
| Respiratory | 1.4 | 0.9–2.3 | | |
| Gastrointestinal | 3.3 | 2.2–5.0 | | |
| Urogenital | 2.2 | 1.3–3.7 | | |
| Locomotor | 2.7 | 1.8–4.0 | | |
| Endocrine | 4.6 | 3.1–6.9 | | |
| CNS | 3.9 | 3.0–5.0 | 2.4 | 1.6–3.4 |



### Predicted Mortality

The observed mortality rate in the total population, including 96 patients who received TLC, was 6.5% (286 of 4,389 patients). The revised Baux score was used to calculate the probability of death for our population. The distribution of the survival probability estimates was divided into 10 equally sized groups (Table 4). Each patient in the RBC had an estimated probability of death. For example, in the 81st to 90th percentile, the expected number of death is 24; the observed number of death was 34 in this group.

**TABLE 4.** Observed and Predicted Deaths (Hosmer-Lemeshow Test)

| Risk of Death* | Total Patients | Revised Baux Score | Predicted Mortality | | Observed Mortality | |
|---|---|---|---|---|---|---|
| **Percentile** | **n** | **Mean** | **Percentage** | **n** | **Percentage** | **n** |
| 1–10 | 564 | 4.5 | 0.0 | 0 | 0.2 | 1 |
| 11–20 | 318 | 8.0 | 0.0 | 0 | 0.0 | 0 |
| 21–30 | 477 | 13.6 | 0.0 | 0 | 0.2 | 1 |
| 31–40 | 414 | 22.9 | 0.1 | 0 | 0.0 | 0 |
| 41–50 | 446 | 32.3 | 0.2 | 1 | 0.2 | 1 |
| 51–60 | 424 | 40.9 | 0.4 | 2 | 0.2 | 1 |
| 61–70 | 431 | 50.5 | 0.8 | 3 | 0.9 | 4 |
| 71–80 | 451 | 60.7 | 1.7 | 8 | 2.7 | 12 |
| 81–90 | 424 | 76.4 | 5.7 | 24 | 8.0 | 34 |
| 91–100 | 431 | 109.1 | 40.2 | 173 | 53.8 | 232 |
| Total | 4,380 | 41.4 | 4.8 | 211 | 6.5 | 286 |

Patients ranked according to increased probability of death. Patients in the 91st to 100th percentile groups are those with the highest predicted probability of death.

The Hosmer-Lemeshow test, which is based on an analysis of the differences between the observed and predicted number of death in each of the percentile groups, was technically not possible because of empty cells in groups with a low Baux or revised Baux index. In the high percentile groups with revised Baux scores greater than 75, predicted mortality underestimated the observed mortality.

The discriminative power of the revised Baux score was assessed by ROC curve analysis (Fig. 1).

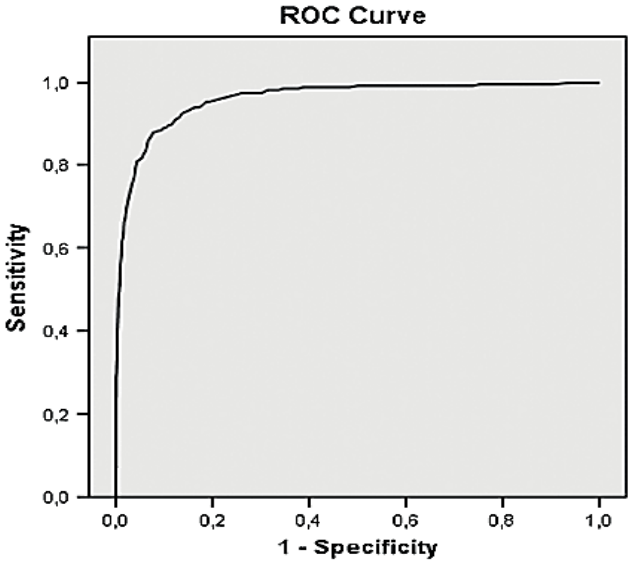


**Figure 1.** ROC curve of predicted mortality compared with observed mortality, based on 4,389 burn patients. AUC analysis, 0.96 (95% CI, 0.95–0.97).

The revised Baux score had a high predictive value for mortality in our patients with acute burn injury; the AUC was 0.96 (95% CI, 0.95-0.97).

An identical curve analysis was made for patients for which the model was suggested to fit the best, namely, patients between 20 and 80 years of age, with a TBS between 30% and 80%[8] (Fig. 2). Of all patients admitted to the RBC, 247 were included in this subgroup, 109 (44.1%) of these patients died. The AUC was 0.81 (95% CI, 0.76Y0.87).

Exclusion of the TLC did not change the goodness of fit of the model.

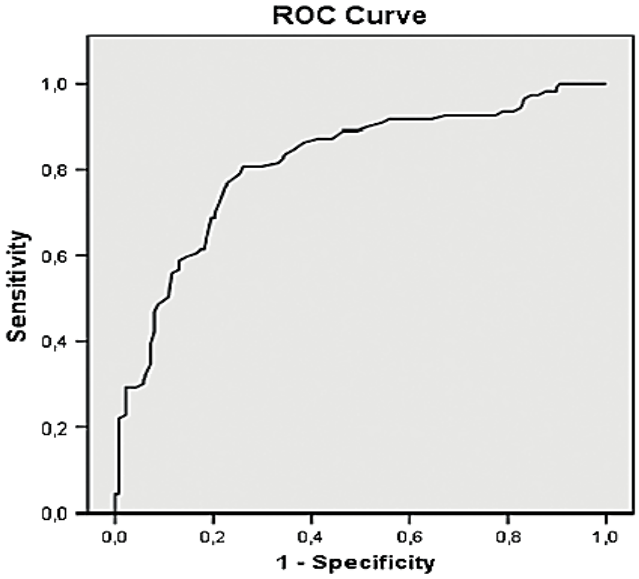


**Figure 2.** ROC curve of predicted mortality compared with observed mortality in a subgroup of 247 burn patients between 20 years and 80 years of age and with a TBS between 30% and 80%. AUC analysis, 0.81 (95% CI, 0.76–0.87).



## DISCUSSION

In the first part of our study, we described demographics and comorbidity of patients admitted to the RBC, comparing survivors and nonsurvivors. Patients who did not survive were significantly older, had a higher TBS, more frequently had an inhalation injury, and apart from preexisting respiratory tract diseases, had more premorbid conditions, compared with survivors.

More specifically looking at factors related to mortality, contrary to the trend in trauma in general, male sex had a higher risk in univariate analysis. In univariable and multivariable analyses, increasing age, TBS involved, and the presence of inhalation injury considerably contributed to mortality: The ORs increased per age period (2.08 per 10 years of age) and percentage of burns (2.60 per 10% TBS). Inhalation injury was the strongest predictor in univariable (OR, 17.8) and multivariable analyses (OR, 3.1). Considering the impact of age, TBS, and inhalation trauma, increasing age and larger TBS at some point will have a higher impact on mortality than inhalation injury.

Concerning comorbidity groups of premorbid conditions were defined. These groups were based on tracts without distinction between complaints and severity. For example, the subgroup CNS contained patients with neurologic problems such as like neuropathy,

cerebrovascular accidents, and psychiatric problems such as depression, dementia, and suicidal attempts. Multivariable logistic regression analysis suggested that circulatory and CNS premorbid conditions were important contributing factors of mortality (OR, 1.6 and 2.4, respectively).

Finally, the revised Baux score was externally validated.

The revised Baux score was developed starting from patients of the American NBR but never before validated in an external population.[8] Calibration was limited in the higher revised Baux scores, underestimating mortality in our population. ROC curve analysis revealed a good discriminative power, with an AUC of 0.96 for the total population, implying a high specificity and sensitivity of the revised Baux score in our patients.

Osler et al. assumed that the revised Baux score performed the best in predicting mortality for patients between the ages of 20 years and 80 years with TBS values between 30% and 80%.[8] Contrary to this assumption, the AUC concerning these patients in our population was slightly lower compared with the overall population and showed a larger CI. This indicates that the revised Baux score has a higher predictive value for mortality in the total population of patients with acute burn injury than in a subgroup of patients suggested to have the best success in predicting mortality.

The differences between our data and the data of Osler et al. can be the consequences of differences in study period, geography, methodology, and patient population.[11]

Data used in the NBR included the time frame 2000 to 2008. Our data from 1987 to 2009 therefore also contained less recent information. Although mortality rates in acute burn injuries were higher in the past, the trend of mortality rates was constant for this entire period in the RBC.

Geographic transportability should not interfere with the results. Our burn center is one of three burn centers in the Netherlands. The data from the NBR were collected from burn centers in America, both continents having a comparable standard of burn care.

Methodological transportability of this study may be suspect. First of all, the number of 39,888 patients studied in the NBR differs from the total of 4,389 patients evaluated in our review. Furthermore, there may be a difference in diagnosing inhalation injury. In the RBC, inhalation injury predominantly is a clinical diagnosis. Osler et al. did not report on which basis the diagnosis inhalation injury was made.

The 6.5% total mortality rate in this study was higher than the 3.7% mortality rate of the NBR. This could be the result of the inclusion of patients who received TLC in the subgroup of nonsurvivors. In our study, 286 patients did not survive, from which 96 received TLC (33.6%). When these patients were excluded, the mortality rate would be 4.3%.

The populations of the RBC and the NBR both include patient with burns admitted to a burn center setting. The population of the RBC contains patients admitted with acute burn injuries; no patients were excluded. In the NBR database, patients with missing data or survival status were excluded.

The mean age of the patients in the RBC was 29.1 years, comparable with the mean age of the patients in the NBR (30.6 years), as was the mean TBS (RBC, 10.5%; NBR, 9.7%). We suggest that the minor difference in mortality rate of patients with an ITT of 4.3% (RBC) versus 3.7% (NBR) may be caused by the difference in incidence of inhalation injury and premorbid conditions. In the RBC patients, 10.5% had an inhalation injury versus 7.4% of the patients in the NBR. In our population, premorbid circulatory and CNS problems were a significant contributing factor of mortality. In the NBR analysis of Osler et al.,[8] data on patients' comorbid conditions were absent.

The absence of the patients' comorbid conditions is an important limitation of the revised Baux score. As stated by Osler et al.,[10] clinicians know that a patient's death is sometimes more of the result of a preexisting condition.

One could presume that the discriminative power of the revised Baux logistic was not maximal, owing to the absence of preexisting circulatory and CNS conditions in the model. Although our results do indicate that inclusion of premorbid conditions could improve the model, we refrained from extension of the formula. Frequently, at the time of admission to a burn center, the patient's history is unknown. Premorbid conditions are limited, available at admission to a burn center, and therefore limit its inclusion in the revised Baux score. Furthermore, the greater is the complexity of the model, the less is its clinical applicability.[9]

The revised Baux score alone does not determine whether to treat a patient with extensive burns. There are obviously more factors involved. The revised Baux score may help the clinician in his or her decision to choose for ITT or TLC.

Lastly, our study contains data of one burn center. We recommend additional external validation studies including data from other burn centers or from different countries.

A recent review by Hussain et al.[12]on the methodology of composite prediction models of burns concluded that the revised Baux score has been constructed using appropriate methodological standards, except for one point (in case of missing data, cases were excluded). In our burn center, we continue to use the revised Baux score because of its simplicity, taking its limitations into account. The score is as easy to calculate as the original Baux score. For a precise prediction of mortality, a nomogram or calculator can be used.

In a recent systematic review, Hussain et al.[12] concluded that although a variety of complex models for predicting mortality in thermal injury have been devised, only a limited number of models have been constructed using appropriate methodological standards. So, progress has been made, but further evaluation in independent patient populations and data sets is necessary to identify the ones best suited for outcome prediction and performance monitoring.[12]

## CONCLUSION

The revised Baux score reveals a high specificity and sensitivity in patients with acute burn injuries in our hospital. The score less adequately predicts survival in case of higher revised Baux scores. Premorbid cardiovascular and CNS disorders could be factors related to mortality, but to gain full insight in the merits of the revised Baux score and its external validation, larger sample sizes, including data from other hospitals, would be required.

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# Chapter 7

## Mortality and causes of death in a burn centre

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## ABSTRACT

Mortality rates are important outcome parameters after burn, and can serve as objective end points for quality control. Causes of death after severe burn have changed over time; in the international literature, multisystem organ failure is seen as the most important cause, but the exact distribution of causes of death remains unknown. Insight into underlying agents of mortality can be directive in research and prevention programs. This comparison between results from the Rotterdam Burn Centre (RBC) and the American National Burn Repository (NBR) examines the most important predictive parameters for fatal outcome, i.e. age, total body surface area involved and presence of inhalation injury. Causes of death were attributed for all fatal outcomes treated in the RBC from 1996 to 2006.

The mortality rate at the RBC was 6.9% and at the NBR was 5.6%, with almost no differences in age or total body surface area involved. The discrepancy in mortality rate might have been due to the high incidence of inhalation injury among the RBC population. However, the mortality rate at the RBC after admission with intention to treat decreased to 4.9%. The most frequent cause of death appeared to be multisystem organ failure, in 64.9% of cases; 93% of these had systemic inflammatory response syndrome at time of death and, in 45.9%, infection was deemed responsible for the fatal clinical deterioration (in 21.3% sepsis was proved and in 24.6% was highly suspected).

To compare mortality rates between different burn centres and periods of time, uniform classifications are needed, particularly for presence of inhalation injury and for causes of death. Prevention of multisystem organ failure, by better management of infection and systemic inflammatory response syndrome, might do most to decrease mortality after burn.

## 1. INTRODUCTION

Outcome measures are the first step in evaluating consequences of trauma and in following health care. In potentially life-threatening conditions, mortality is the outcome measure of greatest concern[1]. Furthermore, mortality rates are used in evaluating new therapeutic interventions and establishing standards of burn survival. The predictive power for mortality is known for age, total body surface area (TBSA) involved and presence of inhalation injury[2–4]. However, in decisions about treatment withdrawal, these parameters should be handled with great care; for example, among severely burned children it has been shown that outcome cannot be predicted by demographic and injury characteristics alone [5].

During the past 50 years, mortality rates following burn have dramatically decreased. Half a century ago, approximately 50% of victims survived if burns involved more than 40% TBSA[6]. Nowadays, burns involving >90% TBSA are sometimes survived by young and healthy people. In the Western world, overall mortality rates following burn have decreased to 5–6% [2,7–9]. This remarkable fall can be attributed to the establishment of specialised burn centres, therapeutic developments including advances in critical care and anesthetic procedures, vigorous fluid resuscitation[10], excision of burn wounds [11], a dynamic, aggressive approach to nutritional management [12,13] and use of topical antimicrobial agents and systemic antibiotics.

There has also been a shift in time and cause of death following burn. Historically, a fatal outcome followed burn in the first few days and was primarily caused by burn shock, respiratory insufficiency and wound sepsis [14]. Today, the first few days after burn are almost always survived and factors such as systemic inflammatory response syndrome (SIRS), sepsis and other complications contribute to later fatality.

Despite their importance for quality control and comparison of results, uniform data on causes of death are surprisingly scarce in the literature. We performed a retrospective review in order to describe our population, compare results and analyse causes of death following burn.

## 2. MATERIALS AND METHODS

### 2.1. Principles of treatment

Standard treatment protocols in the Rotterdam Burn Centre (RBC) from 1996 to 2006 included fluid resuscitation with hypertonic crystalloids (0.45% NaHCO3 in 500 ml 0.9% NaCl; total Na content 202 mmol/l) according to the Parkland formula. Partial-thickness burns involving <10% TBSA were covered with dressings (hydrocolloids, alginates, hydrofibres); larger defects and full-thickness burns were initially treated with topical agents (silver sulfadiazine,

cerium nitrate–silver sulfadiazine). In full-thickness burns, delayed primary excision and biological closure with autografts or allografts or both were started within 7 days.
Isolated one-patient intensive care units were equipped with a laminar downflow system, sluices and overpressure to prevent cross-infection.
Inhalation injury was diagnosed on the basis of suspicion after exposure to smoke or fire, and considered proven in the presence of signs of airway obstruction or carbon particles in sputum or by bronchoscopy. Suspected and proven inhalation injuries were treated by endotracheal intubation and mechanical ventilation.
Antibiotics were not routinely administered at admission apart from selective decontamination of the digestive tract in the presence of burns involving>30% TBSA. Further indications for antibiotic prophylaxis included artificial ventilation in cases of inhalation injury, bacteraemia when the area to be excised exceeded 1% TBSA (one dose preoperatively) and change of a central line. Antibiotics were used therapeutically in the presence of contamination with group Lancefield A *haemolytic streptococci* or clinically suspected or proven infection. The choice of antibiotic was adjusted according to results of culture of the microorganism.
Enteral feeding was started within 24 h after admission and nutritional requirements were calculated using a modified Curreri formula. Gastric mucosal protection was administered if TBSA involved exceeded 20%.

## 2.2. Study design

Mortality was studied for the total population admitted to the RBC and for the subgroup admitted with intention to treat (ITT) over the 10-year period from 1996 to 2006. The decision for tender loving care (TLC) only was always a patient-tailored judgement made by an experienced team of burn specialists on the basis of the important criteria of age, TBSA burned, inhalation injury and also comorbidity. These characteristics were recorded in all cases and are presented for the total population as well as for the subgroups with ITT and TLC (Tables 1 and 2).

For quality control, our overall mortality rate from 1996 to 2006 was compared with results derived from an extensive multicentre database published in the National Burn Repository (NBR) 2005 [9]. These results were derived from 70 centres in the USA plus the District of Colombia from 1995 to 2005.

Causes of death were analysed for burn victims admitted from 1996 to 2006 to the RBC with an ITT. Categorisation included dysfunction of organ system(s), SIRS, sepsis and underlying causes. The concept of MOF as cause of death was defined by dysfunction of more than one organ system responsible for fatal outcome despite organ support.

**Table 1 – Comparison of demographic and injury characteristics of patients admitted to the Rotterdam Burn Centre from 1996 to 2006 with results from the National Burn Repository from 1995 to 2005**

| Characteristic | RBC | NBR | RBC TLC | RBC ITT |
|---|---|---|---|---|
| Number of patients | 1946 | 121,930 | 41 (2.1%) | 1905 (97.9%) |
| Mean age (years) | 28.6 | 33 | 61.1 | 27.9 |
| Mean TBSA involved (%) | 10.9 | 11.9 | 62.3 | 9.7 |
| Number with II | 243 (12.5%) | 7926 (6.5%) | 39 (95.1%) | 204 (10.7%) |
| Number of deaths | 135 (6.9%) | 6797 (5.6%) | 41 (100%) | 94 (4.9%) |

RBC, Rotterdam Burn Centre; NBR, National Burn Repository; TLC, subgroup receiving tender loving care only; ITT, subgroup with an intention to treat; TBSA, total body surface area; II, inhalation injury.

**Table 2 – Demographic and injury characteristics of patients admitted to the Rotterdam Burn Centre with an intention to treat, divided into survivors and non-survivors, from 1996 to 2006**

| Characteristic | Survivors | Non-survivors |
|---|---|---|
| Number of patients | 1811 (95.1%) | 94 (4.9%) |
| Mean age (years) | 26.3 | 58.2 |
| Mean TBSA involved (%) | 8.7 | 29.1 |
| Number with II | 162 (8.9%) | 42 (44.7%) |

TBSA, total body surface area; II, inhalation injury.



In recording dysfunction, definitions[15–17]were modified for the following organ systems: respiratory, defined by the requirement for mechanical ventilation for>72 h; cardiovascular, defined by inotropic dependency to keep mean arterial pressure above 60 mmHg; renal, defined by the use of continuous veno-venous or arterio-venous haemofiltration; hepatic, defined by transaminase level>1.5 of normal; and haematological, defined by a platelet count below 100,000/ml.

For SIRS and sepsis, definitions proposed by the American College of Chest Physicians/ Society of Critical Care Medicine Consensus Conference were used[16,17]. SIRS, regardless of cause, was defined and diagnosed if the patient showed more than one of the following clinical features:

- body temperature>38 $^{0}$C or <36 $^{0}$C
- heart rate>90/min
- respiratory rate>20/min or PaCO2<32 mmHg
- white blood cell count>12,000 cells/ml or <4000 cells/ml.

Sepsis was defined as the clinical syndrome of a systemic inflammation in response to infection. In the International Sepsis Definitions Conference no single specific criterion for sepsis was proposed, but rather a combination of criteria including proven or at least highly suspected infection[18].In our study, sepsis was proved by positive blood culture or was suspected in, for example, the presence of a new radiographic infiltrate together with an overall clinical impression.

Data expression and statistical analyses were performed using SPSS version 15.0. Descriptive statistics included means for continuous variables and proportions for categorical variables, which were compared using $X^2$ tests.

## 3. RESULTS

### 3.1. Burn centre mortality

Causes of burn among victims admitted to the RBC are shown in Fig. 1; flames (48%) or scalds (43%) were the agent of injury in 91% of cases. Demographic and injury characteristics and mortality rates among people admitted to the RBC together with data derived from the NBR are presented in Table 1. From 1996 to 2006, 1946 victims of burn were admitted to the RBC with a mean age of 29 years (range 0–98 years) and a mean TBSA involved of 10.9% (range 0–99%); 243 (12.5%) had suspected or proven inhalation injury according to the criteria mentioned in 2.1. Overall mortality rate among this population was 6.9%.
During almost the same decade, from 1995 to 2005, 121,930 people with burns were admitted to the 70 participating burn centres summarised in the NBR data. Demographic and injury characteristics included a mean age of 33 years and a mean TBSA involved of 11.9%, and 6.5% of cases had inhalation injury. Overall mortality rate in the NBR during this period was 5.6%. Differences between the RBC and the NBR in overall mortality rate and in incidence of inhalation injury proved to be statistically significant ($p<0.05$).

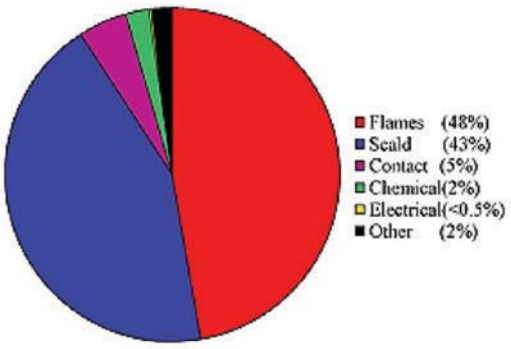


**Fig. 1 – Causes of burn among patients admitted to the Rotterdam Burn Centre from 1996 to 2006.**

Of the 1946 burn victims admitted to the RBC, 41 (2.1%) received TLC only. Mean age was 61.1 years, mean TBSA involved was 62.3% and 95.1% of these patients had inhalation injury. Therefore, 1905 people (97.9%) were admitted to the RBC with ITT. Mean age was 27.9 years, mean TBSA involved was 9.7%, inhalation injury was present in 10.7% and mortality rate was

4.9%. Divided into survivors and non-survivors, their demographic and injury characteristics are shown in Table 2. Mean age among the non-survivors was 58.2 years compared with 26.3 years among the survivors. Compared with survivors, TBSA involved was three times higher among the non-survivors (29.1% versus 8.7%) and the incidence of inhalation injury was five times higher (44.7% versus 8.9%).

### 3.2. Causes of death following burn

All burn victims receiving TLC died of irreversible shock, as resuscitation was withheld. Among the 4.9% of patients with ITT who died, cause of death could be retrieved in 89 (94.7%), as presented in Table 3.

As categorised by organ system, circulatory failure resulted in lethal outcome for eight patients, i.e. four (4.3%) sustained cardiac arrest, three (3.2%) died of burn shock and one (1.1%) died of an uncontrollable haemorrhage.

**Table 3 – Causes of death following burn in the Rotterdam Burn Centre from 1996 to 2006**

| Cause of death | Number | Percentage of total |
|---|---|---|
| Multisystem organ failure | 61 | 64.9 |
| Cardiac arrest | 4 | 4.3 |
| Burn shock | 3 | 3.2 |
| Haemorrhage | 1 | 1.1 |
| Pneumonia | 2 | 2.1 |
| Aspiration | 4 | 4.3 |
| Cerebral stroke | 3 | 3.2 |
| Neurological deterioration | 5 | 5.3 |
| Toxic shock syndrome | 2 | 2.1 |
| Carbon monoxide intoxication | 1 | 1.1 |
| Crush syndrome | 1 | 1.1 |
| Treatment refusal | 2 | 2.1 |
| Unknown | 5 | 5.3 |
| Subtotal | 89 | 94.7 |
| Total | 94 | 100 |

A further six people did not survive respiratory problems, i.e. pneumonia in two cases (2.1%) and aspiration in four cases (4.3%). Neurological problems were the cause of death of eight people, i.e. cerebral stroke in three cases (3.2%) and neurological deterioration in five cases (5.3%). For 61 people (64.9%) MOF resulted in fatal outcome; the remaining six died of toxic shock syndrome (two cases), carbon monoxide intoxication (one case), crush syndrome (one case), refusal of dialysis (one case) and refusal of blood transfusion (one case).

With respect to the inflammatory state among those who died from MOF, almost all (93%) showed signs of SIRS before death; among 28 of these (45.9%) an infectious source was

concurrently identified. In 13 of these 28 cases (46.4%), sepsis was proved by positive blood cultures, a further 14 had a diagnosis of pneumonia and 1 had a diagnosis of infected ascites. From 41 (67.2%) of those who died from MOF, blood cultures were drawn during their final septic episode; 17 microorganisms were cultured from 13 different blood samples, 12 cultures showed Gram-negative strains (*Klebsiella, Acinetobacter, Pseudomonas*) and 5 cultures yielded Grampositive strains (*Staphylococcus, Streptococcus, Enterococcus*).

## 4. DISCUSSION

### 4.1. Mortality

This study aimed to describe, first, the demographic and clinical features of the study population, comparing mortality rates with those published in a multicentre database from 70 burn centres in the USA and the District of Colombia. The number of admissions (1946) for burn to the RBC from 1996 to 2006 was slightly higher than the average number (1742) of admissions (121,930/70) to the participating burn centres in the NBR from 1995 to 2005.The 6.9% mortality rate from the RBC was significantly higher than the 5.6% mortality rate from the NBR and deserves a closer look, not least because mortality is one of the most important outcome parameters following life-threatening trauma and can serve as a measure for quality of care. Before being conclusive about quality of care, an evaluation of the most predictive parameters of fatal outcome should be taken into account.

Even with a higher mean age and higher mean TBSA involved, a 1.3% lower mortality rate was found in the NBR. The differences in age and TBSA involved are too small to explain the differing mortality rates, the reason which is probably the significant difference in incidence of inhalation injury, one of the three most powerful predictive parameters for fatal outcome (12.5% in the RBC compared with 6.5% in the NBR). Unfortunately, the comparison is complicated by the lack of definition in the NBR and by the criteria used in the RBC (see Section 2.1). From 1996 to 2006, burn victims were frequently admitted to the RBC as a tertiary referral centre and intubation had already taken place in another hospital. Bronchoscopy to prove inhalation injury was performed only if there had been no such previous intubation. In 12.5% of cases inhalation injury was diagnosed by suspicion, and in only 16.5% of these was proven by bronchoscopy. The number of cases where inhalation injury was diagnosed on the basis of signs of airway obstruction or carbon particles found in sputum unfortunately could not be retrieved. Because some of the criteria used are less specific than bronchoscopy, this may have resulted in an overestimation of inhalation injury among the RBC population. Nevertheless, the odds are that the difference in incidence of inhalation injury, with its high morbidity and mortality, is the most likely explanation for the difference in mortality rates between the RBC and the NBR. A uniform definition of

inhalation injury is recommended for future comparisons, and the most reliable and specific definition would be positive findings at bronchoscopy. Thus it is also recommended that clinical findings and bronchoscopy results indicating inhalation injury should be mentioned in handovers to tertiary referral centres, and that referred patients should undergo bronchoscopy for suspected inhalation injury even after previous intubation.

Probably more interesting than the outcome parameter of overall mortality is a comparison of mortality rates after admission with an ITT. Unfortunately, no data about this subgroup were available in the NBR and therefore no comparison with the RBC results could be made in this respect. However, comparisons with the NBR results are still of great value because of the multicentre character of the repository and its large amount of data[9]. The mortality rate for burn victims admitted to the RBC with an ITT was 4.9%, and this outcome parameter is in our opinion the most important and should be used in future evaluations of quality of care. Finally, the importance of taking into account the most important risk factors for fatal outcome in evaluation of mortality rates is shown by dividing the patients admitted for burn to the RBC with ITT into survivors and non-survivors.

This division shows that among non-survivors compared with survivors, age is twice, TBSA involved is three times and incidence of inhalation injury five times higher.



## 4.2. Causes of death

The second goal of this retrospective study was analysis of causes of death following burn. According to the literature, MOF is the leading cause of death[16,19]. However, recent studies of the distribution of causes of death are lacking, and therefore we have attempted to categorise causes of death in the RBC from 1996 to 2006. Despite intense investigation the aetiology of MOF remains largely unclear, although all cases seem to exhibit episodes of an uncontrolled inflammatory response (SIRS). A variety of conditions can lead to this response after burn, and underlying causes can be infectious as well as non-infectious[16]. Infectious causes include sepsis [20], bacteraemia following manipulation of colonised wounds, small repetitive infections[21]and bacterial translocation from the gut[22]. In non-infectious aetiology the crucial pathophysiological event is thought to be the tissue damage itself [23]. Several factors can be responsible for this tissue damage and for the prolongation of a systemic inflammatory response to it. After burn, the presence of necrotic tissue, resuscitation failure, ischaemic–reperfusion injury and translocation of endotoxins across the bowel[24]can all lead to SIRS. Sheridan et al.[19]reported MOF to be cause of death after burn injury in 67% of cases. They referred to these fatal cases of MOF as being sterile because no clinical infection was suspected at time of death. In the RBC population MOF was the leading cause of death after burn in 64.9% of cases; 28 of these 61 people (21.8%) had sepsis proved by bacteriological culture, and 15 (24.6%) had highly suspected sepsis. Therefore, in almost half of the RBC population dying from fatal MOF, death could, at

least partially, be attributed to a final infection.
Decreased mortality after burn, and decreased death from MOF in particular, could be achieved with improvement of infection prevention and therapy and prevention of other causes of SIRS. Theoretically, ability to establish an immunological balance between pro-inflammatory and anti-inflammatory biological signals would be the most promising development [25]. However, so far the best approach in practice remains infection prevention and treatment together with patient and organ support to prevent organ failure[26].A minority of people in our population died from theoretically preventable causes of death; in three cases (3.2%) fatal burn shock could not be relieved despite vigorous fluid resuscitation, and in four cases (4.3%) fatal aspiration could not be prevented despite precautions such no tube feeding at night and sleep in a reverse Trendelenburg position for those without intubation.

## 5. CONCLUSION

The availability of demographic and injury characteristics together with outcome variables is necessary for making meaningful comparisons. Risk factors such as age, TBSA involved and the presence of inhalation injury should be taken into account when mortality rates are compared. With respect to comparison of results between the RBC and NBR, the difference in mortality rates can most probably be attributed to differing incidences of inhalation injury, although criteria for its diagnosis were dissimilar. A uniform definition for the diagnosis inhalation injury will be mandatory for reliable comparison of results in future reports and demographic and injury characteristics, not only for the total population but also for the subgroups with and without ITT. After admission to the RBC during the period from 1996 to 2006, overall mortality rate was 6.9%; on an ITT basis, mortality rate was 4.9%. MOF was the most common cause of death, and its fatality was due to a final infection in 45.9% of cases. Decrease in mortality rates after burn is most likely to be achieved by development of better prevention programmes and treatments for infection and of methods for establishing immunological balance.

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# Chapter 8

# Mortality and causes of death of Dutch burn patients during the period 2006–2011

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## ABSTRACT

***Introduction:*** Mortality of burn patients has decreased in the last decades. Literature indicates that the leading cause of death in late mortality is multiple organ failure (MOF), but literature is not clear about the cause of early mortality. The aim of this study was to determine the mortality and causes of death of burn patients in Dutch burn centers between January 2006 and December 2011.

***Methods:*** A retrospective study was performed in patients who died between January 2006 and December 2011 in the burn centers of Rotterdam and Beverwijk, the Netherlands. In this period 2730 patients were admitted.

***Results:*** Of these 2730 patients, 88 patients died as a result of their burn injury. The overall mortality rate was 3.2%. The palliative care group, defined as patients receiving no curative ('active') care and leading to early death (<48 h), consisted of 28 patients (31.8%, 28 out of 88 patients). The most common cause of late mortality (>48 h, in 60 out of 88 patients, 68.2%) was MOF (38.3%, 23 out of 60 patients). One important significant difference between the early and late mortality groups was a higher Baux score in the palliative care group compared to the withdrawal of and active treatment groups. There were no significant differences when the groups were compared regarding the presence of inhalation trauma.

***Conclusions:*** Mortality in burn patients has decreased. Most deaths occur early, in patients who receive only palliative care. In late mortality, MOF is the most common cause of death.

## 1. INTRODUCTION

Even though the mortality of burn patients has decreased in the last decades [1–3], patients still die as a result of their burn injuries. The literature indicates that the leading cause of late mortality is multiple organ failure (MOF) [4–7].
The cause of early mortality is not clear, but appears to occur mainly in patients who are not actively treated and receive palliative care [8,9].
Beside the depth and affected total body surface area, the prognosis after burn wounds is influenced by age, comorbidities and other trauma such as inhalation injury [4,10–15]. Breathing or circulation problems occur mainly in the first 48 h after a burn injury. After this period metabolic and infectious problems occur [16].
Due to changes in burn care, such as early surgery, improved resuscitation, nutritional support and skin replacement techniques, the mortality rate has decreased [5,11]. The aim of this study was to determine the mortality and causes of death of burn patients in two Dutch burn centers between January 2006 and December 2011.

## 2. METHODS



A retrospective study was performed in patients who died between January 2006 and December 2011 in two of the three burn centers in the Netherlands (Rotterdam and Beverwijk). In the Netherlands patients with burns are referred to a burn center if they fulfill the referral criteria presented in Table 1.

**Table 1 – Dutch burn center referral criteria.**

| |
|---|
| TBSA > 10% for adults |
| TBSA > 5% for children |
| Full thickness burn > 5% TBSA |
| Burns on children or elderly |
| Burns on patients with pre-existing conditions, that may affect treatment and healing |
| Burns associated with another trauma or with inhalation trauma |
| Burns on functional areas, such as hand, foot, face, genitalia or large joints |
| Electrical burns |
| Chemical burns |
| Circular burns on trunk or limbs |

Data of the patients admitted to the burn centers in the years 2006–2008 were collected from the (digital) patient files. Data of the patients in the years 2009–2011 were obtained from the joint burn registry of the three burn centers in the Netherlands (Dutch Burn Repository R3) which started in 2009.

Data collection included age, gender, year of admission, burn center, cause of injury, co-morbidities (circulatory, endocrine, locomotor, gastro-intestinal, genitourinary, respiratory, and psychiatric), TBSA, Baux score, inhalation injury,CO-intoxication, survival time, complications and cause and time of death. Co-morbidities were registered by number and not by severity. TBSA was determined by the Lund and Browder charts. The Baux score is defined as the sum of age in years and TBSA and can be used to predict the probability of survival after severe burns [17]. If the score exceeds 100, the patient has a reduced probability of survival (<50%). The revised Baux score is defined as the sum of age in years and TBSA in % and the presence of an inhalation trauma with 17 points [18]. Early mortality was defined as death within 48 h and late mortality as death after 48 h.

Patients who died during hospital admission were subdivided into three groups [19]. The first group consisted of patients for whom no active ('curative') care was started and who received only palliative care. The decision to withhold treatment was made on admission day by the entire burn team according to the hospital protocol. This decision is based on many objective and subjective factors such as age, TBSA, inhalation trauma, co-morbidities, patient's wishes or likely patient choices as reported by the family. In the second group, active treatment was initially started but was discontinued due to complications. The third group received active treatment until death.

Data were analysed using SPSS version 17.0. One-way ANOVA and the Kruskal–Wallis test were used for continuous variables for group comparisons. The Chi-square test was used to compare categorical variables between the patient groups. Two-tailed p values below 0.05 were considered statistically significant.

## 3. RESULTS

During the period January 2006–December 2011 2730 patients were admitted to the burn centers of Rotterdam and Beverwijk in the Netherlands. The mean age and TBSA did not change between 2006 and 2011 (ANOVA, $p = 0.865$ and $p = 0.151$, respectively) (Table 2). Of these patients, 91 patients died during hospital admission. Three patients who died as a result of cancer were excluded from further analysis. The overall mortality rate due to burn injury was 3.2%.

**Table 2 – Age and TBSA of burn patients between 2006 and 2011.**

| Year admission | Total group *N* | Age mean (SD) | TBSA mean (SD) | Died *N* |
|---|---|---|---|---|
| 2006 | 420 | 27.8 (24.6) | 9.4 (12.6) | 18 |
| 2007 | 384 | 27.1 (23.5) | 7.9 (11.6) | 11 |
| 2008 | 427 | 29.2 (24.0) | 7.9 (11.6) | 10 |
| 2009 | 458 | 28.6 (24.5) | 7.5 (10.9) | 15 |
| 2010 | 477 | 27.9 (24.8) | 7.4 (10.7) | 12 |
| 2011 | 564 | 27.8 (24.1) | 7.8 (13.1) | 22 |
| Total | 2730 | 28.1 (24.2) | 8.0 (11.8) | 88 |

**Table 3 – Causes of death.**

| Cause of death | All patients *n* (%) | Active treatment *n* (%) | Withdrawal of active treatment *n* (%) | Palliative care *n* (%) |
|---|---|---|---|---|
| Palliative care | 28 (31.8) | – | – | 28 (100) |
| Multi organ failure | 23 (26.1) | 13 (41.9) | 10 (34.5) | – |
| Cerebral | 3 (3.4) | 3 (9.7) | – | – |
| Cardiac | 3 (3.4) | 3 (9.7) | – | – |
| Embolism | 1 (1.1) | 1 (3.2) | – | – |
| Pulmonary | 1 (1.1) | 1 (3.2) | – | – |
| Sepsis | 2 (2.3) | 2 (6.5) | – | – |
| Haemodynamically insufficient | 1 (1.1) | – | 1 (3.4) | – |
| Respiratory insufficient | 4 (4.5) | – | 4 (13.8) | – |
| Haemodynamically and respiratory insufficient | 3 (3.4) | – | 3 (10.3) | – |
| Euthanasia | 1 (1.1) | – | 1 (3.4) | – |
| Otherwise[a] | 5 (5.7) | 5 (16.1) | – | – |
| Unknown | 13 (14.8) | 3 (9.7) | 10 (34.5) | – |
| Total | 88 (100) | 31 (100) | 29 (100) | 28 (100) |

[a] Circulatory complications, accidental extubation (after which resuscitation failed), bleeding after inserting a thorax drain and hypoglycaemia.

The mean age of the 88 deceased burn patients was 63.5 years (SD 20.0). Half of them were male. The patients had an average TBSA of 42.1% (SD 29.1). The majority of the lethal burn accidents happened in or around the house (73.9%).
Other common accident sites were the public road (5.7%), care facilities (such as nursing homes) (3.4%) and campsites (2.3%). Only one (1.1%) of the accidents happened at work. Most of the lethal burns (89.9%) were caused by flame, followed by scalding (8.0%), and steam or grease (both 1.1%). None of the patients died of electrical or chemical burns.

In the palliative care group no patients were <16 years old, 3 patients between 20 and 40 years, 15 patients 40–70 years and 10 patients >70 years; in the withdrawal of active treatment group no patients <16 years old, 2 patients between 20 and 40 years, 11 patients 40–70 years and 16 patients >70 years; in the active treatment group care group one patient <16 years old, no patients between 20 and 40 years, 18 patients 40–70 years and 12 patients >70 years. Only one child died, who was 3 years old and actively treated.
One third of the deceased patients (n = 28, 31.8%) received only palliative care and died within 48 h as a direct result of their injury. In the remaining 60 deceased patients (68.2% of total), active treatment was started but discontinued in 29 (33.0% of total). All of these 60 patients died after 48 h except one patient who died on the second day after withdrawal of active treatment. The most common cause of late mortality was MOF (23/60, 38.3%) (Table 3).
The burn patients who died after palliative care, withdrawal of active treatment or active treatment did not differ regarding age and gender (Table 4).

Comparing the mean age of the palliative (58.8 years, SD 19.9) with the withdrawal of care group (69.3 years, SD = 20.4) a mean difference of 10.6 years ($p = 0.053$) was observed. The median survival time was 9.0 days (range of 1–108), and was, as expected, shortest in the palliative care group ($p < 0.001$). Patients who received palliative care had the highest percentage TBSA and Baux score ($p < 0.001$), and of course as expected the lowest number of ventilator days ($p < 0.001$).
Patients in the palliative care group (35.7%) had significantly less co-morbidities compared to the withdrawal of care group (86.2%) and the active treatment group (80.6%) ($p < 0.001$). The most common co-morbidities were circulatory and endocrine conditions. The number of co-morbidities per patient in each care group was not significantly different. Fewer patients in the palliative care group developed complications compared to the withdrawal of care group and the active treatment group (42.9% versus 86.2% and 93.5%, $p < 0.001$) caused by their shorter life expectancy. The number of complications per patient was not significantly different ($p = 0.22$). In the active treatment group more patients developed acute renal failure compared to the palliative care group ($p < 0.001$) and compared to the discontinued care group ($p = 0.03$).

**Table 4 – Characteristics of deceased burn patients by type of care.**

| | Active treatment ($n = 31$) | Withdrawal of care ($n = 29$) | Palliative care ($n = 28$) | $p$ Value |
|---|---|---|---|---|
| Burn center, $n$ (%) | | | | 0.66 |
| Beverwijk | 19 (61.3) | 17 (58.6) | 14 (50.0) | |
| Rotterdam | 12 (38.7) | 12 (41.4) | 14 (50.0) | |
| Gender, $n$ (%) | | | | 0.90 |
| Male | 15 (48.4) | 14 (48.3) | 15 (53.6) | |
| Female | 16 (51.6) | 15 (51.7) | 13 (46.2) | |
| Age, mean (SD) | 62.2 (19.0) | 69.3 (20.4) | 58.8 (19.9) | 0.13 |
| Co-morbidities, $n$ (%) | 25 (80.6) | 25 (86.2) | 10 (35.7) | <0.001* |
| Cause of injury, $n$ (%) | | | | 0.25 |
| Flame | 25 (80.6) | 29 (100.0) | 25 (89.3) | |
| Scald | 4 (12.9) | 0 (0.0) | 3 (10.7) | |
| Grease | 1 (3.2) | 0 (0.0) | 0 (0.0) | |
| Steam | 1 (3.2) | 0 (0.0) | 0 (0.0) | |
| Survival time in days, median (range) | 19.0 (2–109) | 10.0 (3–78) | 1.0 (1–2) | <0.001** |
| Percentage TBSA, mean (SD)[a] | 35.2 (24.8) | 26.7 (17.3) | 65.7 (27.7) | <0.001* |
| Baux score, mean (SD)[b] | 97.4 (20.6) | 96.0 (11.6) | 124.5 (22.9) | <0.001* |
| Inhalation trauma, $n$ (%) | 13 (41.9) | 11 (37.9) | 14 (50.0) | 0.65 |
| Revised Baux score, mean (SD)[c] | 104.5 (23.2) | 102.5 (14.3) | 133.0 (25.0) | <0.001* |
| Ventilated, $n$ (%) | 26 (83.9) | 20 (69.0) | 24 (85.7) | 0.22 |
| Days on ventilator, mean (SD) | 19.8 (22.1) | 8.3 (16.0) | 1.2 (0.7) | <0.001** |
| Complications, $n$ (%) | 29 (93.5) | 25 (86.2) | 12 (42.9) | <0.001* |

* Palliative care group significantly different from withdrawal of and active treatment group.
** Significant difference between the three groups.
[a] TBSA, total body surface area.
[b] Baux score: age + %TBSA.
[c] Revised Baux score: age + %TBSA + 17*(inhalation trauma, 1 = yes, 0 = no).

Patients in the active treatment group were significantly more often operated compared to the withdrawal of active treatment group (74% and 34%, respectively) ($p = 0.002$), but the mean number of operations per patient was not different (4.0 versus 3.1 operations, $p = 0.21$).

## 4. DISCUSSION

The aim of this study was to determine the in-hospital mortality of burn patients in two Dutch burn centers between 2006 and 2011. The mortality rate found was 3.2%. In a previous study in a Dutch burn center between 1996 and 2006 performed by Bloemsma et al. [4] a mortality rate of 6.9% was found. The mean age and TBSA in this study was 28.6 years and 10.9%. The age distributions of the active treatment, withdrawal of care and palliative care group were equal. Therefore in comparison with our study the mean age was stable and the mean percentage TBSA declined over time, which may be explained by changing referral patters especially in children [20] and the ongoing improvement of burn care such as better prevention and educational programs [21]. So the mortality rate in Dutch burn centers seems to have declined over time which may be explained by the decreased TBSA of the admitted patients and ongoing improvement of burn care [21]. In the Netherlands, the introduction of the EMSB course (Emergency Management of Severe Burns) for emergency health workers may also have contributed to a lower mortality rate.

Recent studies outside the Netherlands found slightly higher mortality rates of 5.4% [7], 6.8% [15] and 10.5% [22]. Only Åkerlund et al. [3] found a similar mortality rate (3%) and an overall reduction in mortality in Sweden. The studied time periods, populations and numbers of patients in these studies on mortality rate were different, which hampers a direct comparison of the reported mortality rates. A longer studied time period also increases the likelihood of a decline in mortality. Åkerlund et al. [3] studied all patients who were admitted to hospitals in Sweden (24,538 patients) during 1987–2004. Kallinen et al. [7] studied 1370 patients admitted to the Helsinki Burn Center (Finland) during 1995–2005. Edelman et al. [15] analysed 829 consecutive patients admitted to the burn unit of a level one trauma center in Detroit (USA) during 2000–2004 and Belba et al. [22] described the mortality in a group of 2337 patients hospitalized in the Burns Service University Hospital Center Tirana (Albania) during 1998–2008. Especially the last study had a high mean TBSA of 22.8%.

The most common cause of burns within the group of deceased patients in this study was flame (89.9%). This is consistent with other studies [5,23]. In this study 73.2% of the accidents happened at home. Belba et al. [22] found almost the same percentage.

In the active treatment group the most common cause of death was MOF. This was the same in another Dutch study. Bloemsma et al. [4] also divided their patients into subgroups. In

their Intention to Treat (ITT) group, which is comparable with the active treatment group in this study, the most common cause of death was MOF. MOF mostly occurs as a complication of a severe infection [24]. One study found renal failure in all patients with MOF [7]. Acute renal failure was also the most frequent complication in the active treatment group in this study. Acute renal failure is commonly seen after major burns and often coincides with failure in other organs [25].

The patients in the palliative care group had similar age and less comorbidity compared to the patients who received active treatment immediately after admission but they had a significantly higher TBSA percentage and a significantly higher Baux score. It therefore seems that the decision not to treat a patient actively and to give only palliative care is mostly influenced by TBSA and not so much by age or comorbidity. The patients in whom active treatment was discontinued were similar to the patients who received active treatment until death with respect to age, co-morbidity, TBSA and Baux scores. The main reason for withdrawal of the active treatment therefore seems the severity of the complications which ultimately led to the patients' death (Table 3).

The patients in the withdrawal of care group had a higher age (mean of 69.3 years) compared to the palliative care group (mean of 58.8 years) (post-hoc least significant difference (LSD) test, $p = 0.047$). The withdrawal of care patients had a significantly lower mean percentage TBSA and mean Baux score, and had more often co-morbidities than the palliative care group (Table 4). The patients in the withdrawal of care group were also less often operated upon. Therefore the patients in the withdrawal of care group consisted of slightly older patients with smaller injuries which needed fewer operations, and died due to their pre-accident conditions of heart and consecutive lung conditions (Table 3).

The patients who received immediate palliative care had the highest Baux scores and therefore the highest risk of mortality. The palliative care group had an average Baux score higher than 100, the groups that received active treatment had a score below 100. Theoretically this would mean that the patients in the palliative care group had no anticipated chance of survival, which might justify the choice for immediate palliative care for these patients. Wibbenmeyer et al. [26] formed two subgroups ('care withdrawn' and 'treated and died') which were quite similar to the other two groups in this study. They also found no significant differences between these two groups regarding to age and the presence of inhalation trauma.

The percentage of patients with inhalation trauma was similar in the three care groups, moreover not influencing the revised Baux scores.

This study included only patients that died in burn centers. Patients who were admitted because of a burn injury in nonspecialised hospitals were not included. In general, burn patients who are admitted in these hospitals have less severe burns and do not die because of their injury. This study only used the data of two of the three burn centers in the

Netherlands, but the results can be generalised since the patient populations in the three burn centers are very similar.

## 5. CONCLUSION

The mortality rate in Dutch burn centers between 2006 and 2011 was 3.2% and has declined since the preceding years by more than 50%, which may in part be explained by a decline in TBSA. Most in-hospital mortality occurs early, due to palliative care (about one third) or withdrawal of active treatment (about one third). In late mortality, MOF is the most common cause of death.

### Conflict of interest

The authors declare that they have no competing interests. The authors have no financial and personal relationships with other people or organisations that could inappropriately influence (bias) their work

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### Appendix A

The Dutch Burn Repository Group consists of:

- Burn Center Beverwijk: E.C. Kuijper, F.R.H. Tempelman, A.F.P.M. Vloemans, P.P.M. van Zuijlen.
- Burn Center Rotterdam: A. van Es, H. Hofland, J. Dokter.
- Burn Center Groningen: J. Eshuis, J. Hiddingh, S. Scholten Jaegers.
- Association of Dutch Burn Centers: M.E. van Baar, E. Middelkoop, M.K. Nieuwenhuis, A. Novin, M. Novin

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# Chapter 9

## Summary and discussion

Samenvatting en discussie

Epidemiology is the cornerstone of public health. It generates information for policy decisions and evidence-based practice by identifying risk factors for diseases and targets for epidemiological studies that are essential for improving health care. High research design and conduct are essential and results should be interpreted carefully.
The epidemiology of burns in the Netherlands has changed in recent decades, and many factors have contributed to this change. The increase in the elderly among the population because of aging in our society and the numbers of children from other ethnic and cultural groups due to immigration cause the age distribution in society to vary. Although burns happen especially at the extremes of age, the total number of patients with burns is still decreasing.
Public education campaigns, often initiated by the Dutch Burns Foundation and the spread of one-liners for prevention ("Eerst water, de rest komt later" or "Water first, the rest will come later") and first aid measures play an important role in the awareness of burn dangers throughout the population.
Education by healthcare professionals improves care quality, the recognition of small and simple burn wounds, and the acknowledgement of more specialized care in case of severe burn wounds.
Cooperation between burn centers and referral hospitals also increases awareness of the need for adequate early resuscitation, stabilization, referral and admission to specialized hospitals.
Good primary treatment is of major importance for optimal outcomes.
Nationwide registration of burn patients gives insight into care outcomes and can highlight the tools that can allow for further improvement.
Adequate registration and measurement of care outcomes remains necessary and will further change the epidemiology of burns in the future.

The aim of this thesis is to acquire knowledge on the epidemiology, treatment and outcomes of specialized burn care in the Netherlands. The thesis is mainly based on historical data from the Rotterdam Burn Centre since 1986, combined with historical data from the burn centers in Groningen and Beverwijk from 1995 to 2009 and the common Dutch Burn Repository (DBR) R3, established in 2009.

This thesis is divided into three parts:

Part 1: epidemiology
Part 2: management
Part 3: outcome

## PART ONE: EPIDEMIOLOGY

### **Chapter 1** *Introduction and outline of the thesis*

Chapter 1 describes the development of specialized burn care in The Netherlands. It began with the emergence of the Dutch Burns Foundation to generate funds for research and was followed by the opening of three burn centers in non-academic hospitals in Beverwijk, Rotterdam and Groningen.
In the course of time, strengthened cooperation between these three centers resulted in the Association of Dutch Burn Centres (ADBC).
One of the great milestones of the ADBC was achieved with the development and implementation of a common uniform database, the Dutch Burn Repository (DBR R3) in 2009.
The current version of DBR R3 contains all essential information about patients who have been admitted to any of the three burn centers, their treatment and their outcomes. The database is adapted and expanded in close consultation with the users in such a way that the system is up to date with developments in burn care, allowing for better comparison with international databases.
Merging the historical databases of the three burn centers and the start of the DBR R3 enabled an overview of primary admissions in Dutch burn centers from 1995 to 2011 described in Chapter 2. In this study, data were also used from general hospitals, specifically from the National Hospital Discharge Register (NHDR).
Data from these registries underscore their importance for monitoring and improving the quality of care for these patients.

### **Chapter 2** *Epidemiology and trends in severe burns in the Netherlands [1]*

The annual number of patients admitted to the three Dutch burn centers increased from 430 in 1995 to 747 in 2011, an increase from 2.72 to 4.66 per 100,000 inhabitants. There was a trend towards admissions for less extensive burns and lengths of stay decreased over time as well. Overall burn center mortality decreased from 8% to 4%.This reduced mortality could of course be at least partly explained by the fact that more patients with less extensive burns were referred over time to the three centers. In children, the vast majority of patients (four in five) meet the referral criteria for burn centers, as shown by Vloemans et al [2], but children with less severe burns are also admitted to the centers.

In the Netherlands, the referral criteria for burn centers according to the Emergency Management of Severe Burns (EMSB) course are:

- Burns over 10% total body surface area (TBSA) in adults.
- Burns over 5% TBSA in children.
- Full-thickness burns over 5% TBSA.
- Burns at the extremes of age, children and the elderly.
- Burns in patients with preexisting medical disorders that could complicate management and prolong recovery or effect mortality.
- Any burn patient with associated trauma.
- Burns with associated inhalation injury.
- Circumferential burns of the limbs, neck or chest.
- Burns to special areas such as the face, hands, feet, perineum, genitals and major joints.
- Electrical burns.
- Chemical burns.

The introduction in the Netherlands of the Emergency Management of Severe Burns course in 1998, where lower-threshold consultation is encouraged, has contributed to earlier referral to burn centers. Many patients are transferred to tertiary care facilities because of a perceived lack of basic skills in assessing and caring for burn wounds in hospitals that are infrequently confronted with burn patients.

Recently, a working group of burn care professionals, general practitioners, ambulance personnel, emergency medicine physicians, pediatricians and trauma surgeons developed an evidence-based guideline on initial acute care and referral decisions [3]. This was done in close cooperation with the Dutch Burns Foundation, the Dutch Society for Burn Care (Nederlandse Vereniging voor Brandwonden Zorg), the ADBC and experts from the Dutch Institute for Healthcare Improvement (Centraal Begeleidings Orgaan (CBO)). This guideline aims to improve emergency care and to support treatment and decisions about referrals of burn patients. In case of questions or doubt, a burn center expert can always be consulted.

In comparison with other countries, the Netherlands has a relatively low number of burn patients, which is likely related to the broad attention given to burn prevention in the country.

The incidence in children aged 0-4 years who were admitted to Dutch burn centers doubled from 10.26 per 100,000 inhabitants in 1995 to 22.96 per 100,000 in 2011 [4]. This marked increase in the number of pediatric admissions was also noted before by Vloemans et al [2], and it led to the retrospective epidemiological study described in Chapter 3.

**Chapter 3** *Epidemiology of children admitted to the Dutch burn centres. Changes in referral influence admittance rates at the centres*

In this publication, burn patients from 0 to 4 years were compared with patients age 5-17 during the two time periods 1995-1999 and 2000-2007.
From the first (1995-1999) to the second (2000-2007) period, the mean number of admissions to the Dutch burn centers increased from 113 to 163 per year for younger children and from 50 to 71 for older children, increases of 44.0 and 44.3%, respectively.
In patients over 18 years old, the annual mean number of admissions increased from 290 to 303, an increase of 4.3%. The proportion of children admitted to specialized burn centers rather than general hospitals increased over time from approximately 30% in 1995 to nearly 50% in 2007 in both age groups ( $p<0.001$).
Nearly 50% of all children with burns between 0-4 years of age in the Netherlands were admitted to a specialized burn center.
In conclusion, there has been a shift in pediatric burn care towards a greater volume of admissions to burn centers particularly for young children with less severe burns. Together with the general tendency toward centralizing specialized healthcare, the introduction of the Emergency Management of Severe Burns course in 1998 could be a possible explanation because EMSB guidelines dictate stricter and generally accepted referral criteria.
The Netherlands is a small country with three burn centers. The merits of the two studies that were described in chapters 2 and 3 about epidemiology and registration is that they are nationwide and they cover 100% of admitted burn center patients. In other countries with larger numbers of burn centers, such as the UK, Australia and New Zealand, similar burn-center-based registries that include data on all patients, outcomes and quality of care, but nationwide participation is not always reached.
In the USA, the National Burn Repository (NBR, 2014) covers 96 of 123 US burn centers plus 4 centers in Canada and 2 in Sweden. [5]
The National Burn Repository summarizes and compares cases submitted by burn centers internationally and in the United States. The concept behind it is simple: through calls for data, burn centers send a standard set of data elements regarding their burn cases to a central repository. This central repository summarizes data quality, demographic and injury information, and outcomes to prepare various reports.
The American Burn Association (ABA) annually provides an NBR report of data that summarizes the clinical characteristics and courses of some of the annual burn treatment cases that were submitted to the NBR from specialized burn care facilities.
These cases constitute a convenient sample of burn patients who received specialized care; they do not represent a random sample of all patients who were presented to a hospital for burn treatment or who were admitted to burn centers. It is a large sample of patients from facilities that have a strong commitment to excellent burn care. The data include many of

the most challenging burn cases seen at specialized burn care facilities and reflect, in large part, the best possible outcomes of burn care at the beginning of the second decade of the 21st century.

Some shortcomings of our two studies have to be mentioned. First, data are lacking about outpatient treatment. In line with reduced lengths of stay (LOS), outpatient care has gained importance and is currently a crucial part of our specialized burn care. Data on these outpatient burn center activities would add to our knowledge on the full spectrum of specialized burn care. This is acknowledged by other groups as well [6]. In the Netherlands, the Dutch Burn Repository group has already designed a data collection scheme, but implementation has been postponed due to manpower constraints; electronic medical records do however include all necessary information. In the near future, we hope to extract these data and to be able to include them in our repository. Similar developments have been reported, for instance in the Burns Registry of Australia and New Zealand [6].

Second, we did not have access to the digital NHDR data, and thus only limited analyses could be performed on the overall burn-related admissions in the Netherlands. A frequent problem in these datasets is the double counting of patients with an admission to a non-burn centre hospital first and referred to a burn centre afterwards. This problem will apply to the Dutch data as well, but only to a minority of patients; more than 80% of our patients at first are seen in emergency departments at non-burn center hospitals, but after first assessment and resuscitation, they are transferred immediately to burn centers for admission and further treatment because of the short distances to the specialized centers in our country. Thus, the delivered data were of good quality and sufficient for comparing trends in specialized burn care with trends in non-specialized care [7].

A third potential shortcoming is the content of the dataset. We included data such as age, sex, cause of burns, accident location, accident background, etc. into local databases and merged these into one database as much as possible. In the past, specific patient characteristics (e.g. co-morbidity and socioeconomic status) could not be addressed because these variables were absent or partly absent in the historical local databases. However, with the uniform Dutch Burn Repository R3 from 2009 onwards, a number of problems were overcome, and more detailed information became available. For instance, we now have indications of patients' socioeconomic status based on information their postal codes. In addition, information on comorbidity is systematically recorded.

The two studies show that young children especially are an important target group for prevention; the age group of 0-4 years is overrepresented in the patient population in the Dutch burn centers. The Dutch Burns Foundation pays special attention to this age group by means of lectures, special mass media prevention campaigns, in infant welfare centers and by publishing prevention measures on their website.

The fact that children are so frequently involved in burn injuries has implications for therapy, as well. Most of these injuries are scald burns, which require special wound care. This aspect is described in detail in Part 2 of Chapter 4.

A new challenge is evaluating the implementation of the recently developed Dutch guideline on initial care for burn patients in the acute phase [3]. With data from the HDR and the DBR R3, we can better monitor referral patterns, and additional data on burn care consultation will add to our knowledge on the needs of health care professionals outside of specialized burn care. As a result, we can direct prevention, monitor care quality and facilitate scientific research.

## PART TWO: MANAGEMENT, WOUND CARE (A) AND BACTERIOLOGICAL SURVEILLANCE (B)

### a) Wound care

An important milestone in burn treatment was adding silver to local wound care. In his 1968 article "Silver sulfadiazine--a new topical therapy for Pseudomonas in burns. Therapy of Pseudomonas infection in burns," in *Archives of Surgery* [8], C. L. Fox, Jr. describes for the first time the effect of silver sulphadiazine on reducing burn wound sepsis and mortality. Since then, silver sulfadiazine has been the first choice in treating burns and today it is still frequently used worldwide, especially in full-thickness burns [9].
With the introduction of this anti-bacterial cream with its broad antibacterial spectrum, which results in less wound infection and sepsis, it became possible for patients to survive major burns. Especially in full-thickness burns, it has proven its benefits, and in many treatment protocols, the use of silver sulphadiazine is clearly defined [10].
In practice, however, most burn injuries are a mixture of superficial and deeper lesions, especially in scalds in children. In addition, negative side effects of silver sulphadiazine were observed over time. In mixed partial-thickness burn wounds, it is our policy to wait and see which parts will heal spontaneously within 2 weeks and to wait for demarcation of deeper areas that require excision and grafting.
A number of studies showed that silver sulphadiazine inhibits the healing of partial-thickness burn wounds [11]. In the late eighties and early nineties, it became evident that the optimal environment for wound healing is between moist and dry [12]. Therefore, modern wound dressings that create this jelly environment are used more and more, and this prompted the study described in Chapter 4.
In this chapter, a retrospective study is described that compared the clinical outcomes of using silver sulphadiazine with those from the hydrofiber dressing Aquacel®, a modern

wound dressing that creates a jelly environment. The primary endpoint was the need for secondary surgical intervention, and secondary endpoints were length of stay and readmission for the same burn.

**Chapter 4** *Reduction in skin grafting after the introduction of hydrofiber dressings in partial-thickness burns: a comparison between a hydrofiber and silver sulphadiazine[13]*

The study population consisted of 804 children aged 0-4 years with scalds on up to 10% TBSA between January 1987 and January 2010. Of these 804 children, 502 were treated with silver sulphadiazine (Ag-SD) and 302 with the hydrofiber dressing (HFD).
In the total study period, 27.3% of 502 children who were treated with silver sulphadiazine underwent skin grafting, whereas in the group of 302 children who were treated with the hydrofiber, only 11.6% required operative treatment, a significant decrease in the number of operations.
In addition, a second major gain after the introduction of hydrofiber dressings was the reduction in hospital Length Of Stay (LOS). Before the introduction of HFD, the mean LOS was 12.4 days. When HFD was introduced, a change of policy in wound treatment was initiated, and Ag-SD was later replaced by a variety of wound dressings, allowing for less frequent dressing changes and therefore less need for long hospital stays.
This could explain the observation that in the period during which both Ag-SD and hydrofibers were used, LOS for Ag-SD treated patients showed a statistically significant decrease to 9.7 days. However, patients with burns treated with HFD were admitted for 7.5 days, a more significant decrease compared with Ag-SD-treated patients in the same time period.
Although this was a retrospective study, with all the limitations that entails, it gained strength due to the large number of patients. However, as a result of our study combined with other benefits such as decreased pain perception and increased patient comfort (based on fewer dressing changes) at lower total cost, currently hydrofiber dressings are the first choice in treating scald burns over up to 10% TBSA in our burn center [14,15] .

The proverb "All roads lead to Rome" is especially true in the vast range of wound dressings for burns. It should be realized that the ideal wound dressing still does not exist. With one dressing, it will take 14 days for a superficial burn to heal, and with the other, it will take two weeks. In addition to time for wound healing, patient comfort, ease of use and cost also determine the choice of a dressing. Burns are dynamic wounds: superficial-looking wounds can deepen secondary to multiple causes such as inadequate cooling or infection. The best time to assess the depth of burns is after 48-72 hours, and currently, laser Doppler imaging (LDI) is much more reliable than clinical assessment by physicians or nurses [16]. To be able to make LDI scans 2 to 5 days after the burn, the HFD has to be removed first, which is not

always easy after two days because the fragile, just-repairing epithelium may be disrupted. Hydrofibers therefore remain on the wound for approximately 10 days, making interim assessment impossible. It is always possible that there are deeper parts after dressings are removed that sometimes have to be operated on, and this has to be discussed in the beginning of treatment with patients and/or parents.

## b) Bacteriological surveillance

Infection remains one of the major complications in the period following severe burns, facilitated by the defect skin and patients' innate immune responses.
We had the opportunity to merge the patient database of the Rotterdam Burn Centre, with mainly demographic data on causes and localizations of burns, with a very large database from the hospital's Department of Bacteriology, which contained all microbial cultures over a period of 24 years.
After a presentation at the 16th Congress of the International Society for Burn Injuries in 2012 in Edinburgh, there was a discussion of a preliminary survey of bacteriological cultures taken on admission [17] , and the question was raised about the need for and value of standard culturing of burn patients on admission.
This was the impetus for the article described in chapter 5, where the first results are presented of merging these two extensive databases [7,18]. Herein, the rationale for taking bacteriological cultures on admission is discussed, including the frequency of colonization with potentially pathogenic microorganisms on admission and identifying the bacteria involved and their potential roles in later septic complications.

**Chapter 5** *Bacteriological cultures on admission of the burn patient; to do or not to do, that's the question[18]*

In this study, 3271 patients were included who had primarily been admitted to the Rotterdam Burn Centre between January 1987 and August 2010 with complete bacteriological swabs from the nose, throat, perineum and burn wounds.
Resistant bacteria or micro-organisms that can impede wound healing and cause major infections are found in a minority of bacteriological specimens obtained on first presentation of patients with burn wounds. Methicillin-resistant Staphylococcus *aureus* (MRSA) was cultured in 0.4% (14/3271) of patients on admission; 12 out of these 14 patients (85.7%) were repatriated from abroad. Overall, 9.3% (12/129) of repatriated patients were colonized with MRSA. Multi-resistant Acinetobacter or Pseudomonas were detected in 0.3% of patients (11/3271 and 10/3271 respectively). Overall 18 of 129 patients (14%) who were repatriated from abroad had one or more resistant bacteria in cultures taken within the first 24 hours after admission to our burn center.

On admission, Lancefield group A β-hemolytic streptococci (HSA) were found in 3.6% of patients (117/3271), predominantly in children up to 10 years of age (81/1065 =7.6%).These microorganisms were found mainly in the throat but also in the burn wounds.

HSA can cause failure in primary closure or loss of skin grafts and is the only microorganism for which systemic antibiotic treatment is begun as soon as possible after admission.
Consequences in terms of isolation and therapy are of great importance, justifying the rationale for systematic bacteriological surveillance on admission. Our study indicates that special attention to resistant bacteria is required for patients who are repatriated from abroad and for HSA contamination in younger children.
In the Netherlands the incidence of resistant bacteria is relatively low, but misuse of antibiotics and other antimicrobials in humans and animals has led to the development of resistant bacteria: MRSA (Methicillin-resistant Staphylococcus *aureus*), VRE (Vancomycin-Resistant Enterococcus), Extended-Spectrum Beta-Lactamase (ESBL) producing bacteria and Carbapenemase-Producing Enterobacteriaceae (CPE).
Currently, five to ten percent of the Dutch population show colonization with ESBL-producing bacteria [19], and this worrying trend is caused by intensive use of antibiotics in various sectors. As a result of imports from abroad, contamination from livestock and infections in healthcare facilities and in households, it is likely that the increase in ESBL is unavoidable, indicating that bacteriological surveillance is no longer intended for burn patients only [19].



Apart from identifying microorganisms found on admission, we were interested in whether these bacteria were also responsible for later septic complications.
In 62.6% of 195 patients with later clinical signs of sepsis, Staphylococcus *epidermidis* was found in their blood cultures, indicating catheter-related sepsis.
Pseudomonas was cultured in 18.5% of later septic patients. In 0.9% of patients with later positive blood cultures, Pseudomonas was not present on admission; when found on admission, this microorganism was detected in 3.3% of patients with positive blood cultures, a significant difference. A similar trend was found for other gram-negative bacteria, but a predictive value could not be determined.
Staphylococcus *aureus* was found in 17.4% of patients with later clinical signs of sepsis. When it was not detected on admission, Staphylococcus *aureus* was found in the blood cultures of 0.9% of patients who later developed septic complications. In patients who had Staphylococcus initially, only 1.2% had later positive blood cultures for Staphylococcus *aureus*, a non-significant difference.

In conclusion, the results of bacteriological cultures taken on admission have very little predictive value for later septic complications. However, the rationale for culturing burn patients on admission is determined by the identification of bacteria that have consequences for isolation and therapy, for example, isolation in the presence of resistant microorganisms and the choice for early antibiotic therapy if Lancefield group A ß-haemolytic streptococci are cultured.

Infections and sepsis are major complications that can lead to death. Thus, mortality prediction and information are the subjects of the third part of this thesis.

## PART THREE: OUTCOME

A variety of models have been developed for estimating the chances of surviving a burn injury. The most commonly used model is the Baux score. The Baux score is the sum of the total body surface area burned (TBSA) and the age of the patient [20]; it is a comparative indicator of burn severity, with a score over 140 considered unsurvivable. Because inhalation injury was recognized as an important contributor to mortality, Osler et al. developed a revised Baux score for predicting mortality in burn patients in an American population. It was found that inhalation injury resulted in an increase of approximately 17 points on the Baux score, which means that a patient with burns and an inhalation injury would have his revised Baux score calculated by TBSA burned + age of patient + 17 [21].
Chapter 6 describes a study that was performed to validate the revised Baux score with data from patients admitted to our burn center.

**Chapter 6** *External validation of the revised Baux score for predicting mortality in patients with acute burn injury[22]*

Prospectively collected data were analyzed for 4389 patients with an acute burn injury who were admitted to the burn center of the Maasstad Hospital in Rotterdam from 1987 to 2009, including sex, age, total involved body surface area, inhalation injury, mortality, and premorbid conditions. Logistic regression analysis was used to determine the relationships between mortality and possible contributing variables. The discriminative power of the revised Baux score was assessed by receiver operating characteristic curve analysis.

The mortality in the study group of 4389 patients was 6.5% (286/4389). In the group of non-survivors, 96 patients received tender loving care (TLC), and 190 had an intention to treat (ITT). Mortality in patients with ITT was 4.4% (190/4293).

Significant differences between survivors and non-survivors were found regarding age (median 25 vs 62.5 yrs), TBSA (5 vs 38%) and the presence of inhalation injury (7.2 vs 58%). As a result there were significant differences in Baux scores (33 vs 99) and revised Baux scores (33.5 vs 108).

Patients who did not survive had more comorbidities. This applied to the circulatory, gastro-intestinal, urogenital, locomotor and endocrine tracts and the central nervous system (CNS). Age, total body surface area, and inhalation injury as well as premorbid circulatory and central nervous system conditions were significant independent predictors of in-hospital mortality.

The fact that CNS problems have predictive value for mortality could be explained by disorders such as neuropathy and CVA's that lead to decreased sensitivity and mobility, as well as by psychiatric disorders and suicide attempts, which frequently cause more serious burns.

Osler et al. believed that the revised Baux score performed the best in predicting mortality for patients between the ages of 20 and 80 years with TBSA values between 30% and 80% [21]. Contrary to this belief, in our study, the revised Baux score had high predictive value for mortality in the total population (area under the curve, 0.96; 95% confidence interval 0.95-0.97 vs. Osler's area under the curve of 0.81 with 95% confidence interval of 0.76-0.84). Differences in methodology could be responsible for the differences between our data and Osler's, such as different study periods and numbers of patients, the inclusion of all patients including patients with TLC, possible different diagnostics for inhalation injury and records of premorbid conditions.

We concluded that the revised Baux score is a simple and accurate model for predicting mortality in patients with acute burn injuries in a burn centre setting.

Including premorbid conditions in the revised Baux formula is not recommended because relevant historical information is not always available at admission and because of the resulting increased complexity of the model.

Although the Baux score has proven to be a useful tool in itself, it still remains difficult for a treatment team to decide on the basis of a mathematical calculation whether to begin treatment with the aim of survival or to opt for comfort care.

Limitations of the Baux score include the fact that neither the distinction between superficial and full-thickness burns nor the influence of different etiologies, for example, high-voltage electrical burns that can cause limited skin lesions but extensive life-threatening internal damage, are taken into account.

Mortality and causes of death are described in Chapter 7 and Chapter 8.

**Chapter 7** *Mortality and causes of death in a burn center[23]*

In this retrospective study, we described mortality and causes of death for 135 of 1946 patients who were admitted to the burn center of the Maasstad Hospital in Rotterdam (RBC) between 1996 and 2006.
The overall mortality rate, including patients who received tender loving care (n=41), was 6.9%; mortality in patients with an intention to treat (ITT) was 4.9% (94/1905). Mortality, being an important parameter for outcome and quality, was compared with data from the American National Burn Repository (NBR), which were derived from data from 70 burn centers in the USA from 1995 to 2005. In this database, overall mortality of patients who were comparable in demographics such as age and TBSA was 5.6%.
However, in the NBR, it is not clear if patients who received TLC were also included, and there is no clear uniformity about the definition and therefore incidence of inhalation injury. The NBR reports an incidence of inhalation injury in 6.5%, whereas the RBC diagnosed inhalation injury in 12.5% of patients. In the RBC, inhalation injury was considered to be present in cases of clinical signs of airway obstruction, the presence of soot in sputum, or confirmation by bronchoscopy. In the NBR, no strict criteria for the diagnosis inhalation injury are described. The differences between the NBR and the RBC illustrate the need for uniform criteria for the diagnosis of inhalation injury.

Chapter 8 deals with mortality and causes of death of burn patients admitted to the Burn Centres of Rotterdam and Beverwijk between 2006 and 2011, creating the possibility to compare mortality rates in different time periods.

**Chapter 8** *Mortality and causes of death of Dutch burn patients during the period 2006-2011 [24]*

In this period 88 out of 2730 patients died after sustaining a burn injury, an overall mortality of 3.2%.The mean age of these 88 patients was 63.5 years and the average TBSA burned was 42.1%. Most burn injuries (89.9%) were flame burns.
Patients who died were subdivided in three groups. These groups did not differ in age and gender distribution and there was no significant difference in the incidence of inhalation trauma.
The first group of 28 patients received no active curative treatment from the start because of the severity of their injuries without chance of survival. All 28 patients in the palliative Tender Loving Care group were above 16 years of age, had a significant higher TBSA burned (65.7%) and higher Baux scores (124.5) and Revised Baux scores (133.0).
In a second group of 29 patients active treatment was started initially, but discontinued later due to complications like MOF and severe hemodynamic and respiratory insufficiency.

Compared to the group who received TLC these patients had lower TBSA's burned, lower Baux scores and more co-morbidities like pre-existing hart and long conditions. The mean survival time in this group was 10 days with a range of 3 to 78 days.
The third group of 31 patients received active therapy until death, mean 19 days after injury (range 2 to 109 days).
Co-morbidities were more frequently present in the patients who primarily received active curative care.

In table 1 we combined results of the two studies from Chapter 7 and 8.

**Table 1.** Results from studies on mortality after burn injuries

| | | Bloemsma 1996-2006 | Dokter 2006-2011 | NBR*ref 1995-2005 |
|---|---|---|---|---|
| | Number of patients | 1946 | 2730 | 121.930 |
| | Mean age (yrs) | 28.6 | 28.1 | 33 |
| | Mean TBSA (%) | 10.9 | 8.0 | 11.9 |
| | Overall mortality (%) | 6.9 | 3.2 | 5.6 |
| TLC** | Number of patients | 41/1946 (2.1%) | 28/2730 (1.0%) | |
| | Mean age (yrs) | 61.1 | 58.8 | |
| | Mean TBSA (%) | 62.3 | 65.7 | |
| | Inhalation injury (%) | 95.1 | 50.0 | |
| | Mortality | 100% | 100% | |
| ITT*** | Number of patients | 1905/1946(97.9%) | 2702/2730(98.9%) | |
| | Mean age (yrs) | 27.9 | 28.1 | |
| | Mean TBSA (%) | 9.7 | 8.0 | |
| | Inhalation injury (%) | 10.7 | 40.0 | |
| | Mortality | 94/1905(4.9%) | 60/2702 (2.2%) | |

* = National Burn Repository, ** = Tender Loving Care, *** = Intention To Treat

The 3 publications deal with significant differences of numbers of patients in different time periods. Mean ages and TBSA's burned were comparable. Most striking is the lower overall mortality of 3.2% in 2006 to 2011 compared to 6.9% in the period 1996 to 2006. The number of patients where no active therapy was given from the start is low, ranging from 2.1 to 1.0%. The percentage of inhalation injuries in the TLC group of Bloemsma (95.1%) was twice as much as in Dokter's publication (50%), with equal TBSA's burned and ages resulting in higher Baux scores.
In the ITT group comparable ages and TBSA's burned combined with a higher incidence of inhalation injuries of 40.0% in Dokter's publication would result in higher Revised Baux scores with worse prognosis, but mortality decreased from 4.9% to 2.2%.

The second goal of the studies was an analysis of causes of death following burn injury. To compare mortality rates, uniform classification of causes of death is also necessary; in the NBR, these data are lacking.
Multisystem organ failure (MOF) was the leading cause of death in 64.9% of patients (61/94) in the first study and 38.3% (23/60) in the second. Nearly all of these patients showed signs of systemic inflammatory response syndrome (SIRS). In the first study an infectious source in terms of proven or highly suspected sepsis was present in 45.9% of patients who died from MOF.
Preventing and treating MOF and better managing infection and SIRS might further decrease mortality, which has already improved with the institution of burn centers, advances in critical care, fluid resuscitation, operative approaches and techniques, insights in metabolism and the use of topical and systemic antibiotic agents.

The decreased mortality in burn patients in recent decades can be explained best by the decrease in mean TBSAs of admitted patients from 9.4% to 7.5% over the years 2006-2009 e.g.. Another explanation could be a changing referral pattern, especially in children as a result of the introduction of the Emercency Management of Severe Burns course in the Netherlands and ongoing improvement of burn care, prevention and educational programs. From the database of our own burn center in Rotterdam, we see that the mean age of patients with an ITT who died increased slightly over in time. The mean TBSA in these patients remained approximately the same, as shown in figure 1.

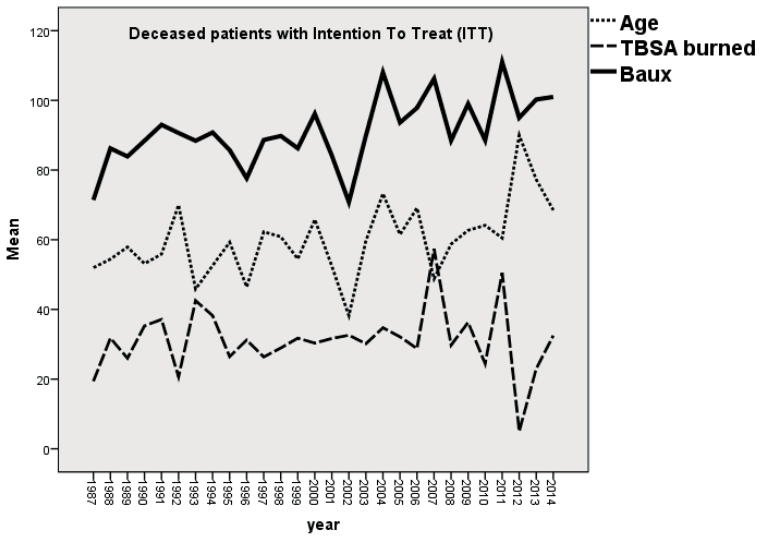


**Figure 1.** Deceased patients with Intention To Treat (ITT)

Mortality is one of the main markers for quality of burn care, but it appears that the limits for achieving burn survival have been reached and that other outcome measures after surviving severe burns have become increasingly important. Long-term outcome measures such as quality of life measures, exercise tolerance and return to pre-burn activities are now becoming of equal importance as the numbers of burn survivors increase.

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# Chapter 9

Summary and discussion

**Samenvatting en discussie**

Epidemiologie is de hoeksteen van de volksgezondheid. De epidemiologie bestudeert het vóórkomen van ziekte en daarmee samenhangende factoren. Inzicht wordt verkregen in risicofactoren voor ziekten en in aandachtspunten voor epidemiologische onderzoek. Met deze informatie kunnen beleidsbeslissingen worden genomen en kan evidence based practice worden ingericht. Daarmee zijn epidemiologische studies van groot belang voor de verbetering van de gezondheidszorg. Een kwalitatief goede opzet en uitvoering van het onderzoek is essentieel, in combinatie met een zorgvuldige interpretatie van de resultaten.
De epidemiologie van brandwonden in Nederland is in de afgelopen decennia veranderd. Vele factoren hebben bijgedragen aan deze verandering. Aan de ene kant is er sprake van een toename van het aantal ouderen door de vergrijzing van onze samenleving en aan de andere kant is er een toename van het aantal kinderen van andere etnische en culturele groepen als gevolg van de immigratie maakt dat de leeftijdsverdeling is veranderd. Hoewel brandwonden vooral voorkomen in deze uitersten van leeftijden daalt het totaal aantal patiënten met brandwonden nog steeds.
Publieke voorlichtingscampagnes, in ons land vaak geïnitieerd door de Nederlandse Brandwonden Stichting en het uitdragen van slogans ("Eerst water, , de rest komt later") gericht op preventie en vergroten van kennis over eerste hulp maatregelen spelen een belangrijke rol in de bewustwording van de gevaren van brandwonden in de bevolking.
De opleiding van professionals in de gezondheidszorg verbetert de kwaliteit van de zorg voor kleine en eenvoudige brandwonden en het herkennen van de noodzaak van meer gespecialiseerde zorg in geval van ernstige brandwonden.
Een goede samenwerking tussen brandwondencentra en verwijzende ziekenhuizen maakt ook het bewustzijn wakker van de noodzaak van adequate vroege resuscitatie en stabilisering en doorverwijzing naar de gespecialiseerde ziekenhuizen bij ernstige brandwonden.
Een goede eerste behandeling is van groot belang voor een optimaal resultaat.
De landelijke registratie van patiënten met brandwonden geeft ons inzicht in de uitkomsten van de zorg en geeft aangrijpingspunten voor verdere verbetering.
Adequate registratie en analyse van de uitkomst van de zorg blijft noodzakelijk en zal de epidemiologie van brandwonden in de toekomst verder veranderen.
Het doel van dit proefschrift is om inzicht te verwerven in de epidemiologie, behandeling en de uitkomsten van gespecialiseerde brandwondenzorg in Nederland. Dit proefschrift is vooral gebaseerd op historische gegevens van het brandwondencentrum in Rotterdam vanaf 1986, gecombineerd met historische data van de brandwondencentra in Groningen en Beverwijk van 1995-2009 en de gemeenschappelijke Nederlandse Brandwonden Registratie (NBR) R3 vanaf 2009.

Dit proefschrift bestaat uit drie delen:

Deel 1: epidemiologie
Deel 2: behandeling
Deel 3: uitkomsten

## DEEL 1: EPIDEMIOLOGIE

### **Hoofdstuk 1** *Inleiding en hoofdstukindeling van het proefschrift*

In hoofdstuk 1 wordt de ontwikkeling van gespecialiseerde brandwonden zorg in Nederland beschreven. Het begon met de oprichting van de Nederlandse Brandwonden Stichting om fondsen te genereren voor onderzoek en werd gevolgd door de start van drie brandwondencentra in niet-academische ziekenhuizen in Beverwijk, Rotterdam en Groningen.
Na verloop van tijd resulteerde een nauwere samenwerking tussen deze drie centra tot de Vereniging van Samenwerkende Brandwondencentra Nederland (VSBN).
Een van de grote mijlpalen van de VSBN werd bereikt met de ontwikkeling en implementatie van een gemeenschappelijke uniforme database, de Nederlandse Brandwonden Registratie (NBR) R3, in 2009.

De huidige versie van de NBR R3 bevat alle essentiële informatie van patiënten uit de drie brandwondencentra, hun behandeling en de uitkomst van de behandeling. De registratie wordt aangepast en uitgebreid in nauw overleg met de gebruikers, zodat de registratie past bij de ontwikkelingen in de brandwondenzorg en dat gegevens vergelijkbaar zijn met andere internationale brandwondenregistraties.
Het samenvoegen van de historische databases van de drie brandwondencentra en de implementatie/ van de NBR R3 leidde tot het overzicht van de primaire opnames in de drie Nederlandse brandwondencentra in de periode van 1995-2011 , zoals is beschreven in hoofdstuk 2. In deze studie werden ook algemene ziekenhuisgegevens gebruikt uit de Landelijke Medische Registratie (LMR).
De resultaten van deze studie benadrukken het belang van deze registraties voor het monitoren en het verbeteren van de kwaliteit van zorg voor deze patiënten.

## **Hoofdstuk 2** *"Epidemiology and trends in severe burns in the Netherlands"[1]*

Het aantal patiënten dat jaarlijks wordt opgenomen in de drie Nederlandse brandwondencentra is gestegen van 430 in 1995 tot 747 in 2011, de incidentie van opnames in brandwondencentra steeg van 2,72 tot 4,66 per 100.000 inwoners. Er was een trend naar meer opnames met minder uitgebreide brandwonden en ook de opnameduur nam af in verloop van tijd. De sterfte van patiënten opgenomen in een brandwondencentrum daalde van 8% naar 4% . Deze daling in mortaliteit wordt gedeeltelijk worden verklaard door het feit dat meer patiënten met minder ernstige brandwonden verwezen worden naar de drie brandwondencentra. Bij kinderen voldoet de overgrote meerderheid (vier van de vijf patiënten) aan de verwijscriteria voor brandwondencentra, zoals beschreven door Vloemans et al [2], maar ook kinderen met minder ernstige brandwonden worden verwezen. In Nederland zijn de criteria voor verwijzing naar brandwondencentra opgenomen in de cursus Emergency Management of Severe Burns (EMSB). Deze zijn:

- Brandwonden > 10% van het lichaamsoppervlak
- Brandwonden > 5% van het lichaamsoppervlak bij kinderen
- Derdegraads brandwonden > 5% van het lichaamsoppervlak
- Brandwonden over functionele gebieden (gelaat, handen, genitalia, gewrichten)
- Circulaire brandwonden aan hals, thorax en ledematen
- Brandwonden gecombineerd met een inhalatietrauma of ander begeleidend letsel
- Brandwonden t.g.v. elektriciteit
- Chemische verbrandingen
- Brandwonden bij slachtoffers met een pre-existente ziekte
- Brandwonden bij kinderen en bejaarden
- Bij twijfel aan de vermelde ongevalstoedracht

De introductie in Nederland van de EMSB cursus in 1998, waar laagdrempelig overleg wordt aangemoedigd, heeft bijgedragen tot een eerdere verwijzing naar brandwondencentra. Veel patiënten zijn overgeplaatst naar de tertiaire zorginstellingen vanwege een vermeend gebrek aan basisvaardigheden in de ziekenhuizen wat betreft de beoordeling en de verzorging van brandwonden. Onlangs is door een werkgroep van professionals in de brandwondenzorg, huisartsen, ambulancepersoneel, spoedeisende geneeskunde artsen, kinderartsen en trauma chirurgen een evidence-based richtlijn ontwikkeld voor de eerste opvang van brandwond patiënten in de acute fase van verbranding en verwijzing [3]. Dit werd gedaan in nauwe samenwerking met de Nederlandse Brandwonden Stichting, de Nederlandse Vereniging voor Brandwonden Zorg, de VSBN en deskundigen van het Kwaliteitsinstituut voor de Gezondheidszorg (CBO). Deze richtlijn is bedoeld om de acute zorg te verbeteren en helpt bij doorverwijzing van patiënten met brandwonden. In geval van vragen of twijfel kan altijd een brandwondenexpert worden geraadpleegd.

In vergelijking met andere landen heeft Nederland een relatief klein aantal patiënten met brandwonden, wat waarschijnlijk mede komt door de brede aandacht voor de preventiecampagnes.

De incidentie bij kinderen van 0-4 jaar, opgenomen in Nederlandse brandwondencentra, verdubbelde van 10,26 per 100.000 inwoners in 1995 naar 22,96 per 100.000 in 2011 [4].
Deze opmerkelijke stijging van het aantal opnames van kinderen werd ook eerder opgemerkt door Vloemans et al [2] en leidde tot de retrospectieve epidemiologische studie zoals beschreven in hoofdstuk 3.

**Hoofdstuk 3** *"Epidemiology of children admitted to the Dutch burn centres. Changes in referral influence admittance rates in burn centres"*

In deze publicatie werden kinderen van 0-4 jaar met brandwonden en kinderen in de leeftijdsgroep 5-17 jaar vergeleken in de perioden 1995-1999 en 2000-2007.
Van de eerste periode (1995-1999) tot de tweede periode (2000-2007) is het gemiddelde aantal opnames in de Nederlandse brandwondencentra per jaar gestegen van 113 naar 163 voor jongere kinderen en van 50 naar 71 voor oudere kinderen, wat neerkomt op een stijging van respectievelijk 44,0 en 44,3%.
Bij patiënten ouder dan 18 jaar steeg het jaarlijks gemiddelde aantal opnames van 290 naar 303, een stijging van 4,3%. Het percentage kinderen opgenomen in gespecialiseerde brandwondencentra steeg van bijna 30% in 1995 tot bijna 50% in 2007 in beide leeftijdsgroepen ($p < 0{,}001$).
Bijna 50% van alle kinderen met brandwonden tussen 0-4 jaar in Nederland werd opgenomen in een gespecialiseerd brandwondencentrum.
Tot slot is er een verschuiving te zien van meer verwijzingen naar brandwondencentra van vooral jonge kinderen met minder ernstige brandwonden. Samen met de algemene tendens om gespecialiseerde zorg meer en meer te centraliseren, zou ook de invoering van het EMSB cursus in 1998 een mogelijke verklaring hiervoor zijn, aangezien EMSB strakke en algemeen geaccepteerde doorverwijzingscriteria hanteert.
Nederland is een klein land met drie brandwondencentra. Het bijzondere van de twee studies beschreven in hoofdstuk 2 en 3 over epidemiologie en registratie van patiënten met brandwonden in brandwondencentra ligt in het feit dat het gegevens betreft van een heel land. In andere landen met meer brandwondencentra, zoals het Verenigd Koninkrijk, Australië en Nieuw-Zeeland, zijn soortgelijke registraties ontwikkeld, maar is volledige landelijk deelname niet altijd bereikt.
In de Verenigde Staten bevat de National Burn Repository (NBR, 2014) gegevens van 96 van de 123 brandwondencentra in de VS plus 4 centra van Canada en 2 uit Zweden. [5]

Het concept achter de NBR is eenvoudig: door middel van een oproep sturen brandwondencentra een standaard dataset naar een centrale database en van hieruit wordt de informatie, over o.a. demografie en uitkomsten van zorg, verwerkt.
De American Burn Association (ABA) publiceert jaarlijks een overzicht van deze gegevens over de klinische kenmerken en het verloop van de behandeling van patiënten met brandwonden in de gespecialiseerde instellingen.
Deze gegevens zijn gebaseerd op een steekproef van patiënten met brandwonden die gespecialiseerde brandwonden zorg ontvangen. Ze omvatten niet alle patiënten die voor de behandeling van brandwonden naar een ziekenhuis gaan en betreffen ook niet alle patiënten die zijn opgenomen in alle brandwondencentra. Het is een grote steekproef van patiënten uit centra die een sterk betrokken zijn bij uitstekende brandwondenzorg.
Enkele tekortkomingen van onze twee studies dienen te worden vermeld.
Ten eerste worden de ontbreken gegevens over poliklinische behandeling. In lijn met de verminderde opnameduur heeft de ambulante zorg aan belang gewonnen en is tegenwoordig een cruciaal onderdeel van onze gespecialiseerde brandwonden zorg. Gegevens over deze poliklinische behandeling in brandwondencentra zou bijdragen aan onze kennis over het hele spectrum van gespecialiseerde brandwonden zorg. Dit beeld wordt bevestigd door andere groepen [6]. In Nederland heeft de Werkgroep NBR R3 hiervoor al een dataset ontworpen, echter de implementatie wordt nog uitgesteld vanwege beperkingen in menskracht en middelen. Elektronische medische dossiers bevatten alle nodige informatie en in de nabije toekomst hopen we hieruit gegevens te kunnen halen via geautomatiseerde dataextractie.. Vergelijkbare ontwikkelingen zijn beschreven voor Australië en Nieuw-Zeeland [6].
Een tweede beperking was het ontbreken van toegang tot de digitale LMR gegevens; daarmee konden dus slechts beperkte analyses worden uitgevoerd op de totale brandwonden opnames in Nederland. Een veel voorkomend probleem in dergelijke ziekenhuisregistraties is de dubbele telling van patiënten met een opname in het eerste opvangende ziekenhuis en een daaropvolgende opname in een brandwondencentrum. Dit probleem is in principe ook van toepassing op de Nederlandse data, maar slechts bij een beperkt deel van de patiënten. Een meerderheid van meer dan 80% van onze patiënten wordt in eerste instantie gezien op spoedeisende hulpafdelingen van niet-brandwondencentrum ziekenhuizen. Echter, na de eerste beoordeling en starten van rehydratie, worden ze direct overgebracht naar een brandwondencentrum, mede vanwege de korte afstanden tot de gespecialiseerde centra in ons land. Dus de geleverde data waren van goede kwaliteit en voldoende om trends in gespecialiseerde brandwondenzorg en niet-gespecialiseerde brandwondenzorg te vergelijken [7].
Een derde mogelijke tekortkoming is de inhoud van de dataset. We namen gegevens zoals leeftijd, geslacht, oorzaak van brandwonden, ongevalsplaats, achtergrond ongeval enz. op

in de lokale databases en deze zijn zo veel mogelijk samengevoegd in één database. In het verleden konden andere karakteristieken van de patiënt (bv co-morbiditeit en socio-economische status) niet worden geanalyseerd, omdat deze variabelen geheel of gedeeltelijk afwezig waren in de historische lokale databases. Echter met de introductie van de NBR R3 vanaf 2009 kon een aantal problemen worden overwonnen en is meer gedetailleerde informatie beschikbaar. Zo hebben we nu een indicatie van de sociaaleconomische status van de patiënten, gebaseerd op informatie met betrekking tot hun postcodes. Daarnaast wordt informatie over co-morbiditeit systematisch geregistreerd.

De twee studies tonen aan dat vooral jonge kinderen een belangrijke doelgroep voor preventie zijn. De leeftijdsgroep van 0-4 jaar is oververtegenwoordigd in de patiëntenpopulatie in de Nederlandse brandwondencentra. De Nederlandse Brandwonden Stichting besteedt bijzondere aandacht aan deze leeftijdsgroep door middel van lezingen, speciale massamedia preventiecampagnes, consultatiebureaus en met bekendmaking van preventiemaatregelen op hun website.
Het feit dat kinderen zo vaak betrokken zijn door brandwonden heeft ook implicaties voor de behandeling. Veel van deze brandwonden zijn veroorzaakt door hete vloeistoffen, die speciale wondverzorging vragen. Dit aspect is in detail beschreven in deel 2, hoofdstuk 4.

Een nieuwe uitdaging is de evaluatie van de uitvoering van de recent ontwikkelde Nederlandse richtlijn over de eerste opvang van patiënten met brandwonden in de acute fase [3]. Met de gegevens uit de LMR en de NBR R3 kunnen verwijspatronen worden onderzocht. Aanvullende gegevens over de mate en inhoud van overleg van zorgprofessionals met professionals in de brandwondenzorg zou bijdragen aan inzicht in de behoefte aan kennis van professionals in de gezondheidszorg buiten gespecialiseerde brandwondenzorg. Daarmee kunnen we direct preventie, kwaliteit van zorg en wetenschappelijk onderzoek vergemakkelijken.

## DEEL 2: BEHANDELING; WONDVERZORGING (A) EN BACTERIOLOGISCHE SURVEILLANCE (B)

### a) Wondverzorging

Een belangrijke mijlpaal in de behandeling van brandwonden was de toevoeging van zilver aan de lokale wondbehandeling. In het artikel "Silver sulfadiazine--a new topical therapy for Pseudomonas in burns. Therapy of Pseudomonas infection in burns" van CLFox Jr. in 1968 in Archives of Surgery [8] beschrijft hij voor het eerst het effect van zilversulfadiazine op het verminderen van wond sepsis en mortaliteit bij brandwonden. Vanaf die tijd werd

zilversulfadiazine de eerste keuze in de behandeling van brandwonden en wordt tot op vandaag wereldwijd nog vaak gebruikt, vooral volledig dikte brandwonden. [9]
Met de introductie van deze antibacteriële crème met een breed antibacterieel spectrum, wat resulteert in minder wondinfectie en wond sepsis, werd het mogelijk om grote brandwonden te overleven. Vooral in de volledige dikte brandwonden heeft het zijn voordelen bewezen en in veel behandelprotocollen is het gebruik van zilversulfadiazine duidelijk omschreven. [10]
In de praktijk zijn de meeste brandwonden echter vaak een mix van oppervlakkige en diepere wonden, vooral bij brandwonden veroorzaakt door hete vloeistoffen bij kinderen. Daarnaast werden na verloop van tijd een aantal negatieve bijwerkingen van zilversulfadiazine waargenomen. In die brandwonden van gemengde dikte is ons beleid om te wachten en te zien welke delen spontaan genezen binnen 2 weken en te wachten op duidelijke afgrenzing van de diepere gebieden waarvoor excisie en transplantatie nodig is.
In verscheidene studies werd aangetoond dat zilversulfadiazine de genezing van gedeeltelijke dikte brandwonden remt [11]. Eind jaren tachtig en begin jaren negentig werd duidelijk dat de optimale omgeving voor wondgenezing tussen nat en droog is[12]. Daarom worden moderne wondverbanden, die deze geleiachtige omgeving creëren, steeds meer gebruikt.
Dit leidde tot het onderzoek beschreven in hoofdstuk 4. In dit hoofdstuk wordt een retrospectieve studie beschreven, waarin de klinische uitkomst van het gebruik van zilversulfadiazine vergeleken wordt met de hydrofiber dressing AQUACEL®, een modern wondverband dat een geleiachtig milieu creëert. Het primaire eindpunt was de noodzaak voor secundaire chirurgische interventie, secundaire eindpunten waren verblijfsduur en heropnames voor dezelfde brandwonden.



**Hoofdstuk 4** *"Reduction in skin grafting after the introduction of hydrofiber dressings in partial thickness burns: a comparison between a hydrofiber and silversulphadiazine".[13]*

De onderzoekspopulatie bestond uit 804 kinderen van 0-4 jaar met brandwonden tot 10% TVLO tussen januari 1987 en januari 2010. Van deze 804 werden 502 kinderen behandeld met zilversulfadiazine (Ag-SD) en 302 met het hydrofiber verband (HFD).
In de totale onderzoeksperiode onderging 27,3% van de 502 kinderen die Ag-SD waren behandeld een huidtransplantatie, terwijl in de groep van 302 kinderen die met HFD waren behandeld slechts 11,6% een operatieve behandeling nodig was, een significante daling.
Daarnaast was de daling in opnameduur in het ziekenhuis een belangrijk tweede voordeel na de invoering HFD. Vóór de invoering van HFD was de gemiddelde opnameduur 12,4 dagen. Rond de tijd dat HFD werd ingevoerd werd reeds een ander beleid in wondbehandeling gestart, waarbij Ag-SD op een later ogenblik werd vervangen door een wondbedekker,

waarbij minder frequente verbandwisselingen nodig waren en daardoor de noodzaak voor ziekenhuisopname minder werd.
Dit kan een verklaring zijn voor de waarneming dat in de periode waarin zowel de Ag-SD als hydrofibers gebruikt werden de opnameduur van de Ag-SD behandelde patiënten al een statistisch significante daling liet zien tot 9,7 dagen. Echter de opnameduur van patiënten met brandwonden behandeld met HFD verminderde tot 7,5 dagen, een verdere significante daling in vergelijking met Ag-SD behandelde patiënten in dezelfde periode.
Hoewel het een retrospectieve studie betreft met alle beperkingen, won het aan kracht door het grote aantal patiënten. Als gevolg van deze studie gecombineerd met andere voordelen, zoals verminderde pijnperceptie en meer comfort voor de patiënt door het beperken van de frequente verbandwisselingen, alsmede lagere totale kosten zijn HFD tegenwoordig eerste keuze in de behandeling van brandwonden tot 10% TVLO in ons brandwondencentrum. [14,15]

Het spreekwoord "Alle wegen leiden naar Rome" is vooral van toepassing voor het maken van een keuze uit het grote scala aan wondbedekking materialen voor brandwonden. Men moet zich realiseren dat het ideaal wondverband nog steeds niet bestaat. Met de ene wondbedekker zal een oppervlakkige brandwonden in 4 dagen genezen, bij een andere zal het twee weken duren...! Naast tijd tot wondgenezing zullen patiënt comfort, gemak en kosten ook de keuze van het verband bepalen. Brandwonden zijn dynamische wonden, aanvankelijk oppervlakkige wonden kunnen secundair verdiepen door verschillende oorzaken, zoals onvoldoende koeling of infectie. Het beste tijdstip om de diepte van de brandwonden te beoordelen is na 48-72 uur en op dat moment is tegenwoordig de Laser Doppler Imaging (LDI) veel betrouwbaarder dan de klinische beoordeling door artsen of verpleegkundigen [16]. Om een LDI scan te kunnen maken op dag 2 tot 5, moet de HFD eerst worden verwijderd, wat niet altijd gemakkelijk is na twee dagen en fragiel, net herstellend epitheel wordt losgetrokken. Hydrofibers blijven dus op de wond gedurende ongeveer 10 dagen, waardoor tussentijdse evaluatie onmogelijk. Het is altijd mogelijk dat er diepere delen na het verwijderen van het verband overblijven die soms moeten worden geopereerd. Dit moet natuurlijk in het begin van de behandeling met de patiënt en / of ouders besproken zijn.

## b) Bacteriologisch surveillance

Infectie blijft een van de belangrijkste complicaties na ernstige brandwonden. Dit wordt makkelijker gemaakt door de defecte huid en een verminderde immuunreactie van de patiënt.
We hadden de kans om de patiënten database met voornamelijk demografische gegevens over o.a. oorzaken en lokalisatie van brandwonden samen te voegen met een

enorme database van de afdeling medische microbiologie van het ziekenhuis, met alle bacteriologische kweken over een periode van 24 jaar.
In de discussie na een presentatie van een eerste inventarisatie van bacteriologische kweken genomen bij opname van patiënten, die werd gehouden op het 16e congres van de International Society Burn Injuries (ISBI) in 2012 in Edinburgh [17], werd de vraag gesteld wat de noodzaak en de waarde is van de standaard kweken van patiënten met brandwonden bij opname in het brandwondencentrum.
Dit was de aanzet voor het in hoofdstuk 5 beschreven artikel waarin de eerste resultaten gepresenteerd zijn van het samenvoegen van de twee uitgebreide databases [7,18]. Hierin worden het belang het afnemen van bacteriologische kweken bij opname besproken, alsmede het voorkomen van kolonisatie met potentieel pathogene micro-organismen bij opname, de identificatie van de betrokken bacteriën en hun mogelijke rol in de latere septische complicaties.

**Hoofdstuk 5** *"Bacteriological cultures on admission of the burn patient; to do or not to do, that's the question"[18]*

Deze studie betrof 3271 primaire brandwondenpatiënten opgenomen in het brandwondencentrum van Rotterdam tussen januari 1987 en augustus 2010 met complete bacteriologische kweken van neus, keel, perineum en de brandwonden.
Resistente bacteriën of micro-organismen die wondgenezing kunnen vertragen of grote infecties kunnen veroorzaken worden bij een minderheid van de bacteriologische monsters verkregen bij de eerste presentatie van de patiënten met brandwonden aangetroffen. Methicilline resistente Staphylococcus *aureus* (MRSA) werd gekweekt in 0,4% (14/3271) bij opname; 12 van deze 14 patiënten (85,7%) waren gerepatrieerd uit het buitenland. Van de gerepatrieerde patiënten was 9,3% (12/129) gekoloniseerd met MRSA. Multiresistente Acinetobacter of Pseudomonas werd ontdekt in 0,3% (respectievelijk 11/3271 en 10/3271). Bij 18 van de 129 (14%) gerepatrieerde patiënten uit het buitenland werden één of meerdere resistente bacteriën gevonden in de eerste kweken die binnen de eerste 24 uur na opname in onze brandwondencentrum waren afgenomen.
Lancefield groep A β-hemolytische streptokokken (HSA) werden bij opname gevonden in 3,6% van de patiënten (117/3271), voornamelijk bij kinderen tot 10 jaar (81/1065 = 7,6%). Deze micro-organismen werden voornamelijk gevonden in de keel, maar ook in brandwonden.
HSA kan verstoring van wondgenezing of verlies van huidtransplantaties veroorzaken en is het enige micro-organisme waar systemische behandeling met antibiotica wordt gestart, het liefst zo snel mogelijk na opname.
Gevolgen in termen van isolatie en behandeling kunnen van groot belang zijn en zij rechtvaardigen een systematische bacteriologische surveillance bij opname. Onze

studie geeft aan dat er speciale aandacht nodig is voor resistente bacteriën bij patiënten gerepatrieerd uit het buitenland en voor HSA kolonisatie bij jonge kinderen.
In Nederland is de incidentie van resistente bacteriën weliswaar relatief laag, maar misbruik van antibiotica en andere antimicrobiële stoffen bij mens en dier leidt wel tot een verdere ontwikkeling van resistente bacteriën. Deze resistente bacteriën MRSA (Methicilline Resistente Staphylococcus aureus), VRE (Vancomycine resistente Enterococcus), ESBL (Extended Spectrum Beta-lactamase) producerende bacteriën en CPE (Carbapenemase Producerende Enterobacteriën) gaan steeds vaker voorkomen. Tegenwoordig blijkt vijf tot tien procent van de Nederlandse bevolking gekoloniseerd te zijn met ESBL-producerende bacteriën [19]. Deze zorgwekkende trend wordt veroorzaakt door intensief gebruik van antibiotica in de verschillende sectoren. Als gevolg van toename van de invoer vanuit het buitenland, besmetting van de veestapel, infecties in zorginstellingen en huishoudens is de stijging van het voorkomen van deze bijzonder resistente micro-organismen onvermijdelijk en is bacteriologische surveillance niet alleen meer bedoeld voor patiënten met brandwonden [19].

Afgezien van het identificeren van micro-organismen bij opname waren we benieuwd of deze bacteriën ook verantwoordelijk zijn voor later septische complicaties.
In 62,6% van de 195 patiënten met later klinische tekenen van sepsis werd Staphylococcus epidermidis gevonden in het bloedkweken, geduid als katheter gerelateerde sepsis.
Pseudomonas werd gekweekt in 18,5% van de latere septische patiënten. In 0,9% van de patiënten met een latere positieve bloedkweek met Pseudomonas was deze niet aanwezig bij opname. Als Pseudomonas werd gevonden bij opname werd dit micro-organisme aangetroffen in 3,3% van de patiënten met positieve bloedkweken, een klein, maar wel significant verschil.
Een soortgelijke trend werd gevonden voor andere Gram-negatieve bacteriën, maar een goede voorspellende waarde kon niet worden aangetoond.
Staphylococcus aureus werd in 17,4% van de patiënten gevonden met latere klinische symptomen van sepsis. Indien de Staphylococcus aureus niet werd gedetecteerd bij opname werd hij wel gevonden in het bloedkweken van 0,9% van de patiënten die later septische complicaties ontwikkelden. Bij patiënten die wel een Staphylococcus hadden bij opname werd slechts in 1,2% van de gevallen een positieve bloedkweken met Staphylococcus aureus gevonden, een niet-significant verschil.
De conclusie is dat bacteriologische kweken genomen bij nauwelijks voorspellende waarde heeft voor latere septische complicaties.
De waarde van opnamekweken bij brandwond patiënten wordt echter wel bepaald door de identificatie van bacteriën die consequenties hebben voor isolatie en therapie; bijvoorbeeld isolatie in aanwezigheid van resistente micro-organismen en de keuze voor

vroege antibiotica als Lancefield groep A ß-hemolytische streptokokken worden gekweekt. Infecties en sepsis zijn ernstige complicaties die kunnen leiden tot de dood.
Voorspelling van en informatie over de sterfte zijn om die reden onderwerp van het derde deel van dit proefschrift.

## DEEL 3: UITKOMSTEN

Een verscheidenheid aan rekenmodellen is ontwikkeld om te kunnen voorspellen wat de kans is om een brandwondletsel te kunnen overleven.
De meest gebruikte model is de Baux score. De Baux score is de som van het totale verbrand lichaamsoppervlak (TVLO) en de leeftijd van de patiënt [20]. De score is indirect een indicator van de ernst van brandwonden, een score meer dan 140 wordt beschouwd als een niet te overleven letsel. Sinds bekend werd dat het inhalatieletsel een belangrijke bijdrage levert aan de mortaliteit, ontwikkelde Osler et al. een Revised Baux score voor de voorspelling van de sterfte van patiënten met brandwonden in een Amerikaanse onderzoekspopulatie. Het bleek dat het inhalatieletsel resulteerde in een toename van ongeveer 17 punten op de Baux score en deze toevoeging betekent dat een patiënt met brandwonden en een inhalatieletsel een Revised Baux Score zou hebben van berekend TVLO + leeftijd van de patiënt + 17 [21] .
Hoofdstuk 6 beschrijft een studie die is uitgevoerd om deze Revised Baux score te valideren met gegevens van patiënten opgenomen in ons brandwondencentrum.



**Hoofdstuk 6** *"External validation of the revised Baux score for the prediction of mortality in patients with acute burn injury"[22]*

Prospectief verzamelde gegevens van 4389 patiënten met acute brandwonden opgenomen in het brandwondencentrum van het Maasstad Ziekenhuis in Rotterdam van 1987-2009 werden geanalyseerd, met inbegrip van geslacht, leeftijd, TVLO, inhalatieletsel, mortaliteit en voorgeschiedenis. Logistische regressieanalyse werd gebruikt om het verband tussen de mortaliteit en mogelijke bijdragende variabelen te bepalen. Het onderscheidend vermogen van de Revised Baux score werd bepaald door de Receiver Operating Characteristic (ROC) curve analyse.

De mortaliteit in de studiegroep van 4.389 patiënten bedroeg 6,5% (286/4389). In de groep van niet-overlevenden kregen 96 patiënten Tender Loving Care (TLC) en 190 had een Intention To Treat (ITT). Mortaliteit bij patiënten met ITT was 4,4% (190 / 4.293).
Er werden significante verschillen tussen overlevenden en niet-overlevenden gevonden wat leeftijd (mediaan 25 versus 62,5 jaar), TVLO (5 versus 38%) en de aanwezigheid van

inhalatieletsel (7,2 vs 58%) betrof. In lijn daarmee waren er ook significante verschillen in Baux scores (33 versus 99) en Revised Baux scores (33,5 versus 108).
Patiënten die niet overleefden hadden meer co-morbiditeit. Dit was van toepassing op tractus circulatorius, gastro-intestinale tractus, tractus urogenitale, tractus locomotorius, endocriene tractus en het centrale zenuwstelsel (CNS).
Leeftijd, TVLO, inhalatie letsel, evenals een voorgeschiedenis in tractus circulatorius en CNS, waren belangrijke onafhankelijke voorspellers van sterfte in het ziekenhuis.
Het feit dat pre-morbide aandoeningen in CNS een voorspellende waarde voor sterfte hebben kan worden verklaard door aandoeningen zoals neuropathie en CVA's, wat leidt tot verminderde gevoeligheid en mobiliteit, naast psychiatrische stoornissen en suïcidepogingen, die vaak leiden tot meer ernstige brandwonden.
Osler et al. nemen aan dat de Revised Baux score het beste in het voorspellen van sterfte is voor patiënten in de leeftijd van 20 jaar tot 80 jaar met TVLO's tussen 30% en 80% [21] .In tegenstelling tot deze aanname vonden wij in onze studie dat de Revised Baux score een hoge voorspellende waarde voor sterfte heeft in de totale populatie (Area under the curve, 0,96; 95% betrouwbaarheidsinterval, 0,95-0,97), maar minder specifiek en gevoelig is in de door Osler's geselecteerde groep patiënten tussen 20 en 80 jaar en TVLO's tussen 30 en 80% (oppervlakte onder de curve, 0,81; 95% betrouwbaarheidsinterval, 0,76-0,84).
Verschillen in methodologie kunnen de verschillen tussen Osler's en onze gegevens mogelijk verklaren, zoals verschillende studieperiodes en aantallen patiënten, het opnemen van alle patiënten waaronder ook de patiënten met TLC, potentieel verschillend diagnostiek betreffende inhalatieletsel en registeren van voorgeschiedenis.
We concludeerden dat de Revised Baux score een eenvoudig en nauwkeurig model is voor het voorspellen van de mortaliteit bij patiënten met acute brandwonden in een brandwondencentrum.
Het meenemen van voorgeschiedenis in de Revised Baux formule wordt afgeraden, omdat relevante voorgeschiedenis niet altijd beschikbaar is bij opname en het resulteert in een complex rekenmodel.
Hoewel de Baux score heeft bewezen een nuttig instrument te zijn, blijft het moeilijk voor een behandelteam om op basis van een mathematische berekening te bepalen of een behandeling wordt gestart met het doel om te overleven of te kiezen voor comfort care.
Beperkingen van de Baux score is het feit dat geen rekening wordt gehouden met de diepte van de wonden, noch met de invloed van de oorzaak van de brandwonden, zoals brandwonden veroorzaakt door hoogvoltage elektriciteit, wat soms slechts beperkte huidletsels maar daarnaast veel levensbedreigende inwendige schade kan veroorzaken.

Mortaliteit en doodsoorzaken worden beschreven in hoofdstuk 7 en 8.

**Hoofdstuk 7** *"Mortality and causes of death in a burn centre"[23].*

In deze retrospectieve studie beschreven we de mortaliteit en doodsoorzaken van 136 van de 1946 patiënten die werden opgenomen in het brandwondencentrum van het Maasstad Ziekenhuis in Rotterdam (RBC) tussen 1996 en 2006.
Het totale sterftecijfer, met inbegrip van patiënten die werden behandeld met Tender Loving Care (TLC, n = 41) was 6,9%. De sterfte van patiënten met een Intention To Treat (ITT) was 4,9% (94/1905). Mortaliteit, als zijnde een belangrijke parameter voor resultaat en kwaliteit, werd vergeleken met de gegevens van de Amerikaanse National Burn Repository (NBR), afgeleid van gegevens van 70 brandwondencentra in de Verenigde Staten van 1995 tot 2005. De mortaliteit van de patiënten, die vergelijkbaar waren in demografie zoals leeftijd en TVLO, was in deze database 5,6%. Echter in de NBR is het niet duidelijk of patiënten die TLC kregen ook meegenomen zijn en er is ook geen duidelijke uniformiteit over de definitie en dus het aanwezig zijn van een inhalatieletsel. De NBR rapporteert een incidentie van inhalatieletsel bij 6,5%, de RBC stelde bij 12,5% van de patiënten een inhalatieletsel vast. In het RBC werd een inhalatieletsel geacht aanwezig te zijn in geval van klinische symptomen van luchtwegobstructie, de aanwezigheid van roet in sputum of bevestiging door bronchoscopie. In de NBR worden geen strikte criteria voor de diagnose inhalatieletsel beschreven. De verschillen tussen de NBR en RBC illustreren de noodzaak van uniforme criteria voor de diagnose inhalatieletsel.

**Hoofdstuk 8** *"Mortality and causes of death of Dutch burn patients during the period 2006-2011" [24]*

Dit hoofdstuk handelt over mortaliteit en oorzaken van overlijden van patiënten opgenomen in de brandwondencentra van Rotterdam en Beverwijk tussen 2006 en 2011.
In deze periode overleden 88 van de 2730 patiënten, een totale sterfte of 3,2%.
De gemiddelde leeftijd van deze 88 patiënten was 63,5 jaar en het gemiddelde TVLO was 42,1%.
Meeste brandwonden (89,9%) waren vlamverbrandingen. De overleden patiënten werden onderverdeeld in drie groepen. De eerste groep van 28 patiënten ontving vanaf het begin geen actieve curatieve behandeling (TLC) vanwege de ernst van hun letsel zonder kans op overleving.
In een tweede werd groep van 29 patiënten werd in eerste instantie een actieve behandeling gestart, maar later stopgezet als gevolg van complicaties.
Bij de derde groep van 31 patiënten werd een actieve behandeling gecontinueerd tot moment van overlijden.
De drie groepen verschillen niet wat betreft geslachtsverdeling en ook was er geen significant verschil in de incidentie van inhalatietrauma.

Alle 28 patiënten die palliatieve comfort care kregen waren ouder dan 16 jaar, hadden een aanzienlijk hoger TVLO (65,7%) en hogere Bauxscore (124,5) en herziene Bauxscore (133,0).

In tabel 1 zijn de resultaten van de twee studies van hoofdstuk 7 en 8 gecombineerd.

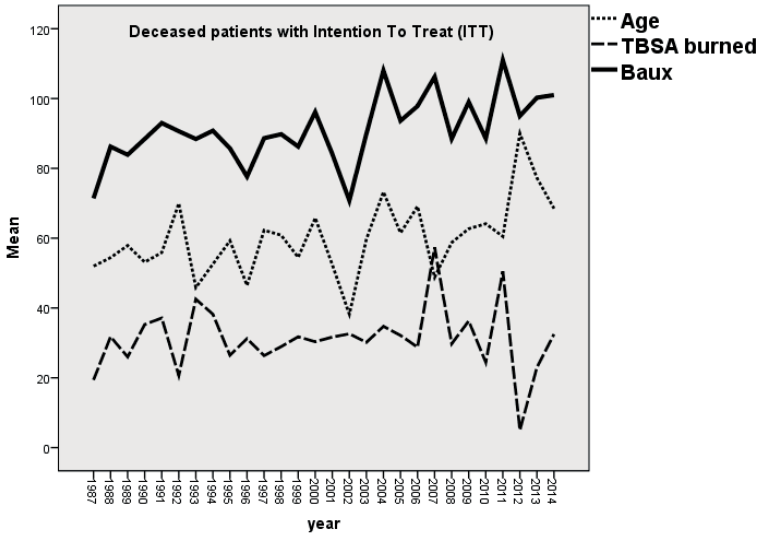
**Tabel 1.** Resultaten van studies naar mortaliteit na brandwonden

| | | **Bloemsma 1996-2006** | **Dokter 2006-2011** | **NBR*ref 1995-2005** |
|---|---|---|---|---|
| | Aantal patiënten | 1946 | 2730 | 121.930 |
| | Gemiddelde leeftijd (jr) | 28.6 | 28.1 | 33 |
| | Gemiddeld TVLO (%) | 10.9 | 8.0 | 11.9 |
| | Mortaliteit (%) | 6.9 | 3.3 | 5.6 |
| TLC** | Aantal patiënten | 41/1946 (2.1%) | 28/2730 (1.0%) | |
| | Gemiddelde leeftijd (jr) | 61.1 | 58.8 | |
| | Gemiddeld TVLO (%) | 62.3 | 65.7 | |
| | Inhalatieletsel (%) | 95.1 | 50.0 | |
| | Mortaliteit | 100% | 100% | |
| ITT*** | Aantal patiënten | 1905/1946(97.9%) | 2702/2730(98.9%) | |
| | Gemiddelde leeftijd (jr) | 27.9 | 28.1 | |
| | Gemiddeld TVLO (%) | 9.7 | 8.0 | |
| | Inhalatieletsel (%) | 10.7 | ? | |
| | Mortaliteit | 94/1905(4.9%) | 60/2702 (2.2%) | |

* = National Burn Repository, ** = Tender Loving Care, *** = Intention To Treat

Om mortaliteit te vergelijken is uniforme classificatie van doodsoorzaken ook noodzakelijk. In de NBR ontbreken deze gegevens.
Naast een analyse van de sterftecijfers, zijn de doodsoorzaken als gevolg van brandwonden geanalyseerd. Multi Orgaan Falen (MOF) was de belangrijkste doodsoorzaak bij 64,9% van de patiënten die overleden (61/94)in de eerste studie en 38,3% (23/60) in de tweede studie. Bijna al deze patiënten vertoonden tekenen van Systemic Inflammatory Response Syndrome (SIRS). Een infectieuze bron in termen van bewezen of sterk verdacht voor sepsis was aanwezig bij 45,9% van de patiënten die aan een MOF overleden.
Preventie en behandeling van MOF en een betere controle over infectie en SIRS kan de mortaliteitscijfers verder laten dalen. Dit is reeds ingezet door de komst van brandwondencentra met verbeterde kritieke zorg, vochttoediening, operatieve benaderingen en technieken en beter inzicht in het metabolisme naast het kritisch gebruik van lokale en systemische antibiotica.

De verminderde mortaliteit van patiënten met brandwonden in de laatste decennia wordt het beste verklaard door de daling van het gemiddelde TVLO van opgenomen patiënten door de jaren heen. Uit de database van onze eigen brandwondencentrum in Rotterdam zien we dat de gemiddelde leeftijd van de patiënten met een ITT die uiteindelijk overleden iets is toegenomen in de tijd. Het gemiddelde TVLO bij deze patiënten bleef ongeveer gelijk, zoals weergegeven in figuur 1.




**Figuur 1.** Overleden patiënten met Intention To Treat (ITT)

Mortaliteit is een van de belangrijkste uitkomstmaten voor de kwaliteit van de zorg, maar het lijkt erop dat de grens om brandwonden te overleven is bereikt en andere uitkomstmaten na het overleven van ernstige brandwonden steeds belangrijker worden. Lange termijn resultaten, zoals kwaliteit van leven, inspanningstolerantie en de evaluatie van terugkeer naar activiteiten van voor het ongeval, worden nu even belangrijk doordat het aantal patiënten dat ernstige brandwonden overleeft stijgt.

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# Curriculum Vitae

Jan Dokter was born on September 6th 1954 in Ridderkerk. He attended secondary school (HBS) at the Develsteincollege where he graduated in 1973. After completing military service from 1973-1974, he studied medicine at Erasmus University in Rotterdam, where he obtained his medical degree in 1983. In that same year he started the training for general practitioner which he completed in 1984 in the former Zuiderziekenhuis.

He continued in that hospital with basic surgical training and became burn physician. From October 1986 until now he is the medical coordinator in the Burn Centre of the Maasstad Hospital.

He is instructor for the Emergency Management of Severe Burns course (EMSB) since 1999 and from 2013 until now Chairman of the Dutch Society for Burn Care (Nederlandse Vereniging voor Brandwonden Zorg, NVBZ).

He is married with Ineke Eijskoot since 1980 and they have three children: Jeanine (1983), Elwin (1986) and Eline (1992) and one grandchild Norah (2013).

## Stellingen behorende bij het proefschrift van Jan Dokter

## “EPIDEMIOLOGY OF BURNS”

1. Ondanks een lagere prevalentie wordt door laagdrempeliger verwijzen een toenemend aantal patiënten met brandwonden opgenomen in de brandwondencentra. *(dit proefschrift)*

2. Verdere verspreiding van kennis, in het bijzonder door de cursus Emergency Management of Severe Burns, leidt ertoe dat meer kinderen worden opgenomen in de Nederlandse brandwondencentra. (*dit proefschrift*)

3. Wondbedekkers in plaats van zalven dienen eerste keus te zijn voor de behandeling van hete vloeistofverbrandingen bij kinderen. (*dit proefschrift*)

4. Het nut van het kweken van patiënten met brandwonden bij opname is gelegen in de identificatie van resistente micro-organismen en bacteriën die vroege antimicrobiële therapie behoeven. *(dit proefschrift)*

5. Bacteriologische kweken bij opname hebben nauwelijks voorspellende waarde voor latere septische complicaties. (*dit proefschrift*)

6. De Revised Baux score is een eenvoudig en nauwkeurig model voor het voorspellen van de mortaliteit bij patiënten met acute brandwonden in een brandwondencentrum. (*dit proefschrift*)

7. Serious Gaming is bij uitstek geschikt als onderwijsmiddel om de opvang van van patiënten met ernstige brandwonden te trainen. (*https://www.zorgvisie.nl/ict/nieuws/2015/1/serious-game-voor-opvang- - 1692024w/*)

8. Meten is weten, registreren is nog meer weten.

9. Beoordelen dient vaak met verschillende zintuigen te gebeuren, zoals het bepalen van de diepte van brandwonden.
   Een uitspraak “ik ruik mooi weer” is dus zo gek nog niet.

10. Brandwondenzorg is teamwerk en vereist een topsportklimaat. *(vrij naar vele voetbaltrainers)*

11. Er is niets mis mee om op oudere leeftijd te promoveren.

12. Omdat je niets ziet door een stethoscoop dient de naam van het instrument veranderd te worden in stethosfoon. *(Boxma, Dokter, van Baar et al; nog niet gepubliceerd onderzoek 2012)*